

As filed with the Securities and Exchange Commission on March 18, 2021

Registration No. 333-

**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION**

Washington, D.C. 20549

FORM S-3
REGISTRATION STATEMENT UNDER

THE SECURITIES ACT OF 1933

TRILLIUM THERAPEUTICS INC.

(Exact name of registrant as specified in its charter)

British Columbia, Canada

(State or other jurisdiction of incorporation or organization)

Not Applicable

(I.R.S. Employer Identification Number)

**Trillium Therapeutics USA Inc.
100 CambridgePark Drive, Suite 510
Cambridge, Massachusetts 02140
(857) 412-7029**

Attention: Chief Financial Officer

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

**Trillium Therapeutics USA Inc.
100 Cambridgepark Drive, Suite 510
Cambridge, Massachusetts 02140
(857) 412-7029**

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

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

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, other than securities offered only in connection with dividend or 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 ☐

Non-accelerated filer ☒

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 ⁽¹⁾	Proposed maximum offering price per unit ⁽¹⁾	Proposed maximum aggregate offering price ⁽¹⁾	Amount of registration fee ⁽²⁾
Common Shares				
First Preferred Shares				
Subscription Receipts				
Warrants				
Units				
Total				

- (1) Pursuant to Form S-3 General Instructions II.E this information is not required to be included. An indeterminate amount of the securities of each identified class are being registered as may from time to time be offered hereunder at indeterminate prices, along with an indeterminate number of securities that may be issued upon exercise, settlement, exchange or conversion of securities offered or sold hereunder. Separate consideration may or may not be received for securities that are issuable upon exercise, settlement, exchange or conversion of other securities. Any securities registered hereunder may be sold separately or as units with other securities registered hereunder.
- (2) In accordance with Rules 456(b) and 457(r) under the Securities Act of 1933, as amended, the registrant is deferring payment of all registration fees and will pay the registration fees subsequently in advance on a “pay-as-you-go” basis.

PROSPECTUS



Common Shares
First Preferred Shares
Subscription Receipts
Warrants
Units

We may from time to time offer and sell our common shares, first preferred shares, subscription receipts, warrants and units (collectively, the “Securities”) separately or together, in amounts, at prices and on terms to be determined based on market conditions at the time of sale and set forth in one or more prospectus supplements. These Securities may be offered and sold in the United States and elsewhere where permitted by law. We will provide the specific terms of these Securities in supplements to this prospectus that will be delivered to purchasers together with this prospectus. You should read this prospectus and any prospectus supplement carefully before you invest in the Securities.

Investment in the Securities involves certain risks that should be considered by a prospective purchaser. See “Risk Factors” on page 5 of this prospectus along with the risk factors described in the applicable prospectus supplement pertaining to the Securities and the other information contained in and incorporated by reference in this prospectus and in the applicable prospectus supplement before purchasing the Securities offered hereby. See “Where You Can Find More Information”.

We may sell the Securities to or through underwriters or dealers purchasing as principals and may also sell the Securities to one or more purchasers directly or through agents. See “Plan of Distribution”. The prospectus supplement relating to a particular offering of Securities will identify each underwriter, dealer or agent, as the case may be, engaged by us in connection with the offering and sale of Securities, and will set forth the terms of the offering of such Securities, including the method of distribution of such Securities, the public offering price, the proceeds to us, any fees, discounts or other compensation payable to underwriters, dealers or agents, and any other material terms of the plan of distribution. Securities may be sold from time to time in one or more transactions at a fixed price or fixed prices, or at non-fixed prices.

Our common shares are listed on the Toronto Stock Exchange (the “TSX”) and on the Nasdaq Capital Market (the “Nasdaq”) under the symbol “TRIL”. On March 16, 2021, the last trading day before the date of this prospectus, the closing price of the common shares on the TSX was C\$13.45 per common share, and the closing price of the common shares on the Nasdaq was US\$10.79 per common share.

Unless otherwise specified in the applicable prospectus supplement, the first preferred shares, subscription receipts, warrants and units will not be listed on any securities or stock exchange. There is no market through which the first preferred shares, subscription receipts, warrant and units may be sold and purchasers may not be able to resell such securities purchased under this prospectus and the applicable prospectus supplement. This may affect the pricing of the first preferred shares, subscription receipts, warrants and units in the secondary market, the transparency and availability of trading prices, the liquidity of the first preferred shares, subscription receipts, warrants and units and the extent of our regulation.

Our principal executive office is located at 100 CambridgePark Drive, Suite 510, Cambridge, Massachusetts, 02140, United States. We also have an office at 2488 Dunwin Drive, Mississauga, Ontario, Canada, L5L 1J9. Our registered office is located at Suite 1750-1055 W. Georgia Street, P.O. Box 11125, Vancouver, British Columbia, V6E 3P3.

Neither the United States Securities and Exchange Commission (the “SEC”) nor any state securities commission has approved or disapproved these Securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offence.

The date of this prospectus is March 18, 2021.

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ABOUT THIS PROSPECTUS

This prospectus is part of an automatic shelf registration statement on Form S-3 that we filed with the Securities and Exchange Commission, or the SEC, as a “well-known seasoned issuer” as defined in Rule 405 of the Securities Act of 1933, as amended, or the Securities Act. Under this shelf registration process, we may, from time to time, sell any combination of the Securities described in this prospectus in one or more offerings. This prospectus provides you with a general description of the Securities that we may offer. Each time we sell Securities, we will provide one or more prospectus supplements that will contain specific information about the terms of that offering of Securities. The applicable prospectus supplement may also add, update or change information contained in this prospectus. Before you invest in the Securities, you should read both this prospectus and any accompanying prospectus supplement together with additional information described under the heading “Where You Can Find More Information” beginning on page [18](#) of this prospectus.

You should rely only on the information contained in or incorporated by reference in this prospectus, the accompanying prospectus supplement or in any related free writing prospectus filed by us with the SEC. We have not authorized anyone to provide you with different information. This prospectus and the accompanying prospectus supplement do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the securities described in the accompanying prospectus supplement or an offer to sell or the solicitation of an offer to buy such securities in any circumstances in which such offer or solicitation is unlawful. You should assume that the information appearing in this prospectus, any prospectus supplement, the documents incorporated by reference and any related free writing prospectus is accurate only as of their respective dates. Our business, financial condition, results of operations and prospects may have changed materially since those dates.

Unless the context otherwise requires, all references in this prospectus and any prospectus supplement to “Trillium”, the “Company”, “we”, “us” and “our” mean Trillium Therapeutics Inc. and its consolidated subsidiaries.

In this prospectus and in any prospectus supplement, unless otherwise specified or the context otherwise requires, all dollar amounts are expressed in United States dollars, references to “dollars”, “\$” or “US\$” are to United States dollars and all references to “C\$” are to Canadian dollars.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, any applicable prospectus supplement, any related free writing prospectus and documents incorporated herein by reference herein or therein contain certain forward-looking statements or information (collectively, “forward-looking statements”) within the meaning of Section 27A of the Securities Act and Section 21E of the Securities Exchange Act of 1934, as amended, the Exchange Act and applicable Canadian securities laws, respectively. Any statements about our expectations, beliefs, plans, objectives, assumptions or future events or performance are not historical and may be forward-looking. These statements are often, but not always, made through the use of words or phrases such as “anticipate”, “believe”, “expect”, “estimate”, “may”, “will”, “could”, “leading”, “intend”, “contemplate”, “shall” and similar expressions, or the negatives of those terms. Accordingly, these statements involve estimates, assumptions, risks and uncertainties which could cause actual results to differ materially from those expressed in them. Any forward-looking statements are qualified in their entirety by reference to the factors discussed throughout this prospectus, and in particular those factors reference in the section “Risk Factors.”

