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, 14th 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: o

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: \boxtimes 333-239318

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, o

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. o

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. o

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	\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

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	Proposed Maximum Aggregate Offering Price(1)	Amount of Registration Fee(2)
Common Shares, no par value per share	(1)	_
Warrants to purchase Common Shares, no par value per share	(1)	-
Total	\$1,753,450	\$191.31

(1) The Registrant previously registered the offer and sale of certain securities, including common shares, no par value (the "Common Shares") and warrants to purchase Common Shares having a proposed maximum aggregate offering price of \$100,000,000 pursuant to a Registration Statement on Form S-3 (File No. 333-239318), which was declared effective by the Securities and Exchange Commission on July 6, 2020 (the "Related Registration Statement"). As of the date hereof, a balance of \$50,000,000 of such securities remains to be offered and sold under the Related Registration Statement. In accordance with Rule 462(b) promulgated under the Securities Act of 1933, as amended (the "Securities Act") an additional amount of the Registrant's Common Shares and warrants to purchase its Common Shares having a proposed maximum aggregate offering price of \$1,753,450 is hereby registered, representing no more than 20% of the maximum aggregate offering price of unsold securities under the Related Registration Statement.

	additional amount of the Registrant's Common Shares and warrants to purchase its Common Shares having a proposed maximum aggregate offering				
	price of \$1,753,450 is hereby registered, representing no more than 20% of the maximum aggregate offering price of unsold securities under the				
	Related Registration Statement.				
(2)	Calculated pursuant to Rule 457(o) under the Securities Act.				
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This Registration Statement shall become effective upon filing in accordance with Rule 462(b) under the Securities Act of 1933, as amended.					

EXPLANATORY NOTE AND INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

This Registration Statement is being filed with the Securities and Exchange Commission (the "Commission") pursuant to Rule 462(b) under the Securities Act and General Instruction IV(A) to Form S-3 to register an additional \$1,753,450 of the Registrant's securities. In accordance with Rule 462(b), this Registration Statement incorporates by reference the contents of the Registrant's Registration Statement on Form S-3 (File No. 333-239318), initially filed with the Commission on June 19, 2020, and declared effective by the Commission on July 6, 2020, including all exhibits thereto and all information incorporated by reference therein, other than the exhibits included herein.

The required opinions and consents are listed on the Exhibit Index set forth below and filed herewith.

EXHIBIT INDEX

Exhibit	Incorporation By Reference		nce		
Number	Exhibit Description	Form	SEC File No.	Exhibit	Filing Date
<u>5.1</u>	Opinion of Osler, Hoskin & Harcourt LLP.		=	<u> </u>	=
<u>5.2</u>	Opinion of Cooley LLP.	Ξ	Ξ	=	Ξ
<u>23.1</u>	Consent of Independent Registered Public Accounting Firm.	Ξ	Ξ	<u>=</u>	Ξ
<u>23.2</u>	Consent of Osler, Hosking & Harcourt LLP (contained in Exhibit 5.1)	Ξ	Ξ	<u>=</u>	Ξ.
<u>23.3</u>	Consent of Cooley LLP (contained in Exhibit 5.2).	=	Ξ	Ξ	Ξ.
<u>24.1</u>	Power of Attorney (incorporated by reference).	<u>S-3</u>	<u>333-239318</u>	<u>24.1</u>	<u>June 19, 2020</u>

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 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 October 22, 2020.

MILESTONE PHARMACEUTICALS INC.

