UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form S-8 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 (IRS employer identification number)

1111 Dr. Frederik-Philips Boulevard, Suite 420 Montréal, Québec CA (Address of Principal Executive Offices)

H4M 2X6 (Zip Code)

2019 Equity Incentive Plan 2019 Employee Share Purchase Plan 2021 Inducement Plan

(Full titles of the plans)

Joseph Oliveto Chief Executive Officer Milestone Pharmaceuticals USA Inc. 6210 Ardrey Kell Road Suite 650 Charlotte, NC 28277 (514) 336-0444

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

Copies to:
Ryan S. Sansom
Nicolas H. R. Dumont
Cooley LLP
500 Boylston Street, 14th Floor
Boston, MA 02116
(617) 937-2300

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," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer		Accelerated filer	
Non-accelerated filer	\boxtimes	Smaller reporting company	\boxtimes
		Emerging growth company	\boxtimes

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. \boxtimes

PART I

EXPLANATORY NOTE

This Registration Statement on Form S-8 (this "Registration Statement") is being filed by Milestone Pharmaceuticals Inc. (the "Registrant") for the purpose of registering (i) an additional 2,361,440 common shares issuable pursuant to the Milestone Pharmaceuticals Inc. 2019 Equity Incentive Plan (the "2019 EIP") and (ii) an additional 342,860 common shares issuable pursuant to the Milestone Pharmaceuticals Inc. 2019 Employee Share Purchase Plan (the "2019 ESPP"). These additional common shares are securities of the same class as other securities for which a Registration Statement on Form S-8 of the Registrant relating to the same employee benefit plans is effective. On July 5, 2022, stockholders of the Registrant approved an amendment to the 2019 EIP that increased the number of shares of Common Stock issuable thereunder by 1,000,000 shares. The prior registration statement that the Registrant filed with the Securities and Exchange Commission ("SEC") on March 24, 2022 (Registration No. 333-263807) relating to the 2019 EIP and the 2019 ESPP is incorporated by reference into this Registration Statement. This incorporation is made under General Instruction E of Form S-8 regarding the registration of additional securities of the same class as other securities for which there has been filed a registration statement on Form S-8 relating to the same employee benefit plan.

PART II

INFORMATION REQUIRED IN THE REGISTRATION STATEMENT

Item 3. Incorporation of Documents by Reference.

The following documents filed by the Registrant with the Securities and Exchange Commission ("SEC") are incorporated by reference into this registration statement (other than information furnished under Item 2.02 or Item 7.01 of Form 8-K or other portions of documents filed with the SEC which are furnished, but not filed, pursuant to applicable rules promulgated by the SEC):

- (a) The Registrant's <u>Annual Report on Form 10-K for the fiscal year ended December 31, 2022 filed on March 29, 2023</u> (the "Annual Report") and the information specifically incorporated by reference into the <u>Annual Report on Form 10-K for the year ended December 31, 2022</u>, from the Registrant's <u>Definitive Proxy Statement on Schedule 14A</u>, filed with the SEC on April 28, 2023;
- (b) The Registrant's Current Reports on Form 8-K filed with the SEC on March 27, 2023, March 28, 2023 and March 31, 2023.
- (c) The description of Common Stock which is contained in a registration statement on Form 8-A filed on May 6, 2019 (File No. 001-38899) under Section 12(b) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), including any amendment or report filed for the purpose of updating such description.
- (d) The Registrant's Registration Statement on Form S-8, previously filed with the Commission on May 9, 2019 (File No. 333-231347), March 6, 2020 (File No. 333-236971), March 29, 2021 (File No. 333-254838), and March 24, 2022 (File No. 333-263807).
- (e) All other reports and documents subsequently filed by the Registrant pursuant to Sections 13(a), 13(c), 14 and 15(d) of the Exchange Act (other than Current Reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits furnished on such form that relate to such items) on or after the date of this Registration Statement and prior to the filing of a post-effective amendment to this Registration Statement which indicates that all securities offered have been sold or which deregisters all securities then remaining unsold, shall be deemed to be incorporated by reference herein and to be a part of this Registration Statement from the date of the filing of such reports and documents. Any statement contained in a document incorporated or deemed to be incorporated by reference herein shall be deemed to be modified or superseded for purposes of this Registration Statement to the extent that a statement contained herein or in any subsequently filed document that also is deemed to be incorporated by reference herein modifies or supersedes such statement. Any such statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this Registration Statement.

Item 4. Description of Securities

See the description of the Registrant's registered securities contained in Exhibit 4.5 to the Annual Report.