This prospectus contains forward-looking statements that are based on our management’s belief and assumptions and on information currently available to our management. These statements relate to future events or our future financial performance, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Forward-looking statements in this prospectus and documents incorporated herein by reference include, but are not limited to, statements with respect to:

- our expected future loss and accumulated deficit levels;
- our projected financial position and estimated cash burn rate;
- our requirements for, and the ability to obtain, future funding on favorable terms or at all;
- our projections for the SIRPaFc development plans and progress of each of our products and technologies, particularly with respect to the timely and successful completion of studies and trials and availability of results from such studies and trials;
- our plans to focus our intravenous TTI-621 & TTI-622 programs on large hematologic malignancy indications, specifically multiple myeloma, acute myeloid leukemia, or AML, peripheral T-cell lymphoma, or PTCL, and diffuse large B-cell lymphoma, or DLBCL, as well as on solid tumors;
- our expectations about our products’ safety and efficacy;
- our expectations regarding our ability to arrange for and scale up the manufacturing of our products and technologies;
- our expectations regarding the progress, and the successful and timely completion, of the various stages of the regulatory approval process;
- our expectations about the timing of achieving milestones and the cost of our development programs;
- our observations and expectations regarding the relative low binding of SIRPaFc to red blood cells, or RBCs, compared to some anti-CD47 monoclonal antibodies and proprietary CD47 blocking agents and the potential benefits to patients;
- our expectation that TTI-621 and TTI-622 are likely to be more effective in combination with other agents;
- our plans to market, sell and distribute our products and technologies;
- our expectations about the timing of data announcements or other clinical updates;
- our expectations regarding the acceptance of our products and technologies by the market;
- our ability to retain and access appropriate staff, management and expert advisers;
- our ability to secure strategic partnerships with larger pharmaceutical and biotechnology companies;

- our expectations with respect to existing and future corporate alliances and licensing transactions with third parties, and the receipt and timing of any payments to be made by us or to us in respect of such arrangements;
- our expectations regarding the impact of the COVID-19 pandemic on our operations; and
- our strategy with respect to the protection of our intellectual property.

All forward-looking statements reflect our beliefs and assumptions based on information available at the time the assumption was made. These forward-looking statements are not based on historical facts but rather on management's expectations regarding future activities, results of operations, performance, future capital and other expenditures (including the amount, nature and sources of funding thereof), competitive advantages, business prospects and opportunities.

By its nature, forward-looking statements involve numerous assumptions, inherent risks and uncertainties, both general and specific, known and unknown, that contribute to the possibility that the predictions, forecasts, projections or other forward-looking statements will not occur or could cause actual results to differ materially from those indicated by these forward looking statements including, without limitation, the risk factors and cautionary statements described in other documents that we file from time to time with the SEC, specifically under "Item 1A. Risk Factors" and elsewhere in our most recent Annual Report on Form 10-K for the year ended December 31, 2020 and our Current Reports on Form 8-K, and the section of any accompanying prospectus supplement entitled "Risk Factors."

Any forward-looking statements in this prospectus and the documents incorporated by reference represent our estimates only as of their respective dates and should not be relied upon as representing our estimates as of any subsequent date. We undertake no obligation to update any forward-looking statement or statements to reflect events or circumstances after the date on which such statement is made or to reflect the occurrence of unanticipated events, except as may be required by applicable law.

You should read carefully the risk factors described in the documents incorporated by reference in this prospectus for a description of certain risks that could, among other things, cause actual results to differ from these forward-looking statements.

TRILLIUM THERAPEUTICS INC.

The following highlights information about us and our business contained elsewhere or incorporated by reference in this prospectus. It is not complete and does not contain all of the information that you should consider before investing in any of our securities. You should carefully read this prospectus together with the more detailed information incorporated by reference in this prospectus.

Overview

We are a clinical stage immuno-oncology company developing innovative therapies for the treatment of cancer. We have two SIRPαFc fusion proteins, TTI-621 and TTI-622, in clinical development. Both molecules target CD47, an innate immune checkpoint inhibitor that binds signal regulator protein alpha (SIRPα) and delivers the inhibitory (“don’t eat me”) signal that suppresses macrophage phagocytosis. TTI-621 and TTI-622 consist of the extracellular CD47-binding domain of human SIRPα, linked to an Fc region of a human immunoglobulin (IgG). They are designed to activate the anti-tumor activity of macrophages by blocking the inhibitory (“don’t eat me”) signal from CD47 and simultaneously delivering a pro-phagocytic (“eat”) signal through the Fc region. The two molecules differ in the identity of the Fc region. Both agents have been well tolerated and have demonstrated monotherapy activity in patients with B- and T-cell lymphomas.

Corporate Information

We were incorporated under the Business Corporations Act (Alberta) on March 31, 2004 as Neurogenesis Biotech Corp. On October 19, 2004, we amended our articles of incorporation to change our name to Stem Cell Therapeutics Corp. (“SCT”), and on November 7, 2013 SCT was continued under the Business Corporations Act (Ontario). Articles of amalgamation were filed on June 1, 2014 to amalgamate SCT with its wholly-owned subsidiary, Trillium Therapeutics Inc., and the amalgamated entity continued to operate under the name Trillium Therapeutics Inc. On December 18, 2019, we were continued under the laws of the Province of British Columbia. We are now governed under the Business Corporations Act (British Columbia) (the “BCBCA”). Additionally, on December 18, 2019, we adopted new articles which are substantially similar to our previous by-laws but for changes that were required to be made in accordance with the BCBCA.

Our principal executive office is located at the offices of our U.S. subsidiary, 100 CambridgePark Drive, Suite 510, Cambridge, Massachusetts, 02140, United States. We also have an office at 2488 Dunwin Drive, Mississauga, Ontario, Canada, L5L 1J9. Our registered office is located at Suite 1750-1055 W. Georgia Street, P.O. Box 11125, Vancouver, British Columbia, V6E 3P3. We have one wholly-owned subsidiary, Trillium Therapeutics USA Inc., which was incorporated March 26, 2015 in the State of Delaware. Our website address is www.trilliumtherapeutics.com. No portion of our website is incorporated by reference into this prospectus and you should not consider any information contained on, or that can be accessed through, our website as a part of this prospectus. We have included our website address in this prospectus solely as an inactive textual reference.

Our common shares are listed on the TSX and the Nasdaq under the symbol “TRIL”.

RISK FACTORS

Trillium's business is subject to uncertainties and risks. You should carefully consider and evaluate the risks referenced below and described in the documents incorporated by reference in this prospectus and any applicable prospectus supplement, as well as other information we include or incorporate by reference into this prospectus and any applicable prospectus supplement, before making an investment decision. This prospectus and the documents incorporated herein by reference also contain forward-looking statements that involve risks and uncertainties. Actual results could differ materially from those anticipated in these forward-looking statements as a result of certain factors, including the risks referenced below and described in the documents incorporated herein by reference, including (i) our most recent Annual Report on Form 10-K, (ii) our Quarterly Reports on Form 10-Q, and (iii) other documents we file with the SEC that are deemed incorporated by reference into this prospectus. If any event arising from these risks occurs, or if any event arising from other risks and uncertainties not presently known to Trillium or that Trillium currently deems immaterial occurs, our business, prospects, financial condition, results of operations or cash flows could be materially adversely affected. This could cause the trading price of Trillium's common shares to decline, perhaps significantly, and investors may lose part or all of their investment.

