

**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION**  
Washington, D.C. 20549

**FORM S-3**

REGISTRATION STATEMENT  
UNDER  
THE SECURITIES ACT OF 1933

**Milestone Pharmaceuticals Inc.**

(Exact name of registrant as specified in its charter)

**Québec**  
(State or other jurisdiction of  
incorporation or organization)

**Not applicable**  
(I.R.S. Employer  
Identification Number)

**1111 Dr. Frederik-Philips Boulevard, Suite 420**  
**Montréal, Québec CA H4M 2X6**  
**(514) 336-0444**

(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

**Joseph Oliveto**  
**Chief Executive Officer**  
**Milestone Pharmaceuticals USA Inc.**  
**7422 Carmel Executive Park Drive**  
**Suite 300**  
**Charlotte, NC 28226**  
**(514) 336-0444**

(Name, address, including zip code, and telephone number, including area code, of agent for service)

**Copies to:**

**Ryan S. Sansom**  
**Marc Recht**  
**Divakar Gupta**  
**Cooley LLP**  
**500 Boylston Street, 14<sup>th</sup> Floor**  
**Boston, MA 02116**  
**(617) 937-2300**

**Nathalie Beauregard**  
**Francois Paradis**  
**Osler, Hoskin & Harcourt LLP**  
**1000 De La Gauchetière Street West,**  
**Suite 2100**  
**Montréal, Québec CA H3B 4W5**  
**(514) 904-8100**

**Approximate date of commencement of proposed sale to the public:** From time to time after the effective date of this Registration Statement.

If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, please check the following box:

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, as amended, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box:

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering:

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box.

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box.

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

Large accelerated filer

Accelerated filer

Non-accelerated filer

Smaller reporting company

Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 7(a)(2)(B) of the Securities Act.

**CALCULATION OF REGISTRATION FEE**

Title of each class of securities to be registered	Amount to be registered <sup>(1)</sup>	Proposed maximum offering price per unit <sup>(2)</sup>	Proposed maximum aggregate offering price <sup>(2)</sup>	Amount of registration fee
Common Shares, no par value per share	910,746	\$5.83	\$ 5,309,649.18	\$579.28

- (1) There are being registered hereunder 910,746 of our common shares issuable upon the exercise of pre-funded warrants with an exercise price of \$0.01 per share held by the selling shareholders named in this registration statement. Pursuant to Rule 416 under the Securities Act of 1933, as amended, this registration statement also covers such additional number of our common shares as may be issuable from time to time upon exercise of such pre-funded warrants as a result of share splits, share dividends, capitalizations or similar events.
- (2) Estimated solely for the purposes of calculating the registration fee. Pursuant to Rule 457(c) under the Securities Act, the registration fee has been calculated based upon the average of the high and low prices, as reported by The Nasdaq Global Market, for our common shares on June 22, 2021.

**The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment that specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933, as amended, or until the Registration Statement shall become effective on such date as the Securities and Exchange Commission, acting pursuant to said Section 8(a), may determine.**

SUBJECT TO COMPLETION, DATED JUNE 25, 2021

## PROSPECTUS

## 910,746 Common Shares



This prospectus covers the offer and resale by the selling shareholders identified in this prospectus of up to an aggregate of 910,746 of our common shares, no par value per share, issuable upon exercise of pre-funded warrants sold to the selling shareholders in a private placement on May 21, 2021. We refer to these underlying common shares as the warrant shares.

We are not selling any common shares under this prospectus and will not receive any proceeds from the sale by the selling shareholders of the warrant shares. We will, however, receive the nominal exercise price per share of \$0.01 for any pre-funded warrants exercised for cash.

Sales of the warrant shares by the selling shareholders may occur at fixed prices, at market prices prevailing at the time of sale, at prices related to prevailing market prices or at negotiated prices. The selling shareholders may sell warrant shares to or through underwriters, broker-dealers or agents, who may receive compensation in the form of discounts, concessions or commissions from the selling shareholders, the purchasers of the warrant shares, or both.

We are paying the cost of registering the warrant shares covered by this prospectus as well as various related expenses. The selling shareholders are responsible for all selling commissions, transfer taxes and other costs related to the offer and sale of their warrant shares.

Our common shares are listed for trading on The Nasdaq Global Select Market under the symbol "MIST." On June 22, 2021, the last reported sale price of our common shares was \$5.84 per share.

**Investing in our common shares involves a high degree of risk. You should review carefully the risks and uncertainties described in the section titled "Risk Factors" on page 2 of this prospectus and any similar section contained in the applicable prospectus supplement and in any free writing prospectuses we have authorized for use in connection with a specific offering, and under similar headings in the documents that are incorporated by reference into 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.**

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The information in this preliminary prospectus is not complete and may be changed. We may not sell these securities or accept an offer to buy these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and it is not soliciting offers to buy these securities in any state where such offer or sale is not permitted.

The date of this prospectus is \_\_\_\_\_, 2021.

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### ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission, or the SEC, using a “shelf” registration process. Under this shelf process, certain selling shareholders may from time to time sell the common shares described in this prospectus in one or more offerings or otherwise as described under “Plan of Distribution.”

This prospectus may be supplemented from time to time by one or more prospectus supplements. Such prospectus supplements may also add, update or change information contained in this prospectus. If there is any inconsistency between the information in this prospectus and the applicable prospectus supplement, you must rely on the information in the prospectus supplement. You should carefully read both this prospectus and any applicable prospectus supplement together with additional information described under the heading “Where You Can Find More Information” before deciding to invest in any shares being offered.

Neither we nor the selling shareholders have authorized anyone to provide any information other than that contained or incorporated by reference in this prospectus or in any related prospectus supplement or any free writing prospectus that we have authorized. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. The shares are not being offered in any jurisdiction where the offer is not permitted. You should not assume that the information contained in or incorporated by reference in this prospectus is accurate as of any date other than the respective dates of such document. Our business, financial condition, results of operations and prospects may have changed since those dates.

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

## SUMMARY

### 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.

### Corporate Background

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](http://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 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.

**RISK FACTORS**

Investing in our common shares involves a high degree of risk. Before deciding whether to invest in our common shares, you should consider carefully the risks and uncertainties described below and under the section titled Risk Factors contained in our most recent Annual Report on Form 10-K, as well as any amendments thereto reflected in subsequent filings with the SEC, which are incorporated by reference into this prospectus in their entirety, together with other information in this prospectus, the documents incorporated by reference herein, any prospectus supplement and any free writing prospectus that we may authorize. If any of the risks described in our most recent Annual Report on Form 10-K, the other filings incorporated by reference herein or in any prospectus supplement or any free writing prospectus that we may authorize occurs, our business, financial condition, results of operations and future growth prospects could be harmed. In these circumstances, the market price of our common shares could decline, and you may lose all or part of your investment. For more information, see the sections entitled “Where You Can Find Additional Information” and “Special Note Regarding Forward-Looking Statements.”

## SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and the documents incorporated by reference herein and any free writing prospectus that we have authorized for use in connection with this offering contain 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 Securities Exchange Act of 1934, or the Exchange Act. These statements 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” incorporated by reference from our most recent Annual Report on Form 10-K and our most recent Quarterly Report on Form 10-Q, as well as any amendments thereto, filed with the SEC.

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, the documents incorporated by reference herein, or in any free writing prospectus that we have authorized for us in connection with this offering about our expectations, beliefs, plans, objectives, assumptions or future events or performance are not historical facts and are forward-looking statements. Forward-looking statements may include, but are not limited to, 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;
- developments relating to our competitors and our industry; and
- other factors that may impact our financial results.

These forward-looking statements are subject to a number of risks and uncertainties. We discuss in greater detail many of these risks in our most recent Annual Report on Form 10-K, as well as any amendments thereto reflected in subsequent filings with the SEC, which are incorporated by reference into this prospectus in their entirety. You should refer to the “Risk Factors” section contained in the documents incorporated by reference herein, and applicable prospectus supplement and any free writing prospectus that we have authorized for use in connection with this offering 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. It is not possible for our management to predict all risks, 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 any forward-looking statements we may make. Given these risks, uncertainties and other factors, many of which are beyond our control, we cannot assure you that the forward-looking statements in this prospectus, the documents incorporated by reference herein or any free writing prospectus that we have authorized for use in connection with this offering will prove to be accurate, and you should not place undue reliance on these forward-looking statements. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified timeframe, or at all.

Except as required by law, we assume no obligation to update these forward-looking statements publicly, or to revise any forward-looking statements to reflect events or developments occurring after the date of this prospectus, even if new information becomes available in the future.

### **USE OF PROCEEDS**

We will not receive any of the proceeds from the sale or other disposition of the warrant shares by the selling shareholders pursuant to this prospectus. Upon any exercise of any of the pre-funded warrants for cash, the applicable selling shareholders would pay us the exercise price set forth in the pre-funded warrants, which is a nominal amount (\$0.01 per common share). The pre-funded warrants are also exercisable on a cashless basis. If any of the pre-funded warrants are exercised on a cashless basis, we would not receive any cash payment from the applicable selling shareholders upon any such exercise of the pre-funded warrants.

We will bear the out-of-pocket costs, expenses and fees incurred in connection with the registration of the warrant shares to be sold by the selling shareholders pursuant to this prospectus. Other than registration expenses, the selling shareholders will bear underwriting discounts, commissions, placement agent fees or other similar expenses payable with respect to sales of the warrant shares.



## SELLING SHAREHOLDERS

On May 21, 2021, we entered into a securities purchase agreement with the selling shareholders named in this prospectus, pursuant to which we sold pre-funded warrants to purchase up to an aggregate of 910,746 of our common shares, no par value per share, at a purchase price of \$5.48 per pre-funded warrant, on May 21, 2021, in a private placement receiving aggregate gross proceeds of approximately \$5 million. The pre-funded warrants have an exercise price of \$0.01 per common share, are exercisable immediately and may be exercised at any time, from time to time, until exercised in full, subject to certain beneficial ownership limitations. A holder (together with its affiliates and other attribution parties) may not exercise any portion of a pre-funded warrant to the extent that immediately prior to or after giving effect to such exercise the holder would own more than 9.99% of our outstanding common shares immediately after exercise, which percentage may be changed at the holder's election to a lower or higher percentage upon 61 days' notice to us, subject to the terms of the pre-funded warrants.

Under the terms of the securities purchase agreement, we also agreed to file a registration statement within 30 days after the closing of the private placement to register for resale the shares underlying the pre-funded warrants and generally to cause the applicable registration statements to be declared effective as soon as practicable.

The selling shareholders may sell some, all or none of the common shares that may be issued to them upon exercise of the pre-funded warrants. We refer to these common shares as warrant shares. We do not know how long the selling shareholders will hold the warrant shares before selling them, and we currently have no agreements, arrangements or understandings with the selling shareholders regarding the sale or other disposition of any of the warrant shares. The warrant shares covered hereby may be offered from time to time by the selling shareholders. As a result, we cannot estimate the number of common shares each of the selling shareholders will beneficially own after termination of sales under this prospectus. In addition, each of the selling shareholders may have sold, transferred or otherwise disposed of all or a portion of its common shares since the date on which it provided information for this table.

Beneficial ownership is determined in accordance with the rules of the SEC and includes voting or investment power with respect to our common shares. Generally, a person "beneficially owns" our common shares if the person has or shares with others the right to vote those shares or to dispose of them, or if the person has the right to acquire voting or disposition rights within 60 days.

The information in the table below and the footnotes thereto regarding common shares to be beneficially owned after the offering assumes the exercise and sale of all warrant shares being offered by the selling shareholders under this prospectus. The percentage of shares owned prior to the offering is based on 29,846,000 common shares outstanding as of April 23, 2021. The percentage of shares owned after the offering is based on 29,846,000 common shares outstanding as of April 23, 2021 plus the maximum number of shares issuable upon exercise of the pre-funded warrants held by the named selling shareholder. This information has been obtained from the selling shareholders or in Schedules 13G or 13D and other public documents filed with the SEC. The address for the selling shareholders is c/o RTW Investments, LP, 40 10th Avenue, Floor 7, New York, NY 10014.

Name and Address <sup>(1)</sup>	Number of Shares Beneficially Owned Before Offering	Number of Shares Offered <sup>(2)</sup>	Beneficial Ownership After Offering	
			Number of Shares Beneficially Owned	Percentage of Shares Beneficially Owned
Entities affiliated with RTW Investments, LP	4,315,102 <sup>(1)</sup>	910,746 <sup>(2)</sup>	4,315,102	14.46%

- (1) Consists of 4,315,102 common shares beneficially owned by each of: (i) RTW Investments, LP ("RTW"), which is deemed the beneficial owner of shares held by RTW Master Fund, Ltd., RTW Venture Fund Limited and RTW Innovation Master Fund, Ltd. (the "Funds"), which are investment funds managed by RTW, and (ii) Roderick Wong, M.D., who serves as the Managing Partner and Chief Investment Officer of RTW. Dr. Wong exercises voting and dispositive control over the securities held by RTW and is therefore deemed to be a beneficial owner of securities owned or controlled by RTW.

Each of RTW and Dr. Wong disclaim beneficial ownership of the reported securities held by the Funds, except to the extent of its or his pecuniary interest therein. The number of shares beneficially owned by RTW and the Funds, in the aggregate, is limited by beneficial ownership limitations applicable to the pre-funded warrants held by the Funds, which limit the number of shares RTW and the Funds can beneficially own, following the exercise of such warrants, to a maximum of 9.99% of our outstanding common shares. As a result of such limitations, the number of shares beneficially owned does not include up to an aggregate of 8,518,257 common shares issuable upon exercise of pre-funded warrants held by the Funds, which includes 910,746 common shares issuable upon exercise of pre-funded warrants held by the Funds and offered under this prospectus.

- (2) Consists of 910,746 common shares issuable upon exercise of pre-funded warrants to purchase common shares held by the Funds and being offered under this prospectus.

## PLAN OF DISTRIBUTION

The selling shareholders, which shall include donees, pledgees, transferees or other successors-in-interest selling warrant shares or interests in warrant shares received after the date of this prospectus from a selling shareholder as a gift, pledge, partnership distribution or other transfer, may, from time to time, sell, transfer or otherwise dispose of any or all of their warrant shares or interests in warrant shares on any stock exchange, market or trading facility on which the warrant shares are traded or in private transactions. These dispositions may be at fixed prices, at prevailing market prices at the time of sale, at prices related to the prevailing market price, at varying prices determined at the time of sale, or at negotiated prices.

The selling shareholders may use any one or more of the following methods when disposing of warrant shares or interests therein:

- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- block trades in which the broker-dealer will attempt to sell the warrant shares as agent, but may position and resell a portion of the block as principal to facilitate the transaction;
- purchases by a broker-dealer as principal and resale by the broker-dealer for its own account;
- an exchange distribution in accordance with the rules of the applicable exchange;
- privately negotiated transactions;
- short sales effected after the date the registration statement of which this prospectus is a part is declared effective by the SEC;
- through the writing or settlement of options or other hedging transactions, whether through an options exchange or otherwise;
- through agreements between broker-dealers and the selling shareholders to sell a specified number of such warrant shares at a stipulated price per share;
- a combination of any such methods of sale; and
- any other method permitted by applicable law.

The selling shareholders may, from time to time, pledge or grant a security interest in some or all of the warrant shares by them and, if they default in the performance of their secured obligations, the pledgees or secured parties may offer and sell the warrant shares, from time to time, under this prospectus, or under an amendment to this prospectus under Rule 424(b) or other applicable provision of the Securities Act amending the list of selling shareholders to include the pledgee, transferee or other successors in interest as selling shareholders under this prospectus. The selling shareholders also may transfer the warrant shares in other circumstances, in which case the pledgees, transferees or other successors in interest will be the selling beneficial owners for purposes of this prospectus.