Item 8. Exhibits.

The exhibits to this Registration Statement are listed below:

Exhibit Number	Exhibit Description
4.1	Amended Articles of Incorporation (incorporated herein by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-38899), filed with the SEC on May 15, 2019).
<u>4.2</u>	Amended and Restated Bylaws (incorporated herein by reference to Exhibit 3.2 to the Registrant's Current Report on Form 8-K (File No. 001-
<u>4.3</u>	38899), filed with the SEC on May 15, 2019). 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).
<u>4.4</u>	2019 Equity Incentive Plan, as amended (incorporated herein by reference to Exhibit 10.1 to the Registrant's Quarterly Report (File No. 001-
<u>4.5</u>	38899), filed with the SEC on November 10, 2022) Form of U.S. Stock Option Grant Notice and Stock Option Agreement under the 2019 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.4 to Amendment No. 1 to the Registrant's Registration Statement on Form S-1 (File No. 333-230846), filed with the SEC on
<u>4.6</u>	April 29, 2019). Form of U.S. Restricted Stock Unit Grant Notice and Restricted Stock Unit Award Agreement under the 2019 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.5 to Amendment No. 1 to the Registrant's Registration Statement on Form S-1 (File No. 333-
<u>4.7</u>	230846), filed with the SEC on April 29, 2019). Form of Canadian Stock Option Grant Notice and Option Agreement under the 2019 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.6 to Amendment No. 1 to the Registrant's Registration Statement on Form S-1 (File No. 333-230846), filed with the SEC on
<u>4.8</u>	<u>April 29, 2019).</u> <u>Form of Canadian Restricted Stock Unit Grant Notice and Restricted Stock Unit Award Agreement under the 2019 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.7 to Amendment No. 1 to the Registrant's Registration Statement on Form S-1 (File No. 333-</u>
<u>4.9</u>	230846), filed with the SEC on April 29, 2019). 2019 Employee Share Purchase Plan (incorporated herein by reference to Exhibit 4.13 to the Registrant's Registration Statement on Form S-8 (File No. 333-231347), filed with the SEC on May 9, 2019).
<u>4.10</u>	2021 Inducement Plan approved by the Board of the Company on November 10, 2021 (incorporated herein by reference to Exhibit 4.10 to the Registrant's Registration Statement on Form S-8 (File No. 333-263807), filed with the SEC on March 24, 2022).
<u>5.1*</u>	Opinion of Osler, Hoskin & Harcourt LLP.
23.1*	Consent of Independent Registered Public Accounting Firm.
23.2*	Consent of Osler, Hoskin & Harcourt LLP. (included in Exhibit 5.1).
24.1*	Power of Attorney (included on the signature page to this Registration Statement).
<u>107*</u>	Filing Fee Table

* Filed herewith.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, as amended, the Registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-8 and has duly caused this Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Montréal, Province of Québec, Canada on April 28, 2023.

Milestone Pharmaceuticals Inc.

By: /s/ Joseph Oliveto

Joseph Oliveto

President and Chief Executive Officer

POWER OF ATTORNEY

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

Pursuant to the requirements of the Securities Act of 1933, as amended, this Registration Statement on Form S-8 has been signed by the following persons in the capacities and on the dates indicated.

Signature	Title	Date April 28, 2023	
/s/ Joseph Oliveto Joseph Oliveto	President, Chief Exetcutive Officer and Director (Principal Executive Officer)		
/s/ Amit Hasija Amit Hasija	Chief Financial Officer (Principal Financial and Accounting Officer)	April 28, 2023	
/s/ Debra K. Liebert Debra K. Liebert	Director	April 28, 2023	
/s/ Richard Pasternak, M.D. Richard Pasternak, M.D.	 Director	April 28, 2023	
/s/ Michael Tomsicek Michael Tomsicek	Director	April 28, 2023	
/s/ Seth Fischer Seth Fischer	Director	April 28, 2023	
Lisa Giles	Director		
/s/ Robert Wills Robert Wills	Director	April 28, 2023	

SIGNATURE OF AUTHORIZED U.S. REPRESENTATIVE OF THE REGISTRANT

Pursuant to the Securities Act, the undersigned, the duly authorized representative in the United States of Milestone Pharmaceuticals Inc. has signed this registration statement or amendment thereto on April 28, 2023.

MILESTONE PHARMACEUTICALS USA, INC.

By:	/s/ Joseph Oliveto				
	Joseph Oliveto				
	President and Chief Executive Officer				

Osler, Hoskin & Harcourt s.E.N.C.R.L./s.r.l.