USE OF PROCEEDS

Unless otherwise indicated in the applicable prospectus supplement relating to an offering of Securities, we intend to use the net proceeds we receive from the sale of any Securities offered under this prospectus for (i) ongoing research and development activities; (ii) working capital and general corporate purposes; and (iii) investment in other development programs. Specific information about the use of net proceeds will be described in the applicable prospectus supplement relating to an offering of Securities. We may invest funds that we do not immediately require in short-term marketable securities. We have not determined the amount of net proceeds to be used specifically for such purposes. As a result, management will retain broad discretion over the allocation of net proceeds.

DESCRIPTION OF SHARE CAPITAL

The following description of our common shares and preferred shares, together with the additional information we include in any applicable prospectus supplements, summarizes the material terms and provisions of the common shares and preferred shares that we may offer under this prospectus. The following description of our capital stock does not purport to be complete and is subject to, and qualified in its entirety by, our Fourth Amended and Restated Certificate of Incorporation (our “certificate of incorporation”) and our Amended and Restated By-laws (our “by-laws” and, together with our certificate of incorporation, our “Charter Documents”), which are exhibits to the registration statement of which this prospectus forms a part, and by applicable law. The terms of our common shares and preferred shares may also be affected by applicable law.

Authorized Capital

Our authorized share capital consists of an unlimited number of common shares, Class B shares and first preferred shares, in each case without nominal or par value. As of March 16, 2021, 103,032,563 common shares were issued and outstanding, no Class B shares were issued, no Series I Non-Voting Convertible First Preferred Shares (the “Series I First Preferred Shares”) were outstanding and 6,750,000 Series II Non-Voting Convertible First Preferred Shares (the “Series II First Preferred Shares”) were issued and outstanding.

The following sets forth the terms and provisions of our existing capital. The particular terms and provisions of the common shares and/or first preferred shares offered by a prospectus supplement and the extent to which these general terms and provisions apply will be described in such prospectus supplement.

Common Shares

The holders of common shares are entitled to receive notice of and to attend all annual and special meetings of our shareholders and to one vote per share held at each such meeting, and they are entitled to receive dividends as determined and declared by our Board of Directors.

Subject to the rights of the holders of any other class of our shares entitled to receive dividends in priority to or concurrently with the holders of the common shares, our board of directors may in its sole discretion declare dividends on the common shares to the exclusion of any other class of shares of the Company.

In the event of our liquidation, dissolution or winding up or other distribution of our assets among our shareholders for the purpose of winding up our affairs, the holders of the common shares shall, subject to the rights of the holders of any other class of shares entitled to receive our assets upon such a distribution in priority to or concurrently with the holders of the common shares, be entitled to participate in the distribution. Such distribution shall be made in equal amounts per share on all the common shares at the time outstanding without preference or distinction.

Class B Shares

The holders of the Class B shares are entitled to receive notice of and to attend any meeting of our shareholders but shall not be entitled to vote any of their Class B shares at any such meeting. Each issued and fully paid Class B share may at any time be converted, at the option of the holder, into one common share.

First Preferred Shares

The first preferred shares may at any time and from time to time be issued in one or more series and our board of directors may before the issue thereof fix the number of shares in, and determine the designation, rights, privileges, restrictions and conditions attaching to the shares of, each series of first preferred shares.

The first preferred shares shall be entitled to priority over the common shares and Class B shares and all other shares ranking junior to the first preferred shares with respect to the payment of dividends and the distribution of our assets in the event of our liquidation, dissolution or winding up or other distribution of our assets among our shareholders for the purpose of winding up our affairs.

The first preferred shares of each series rank on a parity with the first preferred shares of every other series with respect to priority in the payment of dividends and in the distribution of our assets in the event of our liquidation, dissolution or winding up or other distribution of our assets among our shareholders for the purpose of winding up our affairs.

Series I First Preferred Shares

The holders of Series I Non-Voting Convertible First Preferred Shares, or the “Series I First Preferred Shares”, are not entitled to vote at any meeting of our shareholders (except in limited circumstances provided for in the BCBCA).

The holders of Series I First Preferred Shares are entitled to receive dividends as determined and declared at the discretion of our board of directors on a parity basis with the holders of shares of the other series of First Preferred Shares and, at the discretion of our board of directors, either in priority to, or equally on a share-for-share basis with, holders of our Common Shares or Class B Shares. If any amount of cumulative dividends, whether or not declared, or declared non-cumulative dividends, with respect to shares of a series of our First Preferred Shares is not paid in full, the shares of the series will participate on a pro rata basis with the shares of all other series of that class of shares with respect to all accumulated cumulative dividends, whether or not declared, and all declared non-cumulative dividends.

Each issued and fully paid Series I First Preferred Share may at any time be converted, at the option of the holder, into one thirtieth (1/30th) of a common share, subject to adjustment.

In the event of our liquidation, dissolution or winding-up, whether voluntary or involuntary, or in the event of any other distribution of our assets among our shareholders for the purpose of winding-up our affairs, or in the event of a reduction or redemption of our capital stock, the holders of Series I First Preferred Shares are entitled to receive an amount per share equal to that amount of money that we received as consideration for such Series I First Preferred Shares or, in the event that Series I First Preferred Shares were not issued for money, then the amount equal to the fair value of any property we received as consideration for the issuance of such Series I First Preferred Shares divided by the number of Series I First Preferred Shares issued, the whole before any amount shall be paid by us or any of our assets shall be distributed to holders of our common shares and Class B Shares. After such payment, the holders of Series I First Preferred Shares are not entitled to share in any further distribution of our property or assets. If any amount payable on return of capital in the event of our liquidation, dissolution or winding-up in respect of shares of a series of our First Preferred Shares is not paid in full, the shares of the series will participate on a pro rata basis with the shares of all other series of that class of shares with respect to all amounts payable on return of capital in the event of our liquidation, dissolution or winding-up.

If a Fundamental Transaction (as defined below) occurs while any of the Series I First Preferred Shares are outstanding, then a holder of Series I First Preferred Shares shall have the right to receive (in exchange for such shares) in the event that our common shares are exchanged for other securities, cash or property in the Fundamental Transaction, the same kind and amount of securities, cash and property as it would have been entitled to receive upon the occurrence of such fundamental transaction if such holder had been, immediately prior to such Fundamental Transaction, the holder of our common shares. If the holders of our common shares are given any choice as to the securities, cash or property to be received in a Fundamental Transaction, then the holder of our Series I First Preferred Shares shall be given the same choice as to the alternate consideration it receives upon any conversion of Series I First Preferred Shares following such Fundamental Transaction.

In the event of a “takeover bid” that is a “formal bid” (as such terms are defined in the securities laws in the Province of Ontario) for our common shares, the offeror of such bid shall make an offer to acquire the same percentage of our outstanding Series I First Preferred Shares as the percentage of our common shares for which the formal bid is being made, and such offer shall be on the same terms and for the same amount and kind of per share consideration, as adjusted, that is offered to the holders of our common stock under the formal bid. To the extent necessary to effectuate these provisions, to the extent the surviving corporation following a fundamental transaction is not our company, any successor or surviving entity in the fundamental transaction shall include in its organizational documents shares having the same terms and

conditions as our Series I First Preferred Shares and shall issue to the holders of our Series I First Preferred Shares new preferred shares consistent with the foregoing provisions.

“Fundamental Transaction” means (A) we effect any amalgamation, merger, business combination or other transaction with another person, other than a wholly-owned subsidiary, or an arrangement pursuant to the Business Corporations Act (Ontario) or another transaction pursuant to which a person, or group of person acting jointly or in concert, acquires all of our issued and outstanding common shares, (B) we effect any sale, lease or other disposition of all or substantially all of our assets, or (C) we effect any reclassification of our common shares or any compulsory share exchange pursuant (other than as a result of certain dividends or subdivisions) to which our common shares are effectively converted into or exchanged for other securities, cash or property, or any similar transaction or series of transactions involving us or our subsidiaries, directly or indirectly.