In connection with the sale of warrant shares or interests therein, the selling shareholders may enter into hedging transactions with broker-dealers or other financial institutions, which may in turn engage in short sales of the warrant shares in the course of hedging the positions they assume. The selling shareholders may also sell our common shares short and deliver these securities to close out their short positions, or loan or pledge the warrant shares to broker-dealers that in turn may sell these securities. The selling shareholders may also enter into options or other transactions with broker-dealers or other financial institutions or the creation of one or more derivative securities that require the delivery to each such broker-dealer or other financial institution of warrant shares offered by this prospectus, which warrant shares such broker-dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to reflect such transaction).

The aggregate proceeds to the selling shareholders from the sale of the warrant shares offered by them will be the purchase price of the warrant shares less discounts or commissions, if any. Each of the selling shareholders reserves the right to accept and, together with its agents from time to time, to reject, in whole or in part, any proposed purchase of warrant shares to be made directly or through agents. We will not receive

any of the proceeds from the sale of warrant shares in this offering, although we will receive the nominal exercise price upon exercise of the pre-funded warrants for the warrant shares, if such warrants are exercised for cash.

The selling shareholders also may resell all or a portion of the warrant shares in open market transactions in reliance upon Rule 144 under the Securities Act, provided that they meet the criteria and conform to the requirements of that rule.

The selling shareholders and any underwriters, broker-dealers or agents that participate in the sale of the warrant shares or interests therein may be “underwriters” within the meaning of Section 2(11) of the Securities Act. Any discounts, commissions, concessions or profit they earn on any resale of the warrant shares may be underwriting discounts and commissions under the Securities Act. Selling shareholders who are “underwriters” within the meaning of Section 2(11) of the Securities Act will be subject to the prospectus delivery requirements of the Securities Act.

To the extent required, the warrant shares to be sold, the names of the selling shareholders, the respective purchase prices and public offering prices, the names of any agents, dealer or underwriter, and any applicable commissions or discounts with respect to a particular offer will be set forth in an accompanying prospectus supplement or, if appropriate, a post-effective amendment to the registration statement that includes this prospectus.

In order to comply with the securities laws of some states, if applicable, the warrant shares may be sold in these jurisdictions only through registered or licensed brokers or dealers. In addition, in some states the warrant shares may not be sold unless it has been registered or qualified for sale or an exemption from registration or qualification requirements is available and is complied with.

We have advised the selling shareholders that the anti-manipulation rules of Regulation M under the Exchange Act may apply to sales of warrant shares in the market and to the activities of the selling shareholders and their affiliates. In addition, to the extent applicable we will make copies of this prospectus (as it may be supplemented or amended from time to time) available to the selling shareholders for the purpose of satisfying the prospectus delivery requirements of the Securities Act. The selling shareholders may indemnify any broker-dealer that participates in transactions involving the sale of the warrant shares against certain liabilities, including liabilities arising under the Securities Act.

## LEGAL MATTERS

Certain legal matters in connection with this offering relating to U.S. law will be passed upon for us by Cooley LLP. The validity of the issuance of our common shares offered in this prospectus will be passed upon for us by Osler, Hoskin & Harcourt LLP, Montréal, Canada.

## 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 ADDITIONAL INFORMATION

This prospectus is a part of a registration statement on Form S-3 that we filed with the SEC under the Securities Act and does not contain all of the information set forth or incorporated by reference in the registration statement. Whenever a reference is made in this prospectus or the accompanying prospectus supplement to any of our contracts, agreements or other documents, the reference may not be complete and you should refer to the exhibits that are a part of the registration statement or the exhibits to the reports or other documents incorporated by reference into this prospectus for a copy of such contract, agreement or other document. Because we are subject to the information reporting requirements of the Exchange Act, we file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's website at [www.sec.gov](http://www.sec.gov). We also maintain a website at [www.milestonepharma.com](http://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 from other documents that we file with it, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus. Information in this prospectus supersedes information incorporated by reference that we filed with the SEC prior to the date of this prospectus, while information that we file later with the SEC will automatically update and supersede the information in this prospectus. We incorporate by reference into this prospectus and the registration statement of which this prospectus is a part the information or documents listed below that we have filed with the SEC (Commission File No. 001-38899):

- [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 Current Reports on Form 8-K filed with the SEC on [March 30, 2021](#), [May 17, 2021](#), [June 2, 2021](#), and [June 21, 2021](#), to the extent the information in such reports is filed and not furnished; and
- [our definitive Proxy Statement on Schedule 14A, filed with the SEC on April 30, 2021, to the extent the information therein is filed and not furnished.](#)

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 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.

## PART II

## INFORMATION NOT REQUIRED IN THE PROSPECTUS

**Item 14. Other Expenses of Issuance and Distribution**

The following table sets forth an estimate of the fees and expenses payable by us in connection with the sale of the securities being registered.

	<u>Amount</u>
SEC registration fees	\$ 579.28
Accounting fees and expenses	25,000.00
Legal fees and expenses	50,000.00
Miscellaneous fees and expenses	24,720.72
Total	<u>\$100,000.00</u>

**Item 15. Indemnification of Directors and Officers**

Under the Business Corporations Act (Québec), or the QBCA, and our bylaws, we must indemnify our current or former directors and officers, agents or any other persons who act or have acted at our request as a director or officer of a related entity, against all costs, charges and expenses reasonably incurred by such person in connection with any civil, criminal, administrative, investigative or other proceeding in which such person is involved because of his, her or its association with us or such a related entity, provided that such person meets the conditions described below. The QBCA also provides that we must also make an advance payment to such person for costs, charges and expenses reasonably incurred in connection with such a proceeding, provided, however, that such person shall repay such advance payment if he, she or it does not fulfill the conditions described below.

The QBCA provides for such indemnification if the following conditions are met:

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

In the case of actions by or on our behalf, we may make such advance payments or indemnify such persons against all costs, charges and expenses reasonably incurred by such person in connection with such actions, only if (i) the person fulfills the conditions set forth above and (ii) a court approves such advance payments or indemnification.

The QBCA and our bylaws authorize us to purchase and maintain insurance for the benefit of each of our current or former directors or officers and other agents and each person who acts or acted at our request as a director, officer or other agents or a person acting in a similar capacity, of another entity.

In addition, we have entered, or intend to enter, into separate indemnity agreements with each of our directors and officers pursuant to which we agree to indemnify and hold harmless our directors and officers against any and all liability, loss, damage, cost or expense in accordance with the terms and conditions of the QBCA and our bylaws.

We have purchased and currently intend to maintain insurance on behalf of each and every person who is or was a director or officer of our company against any loss arising from any claim asserted against him or her and incurred by him or her in any such capacity, subject to certain exclusions.

**Item 16. Exhibits**

Exhibit Number	Description of Document
3.1	<a href="#">Amended Articles of Incorporation (incorporated herein by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K, filed with the SEC on May 15, 2019).</a>
3.2	<a href="#">Amended and Restated Bylaws (incorporated herein by reference to Exhibit 3.2 to the Registrant's Current Report on Form 8-K, filed with the SEC on May 15, 2019).</a>
4.1	<a href="#">Form of Common Share Certificate (incorporated herein by reference to Exhibit 4.1 to Amendment No. 1 to the Registrant's Registration Statement on Form S-1 (File No. 333-230846), filed with the SEC on April 29, 2019).</a>
5.1	<a href="#">Opinion of Osler, Hoskin &amp; Harcourt LLP.</a>
10.1	<a href="#">Securities Purchase Agreement dated May 21, 2021.</a>
10.2	<a href="#">Form of Pre-Funded Warrant to Purchase Common Shares.</a>
23.1	<a href="#">Consent of PricewaterhouseCoopers LLP, Independent Registered Public Accounting Firm.</a>
23.2	<a href="#">Consent of Osler, Hoskin &amp; Harcourt LLP (included in Exhibit 5.1).</a>
24.1	Power of Attorney (included on signature page).

**Item 17. Undertakings**

- (a) The undersigned registrant hereby undertakes:
- (1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:
    - (i) to include any prospectus required by Section 10(a)(3) of the Securities Act;
    - (ii) to reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the SEC pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20 percent change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement;
    - (iii) to include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement;

*provided, however*, that paragraphs (1)(i), (1)(ii) and (1)(iii) of this section do not apply if the registration statement is on Form S-3 and the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the SEC by the registrant pursuant to Section 13 or Section 15(d) of the Securities Exchange Act of 1934 (the "Exchange Act") that are incorporated by reference in the registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of the registration statement.

- (2) That, for the purpose of determining any liability under the Securities Act, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.
  - (3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.
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- (4) That, for the purpose of determining liability under the Securities Act to any purchaser:
- (i) each prospectus filed by the registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and
  - (ii) each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5) or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii) or (x) for the purpose of providing the information required by Section 10(a) of the Securities Act shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which the prospectus relates, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof. *Provided, however,* that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such effective date.
- (b) The undersigned registrant undertakes that, for purposes of determining any liability under the Securities Act, each filing of the registrant's annual report pursuant to Section 13(a) or Section 15(d) of the Exchange Act (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Exchange Act) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.
- (c) Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers, and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the SEC such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer, or controlling person of the registrant in the successful defense of any action, suit, or proceeding) is asserted by such director, officer, or controlling person of the registrant in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.
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<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ Paul Truex</u> Paul Truex	Director	June 25, 2021
<u>/s/ Robert J. Wills, PhD</u> Robert J. Wills, PhD	Director	June 25, 2021

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**Osler, Hoskin & Harcourt LLP**  
1000 De La Gauchetière Street West  
Suite 2100  
Montréal, Québec, Canada H3B 4W5  
514.904.8100 MAIN  
514.904.8101 FACSIMILE

OSLER

Montréal

Toronto

Calgary

Ottawa

Vancouver

New York

June 25, 2021

**Exhibit 5.1**

**Milestone Pharmaceuticals Inc.**  
1111 Dr. Frederik-Philips Boulevard  
Montreal, Québec  
H4M 2X6

Dear Sirs/Mesdames:

**Re: Milestone Pharmaceuticals Inc. – Registration Statement on Form S-3**

We have acted as Canadian counsel to Milestone Pharmaceuticals Inc. (the “**Corporation**”), a corporation governed by the *Business Corporations Act* (Québec), in connection with the preparation of a registration statement on Form S-3 (the “**Registration Statement**”), including a related prospectus filed with the Registration Statement (the “**Prospectus**”), covering the registration for resale of up to 910,746 common shares of the Corporation (the “**Shares**”) on behalf of the selling shareholders identified in the Prospectus issuable upon the exercise of certain pre-funded warrants sold to the selling shareholders in a private placement on May 21, 2021 (the “**Warrants**”).

We have examined the Registration Statement, the Prospectus and the Warrants and all such corporate and public records, statutes and regulations and have made such investigations and have reviewed such other documents as we have deemed relevant and necessary and have considered such questions of law as we have considered relevant and necessary in order to give the opinion hereinafter set forth. As to various questions of fact material to such opinions which were not independently established, we have relied upon a certificate of an officer of the Corporation.

In reviewing the foregoing documents and in giving this opinion, we have assumed (a) the legal capacity of all individuals, the genuineness of all signatures, the veracity of the information contained therein, the authenticity of all documents submitted to us as originals and the conformity to authentic or original documents of all documents submitted to us as certified, conformed, electronic, photostatic or facsimile copies and (b) the completeness, truth and accuracy of all facts set forth in the official public records, certificates and documents supplied by public officials or otherwise conveyed to us by public officials.

We are qualified to practice law in the Province of Québec and this opinion is rendered solely with respect to the Province of Québec and the federal laws of Canada applicable in the Province of Québec.

osler.com

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Where our opinion expressed herein refers to the Shares having been issued as being “fully- paid and non-assessable” common shares of the Corporation, such opinion assumes that all required consideration (in whatever form) has been paid or provided. No opinion is expressed as to the adequacy of any consideration received.

We express no opinion to the extent that, notwithstanding the Corporation’s current reservation of the Shares as of the date hereof, future issuances of securities of the Corporation, including the Shares, and/or antidilution adjustments to outstanding securities of the Corporation, including the Warrants, may cause the Warrants to be exercisable for more common shares of the Corporation than the number that then remain authorized but unissued.

On the basis of the foregoing, we are of the opinion that the Shares, when issued and paid for upon exercise of the Warrants in accordance with the terms of the Warrants, will be will be validly issued, fully paid and non-assessable.

Our opinion is limited to the matters stated herein and no opinion is implied or may be inferred beyond the matters expressly stated. Our opinion is based on these laws as in effect on the date hereof, and we disclaim any obligation to advise you of facts, circumstances, events or developments which hereafter may be brought to our attention and which may alter, affect or modify the opinion expressed herein.

We consent to the filing of this opinion as an exhibit to the Registration Statement and to the reference to our firm under the caption “Legal Matters” in the Prospectus.

Yours very truly,

*(signed) Osler, Hoskin & Harcourt LLP*

Osler, Hoskin & Harcourt LLP

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## SECURITIES PURCHASE AGREEMENT

This SECURITIES PURCHASE AGREEMENT (this “**Agreement**”) is made and entered into as of May 21, 2021 (the “**Effective Date**”) by and among Milestone Pharmaceuticals Inc., a corporation continuing under the *Business Corporations Act* (Québec) (the “**Company**”) and each of those persons listed as a Purchaser on the Schedule of Purchasers attached as Schedule I hereto (each, a “**Purchaser**” and together, the “**Purchasers**”). Certain terms used and not otherwise defined in the text of this Agreement are defined in Section 11 hereof.

### RECITALS

WHEREAS, the Company and the Purchasers are executing and delivering this Agreement in reliance upon the exemption from securities registration afforded by Section 4(a)(2) of the Securities Act of 1933, as amended (the “**Securities Act**”) and/or Rule 506 of Regulation D as promulgated by the United States Securities and Exchange Commission (the “**Commission**”) under the Securities Act; and

WHEREAS, the Company desires to sell to the Purchasers, and the Purchasers desire to purchase from the Company, one or more pre-funded warrants issued by the Company to purchase up to 910,746 Company common shares, no par value per share (the “**Common Shares**”) at an exercise price of \$0.01 per share (the “**Warrant Shares**”) in substantially the form attached hereto as Exhibit A (the “**Pre-Funded Warrants**”);

NOW, THEREFORE, in consideration of the foregoing and the mutual representations, warranties and covenants herein contained, the parties hereto hereby agree as follows:

Section 1. Authorization of Warrants. The Company has authorized the sale and issuance of the Pre-Funded Warrants on the terms and subject to the conditions set forth in this Agreement.

Section 2. Sale and Purchase of the Pre-Funded Warrants.

2.1 Upon the terms and subject to the conditions herein contained, the Company agrees to sell to the Purchasers, and the Purchasers agree to purchase from the Company, at the Closing (as defined in Section 3), that number of Pre-Funded Warrants set forth on Schedule I hereto (the “**Schedule of Purchasers**”) for the purchase price set forth opposite such Purchaser’s name, which amount represents the number of Pre-Funded Warrants purchased by such Purchaser multiplied by the price per Pre-Funded Warrants of \$5.48. The purchase price to be paid by each Purchaser, as set forth on Schedule I, shall be referred to as the “**Aggregate Purchase Price.**”

2.2 At or prior to the Closing, each Purchaser will pay the purchase price set forth opposite such Purchaser’s name on Schedule I by wire transfer of immediately available funds in accordance with wire instructions provided by the Company to the Purchasers prior to the Closing. On or before the Closing, the Company will deliver duly executed Pre-Funded Warrants to the Purchasers, in each case against delivery of the Aggregate Purchase Price.