1000, rue De La Gauchetière Ouest bureau 2100 Montréal (Québec) Canada H3B 4W5 514.904.8100 TÉLÉPHONE 514.904.8101 TÉLÉCOPIEUR





Milestone Pharmaceuticals Inc.

1111 Dr. Frederik-Philips Boulevard, Suite 420 Montreal, Québec H4M 2X6

Dear Sirs/Mesdames:

Re: Milestone Pharmaceuticals Inc. - Registration Statement on Form S-8

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 registration of (i) an additional 2,361,440 common shares of the Corporation (the "EIP Shares") issuable pursuant to the Corporation's 2019 equity incentive plan (the "2019 Plan"), and (ii) an additional 342,860 common shares of the Corporation (the "ESPP Shares" and, together with the EIP Shares, the "Shares") issuable pursuant to the Corporation's 2019 employee share purchase plan (the "ESPP" and, together with the 2019 Plan, the "Plans"), pursuant to a Registration Statement on Form S-8 (the "Registration Statement") filed on April 28, 2023 with the Securities and Exchange Commission under the *Securities Act of 1933*, as amended, relating to the registration of the Shares.

We have examined the Registration Statement, the Plans 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 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.

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.

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On the basis of the foregoing, we are of the opinion that, when the Shares shall have been issued and sold pursuant to the terms of the Plans and the Registration Statement, the Shares will be validly issued, fully paid and non-assessable.

We hereby consent to the filing of this opinion as an exhibit to the Registration Statement.

Yours very truly,

/s/ Osler, Hoskin & Harcourt LLP Osler, Hoskin & Harcourt LLP

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in this Registration Statement on Form S-8 of Milestone Pharmaceuticals Inc. of our report dated March 29, 2023 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, 2022.

/s/ PricewaterhouseCoopers LLP Montréal, Canada April 28, 2023

Calculation of Filing Fee Tables

Form S-8 (Form Type)

Milestone Pharmaceuticals, Inc.

(Exact Name of Registrant as Specified in its Charter)

<u>Table 1: Newly Registered Securities</u>

Security Type	Security Class Title	Fee Calculation Rule	Amount Registered ⁽¹⁾	Proposed Maximum Offering Price Per Unit	Maximum Aggregate Offering Price	Fee Rate		mount of gistration Fee
Equity	2019 Equity Incentive Plan (Common shares, no par value per share)	Other	2,361,440 ⁽²⁾	\$ 3.78 ⁽⁻	\$ 8,926,243.20 ⁽⁴⁾	\$110.20 per \$1,000,000	\$	983.68
Equity	2019 Employee Share Purchase Plan (Common shares, no par value per share)	Other	342,860 ⁽³⁾			\$110.20 per \$1,000,000	\$	142.82
Total	fering Amount Fee Offsets t Fee Due				\$10,222,254.00 ⁽⁴⁾		\$ \$	1,126.50 — 1,126.50

- (1) Pursuant to Rule 416 under the Securities Act of 1933, as amended (the "Securities Act"), this Registration Statement shall also cover any additional common shares that become issuable under the above-named plans by reason of any share dividend, share split, recapitalization or any other similar transaction effected without receipt of consideration which results in an increase in the number of Milestone Pharmaceuticals Inc.'s (the "Registrant") outstanding common shares, no par value per share (the "Common Shares").
- (2) Represents (i) 1,361,440 Common Shares that were automatically added to the shares authorized for issuance under the Milestone Pharmaceuticals Inc. 2019 Equity Incentive Plan (the "2019 EIP") on January 1, 2023 pursuant to an "evergreen" provision contained in the 2019 Plan and (ii) 1,000,000 additional Common Shares that stockholders of the Registrant approved to be added to the reserve for the 2019 EIP on July 5, 2022 pursuant to an amendment to the 2019 EIP.
- (3) Represents Common Shares that were automatically added to the shares authorized for issuance under the Milestone Pharmaceuticals Inc. 2019 Employee Share Purchase Plan (the "2019 ESPP") on January 1, 2023 pursuant to an "evergreen" provision contained in the 2019 ESPP.
- (4) Estimated pursuant to Rule 457(c) and Rule 457(h) of the Securities Act solely for the purpose of calculating the registration fee. The proposed maximum offering price per share and proposed maximum aggregate offering price are based on the average of the high and low sale prices of the Registrant's common stock as reported on the Nasdaq Global Select Market on April 27, 2023.