Series II First Preferred Shares

The holders of Series II First Preferred Shares are not entitled to vote at any meeting of our shareholders (except in limited circumstances provided for in the BCBCA).

The holders of Series II First Preferred Shares are entitled to receive dividends as determined and declared at the discretion of our board of directors on a parity basis with the holders of shares of the other series of first preferred shares and, at the discretion of our board of directors, either in priority to, or equally on a share-for-share basis with, holders of our common shares or Class B shares. If any amount of cumulative dividends, whether or not declared, or declared non-cumulative dividends, with respect to shares of a series of our first preferred shares is not paid in full, the shares of the series will participate on a pro rata basis with the shares of all other series of that class of shares with respect to all accumulated cumulative dividends, whether or not declared, and all declared non-cumulative dividends.

Each issued and fully paid Series II First Preferred Share may at any time be converted, at the option of the holder, into one common share, subject to adjustment. Notwithstanding the foregoing, holders of Series II First Preferred Shares will be prohibited from converting Series II First Preferred Shares into common shares if, as a result of such conversion, the holder, together with its affiliates, would own more than 4.99% (which the holder may elect to increase or decrease by written notice to us to any other percentage specified in such notice, provided that any increase (but not decrease) will not be effective until the 61st day after such notice) of the total number of our common shares then issued and outstanding, unless the holder gives us at least 61 days prior notice of an intent to convert into common shares that would cause the holder to own more than 4.99% of the total number of our common shares then issued and outstanding.

In addition, we will not be required to deliver to a holder any common shares upon a conversion of our Series II First Preferred Shares into common shares if our common shares are then listed and posted for trading on the TSX, or if applicable, such other stock exchange on which the common shares are principally traded, and to the extent that the conversion would result in the holder, together with any person acting jointly or in concert with the holder within the meaning of the Securities Act (Ontario), beneficially owning or exercising control or direction over common shares representing more than:

1. 9.99% of our outstanding common shares unless the holder (or, where the holder is not an individual, any director, officer or insider of the holder) has first provided:
 - (a) the stock exchange with a personal information form pursuant to the rules of that stock exchange and the form has been approved by the stock exchange; and
 - (b) a copy of the approval of the personal information form by the stock exchange to us; and
2. 19.99% of our outstanding common shares, unless we have received approval from the stock exchange and the holders of our common shares of the issuance of common shares at a meeting of holders of common shares which we will call, at our expense, in accordance with the applicable policies of the stock exchange.

In the event of our liquidation, dissolution or winding-up, whether voluntary or involuntary, or in the event of any other distribution of our assets among our shareholders for the purpose of winding-up our

affairs, or in the event of a reduction or redemption of our capital stock, the holders of Series II First Preferred Shares are entitled to receive an amount per share equal to that amount of money that we received as consideration for such Series II First Preferred Shares or, in the event that Series II First Preferred Shares were not issued for money, then the amount equal to the fair value of any property we received as consideration for the issuance of such Series II First Preferred Shares divided by the number of Series II First Preferred Shares issued, the whole before any amount shall be paid by us or any of our assets shall be distributed to holders of our common shares and Class B shares. After such payment, the holders of Series II First Preferred Shares are not entitled to share in any further distribution of our property or assets. If any amount payable on return of capital in the event of our liquidation, dissolution or winding-up in respect of shares of a series of our first preferred shares is not paid in full, the shares of the series will participate on a pro rata basis with the shares of all other series of that class of shares with respect to all amounts payable on return of capital in the event of our liquidation, dissolution or winding-up.

If a Fundamental Transaction occurs while any of the Series II First Preferred Shares are outstanding, then a holder of Series II First Preferred Shares shall have the right to receive (in exchange for such shares) in the event that our common shares are exchanged for other securities, cash or property in the Fundamental Transaction, the same kind and amount of securities, cash and property as it would have been entitled to receive upon the occurrence of such Fundamental Transaction if such holder had been, immediately prior to such Fundamental Transaction, the holder of our common shares. If the holders of our common shares are given any choice as to the securities, cash or property to be received in a Fundamental Transaction, then the holder of our Series II First Preferred Shares shall be given the same choice as to the alternate consideration it receives upon any conversion of Series II First Preferred Shares following such Fundamental Transaction.

In the event of a “takeover bid” that is a “formal bid” (as such terms are defined under applicable securities laws in the Province of Ontario) for our common shares, the offeror of such bid shall make an offer to acquire the same percentage of our outstanding Series II First Preferred Shares as the percentage of our common shares for which the formal bid is being made, and such offer shall be on the same terms and for the same amount and kind of per share consideration, as adjusted, that is offered to the holders of our common stock under the formal bid.

To the extent necessary to effectuate these provisions, to the extent the surviving corporation following a Fundamental Transaction is not our company, any successor or surviving entity in the Fundamental Transaction shall include in its organizational documents shares having the same terms and conditions as our Series II First Preferred Shares and shall issue to the holders of our Series II First Preferred Shares new preferred shares consistent with the foregoing provisions.

Transfer Agent and Registrar

Our registrar and transfer agent is Computershare Trust Company of Canada, located at 100 University Avenue, Toronto, Ontario, M5J 2Y1.

DESCRIPTION OF SUBSCRIPTION RECEIPTS

Subscription receipts may be offered separately or together with common shares, first preferred shares or warrants. The subscription receipts will be issued under one or more subscription receipt agreements that will be entered into by Trillium and an escrow agent at the time of issuance of the subscription receipts.

A subscription receipt will entitle the holder thereof to receive a common share, first preferred share or warrant of Trillium, for no additional consideration, upon the completion of a particular transaction or event, typically an acquisition of the assets or securities of another entity by Trillium or one or more of its subsidiaries. The subscription proceeds from an offering of subscription receipts will be held in escrow by an escrow agent pending the completion of the transaction or the termination time (the time at which the escrow terminates regardless of whether the transaction or event has occurred). Holders of subscription receipts will receive common shares, first preferred shares or warrants of Trillium upon the completion of the particular transaction or event or, if the transaction or event does not occur by the termination time, a return of the subscription funds for their subscription receipts together with any interest or other income earned thereon, as determined by the terms of the applicable escrow.

Holders of subscription receipts are not shareholders of Trillium. The particular terms and provisions of subscription receipts offered by any prospectus supplement, and the extent to which the general terms and provisions described below may apply to them, will be described in the prospectus supplement filed in respect of such subscription receipts. This description will include, where applicable: (i) the number of subscription receipts offered; (ii) the price at which the subscription receipts will be offered; (iii) the terms, conditions and procedures pursuant to which the holders of subscription receipts will become entitled to receive common shares, first preferred shares or warrants; (iv) the number of common shares, first preferred shares or warrants that may be obtained upon exercise of each subscription receipt; (v) the designation and terms of any other securities with which the subscription receipts will be offered, if any, and the number of subscription receipts that will be offered with each such security; (vi) the terms relating to the holding and release of the gross proceeds from the sale of the subscription receipts plus any interest and income earned thereon; (vii) the material income tax consequences of owning, holding and disposing of the subscription receipts; and (viii) any other material terms and conditions of the subscription receipts including, without limitation, transferability and adjustment terms and whether the subscription receipts will be listed on a stock exchange.

DESCRIPTION OF WARRANTS

Warrants will typically be offered with common shares and/or first preferred shares, with such securities often referred to collectively as a “unit”, but may be offered with subscription receipts or separately and may be attached to or separate from other Securities.