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**Section 3 Closing.** Subject to the satisfaction of the closing conditions set forth in Section 7, the closing with respect to the transactions contemplated in Section 2 hereof (the “**Closing**”), shall take place at the offices of Cooley LLP, 500 Boylston Street, 14<sup>th</sup> Floor, Boston, MA 02116 on the second Business Day after the Effective Date (the “**Closing Date**”) or at such other time and place as the Company and Purchasers may agree, including remotely via the exchange of documents and signatures.

**Section 4. Representations and Warranties of the Purchaser.** Each Purchaser represents and warrants to the Company that the statements contained in this Section 4 are true and correct as of the Effective Date, and will be true and correct as of the date of the Closing Date:

4.1 **Validity.** The execution, delivery and performance of this Agreement, including the purchase of the Pre-Funded Warrants and the other instruments referred to herein, in each case to which such Purchaser is a party, and the consummation by such Purchaser of the transactions contemplated hereby have been duly authorized by all necessary corporate, partnership, limited liability or similar actions, as applicable, on the part of such Purchaser. This Agreement has been duly executed and delivered by such Purchaser, and the other instruments referred to herein to which it is a party will be duly executed and delivered by such Purchaser, and each such agreement and other instruments constitutes or will constitute a valid and binding obligation of such Purchaser, enforceable against it in accordance with its terms, except as limited by applicable bankruptcy, insolvency, reorganization, moratorium, fraudulent conveyance, and any other laws of general application affecting enforcement of creditors’ rights generally, and as limited by laws relating to the availability of specific performance, injunctive relief, or other equitable remedies.

4.2 **Brokers.** There is no broker, investment banker, financial advisor, finder or other Person that has been retained by or is authorized to act on behalf of such Purchaser who might be entitled to any fee or commission for which the Company will be liable in connection with the execution of this Agreement and the consummation of the transactions contemplated hereby.

4.3 **Investment Representations and Warranties.** Such Purchaser understands and agrees that the offering and sale of the Pre-Funded Warrants and the Warrant Shares has not been registered under the Securities Act or any applicable state securities laws and are being made in reliance upon federal and state exemptions for transactions not involving a public offering that depend upon, among other things, the bona fide nature of the investment intent and the accuracy of such Purchaser’s representations as expressed herein.

4.4 **Acquisition for Own Account; No Control Intent.** Such Purchaser is acquiring the Pre-Funded Warrant and the Warrant Shares for its own account for investment and not with a view toward distribution in a manner that would violate the Securities Act or any applicable state securities laws. Such Purchaser is not a broker or dealer registered pursuant to Section 15 of the Exchange Act (a “registered broker-dealer”) and is not affiliated with a registered broker dealer. Such Purchaser is not party to any agreement providing for or contemplating the distribution of any of the Pre-Funded Warrants or the Warrant Shares. Such Purchaser has no present intent to effect a “change of control” of the Company as such term is understood under the rules promulgated pursuant to Section 13(d) of the Exchange Act.



4.5 Ability to Protect Its Own Interests and Bear Economic Risks. Such Purchaser, by reason of the business and financial experience of its management, has the capacity to protect its own interests in connection with the transactions contemplated by this Agreement and is capable of evaluating the merits and risks of the investment in the Pre-Funded Warrants and the Warrant Shares. Such Purchaser is able to bear the economic risk of an investment in the Pre-Funded Warrants and the Warrant Shares and is able to sustain a loss of all of its investment in the Pre-Funded Warrants without economic hardship, if such a loss should occur.

4.6 Accredited Investor; No Bad Actor. Such Purchaser is an “accredited investor” as that term is defined in Rule 501(a) under the Securities Act, a “Qualified Institutional Buyer” as defined in Rule 144A under the Securities Act, and a “qualified purchaser” as defined in Section 2(a)(51) of the Investment Company Act of 1940, as amended. Such Purchaser has not taken any of the actions set forth in, and is not subject to, the disqualification provisions of Rule 506(d)(1) of the Securities Act. Such Purchaser is also an “accredited investor” within the meaning of *Regulation 45-106 respecting Prospectus Exemptions* on the basis that such Purchaser fits within one of the categories of an “accredited investor” which such Purchaser has indicated it so belongs and has provided confirmation of same to the Company. Such Purchaser is also acquiring the Pre-Funded Warrants and the Warrant Shares as principal and has not been created, or is being used, solely to purchase or hold the Pre-Funded Warrants and the Warrant Shares.

4.7 Access to Information. Such Purchaser has been given access to Company documents, records, and other information, and has had adequate opportunity to ask questions of, and receive answers from, the Company’s officers, employees, agents, accountants, and representatives concerning the Company’s business, operations, financial condition, assets, liabilities, and all other matters relevant to its investment in the Pre-Funded Warrants and the Warrant Shares. Such Purchaser understands that an investment in the Pre-Funded Warrants and the Warrant Shares bears significant risk and represents that it has reviewed the SEC Reports (defined below), which serve to qualify certain of the Company representations set forth below.

4.8 Restricted Securities.

(a) Such Purchaser understands that the Pre-Funded Warrants and the Warrant Shares will be characterized as “restricted securities” under the federal securities laws inasmuch as they are being acquired from the Company in a private placement under Section 4(a)(2) of the Securities Act and/or the applicable provisions of Regulation D promulgated thereunder, and that under such laws and applicable regulations such Pre-Funded Warrants and Warrant Shares may be resold without registration under the Securities Act only in certain limited circumstances.

(b) Such Purchaser acknowledges that the Pre-Funded Warrants and the Warrant Shares must be held indefinitely unless subsequently registered under the Securities Act and under applicable state securities laws or an exemption from such registration is available. Such Purchaser understands that the Company is under no obligation to register the Pre-Funded Warrants or the Warrant Shares, except as provided in this Agreement.

(c) Such Purchaser is aware of the provisions of Rule 144 under the Securities Act, which permit limited resale of securities purchased in a private placement.

4.9 Such Purchaser has a substantive, pre-existing relationship with the Company and the management of the Company.

4.10 Such Purchaser became aware of the Pre-Funded Warrants and the Warrant Shares, and the Pre-Funded Warrants and the Warrant Shares were offered to such Purchaser, solely by direct contact between such Purchaser and the Company, and not by any other means, and such Purchaser is unaware of, and is in no way relying on, any form of general solicitation or general advertising, including, without limitation, any article, notice, advertisement or other communication published in any newspaper, magazine or similar media or broadcast over television or radio, or electronic mail over the Internet, in connection with the offer and sale of the Pre-Funded Warrants and the Warrant Shares, and is not subscribing for the Pre-Funded Warrants and the Warrant Shares and did not become aware of the Pre-Funded Warrants or the Warrant Shares through or as a result of any seminar or meeting to which such Purchaser was invited by, or any solicitation of a subscription by, a person not previously known to such Purchaser in connection with investments in securities generally.

Section 5 Representations and Warranties by the Company. Assuming the accuracy of the representations and warranties of the Purchasers set forth in Article 4 and except as set forth in the SEC Reports, which disclosures serve to qualify these representations and warranties in their entirety, the Company represents and warrants to the Purchasers that the statements contained in this Section 5 are true and correct in all material respects as of the Effective Date, and will be true and correct in all material respects as of the date of the Closing Date:

5.1 Organization and Good Standing. The Company and each Subsidiary: (a) is duly incorporated or otherwise organized, validly existing and in good standing under the laws of the jurisdiction of its formation, (b) is duly qualified to do business as a foreign entity and is in good standing in each jurisdiction where the nature of the property owned or leased by it or the nature of the business conducted by it makes such qualification necessary, except where the failure to be so qualified would not have a Material Adverse Effect, and (c) has all requisite corporate power and authority to own or lease and operate its assets and carry on its business as presently being conducted as disclosed in the SEC Reports.

5.2 Corporate Power and Authority; Valid Issuance of Warrants.

(a) The Company has all requisite corporate power and has taken all necessary corporate action required for the due authorization, execution, delivery and performance by the Company of this Agreement and the other Transaction Documents and the consummation of the transactions contemplated hereby and thereby. The execution, delivery and performance by the Company of this Agreement, and the consummation by the Company of the transactions contemplated hereby, have been duly authorized by the Company's board of directors or a duly authorized committee thereof and no further consent or authorization of the Company, its board of directors or its shareholders is required. This Agreement has been duly executed and delivered by the Company, and the other instruments referred to herein to which it is a party will be duly executed and delivered by the Company, and each such agreement constitutes or will constitute a legal, valid and binding obligation of the Company enforceable against it in accordance with its terms, except to the extent that enforceability may be limited by bankruptcy, insolvency, reorganization, moratorium, fraudulent conveyance, and any other laws of general application affecting enforcement of creditors' rights generally, and as limited by laws relating to the availability of specific performance, injunctive relief, or other equitable remedies.

(b) Each Pre-Funded Warrant, upon delivery, will have been duly executed by the Company and, when delivered in accordance with the terms hereof, will constitute a valid and binding obligation of the Company enforceable against the Company in accordance with its terms, except (i) as limited by general equitable principles and applicable bankruptcy, insolvency, reorganization, moratorium and other laws of general application affecting enforcement of creditors' rights generally, (ii) as limited by laws relating to the availability of specific performance, injunctive relief or other equitable remedies and (iii) insofar as indemnification and contribution provisions may be limited by applicable law. The Warrant Shares, when issued and delivered upon exercise of each Pre-Funded Warrant in accordance with its terms, will be validly issued, fully paid and non-assessable and free of any preemptive or similar rights.

5.3 Consents. Neither the execution, delivery or performance of this Agreement by the Company, nor the consummation by it of the obligations and transactions contemplated hereby (including, without limitation, the issuance, the delivery of the Pre-Funded Warrants and the provision to the Purchasers of the rights contemplated by the Transaction Documents) requires any consent of, authorization by, exemption from, filing with or notice to any Governmental Entity or any other Person, other than filings required under applicable U.S. or Canadian federal and state securities laws.

5.4 No Conflicts.

(a) The execution, delivery and performance of this Agreement and the consummation of the transactions contemplated hereby (including, without limitation, the execution and delivery of the Pre-Funded Warrants, and, upon the valid exercise of the Pre-Funded Warrants, the delivery of the Warrant Shares and the provision to the Purchasers of the rights contemplated by the Transaction Documents) will not (a) result in a violation of articles or by-laws, as amended, or any equivalent organizational document of the Company or any Subsidiary (the "**Charter Documents**") or require the approval of the Company's shareholders, (b) violate, conflict with or result in the breach of the terms, conditions or provisions of or constitute a default (or an event which with notice or lapse of time or both would become a default) under, or give rise to any right of termination, acceleration or cancellation under, any material agreement, lease, mortgage, license, indenture, instrument or other contract to which the Company or any Subsidiary is a party, (c) result in a violation of any law, rule, regulation, order, judgment or decree (including, without limitation, U.S. or Canadian federal and state securities laws and regulations and regulations of any self-regulatory organizations to which the Company or its securities are subject) applicable to the Company or any Subsidiary or by which any property or asset of the Company or any Subsidiary is bound or affected, (d) result in a violation of or require shareholder approval under any rule or regulation of The Nasdaq Stock Market, or (e) result in the creation of any encumbrance upon any of the Company's or any of its Subsidiary's assets.

(b) Neither the Company nor any Subsidiary is (i) in violation of its Charter Documents, (ii) in default (and no event has occurred that, with notice or lapse of time or both, would cause the Company or any Subsidiary to be in default) under, nor has there occurred any event giving others (with notice or lapse of time or both) any rights of termination, amendment, acceleration or cancellation of, any material agreement, indenture or instrument to which the Company or any Subsidiary is a party, nor has the Company or any Subsidiary received written notice of a claim that it is in default under, or that it is in violation of, any material contract (whether or not such default or violation has been waived), (iii) in violation of, or in receipt of written notice that it is in violation of, any law, ordinance or regulation of any Governmental Entity, except where the violation would not result in a Material Adverse Effect, and (iv) in violation of any order of any Governmental Entity having jurisdictional over the Company or any Subsidiary or any of the Company's or any Subsidiary's properties or assets.

5.5 Québec Securities Laws. The Company has complied with the securities laws of the Province of Québec, including the rules and regulations made thereunder together with applicable published national and local instruments, policy statements, notices, blanket rulings and orders of the *Autorité des marchés financiers* (Québec), and all discretionary rulings and orders applicable to the Company, if any, of the Canadian securities commissions required to be complied with by the Company in order to sell the Pre-Funded Warrants and the Warrant Shares outside Canada as contemplated by this Agreement. To the Company's knowledge, no order, ruling or decision of any court or any securities regulatory authority in Canada is in effect that restricts or ceases trades in securities of the Company.

5.6 The Nasdaq Stock Market. The Common Shares are listed on The Nasdaq Global Select Market. To the Company's knowledge, there are no proceedings to revoke or suspend such listing or the listing of the Common Shares. The Company is in compliance with the requirements of Nasdaq for continued listing of the Common Shares thereon and any other Nasdaq listing and maintenance requirements, and the execution, delivery and performance of this Agreement by the Company and the consummation by the Company of the transactions contemplated hereby (including the issuance of the Pre-Funded Warrants) will not result in any noncompliance by the Company with any such requirements.

5.7 No Integrated Offering. Neither the Company, any Subsidiary, nor any of the Company's or any Subsidiary's Affiliates or any other Person acting on the Company's or any Subsidiary's behalf, has directly or indirectly engaged in any form of general solicitation or general advertising with respect to the Pre-Funded Warrants, nor have any of such Persons made any offers or sales of any security of the Company, any Subsidiary or any of the Company's or any Subsidiary's Affiliates or solicited any offers to buy any security of the Company, any Subsidiary or any of the Company's or any Subsidiary's Affiliates under circumstances that would require registration of the Pre-Funded Warrants under the Securities Act or any other securities laws or cause this offering of Pre-Funded Warrants to be integrated with any prior offering of securities of the Company or any Subsidiary for purposes of the Securities Act in any manner that would affect the validity of the private placement exemption under the Securities Act for the offer and sale of the Pre-Funded Warrants hereunder.

5.8 SEC Reports; Financial Statements; Shell Company Status.

(a) The Company's Common Shares are registered under Section 12 of the Exchange Act. The Company has filed all reports, schedules, forms, statements and other documents required to be filed by the Company under the Exchange Act, including pursuant to Section 13(a) or 15(d) thereof, since May 8, 2019 (the foregoing materials, including the exhibits thereto and documents incorporated by reference therein, being collectively referred to herein as the "**SEC Reports**") on a timely basis or has received a valid extension of such time of filing and has filed any such SEC Reports prior to the expiration of any such extension. As of their respective dates, the SEC Reports complied in all material respects with the requirements of the Exchange Act and, in each case, to the rules promulgated thereunder, as applicable, and none of the SEC Reports, when filed, contained any untrue statement of a material fact or omitted to state a material fact required to be stated therein or necessary in order to make the statements therein, in the light of the circumstances under which they were made, not misleading.