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

Signature	Title	Date
/s/ Joseph Oliveto	President, Chief Executive	October 22, 202
Joseph Oliveto	Officer and Director (Principal Executive Officer)	
/s/ Amit Hasija	Chief Financial Officer and Executive Vice President of Corporate	October 22, 202
Amit Hasija	Development (Principal Financial Officer and Principal Accounting Officer)	
*	Director	October 22, 202
Paul Edick		
*	Director	October 22, 202
Debra K. Liebert		
*	Director	October 22, 202
Richard Pasternak, M.D.		
*	Director	October 22, 202
Michael Tomsicek		
*	Director	October 22, 202
Paul Truex		
D. L. L. L. L. D. D.	Director	October 22, 202
Robert J. Wills. PhD		
Lisa M. Giles	Director	October 22, 202
Lisa W. Gues		
/s/ Joseph Oliveto		
Joseph Oliveto Attorney-in-Fact		

SIGNATURE OF AUTHORIZED U.S. REPRESENTATIVE OF THE REGISTRANT

Pursuant to the Securities Act of 1933, the undersigned, the duly authorized representative in the United States of Milestone Pharmaceuticals Inc. has signed this registration statement on the 22nd day of October, 2020.

MILESTONE PHARMACEUTICALS INC.		
Ву:	/s/ Joseph Oliveto	
	Joseph Oliveto	
	President and Chief Executive Officer	

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



Montréal

Toronto

Calgary

Ottawa

Vancouver

New York

October 22, 2020

Milestone Pharmaceuticals Inc.

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

Dear Sirs/Mesdames:

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 filing by the Corporation with the Securities and Exchange Commission (the "Commission") of a Registration Statement on Form S-3 (the "Registration Statement") filed by the Corporation pursuant to Rule 462(b) under the Securities Act of 1933, as amended (the "Act"), relating to an aggregate of \$1,753,450 of (i) common shares, without par value, of the Corporation (the "Shares"), and (ii) warrants (the "Warrants") to purchase common shares of the Corporation (the "Warrant Shares"), which may be issued under one or more warrant certificates, to be dated on or about the date of the first issuance of the Warrants thereunder, in the form filed as an exhibit to the Prior Registration Statement (as defined below) (the "Warrant Certificate"). The Registration Statement incorporates by reference the Registration Statement on Form S-3 (Registration No. 333-239318), which was declared effective by the Commission on July 6, 2020 (the "Prior Registration Statement"), including the prospectus which forms part of the Prior Registration Statement (the "Base Prospectus"), which provides that it will be supplemented in the future by one or more prospectus supplements (each, a "Prospectus Supplement").

The Shares and the Warrants are being registered for offer and sale from time to time pursuant to Rule 415 under the Act.

In connection with this opinion, we have examined and relied upon the Registration Statement, (b) the Warrant Certificate, and (c) 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 opinions 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 certifying, among other things, (i) the certificate, articles of incorporation and by-laws of the Corporation, and (ii) certain resolutions passed by the board of directors of the Corporation relating to the foregoing and the issuance of the Shares, the Warrants and the Warrant Shares.

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

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.

Our opinions are expressed with respect to the laws in effect on the date of this opinion and we do not accept any responsibility to take into account or inform the addressee, or any other person authorized to rely on this opinion, of any changes in law, facts or other developments subsequent to this date that do or may affect the opinions we express, nor do we have any obligation to advise you of any other change in any matter addressed in this opinion or to consider whether it would be appropriate for any other person other than the addressee to rely on our opinion.

Where our opinion below refers to the Shares and the Warrant Shares as being "fully-paid and non-assessable", such opinion assumes that all required consideration (in whatever form) has been or will be paid or provided. No opinion is expressed as to the adequacy of any consideration received.