Holders of warrants are not shareholders of Trillium. The particular terms and provisions of warrants offered by any prospectus supplement, and the extent to which the general terms and provisions described below may apply to them, will be described in the prospectus supplement filed in respect of such warrants. This description will include, where applicable: (i) the title or designation of the warrants; (ii) the number of warrants offered; (iii) the number of common shares or first preferred shares of Trillium purchasable upon exercise of the warrants and the procedures for exercise; (iv) the exercise price of the warrants; (v) the dates or periods during which the warrants are exercisable and when they expire; (vi) the designation and terms of any other securities with which the warrants will be offered, if any, and the number of warrants that will be offered with each such security; (vii) the material income tax consequences of owning, holding and disposing of the warrants; and (viii) any other material terms and conditions of the warrants including, without limitation, transferability and adjustment terms and whether the warrants will be listed on a stock exchange.

We reserve the right to set forth in a prospectus supplement specific terms of the warrants that are not within the parameters set forth in this prospectus. In addition, to the extent that any particular terms of the warrants described in a prospectus supplement differ from any of the terms described in this prospectus, the description of such terms set forth in this prospectus shall be deemed to have been superseded by the description of such differing terms set forth in such prospectus supplement with respect to such warrants.

DESCRIPTION OF UNITS

Trillium may issue units comprised of one or more of the other Securities described in this prospectus in any combination. Each unit will be issued so that the holder of the unit is also the holder of each Security included in the unit. Thus, the holder of a unit will have the rights and obligations of a holder of each included Security. The unit agreement under which a unit is issued may provide that the Securities included in the unit may not be held or transferred separately, at any time or at any time before a specified date.

The particular terms and provisions of units offered by any prospectus supplement, and the extent to which the general terms and provisions described below may apply to them, will be described in the prospectus supplement filed in respect of such units. This description will include, where applicable: (i) the designation and terms of the units and of the Securities comprising the units, including whether and under what circumstances those Securities may be held or transferred separately; (ii) any provisions for the issuance, payment, settlement, transfer or exchange of the units or of the Securities comprising the units; (iii) whether the units will be issued in fully registered or global form; and (iv) any other material terms and conditions of the units.

We reserve the right to set forth in a prospectus supplement specific terms of the units that are not within the parameters set forth in this prospectus. In addition, to the extent that any particular terms of the units described in a prospectus supplement differ from any of the terms described in this prospectus, the description of such terms set forth in this prospectus shall be deemed to have been superseded by the description of such differing terms set forth in such prospectus supplement with respect to such units.

CERTAIN INCOME TAX CONSIDERATIONS

The applicable prospectus supplement will describe certain U.S. federal income tax consequences of the acquisition, ownership and disposition of any Securities offered thereunder by an initial investor who is a U.S. person (within the meaning of the U.S. Internal Revenue Code).

The applicable prospectus supplement will also describe certain Canadian federal income tax consequences to an investor of acquiring any Securities offered thereunder, including, for investors who are non-residents of Canada, whether the payment of dividends or distributions, if any, on the Securities will be subject to Canadian non-resident withholding tax.

PLAN OF DISTRIBUTION

We may offer and sell Securities to or through underwriters or dealers and also may sell Securities directly to purchasers or through agents. The Securities may be offered and sold in the United States and elsewhere where permitted by law.

The distribution of Securities may be effected from time to time in one or more transactions:

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

If offered on a non-fixed price basis, Securities may be offered at market prices prevailing at the time of sale or at prices to be negotiated with purchasers at the time of sale, which prices may vary as between purchasers and during the period of distribution and which may include sales of our common shares in transactions that are deemed to be “at-the-market” distributions, including sales made directly on the TSX and the Nasdaq or other existing trading markets for our common shares, and as may be set forth in an accompanying prospectus supplement. If Securities are offered on a non-fixed price basis, the underwriters’, dealers’ or agents’ compensation will be increased or decreased by the amount by which the aggregate price paid for Securities by the purchasers exceeds or is less than the gross proceeds paid to us by the underwriters, dealers or agents.

Subject to any applicable securities legislation, and other than in relation to an “at-the-market” distribution, in connection with any offering of Securities, the underwriters, dealers or agents may over-allot or effect transactions which stabilize, maintain or otherwise affect the market price of the Securities at a level above that which otherwise might prevail on the open market. Such transactions may be commenced, interrupted or discontinued at any time.

In connection with the sale of Securities, underwriters may receive compensation from us or from purchasers of Securities for whom they may act as agents in the form of concessions or commissions. Underwriters, dealers and agents that participate in the distribution of Securities may be deemed to be underwriters and any commissions received by them from us and any profit on the resale of Securities by them may be deemed to be underwriting commissions under the Securities Act.

The applicable prospectus supplement will also set forth the terms of the offering relating to particular Securities, including to the extent applicable, the initial offering price, our proceeds from the offering, the underwriting concessions or commissions, and any other discounts or concessions to be allowed or reallocated to dealers. Underwriters with respect to the particular Securities sold to or through underwriters will be named in the prospectus supplement relating to such Securities.

Under agreements which may be entered into by us, underwriters, dealers and agents who participate in the distribution of Securities may be entitled to indemnification by us against certain liabilities, including liabilities under the Securities Act, or to contributions with respect to payments which such underwriters, dealers or agents may be required to make in respect thereof. The underwriters, dealers and agents with whom we enter into agreements may be customers of, engage in transactions with or perform services for us in the ordinary course of business.

Any offering of first preferred shares, subscription receipts, warrants or units will be a new issue of securities with no established trading market. Unless otherwise specified in a prospectus supplement, the first preferred shares, subscription receipts, warrants or units will not be listed on any securities exchange or on any automated dealer quotation system. This may affect the pricing of the first preferred shares, subscription receipts, warrants or units in the secondary market, the transparency and availability of trading prices, the liquidity of the first preferred shares, subscription receipts, warrants or units and the extent of issuer regulation. Certain broker-dealers may make a market in the first preferred shares, subscription receipts, warrants or units, but will not be obligated to do so and may discontinue any market making at any time without notice. We cannot assure you that any broker-dealer will make a market in the first preferred shares, subscription receipts, warrants or units of any series or as to the liquidity of the trading market, if any, for such securities.

LEGAL MATTERS

Unless otherwise indicated in any supplement to this prospectus, certain legal matters with respect to United States will be passed upon for us by Goodwin Procter LLP, Boston, MA. Unless otherwise indicated in any supplement to this prospectus, certain legal matters with respect to Canadian law, including in connection with the validity of the offered securities, will be passed upon for us by Baker & McKenzie LLP, Toronto, Ontario. Additional legal matters may be passed upon for any underwriters, dealers or agents by counsel that we will name in the applicable prospectus supplement.

EXPERTS

The consolidated financial statements of Trillium Therapeutics Inc. included in our Annual Report on Form 10-K for the year ended December 31, 2020, have been audited by Ernst & Young LLP, independent registered public accounting firm as set forth in their report, thereon, included therein, and incorporated herein by reference in this prospectus and elsewhere in the registration statement of which this prospectus forms a part. Such consolidated financial statements are incorporated herein by reference in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

ENFORCEABILITY OF CIVIL LIABILITIES

We are a corporation incorporated under and governed by the BCBCA. Some of our officers and directors are Canadian residents, and many of our assets or the assets of our officers and directors are located outside the United States. We have appointed an agent for service of process in the United States, but it may be difficult for holders of Securities who reside in the United States to effect service within the United States upon those directors, officers who are not residents of the United States. It may also be difficult for holders of Securities who reside in the United States to realize in the United States upon judgments of courts of the United States predicated upon our civil liability and the civil liability of our officers and directors under the United States federal securities laws. We have been advised by our Canadian counsel, Baker & McKenzie LLP, that a judgment of a United States court predicated solely upon civil liability under U.S. federal securities laws would probably be enforceable in Canada if the United States court in which the judgment was obtained has a basis for jurisdiction in the matter that would be recognized by a Canadian court for the same purposes and if certain other conditions are met. We have also been advised by Baker & McKenzie LLP, however, that there is substantial doubt whether an action could be brought in Canada in the first instance on the basis of liability predicated solely upon U.S. federal securities laws.