(b) The financial statements and the related notes of the Company included in the SEC Reports comply in all material respects with applicable accounting requirements and the rules and regulations of the Commission with respect thereto as in effect at the time of filing. Such financial statements have been prepared in accordance with GAAP, except as may be otherwise specified in such financial statements or the notes thereto and except that unaudited financial statements may not contain all footnotes required by GAAP, and fairly present the consolidated financial position of the Company as of and for the dates thereof and the consolidated results of operations and cash flows for the periods then ended, subject, in the case of unaudited statements, to normal, immaterial, year-end audit adjustments. There is no transaction, arrangement, or other relationship between the Company or any Subsidiary and an unconsolidated or other off balance sheet entity that is required to be disclosed by the Company in SEC Reports and is not so disclosed and would have or reasonably be expected to result in a Material Adverse Effect.

(c) The Company is not, and has never been, an issuer identified in Rule 144(i)(1) under the Securities Act.

5.9 Disclosure Controls and Procedures; Internal Controls Over Financial Reporting.

(a) The Company has established and maintains disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) that are effective in all material respects to ensure that material information relating to the Company, including any consolidated Subsidiaries, is made known to its principal executive officer and principal financial officer by others within those entities. The Company's certifying officers have evaluated the effectiveness of the Company's disclosure controls and procedures as of the end of the period covered by the most recently filed quarterly or annual periodic report under the Exchange Act (such date, the "**Evaluation Date**"). The Company presented in its most recently filed quarterly or annual periodic report under the Exchange Act the conclusions of the certifying officers about the effectiveness of the disclosure controls and procedures based on their evaluations as of the Evaluation Date.

(b) The Company maintains internal control over financial reporting (as such term is defined in Exchange Act Rule 13a-15(f) and 15d-15(f)) designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with GAAP and such internal control over financial reporting is effective. The Company presented in its most recently filed annual report under the Exchange Act the conclusions of the certifying officers about the effectiveness of the Company's internal control over financial reporting based on their evaluations as of the end of the period covered by such report. Since the Evaluation Date, there have been no significant changes in the Company's internal control over financial reporting or, to the Company's knowledge, in other factors that could significantly affect the Company's internal control over financial reporting.

5.10 Absence of Litigation. There is no claim, action, suit, arbitration, investigation or other proceeding pending against, or to the knowledge of the Company and each Subsidiary, threatened against or affecting, the Company, any Subsidiary or any of the Company's or any Subsidiary's properties or, to the knowledge of the Company and each Subsidiary, any of its respective officers or directors before any Governmental Entity, in each case other than legal proceedings that are not reasonably expected to result in a Material Adverse Effect. Neither the Company nor any Subsidiary, nor any director or officer thereof, is or has been the subject of any action involving a claim of violation of or liability under federal or state securities laws or a claim of breach of fiduciary duty relating to the Company or any Subsidiary. There has not been, and to the knowledge of the Company and each Subsidiary, there is not pending or contemplated, any investigation by the Commission of the Company or any Subsidiary or any current or former director or officer of the Company or any Subsidiary. The Company has not received any stop order or other order suspending the effectiveness of any registration statement filed by the Company under the Exchange Act or the Securities Act and, to the Company's knowledge, the Commission has not issued any such order.

5.11 Taxes. The Company and the Subsidiary have filed all U.S. and Canadian federal, and material state, provincial, municipal and local and any other foreign tax returns that are required to be filed or have properly requested extensions thereof and have paid all taxes required to be paid by any of them and, if due and payable, any related or similar assessment, fine or penalty levied against any of them except as may be contested in good faith and by appropriate proceedings and except where the failure to file or pay would not reasonably be expected, individually or in the aggregate, to have a Material Adverse Effect. The Company has made adequate charges, accruals and reserves in the applicable financial statements referred to in Section 5.8(b) above in respect of all U.S. and Canadian federal, state, provincial, municipal, local and foreign taxes for all periods as to which the tax liability of the Company or the Subsidiary has not been finally determined, except where the failure to make such adequate charge, accrual or reserve would not reasonably be expected, individually or in the aggregate, to have a Material Adverse Effect.

5.12 Compliance with Laws.

(a) The preclinical tests and clinical trials, and other studies (collectively, “studies”) that are described in, or the results of which are referred to in, the SEC Reports were and, if still pending, are being conducted in all material respects in accordance with the protocols, procedures and controls designed and approved for such studies and with standard medical and scientific research procedures; each description of the results of such studies is accurate and complete in all material respects and fairly presents the data derived from such studies, and the Company and the Subsidiary have no knowledge of any other studies the results of which are inconsistent with, or otherwise call into question, the results described or referred to in the SEC Reports; the Company and the Subsidiary have made all such filings and obtained all such approvals as may be required by the Food and Drug Administration of the U.S. Department of Health and Human Services or any committee thereof or from any other U.S. or foreign government or drug or medical device regulatory agency, or health care facility Institutional Review Board (collectively, the “**Regulatory Agencies**”); neither the Company nor the Subsidiary has received any notice of, or correspondence from, any Regulatory Agency requiring the termination, suspension or modification of any clinical trials that are described or referred to in the SEC Reports; and the Company and the Subsidiary have each operated and currently are in compliance in all material respects with all applicable rules, regulations and policies of the Regulatory Agencies.

(b) To the Company’s knowledge, neither the Company nor any of its directors, officers, employees or agents, has made, or caused the making of, any false statements on, or material omissions from, any other records or documentation prepared or maintained to comply with the requirements of the FDA or any other Governmental Entity.

5.13 Brokers. There is no investment banker, broker, finder, financial advisor, placement agent or other Person that has been retained by or is authorized to act on behalf of the Company or any Subsidiary who might be entitled to any fee or commission in connection with the transactions contemplated by this Agreement.

5.14 Environmental Matters. Except as would not reasonably be expected, individually or in the aggregate, to have a Material Adverse Effect: (i) neither the Company nor the Subsidiary is in violation of any federal, state, provincial, local or foreign statute, law, rule, regulation, ordinance, code, policy or rule of common law or any judicial or administrative interpretation thereof, including any judicial or administrative order, consent, decree or judgment, relating to pollution or protection of human health, the environment (including, without limitation, ambient air, surface water, groundwater, land surface or subsurface strata) or wildlife, including, without limitation, laws and regulations relating to the release or threatened release of chemicals, pollutants, contaminants, wastes, toxic substances, hazardous substances, petroleum or petroleum products (collectively, “**Hazardous Materials**”) or to the manufacture, processing, distribution, use, treatment, storage, disposal, transport or handling of Hazardous Materials (collectively, “**Environmental Laws**”); (ii) the Company and the Subsidiary have all permits, authorizations and approvals required under any applicable Environmental Laws and are each in compliance with their requirements; (iii) there are no pending or, to the Company’s knowledge, threatened administrative, regulatory or judicial actions, suits, demands, demand letters, claims, liens, notices of noncompliance or violation, investigation or proceedings relating to any Environmental Law against the Company or the Subsidiary; and (iv) to the Company’s knowledge, there are no events or circumstances that might reasonably be expected to form the basis of an order for clean-up or remediation, or an action, suit or proceeding by any private party or governmental body or agency, against or affecting the Company or the Subsidiary relating to Hazardous Materials or any Environmental Laws.

5.15 Intellectual Property Matters. To the knowledge of the Company, the Company owns, possesses, licenses or has other rights to use, on reasonable terms, all patents, patent applications, trade and service marks, trade and service mark registrations, trade names, copyrights, licenses, inventions, trade secrets, technology, know-how and other intellectual property (collectively, the “**Intellectual Property**”) necessary for the conduct of the Company’s business as now conducted or as proposed in the SEC Reports to be conducted (the “**Company Intellectual Property**”) except where the failure to have such Intellectual Property would not reasonably be expected to have, individually or in the aggregate, a Material Adverse Effect. To the Company’s knowledge: (i) there are no third parties who have rights to any Intellectual Property that is disclosed in the SEC Reports; and (ii) there is no infringement by third parties of any Intellectual Property. There is no pending or, to the Company’s knowledge, threatened action, suit, proceeding or claim by others: (A) challenging the Company’s rights in or to any Intellectual Property, and the Company is unaware of any facts which would form a reasonable basis for any such action, suit, proceeding or claim; (B) challenging the validity, enforceability or scope of any material Intellectual Property, and the Company is unaware of any facts which would form a reasonable basis for any such action, suit, proceeding or claim; or (C) asserting that the Company or the Subsidiary infringes or otherwise violates, or would, upon the commercialization of any product or service described in the SEC Reports as under development, infringe or violate, any patent, trademark, trade name, service name, copyright, trade secret or other proprietary rights of others, and the Company is unaware of any facts which would form a reasonable basis for any such action, suit, proceeding or claim. The product candidates described in the SEC Reports as under development by the Company or the Subsidiary fall within the scope of the claims of one or more patents owned by, or exclusively licensed to, the Company or the Subsidiary.

5.16 Absence of Changes. Since the Evaluation Date: (a) there has not been any Material Adverse Effect or any event or events that individually or in the aggregate would reasonably be expected to have a Material Adverse Effect; (b) there has not been any dividend or distribution of any kind declared, set aside for payment, paid or made by the Company on any class of capital stock, (c) neither the Company nor any Subsidiary has sustained any material loss or interference with the Company’s or any Subsidiary’s business from fire, explosion, flood or other calamity, whether or not covered by insurance, or from any labor disturbance or dispute or any action, order or decree of any court or arbitrator or governmental or regulatory authority, and (d) neither the Company nor any Subsidiary has incurred any material liabilities except in the ordinary course of business.

5.17 Suppliers and Customers. Neither the Company nor any Subsidiary has any knowledge of any termination, cancellation or threatened termination or cancellation or limitation of, or any material dissatisfaction with, the business relationship between the Company or any Subsidiary and any material supplier, customer, vendor, customer or client.



5.18 Application of Takeover Protections. The Company and its Board of Directors have taken all necessary action, if any, in order to render inapplicable any control share acquisition, business combination, poison pill (including any distribution under a rights agreement) or other similar anti-takeover provision under the Company's Charter Documents or the laws of its state of incorporation that is or could become applicable to each Purchaser as a result of such Purchaser and the Company fulfilling their obligations or exercising their rights under this Agreement, including without limitation as a result of the Company's issuance of the Pre-Funded Warrants and such Purchaser's ownership of the Pre-Funded Warrants.

5.19 Foreign Corrupt Practices. Since December 31, 2018, neither the Company nor the Subsidiary nor, to the Company's knowledge, any director, officer, agent, employee, Affiliate or other person acting on behalf of the Company or the Subsidiary has, in the course of its actions for, or on behalf of, the Company or the Subsidiary (i) used any corporate funds for any unlawful contribution, gift, entertainment or other unlawful expenses relating to political activity; (ii) made any direct or indirect unlawful payment to any domestic government official, "foreign official" (as defined in the U.S. Foreign Corrupt Practices Act of 1977, as amended, and the rules and regulations thereunder (collectively, the "**FCPA**")) or employee from corporate funds; (iii) violated or is in violation of any provision of the FCPA or any applicable non-U.S. anti-bribery statute or regulation; or (iv) made any unlawful bribe, rebate, payoff, influence payment, kickback or other unlawful payment to any domestic government official, such foreign official or employee; and the Company and the Subsidiary and, to the Company's knowledge, the Company's Affiliates have conducted their respective businesses in compliance with the FCPA and have instituted and maintain policies and procedures designed to ensure, and which are reasonably expected to continue to ensure, continued compliance therewith.

5.20 Insurance. Each of the Company and its Subsidiaries are insured by recognized, financially sound and reputable institutions with policies in such amounts and with such deductibles and covering such risks as are generally deemed adequate and customary for their businesses including, but not limited to, policies covering material real and personal property owned or leased by the Company and each Subsidiary against theft, damage, destruction, acts of vandalism and earthquakes and policies covering the Company and the Subsidiary for product liability claims and clinical trial liability claims. The Company has no reason to believe that it or the Subsidiary will not be able (i) to renew its existing insurance coverage as and when such policies expire or (ii) to obtain comparable coverage from similar institutions as may be necessary or appropriate to conduct its business as now conducted and at a cost that could not be expected to have a Material Adverse Effect. Neither the Company nor any Subsidiaries has been denied any insurance coverage which it has sought or for which it has applied.

5.21 No Manipulation of Shares. The Company has not taken, nor will it take, directly or indirectly, any action designed to stabilize or manipulate the price of the Common Shares or any security of the Company to facilitate the sale or resale of any of the Pre-Funded Warrants.

5.22 Disclosure. The Company understands and confirms that the Purchasers will rely on the foregoing representations in effecting transactions in securities of the Company. No representation or warranty by the Company contained in this Agreement contains any untrue statement of a material fact or omits to state any material fact necessary in order to make the statements made therein, in light of the circumstances under which they were made, not misleading. The Company acknowledges and agrees that the Purchasers do not make and have not made any representations or warranties with respect to the transactions contemplated hereby other than those specifically set forth in Section 4 hereof.

Section 6. Covenants.

6.1 Reasonable Best Efforts. Each party shall use its reasonable best efforts to timely satisfy each of the conditions to be satisfied by it as provided in Section 7 of this Agreement.

6.2 Reporting Status. During the Reporting Period, the Company shall use reasonable best efforts to: (a) timely file all reports required to be filed with the Commission pursuant to the Exchange Act or the rules and regulations thereunder, and (b) not take any action or file any document (whether or not permitted by the Securities Act or the rules promulgated thereunder) to terminate or suspend the Company's reporting and filing obligations under the Exchange Act or Securities Act.

6.3 Use of Proceeds. The Company will use the proceeds from the sale of the Pre-Funded Warrants for general corporate purposes, research and development, business development, working capital and general and administrative expenses.

6.4 Disclosure of Transactions and Other Material Information. On or before 9:00 a.m., New York City time, on the Business Day following the date of this Agreement, the Company shall file a Current Report on Form 8-K (or an amendment to a prior Current Report on Form 8-K) describing the terms and conditions of the transactions contemplated by the Transaction Documents in the form required by the Exchange Act and attaching the Agreement as an exhibit to such filing (including all attachments, the "**8-K Filing**") in each case, to the extent not previously disclosed on a Current Report on Form 8-K. The Company shall not publicly disclose the name of any Purchaser or any Affiliate or investment adviser of the Purchaser, or include the name of any Purchaser or any Affiliate or investment adviser of the Purchaser in any filing with the Commission (other than in a Registration Statement and any exhibits to filings made in respect of this transaction in accordance with periodic report or current report filing requirements under the Exchange Act) or any regulatory agency, without the prior written consent of such Purchaser, except to the extent such disclosure is required by law or regulations, in which case the Company shall provide each Purchaser whose name is to be disclosed with prior notice of such disclosure and a reasonable opportunity to comment on the proposed disclosure insofar as it relates specifically to such Purchaser. Subject to the foregoing, neither the Company nor the Purchasers shall issue any press releases or any other public statements with respect to the transactions contemplated hereby without the prior written consent of the other party, such consent not to be unreasonably withheld or delayed.

6.5 Expenses. The Company and each Purchaser is liable for, and will pay, its own expenses incurred in connection with the negotiation, preparation, execution and delivery of this Agreement, including, without limitation, attorneys' and consultants' fees and expenses.

Section 7. Conditions of Parties' Obligations.

7.1 Conditions of the Purchasers' Obligations at the Closing. The obligations of the Purchasers under Section 2 hereof are subject to the fulfillment, prior to the Closing, of all of the following applicable conditions, any of which may be waived in whole or in part by the Purchasers in their absolute discretion. If the following conditions are not satisfied on or before 5:00 p.m. (Eastern Time) on the tenth Business Day following the Effective Date (the "**Outside Date**"), then the Purchasers may terminate this Agreement upon providing written notice to the Company.