Based upon and subject to the foregoing and to the qualifications set forth herein, we are of the opinion that, with respect to the Shares and the Warrant Shares offered under the Registration Statement, provided that (a) the Base Prospectus and any and all Prospectus Supplement(s) required by applicable laws have been delivered and filed as required by such laws; (b) the issuance of the Shares and the Warrants have been duly authorized by all necessary corporate action on the part of the Corporation; (c) the issuance and sale of the Shares and the Warrants do not violate any applicable law, are in conformity with the Corporation's articles and by-laws, do not result in a default under or breach of any agreement or instrument binding upon the Corporation and comply with any applicable requirement or restriction imposed by any court or governmental body having jurisdiction over the Corporation; (d) the full consideration for the issuance of the Shares and the Warrants (including the Warrant Shares upon exercise of the Warrants pursuant to its terms) have been received by the Corporation, and (e) the certificates, if any, for the Shares, the Warrants and the Warrant Shares have been duly executed by the Corporation, countersigned by the transfer agent therefor, as applicable, and duly delivered to the purchasers thereof against payment therefor, then the Shares and the Warrant Shares, when issued and sold as contemplated in the Registration Statement, the Base Prospectus and the related Prospectus Supplement(s) and in accordance with the Warrant Certificate and a duly authorized, executed and delivered purchase, underwriting or similar agreement, or upon exercise of any Warrants in accordance with their terms, will be validly issued, fully paid and non-assessable.



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We hereby consent to the filing of this opinion letter as an exhibit to the Registration Statement and to the use of our name under the caption "Legal Matters" in the Registration Statement. In giving this consent, we do not admit that we are in the category of persons whose consent is required under Section 7 of the Act.

Yours very truly,

(signed) Osler, Hoskin & Harcourt LLP

Osler, Hoskin & Harcourt LLP



Ryan S Sansom +1 617 937 2335 rsansom@cooley.com

October 22, 2020

Milestone Pharmaceuticals Inc.

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

Ladies and Gentlemen:

We have acted as special counsel for Milestone Pharmaceuticals Inc., a corporation organized under the Business Corporations Act (Québec) (the "Company"), in connection with the Registration Statement on Form S-3 (the "Registration Statement") filed by the Company pursuant to Rule 462(b) promulgated under the Securities Act of 1933, as amended (the "Act"), relating to an aggregate of \$1,753,450 of common shares, without par value, of the Company (the "Shares") and warrants to purchase common shares of the Company (the "Warrants"), which may be issued under one or more warrant agreements, to be dated on or about the date of the first issuance of the Warrants thereunder, by and between a warrant agent to be selected by the Company (the "Warrant Agent") and the Company, in the form filed as an exhibit to the Prior Registration Statement (as defined below) (the "Warrant Agreement"). The Registration Statement incorporates by reference the registration statement on Form S-3 (File No.333-239318), which was declared effective by the Securities and Exchange Commission on July 6, 2020 (the "Prior Registration Statement"), including the prospectus which forms a part of the Prior Registration Statement (the "Base Prospectus"), which provides that it will be supplemented in the future by one or more prospectus supplements (each a "Prospectus Supplement").

The Shares and the Warrants are collectively referred to as the "Securities". The Securities are being registered for offer and sale from time to time pursuant to Rule 415 under the Securities Act. In connection with this opinion, we have examined and relied upon originals, or copies certified to our satisfaction, of such records, documents, certificates, opinions, memoranda and other instruments as in our judgment are necessary or appropriate to enable us to render the opinion expressed below. As to certain factual matters, we have relied upon a certificate of an officer of the Company and have not independently verified such matters.

In rendering this opinion, we have assumed the genuineness of all signatures, the authenticity of all documents submitted to us as originals, the conformity to originals of all documents submitted to us as copies; the accuracy, completeness and authenticity of certificates of public officials, and the due authorization, execution and delivery of all documents by all persons other than the Company where authorization, execution and delivery are prerequisites to the effectiveness of such documents.

With respect to our opinion as to the Warrants, we have also assumed that any Warrants offered under the Registration Statement, and the related Warrant Agreement are executed in the form filed as exhibits to the Registration Statement or incorporated by reference therein.

Our opinion herein is expressed solely with respect to the laws of the State of New York. We express no opinion to the extent that any other laws are applicable to the subject matter hereof and express no opinion and provide no assurance as to compliance with any federal or state securities law, rule or regulation. We understand you are obtaining a separate opinion with respect to the Shares.