WHERE YOU CAN FIND MORE INFORMATION

We are subject to the informational requirements of the United States Securities Exchange Act of 1934, as amended (the “Exchange Act”) and, in accordance with the Exchange Act, we also file reports with and furnish other information to the SEC. These documents can be accessed through the SEC’s Electronic Document Gathering, Analysis, and Retrieval system (“EDGAR”), via electronic means, including the SEC’s home page on the Internet (www.sec.gov). Copies of certain information filed by us with the SEC are also available on our website at www.trilliumtherapeutics.com. The information contained on our website is not incorporated by reference into this registration statement and, therefore, is not part of this registration statement or any accompanying prospectus supplement.

Additionally, we file documents with securities commissions or similar authorities in the provinces of British Columbia, Alberta, Manitoba, Ontario, Nova Scotia in Canada. These documents are available through the internet on the Canadian System for Electronic Document Analysis and Retrieval (“SEDAR”), which can be accessed at www.sedar.com.

INCORPORATION BY REFERENCE

The SEC allows us to incorporate by reference certain information and reports that we file with it, which means that we can disclose important information to you by referring you to those documents. Information that is incorporated by reference is an important part of this prospectus and information that we file later with the SEC will automatically update and supersede the information already incorporated by reference. We incorporate by reference the documents listed below, which were filed with the SEC (SEC File No. 001-36596), and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, including all filings made after the date of the filing of this registration statement, except as to any portion of any future report or document that is not deemed filed under such provisions until we sell all of the securities:

- [Our Annual Report on Form 10-K for the fiscal year ended December 31, 2020, filed with the SEC on March 18, 2021, including the description of common shares filed as an exhibit thereto.](#)

We also incorporate by reference each of the following documents we file with the SEC after the date of this prospectus and prior to the filing of a post-effective amendment that indicates that all Securities offered hereby have been sold or which deregisters all Securities then remaining unsold: (i) all annual reports on Form 10-K; (ii) all quarterly reports on Form 10-Q; (iii) and all current reports on Form 8-K.

Any statement contained in this prospectus or in a document (or part thereof) incorporated by reference, or deemed to be incorporated by reference, in this prospectus shall be deemed to be modified or superseded, for purposes of this prospectus, to the extent that a statement contained in the prospectus or in any subsequently filed document (or part thereof) that also is, or is deemed to be, incorporated by reference in this prospectus modifies or replaces such statement. Any statement so modified or superseded shall not be deemed, except as so

modified or superseded, to constitute part of this prospectus. The modifying or superseding statement need not state that it has modified or superseded a prior statement or include any other information set forth in the document which it modifies or supersedes.

You may obtain a copy of any of any filings that are incorporated by reference into this prospectus, at no cost, by writing to or telephoning us at the following address:

Trillium Therapeutics Inc.
100 CambridgePark Drive, Suite 510
Cambridge, Massachusetts 02140
United States
(857) 412-7029
Attention: Corporate Secretary

All shelf information permitted under applicable law to be omitted from this prospectus will be contained in one or more prospectus supplements that will be delivered to purchasers together with this prospectus. A prospectus supplement or prospectus supplements containing the specific terms for an issue of Securities will be delivered to purchasers of such Securities together with this prospectus and will be deemed to be incorporated by reference into this prospectus as of the date of such prospectus supplement but only for the purposes of the Securities issued thereunder.



Common Shares
First Preferred Shares
Subscription Receipts
Warrants
Units

PROSPECTUS

March 18, 2021

PART II

INFORMATION NOT REQUIRED IN PROSPECTUS

Item 8. Indemnification

We are subject to the provisions of Part 5, Division 5, of the BCBCA. Under Section 160 of the BCBCA, we may, subject to Section 163 of the BCBCA:

1. indemnify an individual who:
 - a. is or was a director or officer of our company;
 - b. is or was a director or officer of another corporation (i) at a time when such corporation is or was an affiliate of our company; or (ii) at our request or,
 - c. at our request, is or was, or holds or held a position equivalent to that of, a director or officer of a partnership, trust, joint venture or other unincorporated entity, and including, subject to certain limited exceptions, the heirs and personal or other legal representatives of that individual (collectively, an “eligible party”), against all eligible penalties to which the eligible party is or may be liable; and
2. after final disposition of an eligible proceeding, pay the expenses actually and reasonably incurred by an eligible party in respect of that proceeding where:
 - a. “eligible penalty” means judgement, penalty or fine awarded or imposed in, or an amount paid in settlement of, an eligible proceeding.
 - b. “eligible proceeding” means a proceeding in which an eligible party or any of the heirs and personal or other legal representatives of the eligible party, by reason of the eligible party being or having been a director or officer of, or holding or having held a position equivalent to that of a director or officer of, our company or an associated corporation (i) is or may be joined as a party, or (ii) is or may be liable for or in respect of a judgment, penalty or fine in, or expenses related to, the proceeding.
 - c. “proceeding” includes any legal proceeding or investigative action, whether current, threatened, pending or completed.

Under Section 161 of the BCBCA, and subject to Section 163 of the BCBCA, we must, after the final disposition of an eligible proceeding, pay the expenses actually and reasonably incurred by an eligible party in respect of that proceeding if the eligible party (i) has not been reimbursed for those expenses, and (ii) is wholly successful, on the merits or otherwise, in the outcome of the proceeding or is substantially successful on the merits in the outcome of the proceeding.

Under Section 162 of the BCBCA, and subject to Section 163 of the BCBCA, we may pay, as they are incurred in advance of the final disposition of an eligible proceeding, the expenses actually and reasonably incurred by an eligible party in respect of the proceeding, provided that we must not make such payments unless we first receive from the eligible party a written undertaking that, if it is ultimately determined that the payment of expenses is prohibited under Section 163 of the BCBCA, the eligible party will repay the amounts advanced.

Under Section 163 of the BCBCA, we must not indemnify an eligible party against eligible penalties to which the eligible party is or may be liable or pay the expenses of an eligible party in respect of that proceeding under Sections 160, 161 or 162 of the BCBCA, as the case may be, if any of the following circumstances apply:

- a. if the indemnity or payment is made under an earlier agreement to indemnify or pay expenses and, at the time that the agreement to indemnify or pay expenses was made, we were prohibited from giving the indemnity or paying the expenses by our memorandum or articles;
- b. if the indemnity or payment is made otherwise than under an earlier agreement to indemnify

or pay expenses and, at the time that the indemnity or payment is made, we are prohibited from giving the indemnity or paying the expenses by our memorandum or articles;

- c. if, in relation to the subject matter of the eligible proceeding, the eligible party did not act honestly and in good faith with a view to the best interests of our company or the associated corporation, as the case may be; or
- d. in the case of an eligible proceeding other than a civil proceeding, if the eligible party did not have reasonable grounds for believing that the eligible party's conduct in respect of which the proceeding was brought was lawful.

If an eligible proceeding is brought against an eligible party by or on behalf of us or by or on behalf of an associated corporation, we must not either indemnify the eligible party against eligible penalties to which the eligible party is or may be liable, or pay the expenses of the eligible party under Sections 160, 161 or 162 of the BCBCA, as the case may be, in respect of the proceeding.