(a) Representations and Warranties. The representations and warranties of the Company contained in this Agreement and in any certificate, if any, or other writing, if any, delivered by the Company pursuant hereto shall be true and correct in all material respects on and as of the Closing Date with the same effect as though such representations and warranties had been made on and as of the Closing Date (except to the extent expressly made as of an earlier date in which case as of such earlier date).

(b) Performance. The Company shall have performed and complied in all material respects with all covenants, agreements, obligations and conditions contained in this Agreement that are required to be performed or complied by it on or prior to the Closing Date.

(c) Delivery. The Company shall deliver this Agreement duly executed by the Company.

(d) Qualification under State Securities Laws. All registrations, qualifications, permits and approvals, if any, required under applicable state securities laws shall have been obtained for the lawful execution, delivery and performance of this Agreement.

(e) Consents and Waivers. The Company shall have obtained all consents or waivers necessary to execute and perform its obligations under this Agreement. All corporate and other action and governmental filings necessary for the Company to effectuate the terms of this Agreement and other agreements and instruments executed and delivered by the Company in connection herewith shall have been made or taken by the Company, and no Material Adverse Effect has occurred with respect to the operation of the Company's business.

(f) Absence of Litigation. No proceeding challenging this Agreement or the transactions contemplated hereby, or seeking to prohibit, alter, prevent or materially delay the Closing, shall have been instituted or be pending before any court, arbitrator, governmental body, agency or official. The sale of the Pre-Funded Warrants by the Company shall not be prohibited by any law or governmental order or regulation.

7.2 Conditions of the Company's Obligations. The Company's obligations under Section 2 hereof are subject to the fulfillment prior to or on the Closing Date of all of the following conditions, any of which may be waived in whole or in part by the Company: (a) each Purchaser at the Closing shall have performed all of its obligations hereunder required to be performed by it at or prior to the Closing, and (b) the representations and warranties of the Purchasers at the Closing contained in this Agreement shall be true and correct at and as of the Closing as if made at and as of the Closing (except to the extent expressly made as of an earlier date, in which case as of such earlier date). If the foregoing conditions are not satisfied on or the Outside Date, then the Company may terminate this Agreement upon providing written notice to the Purchasers.

Section 8. Transfer Restrictions; Restrictive Legend. The Purchasers understand that the Company may, as a condition to the transfer of any of the Pre-Funded Warrants or Warrant Shares, require that the request for transfer be accompanied by an opinion of counsel reasonably satisfactory to the Company, to the effect that the proposed transfer does not result in a violation of the Securities Act, unless such transfer is covered by an effective registration statement or by Rule 144 or Rule 144A under the Securities Act; provided, however, that an opinion of counsel shall not be required for a transfer: (A) to its partners or former partners in accordance with partnership interests, (B) to any Affiliate or other Person under common management with such Purchaser, or (C) a transfer that is made pursuant to a bona fide gift to a third party; provided, further, that (i) the transferee in each case agrees to be subject to the restrictions in this Section 8 and provides the Company with a representation letter containing customary investment representations under the Securities Act, (ii) the Company reasonably satisfies itself that the number of transferees is sufficiently limited and (iii) in the case of transferees that are partners or limited liability company members, the transfer is for no consideration. It is understood that the certificates evidencing the Pre-Funded Warrants or the book-entry registrations for the Warrant Shares may bear substantially the following legends:

8.1 “THESE SECURITIES HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933 OR ANY APPLICABLE STATE SECURITIES LAWS. THEY MAY NOT BE SOLD, OFFERED FOR SALE, PLEDGED OR HYPOTHECATED IN THE ABSENCE OF A REGISTRATION STATEMENT IN EFFECT WITH RESPECT TO THE SECURITIES UNDER SUCH ACT OR APPLICABLE STATE SECURITIES LAWS OR AN OPINION OF COUNSEL SATISFACTORY TO THE COMPANY THAT SUCH REGISTRATION IS NOT REQUIRED OR UNLESS SOLD PURSUANT TO RULE 144 OR RULE 144A OF SUCH ACT.”

and

“UNLESS PERMITTED UNDER SECURITIES LEGISLATION, THE HOLDER OF THIS SECURITY MUST NOT TRADE THE SECURITY BEFORE SEPTEMBER\_\_\_\_, 2021.”

Section 9. Registration, Transfer and Substitution of Warrants.

9.1 Register; Ownership of Pre-Funded Warrants. The Company will keep at its principal office, or will cause its transfer agent to keep, a register in which the Company will provide for the registration of transfers of the Pre-Funded Warrants. The Company may treat the Person in whose name any of the Pre-Funded Warrants are registered on such register as the owner thereof and the Company shall not be affected by any notice to the contrary. All references in this Agreement to a “holder” of any Warrants shall mean the Person in whose name such Warrants are at the time registered on such register.

9.2 Replacement of Pre-Funded Warrants. Upon receipt of evidence reasonably satisfactory to the Company of the loss, theft, destruction or mutilation of any certificate representing any of the Pre-Funded Warrants, and, in the case of any such loss, theft or destruction, upon delivery of an indemnity agreement and surety bond reasonably satisfactory to the Company or, in the case of any such mutilation, upon surrender of such certificate for cancellation at the office of the Company maintained pursuant to Section 9.1 hereof, the Company at its expense will execute and deliver, in lieu thereof, a new Warrant representing such Warrants, of like tenor.

Section 10. Registration Rights.

10.1 Mandatory Registration. The Company shall prepare, and, as soon as practicable but in no event later than 30 days after the Closing Date (the "**Filing Deadline**"), file with the Commission a Registration Statement under the Securities Act on appropriate form covering the resale of the full amount of the Registrable Securities. The Company shall use its commercially reasonable efforts to have the Registration Statement declared effective by the Commission as soon as practicable, but in no event later than the date (the "**Effectiveness Deadline**"), which shall be either: (i) in the event that the Commission does not review the Registration Statement, 90 days after the Closing Date, or (ii) in the event that the Commission reviews the Registration Statement, 120 days after the Closing Date (but in any event, no later than five Business Days following the Commission indicating that it has no further comments on the Registration Statement). Subject to any comments from the staff of the Commission (the "**Staff**"), such Registration Statement shall include the plan of distribution attached hereto as Exhibit B; provided, however, that no Purchaser shall be named as an "underwriter" in the Registration Statement without the Purchaser's prior written consent. Such Registration Statement shall not include any securities for the account of any other holder without the prior written consent of the Purchasers.

10.2 Rule 415; Cutback. If at any time the Staff takes the position that the offering of some or all of the Registrable Securities in a Registration Statement is not eligible to be made on a delayed or continuous basis under the provisions of Rule 415 under the Securities Act or requires any Purchaser to be named as an "underwriter," the Company shall use its reasonable best efforts to persuade the Commission that the offering contemplated by the Registration Statement is a valid secondary offering and not an offering "by or on behalf of the issuer" as defined in Rule 415 and that none of the Purchasers is an "underwriter." In the event that, despite the Company's reasonable best efforts and compliance with the terms of this Section 10.2, the Staff refuses to alter its position, the Company shall (i) remove from the Registration Statement such portion of the Registrable Securities (the "**Cut Back Securities**") and/or (ii) agree to such restrictions and limitations on the registration and resale of the Registrable Securities as the Staff may require to assure the Company's compliance with the requirements of Rule 415 (collectively, the "**SEC Restrictions**"); provided, however, that the Company shall not agree to name any Purchaser as an "underwriter" in such Registration Statement without the prior written consent of such Purchaser. Any cutback imposed on the Purchasers pursuant to this Section 10.2 shall be allocated among the Purchasers on a pro rata basis, unless the SEC Restrictions otherwise require or provide or the Purchasers otherwise agree.

### 10.3 Obligations of the Purchasers.

(a) At least ten Business Days prior to the first anticipated filing date of the Registration Statement, the Company shall notify each Purchaser in writing of any information the Company requires from such Purchaser in order to have that Purchaser's Registrable Securities included in such Registration Statement. It shall be a condition precedent to the obligations of the Company to complete the registration pursuant to this Agreement with respect to the Registrable Securities of a particular Purchaser that the Purchaser shall furnish to the Company such information regarding itself, the Registrable Securities held by it and the intended method of disposition of the Registrable Securities held by it as shall be reasonably required to effect the effectiveness of the registration of such Registrable Securities and shall execute such documents in connection with such registration as the Company may reasonably request.

(b) Each Purchaser, by its acceptance of the Registrable Securities, agrees to cooperate with the Company as reasonably requested by the Company in connection with the preparation and filing of any Registration Statement hereunder, unless the Purchaser has notified the Company in writing of the Purchaser's election to exclude all of the Purchaser's Registrable Securities from such Registration Statement.

(c) Each Purchaser agrees that, upon receipt of any notice from the Company of the issuance of any stop order or other suspension of effectiveness of a Registration Statement, or the suspension of the qualification of any of the Registrable Securities for sale in any jurisdiction or the happening of any event, as a result of which the prospectus included in a Registration Statement, as then in effect, includes an untrue statement of a material fact or omission to state a material fact required to be stated therein or necessary to make the statements therein, in the light of the circumstances under which they were made, not misleading, the Purchaser will immediately discontinue disposition of Registrable Securities pursuant to any Registration Statement(s) covering such Registrable Securities until the Purchaser's receipt of the copies of the supplemented or amended prospectus or receipt of notice that no supplement or amendment is required.

(d) Each Purchaser covenants and agrees that it will comply with the prospectus delivery requirements of the Securities Act as applicable to it or an exemption therefrom in connection with sales of Registrable Securities pursuant to the Registration Statement.

10.4 Expenses of Registration. All reasonable expenses incurred in connection with registrations, filings or qualifications pursuant to this Section 10, including, without limitation, all registration, listing and qualifications fees, printers and accounting fees, and fees and disbursements of counsel for the Company, shall be paid by the Company. Notwithstanding the foregoing, in no event shall the Company be responsible for underwriting discounts, commissions, placement agent fees or other similar expenses payable with respect to Registrable Securities being sold or offered for sale by the Purchasers.

10.5 Reports under the Exchange Act. With a view to making available to the Purchasers the benefits of Rule 144 promulgated under the Securities Act or any other similar rule or regulation of the Commission that may at any time permit the Purchasers to sell securities of the Company to the public without registration (“**Rule 144**”), the Company agrees to:

- (a) make and keep public information available, as those terms are understood and defined in Rule 144, during the Reporting Period; and
- (b) file with the Commission in a timely manner all reports and other documents required of the Company under the Exchange Act.

Section 11. Definitions. Unless the context otherwise requires, the terms defined in this Section 11 shall have the meanings specified for all purposes of this Agreement. All accounting terms used in this Agreement, whether or not defined in this Section 11, shall be construed in accordance with GAAP. If the Company has one or more Subsidiaries, such accounting terms shall be determined on a consolidated basis for the Company and each of its Subsidiaries, and the financial statements and other financial information to be furnished by the Company pursuant to this Agreement shall be consolidated and presented with consolidating financial statements of the Company and each of its Subsidiaries.

“**Affiliate**” shall have the meaning ascribed to such term in Rule 12b-2 of the General Rules and Regulations under the Exchange Act.

“**Business Day**” means any day other than Saturday, Sunday or other day on which commercial banks in The City of New York are authorized or required by law to remain closed.

“**Effectiveness Date**” means the date the Registration Statement pursuant to Section 10 has been declared effective by the Commission.

“**Exchange Act**” means the Securities Exchange Act of 1934, as amended.

“**GAAP**” means U.S. generally accepted accounting principles consistently applied.

“**Governmental Entity**” means any national, federal, state, municipal, local, territorial, foreign or other government or any department, commission, board, bureau, agency, regulatory authority, self-regulatory organization or instrumentality thereof, or any court, judicial, administrative or arbitral body or public or private tribunal.

“**Knowledge**” by a Person of a particular fact or other matter means the following: (a) if the Person is an individual, that such individual is actually aware or reasonably should be aware, after due inquiry, by virtue of such person’s office, of such fact or other matter; and (b) if the Person is an entity, that any executive officer of such Person is actually aware or reasonably should be aware, after due inquiry, of such fact or other matter.

“**Material Adverse Effect**” means any (i) adverse effect on the reservation, issuance, delivery or validity of the Pre-Funded Warrants, as applicable, or the transactions contemplated hereby or on the ability of the Company to perform its obligations under this Agreement, or (ii) material adverse effect on the condition (financial or otherwise), prospects, properties, assets, liabilities, business or operations of the Company or any of its Subsidiaries.

“**Person**” means and includes all natural persons, corporations, business trusts, associations, companies, partnerships, joint ventures, limited liability companies and other entities and governments and agencies and political subdivisions.

“**Pro Rata Interest**” means the number of Pre-Funded Warrants purchased by each Purchaser, relative to the total number of Pre-Funded Warrants being sold hereunder, as reflected on Schedule I attached hereto.

“**Registrable Securities**” means the Warrant Shares (including any equity securities of the Company that may be issued or distributed in respect thereof by way of dividend or split or other distribution, recapitalization or reclassification). Registrable Securities will cease to be Registrable Securities upon the earliest to occur of (i) a registration statement with respect to the resale by the Purchasers of such securities has become effective under the Securities Act or the comparable statute of any applicable jurisdiction and such securities have been disposed of in accordance with such registration statement, (ii) such securities have been sold or otherwise transferred or assigned pursuant to Rule 144 (or any successor provision) under the Securities Act or another available exemption from the registration requirements of the Securities Act, or (iii) all of such securities may be sold pursuant to Rule 144 during any ninety (90) day period.

“**Registration Statement**” means a registration statement or registration statements of the Company filed under the Securities Act pursuant to Section 10 hereof.

“**Reporting Period**” means the period commencing on the Closing Date and ending on the earliest of: (i) the date as of which the Purchasers may sell all of the Warrant Shares under Rule 144 without volume or manner-of-sale restrictions and without the requirement for the Company to be in compliance with the current public information requirements under Rule 144(c)(1) (or any successor thereto) promulgated under the Securities Act; and (ii) the date on which such Purchaser shall have sold all of the Warrant Shares pursuant to a registration statement.

“**Subsidiary**” means any corporation, association trust, limited liability company, partnership, joint venture or other business association or entity, at least 50% of the outstanding voting securities of which are at the time owned or controlled directly or indirectly by the Company.

“**Trading Day**” means any day on which the Common Shares is traded on the Trading Market; provided that “Trading Day” shall not include any day on which the Common Shares are scheduled to trade on such exchange or market for less than 4.5 hours or any day that the Common Shares are suspended from trading during the final hour of trading on such exchange or market (or if such exchange or market does not designate in advance the closing time of trading on such exchange or market, then during the hour ending at 4:00:00 p.m., New York time).

“**Trading Market**” means the following markets or exchanges on which the Common Shares are listed or quoted for trading on the date in question: NYSE Amex Equities, the Nasdaq Capital Market, the Nasdaq Global Market, the Nasdaq Global Select Market, the New York Stock Exchange or the OTC Markets Group Inc.



“**Transaction Documents**” means this Agreement and all exhibits and schedules thereto and hereto and any other documents or agreements executed in connection with the transactions contemplated hereunder.

Section 12.      Miscellaneous.

12.1      Waivers and Amendments. Upon the approval of the Company and the written consent of the Purchasers, the obligations of the Company and the rights of the Purchasers under this Agreement may be waived (either generally or in a particular instance, either retroactively or prospectively and either for a specified period of time or indefinitely). Neither this Agreement, nor any provision hereof, may be changed, waived, discharged or terminated orally or by course of dealing, but only by an instrument in writing executed by the Company and the Purchasers.