We have assumed that (i) the Company is validly existing under the laws of the Provence of Quebec, has the corporate power to enter into and perform its obligations under the Warrants and the Warrant Agreement in accordance with their terms, (ii) upon issuance, the Company will have duly authorized, executed and delivered, the Warrants and the Warrant Agreements in accordance with its organizational documents and the laws of the Provence of Quebec, (iii) any Shares to be issued upon exercise of the Warrants will be duly authorized, validly issued, fully paid and non-assessable, and (iv) the execution, delivery and performance by the Company of its obligations under the Warrants and the Warrant Agreement will not violate the laws of the Provence of Quebec or any other applicable laws (excepting from such assumption the laws of the State of New York).

Cooley LLP 500 Boylston Street Boston, MA 02116-3736 t: (617) 937-2300 f: (617) 937-2400 cooley.com

Milestone Pharmaceuticals Inc. October 22, 2020 Page Two

On the basis of the foregoing and in reliance thereon, and subject to the qualifications herein stated, we are of the opinion that:

With respect to the Warrants issued under the Warrant Agreement and offered under the Registration Statement, provided that (i) any and all Prospectus Supplement(s) required by applicable laws have been delivered and filed as required by such laws; (ii) the Warrant Agreement has been duly authorized by the Company and the Warrant Agent; (iv) the issuance and terms of the Warrants have been duly authorized by the Company by all necessary corporate action; (v) the terms of the Warrants and of their issuance and sale have been duly established in conformity with the Warrant Agreement and as described in the Registration Statement, the Base Prospectus and the related Prospectus Supplement(s), so as not to violate any applicable law or result in a default under or breach of any agreement or instrument binding upon the Company, so as to be in conformity with the Company's articles of association, and so as to comply with any requirement or restriction imposed by any court or governmental body having jurisdiction over the Company; and (vi) the Warrants have been duly executed and delivered by the Company and authenticated by the Warrant Agent pursuant to the Warrant Agreement and delivered against payment therefor, then the Warrants, when issued and sold as contemplated in the Registration Statement, the Base Prospectus and the Prospectus Supplement(s) and in accordance with the Warrant Agreement and a duly authorized, executed and delivered purchase, underwriting or similar agreement, will be valid and legally binding obligations of the Company, enforceable against the Company in accordance with their terms, except as enforcement thereof may be limited by bankruptcy, insolvency, reorganization, moratorium or other similar laws relating to or affecting creditors' rights generally, and by general equitable principles (regardless of whether such enforceability is considered in a proceeding at law or in equity).

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

Our opinion set forth above is limited to the matters expressly set forth in this letter, and no opinion is implied or may be inferred beyond the matters expressly stated. This opinion speaks only as to law and facts in effect or existing as of the date hereof, and we undertake no obligation or responsibility to update or supplement this opinion to reflect any facts or circumstances that may hereafter come to our attention or any changes in law that may hereafter occur.

Cooley LLP 500 Boylston Street Boston, MA 02116-3736 t: (617) 937-2300 f: (617) 937-2400 cooley.com

Milestone Pharmaceuticals I	nc.
October 22, 2020	
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Sincerely,

COOLEY LLP

By: /s/ Ryan Sansom
Ryan Sansom

Cooley LLP 500 Boylston Street Boston, MA 02116-3736 t: (617) 937-2300 f: (617) 937-2400 cooley.com



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 5, 2020 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, 2019. We also consent to the reference to us under the heading "Experts" in such Registration Statement.

/s/PricewaterhouseCoopers LLP

Partnership of Chartered Professional Accountants

Montréal, Québec, Canada October 22, 2020

PricewaterhouseCoopers LLP/s.r.l./s.e.n.c.r.l. 1250 René-Lévesque Boulevard West, Suite 2500, Montréal, Quebec, Canada H3B 4Y1 T: +1 514 205 5000, F: +1 514 876 1502, www.pwc.com/ca

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