Under Section 164 of the BCBCA, and despite any other provision of Part 5, Division 5 of the BCBCA and whether or not payment of expenses or indemnification has been sought, authorized or declined under Part 5, Division 5 of the BCBCA, on application of our company or an eligible party, the Supreme Court of British Columbia may do one or more of the following:

- a. order us to indemnify an eligible party against any liability incurred by the eligible party in respect of an eligible proceeding;
- b. order us to pay some or all of the expenses incurred by an eligible party in respect of an eligible proceeding;
- c. order the enforcement of, or payment under, an agreement of indemnification entered into by us;
- d. order us to pay some or all of the expenses actually and reasonably incurred by any person in obtaining an order under Section 164 of the BCBCA; or
- e. make any other order the court considers appropriate.

Under our articles, and subject to the BCBCA, we must indemnify our director, former director or alternate director and his or her heirs and legal personal representatives against all eligible penalties to which such person is or may be liable, and we must, after the final disposition of an eligible proceeding, pay the expenses actually and reasonably incurred by such person in respect of that proceeding. Each of our directors and alternate directors are deemed to have contracted with us on the terms of the indemnity contained in our articles. Under our articles, and subject to the BCBCA, we may also indemnify any other person.

We have entered into indemnification agreements ("Indemnification Agreements") with each of our officers and directors, pursuant to which we are obligated to indemnify and hold harmless such persons to the greatest extent permitted by law for liabilities arising out of their service to the company as directors and officers. However, such indemnification obligations arise only to the extent that the party seeking indemnification was acting honestly and in good faith with a view to our best interests, and, in the case of criminal or administrative actions or other non-civil proceedings that are enforced by monetary penalties, that such person had reasonable grounds for believing that his or her conduct was lawful. Under these Indemnification Agreements, we may advance to the indemnified parties the expenses incurred in defending any such actions or proceedings.

We have also purchased directors' and officers' liability insurance for the benefit of our directors and officers, to back up our indemnification of them against liability incurred in their capacity as directors and officers, subject to certain limitations under applicable law.

Insofar as indemnification for liabilities arising under the Securities Act, may be permitted to directors, officers or persons controlling Trillium pursuant to the foregoing provisions, Trillium has been informed that

in the opinion of the Commission such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

Reference is made to Item 10 for the undertakings of the Registrant with respect to indemnification for liabilities arising under the Securities Act.

Item 9. Exhibits

(a) EXHIBITS: The following exhibits have been filed as part of this Registration Statement:

Exhibit Number	Description
1.1†	Form of Underwriting Agreement.
4.1*	Articles of the Registrant.
4.2†	Specimen First Preferred Share Certificate.
4.3†	Form of Subscription Receipt Agreement.
4.4†	Form of Warrant Agreement.
4.5†	Form of Unit Agreement.
5.1	Opinion of Baker & McKenzie LLP.
23.1	Consent of Ernst & Young LLP.
23.2	Consent of Baker & McKenzie LLP (included in Exhibit 5.1 above).
24.1	Powers of Attorney (included on the signature page to the Registration Statement).

* Previously filed as Exhibit 99.1 to the Company's Form 6-K filed on April 23, 2020.

† To be filed as an exhibit to a post-effective amendment to this Registration Statement or as an exhibit to a report filed on Form 6-K or Form 8-K under the Securities Exchange Act of 1934 and incorporated herein by reference.

Item 10. 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 this 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 this 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 Commission pursuant to Rule 424(b), if, in the aggregate, the changes in volume and price represent no more than a 20% change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective Registration Statement; and
 - (iii) to include any material information with respect to the plan of distribution not previously disclosed in this Registration Statement or any material change to such information in this Registration Statement;

provided, however, that paragraphs (a)(1)(i), (a)(1)(ii) and (a)(1)(iii) above do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the Commission by the Registrant pursuant to section 13 or section 15(d) of the U.S. Exchange Act that are incorporated by reference in the Registration Statement, or is contained in the 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.
- (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 this Registration Statement as of the date the filed prospectus was deemed part of and included in this 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 this 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 this Registration Statement relating to the securities in this Registration Statement to which that 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 this Registration Statement or made in a document incorporated or deemed incorporated by reference into this Registration Statement or prospectus that is part of this 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 this Registration Statement or prospectus that was part of this Registration Statement or made in any such document immediately prior to such effective date.
- (5) That, for the purpose of determining liability of the Registrant under the Securities Act to any purchaser in the initial distribution of the securities, the undersigned Registrant undertake that in a primary offering of securities of the undersigned Registrant pursuant to this Registration Statement, regardless of the underwriting method used to sell the securities to the purchaser, if the securities are offered or sold to such purchaser by means of any of the following communications, the undersigned Registrant will be a seller to the purchaser and will be considered to offer or sell such securities to such purchaser:
 - (i) Any preliminary prospectus or prospectus of the undersigned Registrant relating to the offering required to be filed pursuant to Rule 424;
 - (ii) Any free writing prospectus relating to the offering prepared by or on behalf of the undersigned Registrant or used or referred to by the undersigned Registrant;
 - (iii) The portion of any other free writing prospectus relating to the offering containing material information about the undersigned Registrant or its securities provided by or on behalf of the undersigned Registrant; and
 - (iv) Any other communication that is an offer in the offering made by the undersigned Registrant to the purchaser.
- (b) The undersigned Registrant hereby 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 have been advised that in the opinion of the Commission 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 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.

Item 14. Other Expenses of Issuance and Distribution

The expenses payable by Trillium Therapeutics Inc. (the “Registrant” or the “Company”) in connection with the issuance and distribution of the securities being registered (other than underwriting discounts and commissions, if any) are set forth below. Each item listed is estimated, except for the Securities and Exchange Commission (the “SEC”) registration fee.

Securities and Exchange Commission registration fee	\$	*
Legal fees and expenses		**
Accounting fees and expenses		**
Printing fees and expenses		**
Transfer agent and trustee fees		**
Miscellaneous		**
Total	\$	**

* In accordance with Rules 456(b) and 457(r), we are deferring payment of the registration fee for the securities offered under this registration statement.

** These fees and expenses depend on the securities offered and the number of issuances and accordingly cannot be estimated at this time.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, as amended, Trillium Therapeutics Inc. 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 Mississauga, Ontario, Canada, on this 18th day of March 2021.

TRILLIUM THERAPEUTICS INC.

By: /s/ James Parsons

Name: James Parsons

Title: Chief Financial Officer

POWERS OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each officer or director of Trillium Therapeutics Inc. whose signature appears below constitutes and appoints Jan Skvarka and James Parsons, and each of them, with full power to act without the other, his or her true and lawful attorneys-in-fact and agents, with full and several power of substitution, for him or her and in his or her name, place and stead, in any and all capacities, to sign any or all amendments, including post-effective amendments, and supplements 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 full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as they or he or she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents or his or her or their substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act, this Registration Statement has been signed below by or on behalf of the following persons in the capacities indicated on March 18, 2021.

<u>Signature</u>	<u>Capacity</u>	<u>Date</u>
<u>/s/ Jan Skvarka</u> Jan Skvarka	President, Chief Executive Officer and Director (Principal Executive Officer)	March 18, 2021
<u>/s/ James Parsons</u> James Parsons	Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer)	March 18, 2021
<u>/s/ Robert Kirkman</u> Robert Kirkman	Chairman of the Board of Directors	March 18, 2021
<u>/s/ Luke Beshar</u> Luke Beshar	Director	March 18, 2021
<u>/s/ Michael Kamarck</u> Michael Kamarck	Director	March 18, 2021
<u>/s/ Paolo Pucci</u> Paolo Pucci	Director	March 18, 2021
<u>/s/ Thomas Reynolds</u> Thomas Reynolds	Director	March 18, 2021
<u>/s/ Helen Tayton-Martin</u> Helen Tayton-Martin	Director	March 18, 2021
<u>/s/ Paul Walker</u> Paul Walker	Director	March 18, 2021

AUTHORIZED REPRESENTATIVE

Pursuant to the requirements of Section 6(a) of the Securities Act of 1933, as amended, the Authorized Representative has duly caused this Registration Statement to be signed on its behalf by the undersigned, solely in its capacity as the duly authorized representative of Trillium Therapeutics Inc. in the United States, on this 18 day of March 2021.