12.2      Notices. All notices, requests, consents, and other communications under this Agreement shall be in writing and shall be deemed delivered: (a) when delivered, if delivered personally, (b) four Business Days after being sent by registered or certified mail, return receipt requested, postage prepaid, (c) one Business Day after being sent via a reputable nationwide overnight courier service guaranteeing next Business Day delivery, or (d) when receipt is acknowledged, in the case of email, in each case to the intended recipient as set forth below, with respect to the Company, and to the addresses set forth on the signature pages hereto, with respect to the Purchasers.

If to the Company:            Attn: Amit Hasija, Chief Financial Officer  
Milestone Pharmaceuticals Inc.  
1111 Dr. Frederik-Philips Blvd., Suite 420 Montréal, Québec H4M 2X6  
Email: [ahasija@milestonepharma.com](mailto:ahasija@milestonepharma.com)

with copies (which shall not constitute notice) to:

Attn: Ryan Sansom  
Cooley LLP  
500 Boylston Street, 14<sup>th</sup> Floor Boston, MA 02116  
Email: [rsansom@cooley.com](mailto:rsansom@cooley.com)

or at such other address as the Company or each Purchaser may specify by written notice to the other parties hereto in accordance with this Section 12.2.

12.3      Cumulative Remedies. None of the rights, powers or remedies conferred upon the Purchasers on the one hand or the Company on the other hand shall be mutually exclusive, and each such right, power or remedy shall be cumulative and in addition to every other right, power or remedy, whether conferred by this Agreement or now or hereafter available at law, in equity, by statute or otherwise.

12.4 Successors and Assigns. All the terms and provisions of this Agreement shall be binding upon and inure to the benefit of and be enforceable by the respective parties hereto, the successors and permitted assigns of each Purchaser and the successors of the Company, whether so expressed or not. None of the parties hereto may assign its rights or obligations hereof without the prior written consent of the Company, except that a Purchaser may, without the prior consent of the Company, assign its rights to purchase the Pre-Funded Warrants hereunder to any of its Affiliates (provided each such Affiliate agrees to be bound by the terms of this Agreement and makes the same representations and warranties set forth in Section 4 hereof). This Agreement shall not inure to the benefit of or be enforceable by any other Person.

12.5 Headings. The headings of the Sections and paragraphs of this Agreement have been inserted for convenience of reference only and do not constitute a part of this Agreement.

12.6 Governing Law; Jurisdiction. This Agreement shall be governed by and construed in accordance with the laws of the State of New York without regard to its conflict of law principles. Any suit, action or proceeding seeking to enforce any provision of, or based on any matter. Any action, suit or proceeding arising out of or in connection with, Agreement or the transactions contemplated hereby may be brought in any federal or state court located in the City of New York and State of New York, and each of the Parties hereby consents to the jurisdiction of such courts (and of the appropriate appellate courts therefrom) in any such suit, action or proceeding and irrevocably waives, to the fullest extent permitted by law, any objection which it may now or hereafter have to the laying of the venue of any such suit, action or proceeding in any such court or that any such suit, action or proceeding which is brought in any such court has been brought in an inconvenient forum. Process in any such suit, action or proceeding may be served on any party anywhere in the world, whether within or without the jurisdiction of any such court. The Company has the power to submit, and pursuant to this Agreement has, to the extent permitted by law, legally, validly, effectively and irrevocably submitted, to the jurisdiction of the courts herein described.

12.7 Counterparts; Effectiveness. This Agreement may be executed in any number of counterparts and by different parties hereto in separate counterparts, with the same effect as if all parties had signed the same document. All such counterparts (including counterparts delivered by facsimile or other electronic format) shall be deemed an original, shall be construed together and shall constitute one and the same instrument. This Agreement shall become effective when each party hereto shall have received counterparts hereof signed by all of the other parties hereto.

12.8 Entire Agreement. This Agreement contains the entire agreement among the parties hereto with respect to the subject matter hereof and thereof and, except as set forth below, this agreement supersedes and replaces all other prior agreements, written or oral, among the parties hereto with respect to the subject matter hereof and thereof. Notwithstanding the foregoing, this Agreement shall not supersede any confidentiality or other non-disclosure agreements that may be in place between the Company and any Purchaser.

12.9 Severability. If any provision of this Agreement shall be found by any court of competent jurisdiction to be invalid or unenforceable, the parties hereby waive such provision to the extent that it is found to be invalid or unenforceable. Such provision shall, to the maximum extent allowable by law, be modified by such court so that it becomes enforceable, and, as modified, shall be enforced as any other provision hereof, all the other provisions hereof continuing in full force and effect.

\* \* \*

IN WITNESS WHEREOF, the parties hereto have caused this Securities Purchase Agreement to be duly executed as of the Effective Date.

THE COMPANY:

**MILESTONE PHARMACEUTICALS INC.**

By: /s/ Joseph Oliveto  
Name: Joseph Oliveto  
Title: President and CEO

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IN WITNESS WHEREOF, the parties hereto have caused this Securities Purchase Agreement to be duly executed as of the Effective Date.

PURCHASERS:

**RTW MASTER FUND, LTD.**

By: /s/ Roderick Wong

Name: Roderick Wong

Title: Director

**RTW INNOVATION MASTER FUND, LTD.**

By: /s/ Roderick Wong

Name: Roderick Wong

Title: Director

**RTW VENTURE FUND LIMITED**

By: RTW Investments, LP, its Investment Manager

By: /s/ Roderick Wong

Name: Roderick Wong

Title: Managing Partner

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SCHEDULE I

Purchaser Name	No. of Pre-Funded Warrants	Aggregate Purchase Price
<b>RTW MASTER FUND, LTD.</b> , a company existing under the laws of the Cayman Islands, having its head office at 190 Elgin Avenue, George Town, Grand Cayman KY1-9005, Cayman Islands, represented herein by its Director, Roderick Wong.	587,721 \$	3,220,711.08
<b>RTW INNOVATION MASTER FUND, LTD.</b> , a company existing under the laws of the Cayman Islands, having its head office at 190 Elgin Avenue, George Town, Grand Cayman KY1-9005, Cayman Islands, represented herein by its Director, Roderick Wong.	259,150 \$	1,420,142.00
<b>RTW VENTURE FUND LIMITED</b> , a company existing under the laws of Guernsey, having its head office at P.O. Box 286, Floor 2, Trafalgar Court, Les Banques, St Peter Port, Guernsey GY1 4LY, represented herein by the Managing Partner of its Investment Manager, Roderick Wong.	63,875 \$	350,035.00

**EXHIBIT A**

**FORM OF PRE-FUNDED WARRANT**

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**SCHEDULE 1**

**FORM OF EXERCISE NOTICE**

[To be executed by the Holder to purchase Common Shares under the Warrant]

Ladies and Gentlemen:

(1) The undersigned is the Holder of Warrant No.\_\_\_\_(the "Warrant") issued by Milestone Pharmaceuticals Inc., an exempted company incorporated and existing under the laws of the Province of Québec, Canada (the "Company"). Capitalized terms used herein and not otherwise defined herein have the respective meanings set forth in the Warrant.

(2) The undersigned hereby exercises its right to purchase \_\_\_\_\_Warrant Shares pursuant to the Warrant.

(3) Pursuant to this Exercise Notice, the Company shall deliver to the Holder Warrant Shares determined in accordance with the terms of the Warrant. If permissible, the Warrant Shares shall be delivered to the following DWAC Account Number:

\_\_\_\_\_  
\_\_\_\_\_

(4) By its delivery of this Exercise Notice, the undersigned represents and warrants to the Company that in giving effect to the exercise evidenced hereby the Holder will not beneficially own in excess of the number of Common Shares (as determined in accordance with Section 13(d) of the Securities Exchange Act of 1934, as amended) permitted to be owned under Section 11(a) of the Warrant to which this notice relates.

(5) The undersigned is an "accredited investor" as defined in Regulation D promulgated under the Securities Act of 1933, as amended.

Dated: \_\_\_\_\_

Name of  
Holder: \_\_\_\_\_

By: \_\_\_\_\_

Name: \_\_\_\_\_

Title: \_\_\_\_\_

(Signature must conform in all respects to name of Holder as specified on the face of the Warrant)

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## EXHIBIT B

### PLAN OF DISTRIBUTION

The selling shareholders, which shall include donees, pledgees, transferees or other successors-in-interest selling warrant shares or interests in warrant shares received after the date of this prospectus from a selling shareholders as a gift, pledge, partnership distribution or other transfer, may, from time to time, sell, transfer or otherwise dispose of any or all of their warrant shares or interests in warrant shares on any stock exchange, market or trading facility on which the warrant shares are traded or in private transactions. These dispositions may be at fixed prices, at prevailing market prices at the time of sale, at prices related to the prevailing market price, at varying prices determined at the time of sale, or at negotiated prices.

The selling shareholders may use any one or more of the following methods when disposing of warrant shares or interests therein:

- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- block trades in which the broker-dealer will attempt to sell the warrant shares as agent, but may position and resell a portion of the block as principal to facilitate the transaction;
- purchases by a broker-dealer as principal and resale by the broker-dealer for its own account;
- an exchange distribution in accordance with the rules of the applicable exchange;
- privately negotiated transactions;
- short sales effected after the date the registration statement of which this prospectus is a part is declared effective by the SEC;
- through the writing or settlement of options or other hedging transactions, whether through an options exchange or otherwise;
- through agreements between broker-dealers and the selling shareholders to sell a specified number of such warrant shares at a stipulated price per share;
- a combination of any such methods of sale; and
- any other method permitted by applicable law.

The selling shareholders may, from time to time, pledge or grant a security interest in some or all of the warrant shares by them and, if they default in the performance of their secured obligations, the pledgees or secured parties may offer and sell the warrant shares, from time to time, under this prospectus, or under an amendment to this prospectus under Rule 424(b) or other applicable provision of the Securities Act amending the list of selling shareholders to include the pledgee, transferee or other successors in interest as selling shareholders under this prospectus. The selling shareholders also may transfer the warrant shares in other circumstances, in which case the pledgees, transferees or other successors in interest will be the selling beneficial owners for purposes of this prospectus.

In connection with the sale of warrant shares or interests therein, the selling shareholders may enter into hedging transactions with broker-dealers or other financial institutions, which may in turn engage in short sales of the warrant shares in the course of hedging the positions they assume. The selling shareholders may also sell our common shares short and deliver these securities to close out their short positions, or loan or pledge the warrant shares to broker-dealers that in turn may sell these securities. The selling shareholders may also enter into options or other transactions with broker-dealers or other financial institutions or the creation of one or more derivative securities that require the delivery to each such broker-dealer or other financial institution of warrant shares offered by this prospectus, which warrant shares such broker-dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to reflect such transaction).

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The aggregate proceeds to the selling shareholders from the sale of the warrant shares offered by them will be the purchase price of the warrant shares less discounts or commissions, if any. Each of the selling shareholders reserves the right to accept and, together with its agents from time to time, to reject, in whole or in part, any proposed purchase of warrant shares to be made directly or through agents. We will not receive any of the proceeds from the sale of warrant shares in this offering, although we will receive the nominal exercise price upon exercise of the pre-funded warrants for the warrant shares, if such warrants are exercised for cash.

The selling shareholders also may resell all or a portion of the warrant shares in open market transactions in reliance upon Rule 144 under the Securities Act of 1933, provided that they meet the criteria and conform to the requirements of that rule.

The selling shareholders and any underwriters, broker-dealers or agents that participate in the sale of the warrant shares or interests therein may be “underwriters” within the meaning of Section 2(11) of the Securities Act. Any discounts, commissions, concessions or profit they earn on any resale of the warrant shares may be underwriting discounts and commissions under the Securities Act. Selling shareholders who are “underwriters” within the meaning of Section 2(11) of the Securities Act will be subject to the prospectus delivery requirements of the Securities Act.

To the extent required, the warrant shares to be sold, the names of the selling shareholders, the respective purchase prices and public offering prices, the names of any agents, dealer or underwriter, and any applicable commissions or discounts with respect to a particular offer will be set forth in an accompanying prospectus supplement or, if appropriate, a post-effective amendment to the registration statement that includes this prospectus.

In order to comply with the securities laws of some states, if applicable, the warrant shares may be sold in these jurisdictions only through registered or licensed brokers or dealers. In addition, in some states the warrant shares may not be sold unless it has been registered or qualified for sale or an exemption from registration or qualification requirements is available and is complied with.

We have advised the selling shareholders that the anti-manipulation rules of Regulation M under the Exchange Act may apply to sales of warrant shares in the market and to the activities of the selling shareholders and their affiliates. In addition, to the extent applicable we will make copies of this prospectus (as it may be supplemented or amended from time to time) available to the selling shareholders for the purpose of satisfying the prospectus delivery requirements of the Securities Act. The selling shareholders may indemnify any broker-dealer that participates in transactions involving the sale of the warrant shares against certain liabilities, including liabilities arising under the Securities Act.

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NEITHER THIS SECURITY NOR THE SECURITIES FOR WHICH THIS SECURITY IS EXERCISABLE HAVE BEEN REGISTERED WITH THE SECURITIES AND EXCHANGE COMMISSION OR THE SECURITIES COMMISSION OF ANY STATE IN RELIANCE UPON AN EXEMPTION FROM REGISTRATION UNDER THE SECURITIES ACT OF 1933, AS AMENDED (THE "SECURITIES ACT"), AND, ACCORDINGLY, MAY NOT BE OFFERED OR SOLD EXCEPT PURSUANT TO AN EFFECTIVE REGISTRATION STATEMENT UNDER THE SECURITIES ACT OR PURSUANT TO AN AVAILABLE EXEMPTION FROM, OR IN A TRANSACTION NOT SUBJECT TO, THE REGISTRATION REQUIREMENTS OF THE SECURITIES ACT AND IN ACCORDANCE WITH APPLICABLE STATE SECURITIES LAWS. THIS SECURITY AND THE SECURITIES ISSUABLE UPON EXERCISE OF THIS SECURITY MAY BE PLEDGED IN CONNECTION WITH A BONA FIDE MARGIN ACCOUNT OR OTHER LOAN SECURED BY SUCH SECURITIES.

UNLESS PERMITTED UNDER SECURITIES LEGISLATION, THE HOLDER OF THIS SECURITY MUST NOT TRADE THE SECURITY BEFORE SEPTEMBER [ • ], 2021.

**MILESTONE PHARMACEUTICALS INC.**

**FORM OF PRE-FUNDED WARRANT TO PURCHASE COMMON SHARES**

Number of Shares: [ • ] (subject to adjustment)

Warrant No. PFW2021 - [ ]

Original Issue Date: May [ • ], 2021

Milestone Pharmaceuticals Inc., an exempted company incorporated and existing under the laws of the Province of Québec, Canada (the "**Company**"), hereby certifies that, for good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, [ ] or its registered assigns (the "**Holder**"), is entitled, subject to the terms set forth below, to purchase from the Company up to a total of [ • ] common shares, no par value per share (the "**Common Shares**"), of the Company (each such share, a "**Warrant Share**" and all such shares, the "**Warrant Shares**") at an exercise price per share equal to \$0.01 per share (as adjusted from time to time as provided in Section 9 herein, the "**Exercise Price**") upon surrender of this Warrant to Purchase Common Shares (including any Warrants to Purchase Common Shares issued in exchange, transfer or replacement hereof, the "**Warrant**") at any time and from time to time on or after the date hereof (the "**Original Issue Date**") until the Warrant has been exercised in full, subject to the following terms and conditions:

1. *Definitions.* For purposes of this Warrant, the following terms shall have the following meanings:

(a) "**Affiliate**" means any Person directly or indirectly controlled by, controlling or under common control with, a Holder, as such terms are used in and construed under Rule 405 under the Securities Act, but only for so long as such control shall continue.

(b) "**Commission**" means the United States Securities and Exchange Commission.

(c) "**Closing Sale Price**" means, for any security as of any date, the last trade price for such security on the Principal Trading Market for such security, as reported by Bloomberg L.P., or, if such Principal Trading Market begins to operate on an extended hours basis and does not designate the last trade price, then the last trade price of such security prior to 4:00 P.M., New York City time, as reported by Bloomberg L.P., or if the security is not listed for trading on a national securities exchange or other trading market on the relevant date, the last quoted bid price for the security in the over-the-counter market on the relevant date as reported by OTC Markets Group Inc. (or a similar organization or agency succeeding to its functions of reporting prices). If the Closing Sale Price cannot be calculated for a security on a particular date on any of the foregoing bases, the Closing Sale Price of such security on such date shall be the fair market value as mutually determined in good faith by the Company and the Holder. All such determinations shall be appropriately adjusted for any share dividend, share split, share combination or other similar transaction during the applicable calculation period.

(d) "**Principal Trading Market**" means the national securities exchange or other trading market on which the Common Shares are primarily listed on and quoted for trading, which, as of the Original Issue Date, shall be the Nasdaq Global Select Market.

(e) “**Securities Act**” means the Securities Act of 1933, as amended.

(f) “**Trading Day**” means any weekday on which the Principal Trading Market is open for trading. If the Common Shares are not listed or admitted for trading, “Trading Day” means any day except any Saturday, any Sunday, any day which is a federal legal holiday in the United States or any day on which banking institutions in New York City are authorized or required by law or other governmental action to close.

(g) “**Transfer Agent**” means Computershare Investor Services Inc. and Computershare Trust Company, N.A., collectively, the Company’s transfer agent and registrar for the Common Share, and any successor appointed in such capacity.

2. *Warrant Register.* The Company shall register ownership of this Warrant, upon records to be maintained by the Company for that purpose (the “**Warrant Register**”), in the name of the record Holder (which shall include the initial Holder or, as the case may be, any assignee to which this Warrant is assigned hereunder) from time to time. The Company may deem and treat the registered Holder of this Warrant as the absolute owner hereof for the purpose of any exercise hereof or any distribution to the Holder, and for all other purposes, absent actual notice to the contrary.

3. *Registration of Transfers.* Subject to compliance with all applicable securities laws, the Company shall, or will cause its Transfer Agent to, register the transfer of all or any portion of this Warrant in the Warrant Register, upon surrender of this Warrant, and payment for all applicable transfer taxes (if any). Upon any such registration or transfer, a new warrant to purchase Common Shares in substantially the form of this Warrant (any such new warrant, a “**New Warrant**”) evidencing the portion of this Warrant so transferred shall be issued to the transferee, and a New Warrant evidencing the remaining portion of this Warrant not so transferred, if any, shall be issued to the transferring Holder. The acceptance of the New Warrant by the transferee thereof shall be deemed the acceptance by such transferee of all of the rights and obligations in respect of the New Warrant that the Holder has in respect of this Warrant. The Company shall, or will cause its Transfer Agent to, prepare, issue and deliver at the Company’s own expense any New Warrant under this Section 3. Until due presentment for registration of transfer, the Company may treat the registered Holder hereof as the owner and holder for all purposes, and the Company shall not be affected by any notice to the contrary.

#### 4. *Exercise and Duration of Warrants.*

(a) All or any part of this Warrant shall be exercisable by the registered Holder in the manner set forth in Section 4(b) at any time and from time to time on or after the Original Issue Date subject to the limitations set forth in Section 11.

(b) The Holder may exercise this Warrant by delivering to the Company (i) an exercise notice, in the form attached as Schedule 1 hereto (the “**Exercise Notice**”), completed and duly signed, and (ii) payment of the Exercise Price (if applicable) in cash or immediately available funds (or pursuant to cashless exercise provisions in accordance herewith and with Section 10) for the number of Warrant Shares as to which this Warrant is being exercised. The date on which such Exercise Notice is delivered to the Company (as determined in accordance with the notice provisions hereof) is an “**Exercise Date.**” The Holder shall not be required to deliver the original Warrant in order to effect an exercise hereunder. Execution and delivery of the Exercise Notice shall have the same effect as cancellation of the original Warrant and issuance of a New Warrant evidencing the right to purchase the remaining number of Warrant Shares, if any. **The Holder and any assignee, by acceptance of this Warrant, acknowledge and agree that, by reason of the provisions of this paragraph, following the purchase of a portion of the Warrant Shares hereunder, the number of Warrant Shares available for purchase hereunder at any given time may be less than the amount stated on the face hereof.**

#### 5. *Delivery of Warrant Shares.*

(a) The Company shall cause the Warrant Shares purchased hereunder to be transmitted by the Transfer Agent to the Holder by crediting the account of the Holder’s or its designee’s balance account with The Depository Trust Company (“**DTC**”) through its Deposit or Withdrawal at Custodian system (“**DWAC**”) if the Company is then a participant in such system and either (A) there is an effective registration statement permitting the issuance of the Warrant Shares to or resale of the Warrant Shares by the Holder or (B) the Warrant Shares are eligible for resale by the Holder without volume or manner-of-sale limitations pursuant to Rule 144 (assuming cashless exercise of the Warrants), and otherwise by issuing such Warrant Shares in the name of the Holder or its designee in restricted book-entry form in the Company’s share register, for the number of Warrant Shares to which the Holder is entitled pursuant to such exercise by the date that is two (2) Trading Days after the delivery to the Company of the Notice of Exercise and delivery of the aggregate Exercise Price (if applicable) to the Company. The Holder, or any natural person or legal entity (each, a “**Person**”) so designated by the Holder to receive Warrant Shares, shall be deemed to have become the holder of record of such Warrant Shares as of the Exercise Date, irrespective of the date such Warrant Shares are credited to the Holder’s DTC account or the date of restricted book-entry evidencing such Warrant Shares, as the case may be.

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(b) If by the close of the second (2nd) Trading Day after the Exercise Date, the Company fails to deliver to the Holder the required number of Warrant Shares in the manner required pursuant to Section 5(a) or fails to credit the Holder's DTC account for such number of Warrant Shares to which the Holder is entitled, and if after such third (3rd) Trading Day and prior to the receipt of such Warrant Shares, the Holder purchases (in an open market transaction or otherwise) Common Shares to deliver in satisfaction of a sale by the Holder of the Warrant Shares which the Holder anticipated receiving upon such exercise (a "**Buy-In**"), then the Company shall, within two (2) Trading Days after the Holder's request promptly honor its obligation to deliver to the Holder such Warrant Shares and pay cash to the Holder in an amount equal to the excess (if any) of Holder's total purchase price (including brokerage commissions, if any) for the Common Shares so purchased in the Buy-In less the product of (A) the number of Common Shares purchased in the Buy-In, times (B) the Closing Sale Price of a Common Share on the Exercise Date.

(c) To the extent permitted by law and subject to Section 5(b), the Company's obligations to issue and deliver Warrant Shares in accordance with and subject to the terms hereof (including the limitations set forth in Section 11 below) are absolute and unconditional, irrespective of any action or inaction by the Holder to enforce the same, any waiver or consent with respect to any provision hereof, the recovery of any judgment against any Person or any action to enforce the same, or any setoff, counterclaim, recoupment, limitation or termination, or any breach or alleged breach by the Holder or any other Person of any obligation to the Company or any violation or alleged violation of law by the Holder or any other Person, and irrespective of any other circumstance that might otherwise limit such obligation of the Company to the Holder in connection with the issuance of Warrant Shares. Subject to Section 5(b), nothing herein shall limit the Holder's right to pursue any other remedies available to it hereunder, at law or in equity including, without limitation, a decree of specific performance and/or injunctive relief with respect to the Company's failure to timely deliver Common Shares upon exercise of the Warrant as required pursuant to the terms hereof.

6. *Charges, Taxes and Expenses.* Issuance and delivery of Common Shares upon exercise of this Warrant shall be made without charge to the Holder for any issue or transfer tax, transfer agent fee or other incidental tax or expense (excluding any applicable stamp duties) in respect of the issuance of such shares, all of which taxes and expenses shall be paid by the Company; *provided, however*, that the Company shall not be required to pay any tax that may be payable in respect of any transfer involved in the registration of any Warrant Shares or the Warrants in a name other than that of the Holder or an Affiliate thereof. The Holder shall be responsible for all other tax liability that may arise as a result of holding or transferring this Warrant or receiving Warrant Shares upon exercise hereof.

7. *Replacement of Warrant.* If this Warrant is mutilated, lost, stolen or destroyed, the Company shall issue or cause to be issued in exchange and substitution for and upon cancellation hereof, or in lieu of and substitution for this Warrant, a New Warrant, but only upon receipt of evidence reasonably satisfactory to the Company of such loss, theft or destruction (in such case) and, in each case, a customary and reasonable indemnity and surety bond, if requested by the Company. Applicants for a New Warrant under such circumstances shall also comply with such other reasonable regulations and procedures and pay such other reasonable third-party costs as the Company may prescribe. If a New Warrant is requested as a result of a mutilation of this Warrant, then the Holder shall deliver such mutilated Warrant to the Company as a condition precedent to the Company's obligation to issue the New Warrant.

8. *No Pre-Emptive Rights; Duly Issued Warrant Shares.* The Company covenants that all Warrant Shares issuable and deliverable upon exercise in full of this Warrant shall, upon issuance and the payment of the applicable Exercise Price in accordance with the terms hereof, be duly and validly authorized, issued and fully paid and non-assessable. The Company will take all such action as may be reasonably necessary to assure that such Common Shares may be issued as provided herein without violation of any applicable law or regulation, or of any requirements of any securities exchange or automated quotation system upon which the Common Shares may be listed.

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9. *Certain Adjustments.* The Exercise Price and number of Warrant Shares issuable upon exercise of this Warrant are subject to adjustment from time to time as set forth in this Section 9.

(a) Share Dividends and Splits. If the Company, at any time while this Warrant is issued and outstanding, (i) pays a share dividend on its Common Shares or otherwise makes a distribution on any class of capital shares issued and outstanding on the Original Issue Date and in accordance with the terms of such shares on the Original Issue Date or as amended, that is payable in Common Shares, (ii) subdivides its issued and outstanding Common Shares into a larger number of Common Shares, (iii) combines its issued and outstanding Common Shares into a smaller number of Common Shares or (iv) issues by reclassification of capital shares any additional Common Shares of the Company, then in each such case the Exercise Price shall be multiplied by a fraction, the numerator of which shall be the number of Common Shares issued and outstanding immediately before such event and the denominator of which shall be the number of Common Shares issued and outstanding immediately after such event. Any adjustment made pursuant to clause (i) of this paragraph shall become effective immediately after the record date for the determination of shareholders entitled to receive such dividend or distribution, provided, however, that if such record date shall have been fixed and such dividend is not fully paid on the date fixed therefor, the Exercise Price shall be recomputed accordingly as of the close of business on such record date and thereafter the Exercise Price shall be adjusted pursuant to this paragraph as of the time of actual payment of such dividends. Any adjustment pursuant to clause (ii) or (iii) of this paragraph shall become effective immediately after the effective date of such subdivision or combination.

(b) Pro Rata Distributions. If the Company, at any time while this Warrant is issued and outstanding, distributes to all holders of Common Shares for no consideration (i) evidences of its indebtedness, (ii) any security (other than a distribution of Common Shares covered by the preceding paragraph), (iii) rights or warrants to subscribe for or purchase any security, or (iv) cash or any other asset (in each case, a “**Distribution**”), other than a reclassification as to which Section 9(c) applies, then in each such case, the Holder shall be entitled to participate in such Distribution to the same extent that the Holder would have participated therein if the Holder had held the number of Common Shares acquirable upon complete exercise of this Warrant (without regard to any limitations on exercise hereof, including without limitation, the ownership limitation set forth in Section 11(a) hereof) immediately before the date of which a record is taken for such Distribution, or, if no such record is taken, the date as of which the record holders of Common Shares are to be determined for the participation in such Distribution (provided, however, to the extent that the Holder’s right to participate in any such Distribution would result in the Holder exceeding the ownership limitation set forth in Section 11(a) hereof, then the Holder shall not be entitled to participate in such Distribution to such extent (or in the beneficial ownership of any Common Shares as a result of such Distribution to such extent)) and the portion of such Distribution shall be held in abeyance for the benefit of the Holder until the earlier of (i) such time, if ever, as the delivery to such Holder of such portion would not result in the Holder exceeding the ownership limitation set forth in Section 11(a) hereof and (ii) such time as the Holder has exercised this Warrant.

(c) Fundamental Transactions. If, at any time while this Warrant is issued and outstanding (i) the Company effects any amalgamation, merger or consolidation of the Company with or into another Person, in which the Company is not the surviving entity and in which the shareholders of the Company immediately prior to such amalgamation, merger or consolidation do not own, directly or indirectly, at least 50% of the voting power of the surviving entity immediately after such amalgamation, merger or consolidation, (ii) the Company effects any sale to another Person of all or substantially all of its assets in one transaction or a series of related transactions, (iii) pursuant to any tender offer or exchange offer (whether by the Company or another Person), holders of share capital tender shares representing more than 50% of the voting power of the capital shares of the Company and the Company or such other Person, as applicable, accepts such tender for payment, (iv) the Company consummates a share purchase agreement or other business combination (including, without limitation, a reorganization, recapitalization, spin-off or scheme of arrangement) with another Person whereby such other Person acquires more than the 50% of the voting power of the capital shares of the Company (except for any such transaction in which the shareholders of the Company immediately prior to such transaction maintain, in substantially the same proportions, the voting power of such Person immediately after the transaction) or (v) the Company effects any reclassification of the Common Shares or any compulsory share exchange pursuant to which the Common Shares are effectively converted into or exchanged for other securities, cash or property (other than as a result of a subdivision or combination of Common Shares covered by Section 9(a) above) (in any such case, a “**Fundamental Transaction**”), then following such Fundamental Transaction the Holder shall have the right to receive, upon exercise of this Warrant, the same amount and kind of securities, cash or property as it would have been entitled to receive upon the occurrence of such Fundamental Transaction if it had been, immediately prior to such Fundamental Transaction, the holder of the number of Warrant Shares then issuable upon exercise in full of this Warrant without regard to any limitations on exercise contained herein (the “**Alternate Consideration**”). The Company shall not effect any Fundamental Transaction in which the Company is not the surviving entity or the Alternate Consideration includes securities of another Person unless (i) the Alternate Consideration is solely cash and the Company provides for the simultaneous “cashless exercise” of this Warrant pursuant to Section 10 below or (ii) prior to or simultaneously with the consummation thereof, any successor to the Company, surviving entity or other Person (including any purchaser of assets of the Company) shall assume the obligation to deliver to the Holder such Alternate Consideration as, in accordance with the foregoing provisions, the Holder may be entitled to receive, and the other obligations under this Warrant. The provisions of this paragraph (c) shall similarly apply to subsequent transactions analogous of a Fundamental Transaction type.

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(d) Number of Warrant Shares. Simultaneously with any adjustment to the Exercise Price pursuant to Section 9 (including any adjustment to the Exercise Price that would have been effected but for the final sentence in this paragraph (d)), the number of Warrant Shares that may be purchased upon exercise of this Warrant shall be increased or decreased proportionately, so that after such adjustment the aggregate Exercise Price (if applicable) payable hereunder for the increased or decreased number of Warrant Shares shall be the same as the aggregate Exercise Price in effect immediately prior to such adjustment.

(e) Calculations. All calculations under this Section 9 shall be made to the nearest one-millionth of one cent or the nearest share, as applicable.

(f) Notice of Adjustments. Upon the occurrence of each adjustment pursuant to this Section 9, the Company at its expense will, at the written request of the Holder, promptly compute such adjustment, in good faith, in accordance with the terms of this Warrant and prepare a certificate setting forth such adjustment, including a statement of the adjusted Exercise Price and adjusted number or type of Warrant Shares or other securities issuable upon exercise of this Warrant (as applicable), describing the transactions giving rise to such adjustments and showing in detail the facts upon which such adjustment is based. Upon written request, the Company will promptly deliver a copy of each such certificate to the Holder and to the Company's transfer agent.

(g) Notice of Corporate Events. If, while this Warrant is issued and outstanding, the Company (i) declares a dividend or any other distribution of cash, securities or other property in respect of its Common Shares, including, without limitation, any granting of rights or warrants to subscribe for or purchase any capital shares of the Company or any subsidiary, (ii) authorizes or approves, enters into any agreement contemplating or solicits shareholder approval for any Fundamental Transaction or (iii) authorizes the voluntary dissolution, liquidation or winding up of the affairs of the Company, then, except if such notice and the contents thereof shall be deemed to constitute material non-public information, the Company shall deliver to the Holder a notice of such transaction at least ten (10) days prior to the applicable record or effective date on which a Person would need to hold Common Shares in order to participate in or vote with respect to such transaction; provided, however, that the failure to deliver such notice or any defect therein shall not affect the validity of the corporate action required to be described in such notice. In addition, if while this Warrant is issued and outstanding, the Company authorizes or approves, enters into any agreement contemplating or solicits shareholder approval for any Fundamental Transaction contemplated by Section 9(c), other than a Fundamental Transaction under clause (iii) of Section 9(c), then, except if such notice and the contents thereof shall be deemed to constitute material non-public information, the Company shall deliver to the Holder a notice of such Fundamental Transaction at least ten (10) days prior to the date such Fundamental Transaction is consummated.

10. Payment of Cashless Exercise Price. Upon the cashless exercise of this Warrant pursuant to Section 4(b) or Section 9(c) hereof, the Company shall issue to the Holder the number of Warrant Shares in an exchange of securities effected pursuant to Section 3(a)(9) of the Securities Act as determined as follows:

$$X = Y [(A-B)/A]$$

where:

“X” equals the number of Warrant Shares to be issued to the Holder;

“Y” equals the total number of Warrant Shares with respect to which this Warrant is then being exercised;

“A” equals the Closing Sale Price per Common Share as of the Trading Day on the date immediately preceding the Exercise Date; and

“B” equals the Exercise Price per Warrant Share then in effect on the Exercise Date.

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For purposes of Rule 144 promulgated under the Securities Act, it is intended, understood and acknowledged that the Warrant Shares issued in such a “cashless exercise” transaction pursuant to Section 9(c) hereof shall be deemed to have been acquired by the Holder, and the holding period for the Warrant Shares shall be deemed to have commenced, on the date this Warrant was originally issued (provided that the Commission continues to take the position that such treatment is proper at the time of such exercise).

For the avoidance of doubt, any exercise of this Warrant pursuant to Section 4 hereof shall only be settled in cash.

11. *Limitations on Exercise.*

(a) Notwithstanding anything to the contrary contained herein, the Company shall not effect any exercise of this Warrant, and the Holder shall not be entitled to exercise this Warrant for a number of Warrant Shares in excess of that number of Warrant Shares which, upon giving effect or immediately prior to such exercise, would cause (i) the aggregate number of Common Shares beneficially owned by the Holder, its Affiliates and any other Persons whose beneficial ownership of Common Shares would be aggregated with the Holder’s for purposes of Section 13(d) of the Exchange Act (such as any other members of a Section 13(d) “group”) to exceed 9.99% (the “**Maximum Percentage**”) of the total number of issued and outstanding Common Shares of the Company following such exercise, or (ii) the combined voting power of the securities of the Company beneficially owned by the Holder and its Affiliates and any other Persons whose beneficial ownership of Common Shares would be aggregated with the Holder’s for purposes of Section 13(d) of the Exchange Act (such as any other members of a Section 13(d) “group”) to exceed 9.99% of the combined voting power of all of the securities of the Company then outstanding following such exercise. For purposes of this Warrant, in determining the number of outstanding Common Shares, the Holder may rely on the number of outstanding Common Shares as reflected in (x) the Company’s most recent Form 10-Q or Form 10-K, as the case may be, filed with the Commission prior to the date hereof, (y) a more recent public announcement by the Company or (z) any other notice by the Company or its transfer agent setting forth the number of Common Shares outstanding. Upon the written request of the Holder, the Company shall within two (2) Trading Days confirm in writing or by electronic mail to the Holder the number of Common Shares then outstanding. In any case, the number of outstanding Common Shares shall be determined after giving effect to the conversion or exercise of securities of the Company, including this Warrant, by the Holder since the date as of which such number of outstanding Common Shares was reported. By written notice to the Company, the Holder may from time to time increase or decrease the Maximum Percentage to any other percentage specified not in excess of 9.99% as specified in such notice; provided that any such increase will not be effective until the sixty-first (61st) day after such notice is delivered to the Company. For purposes of this Section 11(a), the aggregate number of Common Shares or voting securities beneficially owned by the Holder and its Affiliates and any other Persons whose beneficial ownership of Common Shares would be aggregated with the Holder’s for purposes of Section 13(d) of the Exchange Act (such as any other members of a Section 13(d) “group”) shall include the Common Shares issuable upon the exercise of this Warrant with respect to which such determination is being made, but shall exclude the number of Common Shares which would be issuable upon (x) exercise of the remaining unexercised and non-cancelled portion of this Warrant by the Holder and (y) exercise or conversion of the unexercised, non-converted or non-cancelled portion of any other securities of the Company that do not have voting power (including without limitation any securities of the Company which would entitle the holder thereof to acquire at any time Common Shares, including without limitation any debt, preferred share, right, option, warrant or other instrument that is at any time convertible into or exercisable or exchangeable for, or otherwise entitles the holder thereof to receive, Common Shares), is subject to a limitation on conversion or exercise analogous to the limitation contained herein and is beneficially owned by the Holder or any of its Affiliates and other Persons whose beneficial ownership of Common Shares would be aggregated with the Holder’s for purposes of Section 13(d) of the Exchange Act (such as any other members of a Section 13(d) “group”).

(b) This Section 11 shall not restrict the number of Common Shares that a Holder may receive or beneficially own in order to determine the amount of securities or other consideration that such Holder may receive in the event of a Fundamental Transaction as contemplated in Section 9(c) of this Warrant.

12. *No Fractional Shares.* No fractional Warrant Shares will be issued in connection with any exercise of this Warrant. In lieu of any fractional shares that would otherwise be issuable, the number of Warrant Shares to be issued shall be rounded down to the next whole number and the Company shall pay the Holder in cash the fair market value (based on the Closing Sale Price) for any such fractional shares.

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13. *Notices.* Any and all notices or other communications or deliveries hereunder (including, without limitation, any Exercise Notice) shall be in writing and shall be deemed given and effective on the earliest of (i) the date of transmission, if such notice or communication is delivered via confirmed e-mail prior to 5:30 P.M., New York City time, on a Trading Day, (ii) the next Trading Day after the date of transmission, if such notice or communication is delivered via confirmed e-mail on a day that is not a Trading Day or later than 5:30 P.M., New York City time, on any Trading Day, (iii) the Trading Day following the date of mailing, if sent by nationally recognized overnight courier service specifying next business day delivery, or (iv) upon actual receipt by the Person to whom such notice is required to be given, if by hand delivery. The addresses and e-mail addresses for such communications shall be:

If to the Company:

Attention: Amit Hasija, Chief Financial Officer Milestone Pharmaceuticals Inc.  
1111 Dr. Frederik-Philips Blvd., Suite 420 Montréal, Québec H4M 2X6  
Email: [ahasija@milestonepharma.com](mailto:ahasija@milestonepharma.com)

with copies (which shall not constitute notice) to:

Attention: Ryan Sansom Cooley LLP  
500 Boylston Street, 14<sup>th</sup> Floor Boston, Massachusetts 02116  
Facsimile: (617) 937-2400 Email: [rsansom@cooley.com](mailto:rsansom@cooley.com)

If to the Holder, to its address or e-mail address set forth herein or on the books and records of the Company.

Or, in each of the above instances, to such other address or e-mail address as the recipient party has specified by written notice given to each other party at least five (5) days prior to the effectiveness of such change.

14. *Warrant Agent.* The Company shall initially serve as warrant agent under this Warrant. Upon ten (10) days' notice to the Holder, the Company may appoint a new warrant agent. Any corporation into which the Company or any new warrant agent may be merged or any corporation resulting from any consolidation or amalgamation to which the Company or any new warrant agent shall be a party or any corporation to which the Company or any new warrant agent transfers substantially all of its corporate trust or shareholders services business shall be a successor warrant agent under this Warrant without any further act. Any such successor warrant agent shall promptly cause notice of its succession as warrant agent to be mailed (by first class mail, postage prepaid) to the Holder at the Holder's last address as shown on the Warrant Register.

15. *Miscellaneous.*

(a) No Rights as a Shareholder. The Holder, solely in such Person's capacity as a holder of this Warrant, shall not be entitled to vote or receive dividends or be deemed the holder of share capital of the Company for any purpose, nor shall anything contained in this Warrant be construed to confer upon the Holder, solely in such Person's capacity as the Holder of this Warrant, any of the rights of a shareholder of the Company or any right to vote, give or withhold consent to any corporate action (whether any reorganization, issue of shares, reclassification of shares, consolidation, merger, amalgamation, conveyance or otherwise), receive notice of meetings, receive dividends or subscription rights, or otherwise, prior to the issuance to the Holder of the Warrant Shares which such Person is then entitled to receive upon the due exercise of this Warrant. In addition, nothing contained in this Warrant shall be construed as imposing any liabilities on the Holder to purchase any securities (upon exercise of this Warrant or otherwise) or as a shareholder of the Company, whether such liabilities are asserted by the Company or by creditors of the Company.

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(b) Successors and Assigns. Subject to compliance with applicable securities laws, this Warrant may be assigned by the Holder. This Warrant may not be assigned by the Company without the written consent of the Holder, except to a successor in the event of a Fundamental Transaction. This Warrant shall be binding on and inure to the benefit of the Company and the Holder and their respective successors and assigns. Subject to the preceding sentence, nothing in this Warrant shall be construed to give to any Person other than the Company and the Holder any legal or equitable right, remedy or cause of action under this Warrant. This Warrant may be amended only in writing signed by the Company and the Holder, or their successors and assigns.

(c) Amendment and Waiver. Except as otherwise provided herein, this Warrant may be modified or amended or the provisions hereof waived with the written consent of the Company and the Holder.

(d) Acceptance. Receipt of this Warrant by the Holder shall constitute acceptance of and agreement to all of the terms and conditions contained herein.

(e) Governing Law; Jurisdiction. ALL QUESTIONS CONCERNING THE CONSTRUCTION, VALIDITY, ENFORCEMENT AND INTERPRETATION OF THIS WARRANT SHALL BE GOVERNED BY AND CONSTRUED AND ENFORCED IN ACCORDANCE WITH THE LAWS OF THE STATE OF NEW YORK WITHOUT REGARD TO THE PRINCIPLES OF CONFLICTS OF LAW THEREOF. EACH OF THE COMPANY AND THE HOLDER HEREBY IRREVOCABLY SUBMITS TO THE EXCLUSIVE JURISDICTION OF THE STATE AND FEDERAL COURTS SITTING IN THE CITY OF NEW YORK, BOROUGH OF MANHATTAN, FOR THE ADJUDICATION OF ANY DISPUTE HEREUNDER OR IN CONNECTION HERewith OR WITH ANY TRANSACTION CONTEMPLATED HEREBY OR DISCUSSED HEREIN (INCLUDING WITH RESPECT TO THE ENFORCEMENT OF ANY OF THE TRANSACTION DOCUMENTS), AND HEREBY IRREVOCABLY WAIVES, AND AGREES NOT TO ASSERT IN ANY SUIT, ACTION OR PROCEEDING, ANY CLAIM THAT IT IS NOT PERSONALLY SUBJECT TO THE JURISDICTION OF ANY SUCH COURT. EACH OF THE COMPANY AND THE HOLDER HEREBY IRREVOCABLY WAIVES PERSONAL SERVICE OF PROCESS AND CONSENTS TO PROCESS BEING SERVED IN ANY SUCH SUIT, ACTION OR PROCEEDING BY MAILING A COPY THEREOF VIA REGISTERED OR CERTIFIED MAIL OR OVERNIGHT DELIVERY (WITH EVIDENCE OF DELIVERY) TO SUCH PERSON AT THE ADDRESS IN EFFECT FOR NOTICES TO IT AND AGREES THAT SUCH SERVICE SHALL CONSTITUTE GOOD AND SUFFICIENT SERVICE OF PROCESS AND NOTICE THEREOF. NOTHING CONTAINED HEREIN SHALL BE DEEMED TO LIMIT IN ANY WAY ANY RIGHT TO SERVE PROCESS IN ANY MANNER PERMITTED BY LAW. EACH OF THE COMPANY AND THE HOLDER HEREBY WAIVES ALL RIGHTS TO A TRIAL BY JURY.

(f) Headings. The headings herein are for convenience only, do not constitute a part of this Warrant and shall not be deemed to limit or affect any of the provisions hereof.

(g) Severability. In case any one or more of the provisions of this Warrant shall be invalid or unenforceable in any respect, the validity and enforceability of the remaining terms and provisions of this Warrant shall not in any way be affected or impaired thereby, and the Company and the Holder will attempt in good faith to agree upon a valid and enforceable provision which shall be a commercially reasonable substitute therefor, and upon so agreeing, shall incorporate such substitute provision in this Warrant.

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**IN WITNESS WHEREOF**, the Company has caused this Warrant to be duly executed by its authorized officer as of the date first indicated above.

MILESTONE PHARMACEUTICALS INC.

By: \_\_\_\_\_  
Name: Joseph G. Oliveto  
Title: President and CEO

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**Consent of Independent Registered Public Accounting Firm**

We hereby consent to the incorporation by reference in this Registration Statement on Form S-3 of Milestone Pharmaceuticals Inc. of our report dated March 29, 2021 relating to the consolidated financial statements, which appears in Milestone Pharmaceuticals Inc.'s Annual Report on Form 10-K for the year ended December 31, 2020.

We also consent to the reference to us under the heading "Experts" in the Registration Statement on Form S-3.

*PricewaterhouseCoopers LLP*

**Partnership of Chartered Professional Accountants**

Montreal, Quebec,  
Canada June 25, 2021

*PricewaterhouseCoopers LLP/ s.r.l./ s.e.n.c.r.l.*  
*1250 Rene-Levesque Boulevard West, Suite 2500, Montr eal, Quebec, Canada H3B*  
*4Y1 T: +1514205 5000, F: +1514 8761502, www.pwc.com/ ca*

"PwC" refers to PricewaterhouseCoopers LLP /s.r.l./ s.e.n.c.r.l., an Ontario limited liability partnership.

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