TRILLIUM THERAPEUTICS USA INC.

By: /s/ Jan Skvarka

Name: Jan Skvarka

Title: President

EXHIBITS

Exhibit Number	Description
1.1†	Form of Underwriting Agreement.
4.1*	Articles of the Registrant.
4.2†	Specimen First Preferred Share Certificate.
4.3†	Form of Subscription Receipt Agreement.
4.4†	Form of Warrant Agreement.
4.5†	Form of Unit Agreement.
5.1	Opinion of Baker & McKenzie LLP.
23.1	Consent of Ernst & Young LLP.
23.2	Consent of Baker & McKenzie LLP (included in Exhibit 5.1 above).
24.1	Powers of Attorney (included on the signature page to the Registration Statement).
*	Previously filed as an exhibit to the Company's Form 6-K filed on April 23, 2020.
†	To be filed as an exhibit to a post-effective amendment to this Registration Statement or as an exhibit to a report filed on Form 8-K under the Securities Exchange Act of 1934 and incorporated herein by reference.



Asia Pacific
Bangkok
Beijing
Brisbane
Hanoi
Ho Chi Minh City
Hong Kong
Jakarta
Kuala Lumpur*
Manila*
Melbourne
Seoul
Shanghai
Singapore
Sydney
Taipei
Tokyo
Yangon

Europe, Middle East & Africa
Abu Dhabi

Almaty
Amsterdam
Antwerp
Bahrain
Baku
Barcelona
Berlin
Brussels
Budapest
Cairo
Casablanca
Doha
Dubai
Dusseldorf
Frankfurt/Main
Geneva
Istanbul
Jeddah*
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Kyiv
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Palo Alto
Porto Alegre**
Rio de Janeiro**
San Francisco
Santiago
Sao Paulo**
Tijuana
Toronto
Valencia
Washington, DC

* Associated Firm

** In cooperation with Trench, Rossi & Watanabe Advogados

Baker & McKenzie LLP
Barristers & Solicitors

Brookfield Place
Bay/Wellington Tower
181 Bay Street, Suite 2100
Toronto, ON M5J 2T3
Canada

Tel: +1 416 863 1221
Fax: +1 416 863 6275
www.bakermckenzie.com

March 18, 2021

Trillium Therapeutics Inc.
2488 Dunwin Drive
Mississauga, Ontario L5L 1J9

Dear Sirs/Mesdames:

Re: Trillium Therapeutics Inc. – Registration Statement on Form S-3

We have acted as Canadian counsel to Trillium Therapeutics Inc. (the “**Corporation**”), a corporation existing under the laws of the Province of British Columbia, in connection with the preparation and filing with the United States Securities and Exchange Commission (the “**Commission**”) of a Registration Statement (the “**Registration Statement**”) on Form S-3 under the *United States Securities Act of 1933*, as amended (the “**Act**”). The Registration Statement registers the issuance and sale of the Corporation’s common shares (“**Common Shares**”), First Preferred shares (“**First Preferred Shares**”), warrants to purchase other Securities (“**Warrants**”), units, comprised of one or more other Securities, in any combination (“**Units**”), and subscription receipts convertible into other Securities (“**Subscription Receipts**” and together with the Common Shares, First Preferred Shares, Warrants and Units, the “**Securities**”), all of which may be issued from time to time on a delayed or continuous basis pursuant to Rule 415 under the Act.

The Registration Statement includes a prospectus (the “**Prospectus**”), which provides that it will be supplemented in the future by one or more prospectus supplements.

We are qualified to express opinions with respect to the laws of the Province of Ontario and the federal laws of Canada applicable therein. However, we are entitled, under the National Mobility Agreement of the Federation of Law Societies (the “**National Mobility Agreement**”), to provide an opinion with respect to the laws of the provinces of Canada, other than Ontario, and insofar as the laws of the Province of British Columbia apply to this opinion, we have provided this opinion under the National Mobility Agreement only.

As Canadian counsel for the Corporation, we have examined a copy of the Registration Statement and the Prospectus. We have also considered such questions of law, examined such statutes, regulations, corporate documents, records and certificates, opinions and instruments and have made such other investigations as we have considered necessary or desirable in connection with the opinions hereinafter set forth including, without limitation, a certificate of an officer of the Corporation (the “**Corporate Certificate**”) dated the date hereof addressed to Baker & McKenzie LLP, with respect to certain factual matters.

We have relied upon the Corporate Certificate with respect to the accuracy of the factual matters contained in the Corporate Certificate, which matters have not been independently investigated or verified by us, and we have assumed that all factual statements made in the Corporate Certificate are complete, true and accurate as of the date of this opinion letter. To the extent that the Corporate Certificate, and any other certificate or document referenced herein, is based on any assumption, given in reliance on any other certificate or document, understanding or other criteria or is made subject to any limitation, qualification or exception, our opinions are also so based, given on such reliance and is so made subject.

In connection with our opinions, we have assumed (i) all information contained in all documents reviewed by us is true and correct, (ii) the genuineness of all signatures on all documents reviewed by us, (iii) the authenticity and completeness of all documents submitted to us as originals, (iv) the conformity to authentic originals of all documents submitted to us as certified or photostatic copies, (v) each natural person signing any document reviewed by us had the legal capacity to do so, none of which facts we have independently verified, (vi) no order, ruling or decision of any court or regulatory or administrative body is in effect at any relevant time that restricts the issuance of the Securities, (vii) there is no foreign law that would affect the opinion expressed herein, and (viii) at the time of the execution and delivery of any documents relating to the Securities or the offering thereof, to the extent such documents purport to constitute agreements, such documents constitute valid and binding obligations of such parties. We also have assumed the due authorization, execution and delivery of all documents where authorization, execution and delivery are prerequisites to the effectiveness of such documents.

We have also assumed that at all relevant times:

1. the Corporation has the necessary corporate power and capacity to execute, deliver and perform its obligations under the terms and conditions of any purchase, underwriting or other agreement, indenture or instrument relating to the Corporation's creation, authentication, issuance, sale and/or delivery of the Securities to which the Corporation is party (any such agreements, collectively, the "**Agreement**");
2. the Corporation has the necessary corporate power and capacity to authorize, create, authenticate, validly issue, sell and deliver the Securities and perform its obligations under the terms and conditions of the Securities;
3. all necessary corporate action has been taken by the Corporation to duly authorize the execution and delivery by the Corporation of the Agreement and the performance of its obligations under the terms and conditions thereof;
4. all necessary corporate action has been taken by the Corporation to duly authorize, create, authenticate, sell, deliver and validly issue the Securities and to perform its obligations under the terms and conditions of the Securities, and all of the terms and conditions relevant to the execution, delivery and issuance of the Securities in the applicable Agreement have been complied with;
5. all necessary corporate action has been taken by the Corporation to duly authorize the terms of the offering of the Securities and related matters;
6. the Agreement (i) has been duly authorized, executed and delivered by all parties thereto and such parties have the capacity to do so; (ii) constitutes a legal, valid and binding obligation of all parties thereto; (iii) is enforceable in accordance with its terms against all parties thereto; and (iv) is governed by the laws of the Province of Ontario;
7. the Securities have been duly authorized, created, authenticated, sold and delivered and validly issued by the Corporation and any other person signing or authenticating the Securities, as applicable;
8. the terms of the offering of the Securities and related matters have been duly authorized by the Corporation;

9. the execution and delivery of the Agreement and the performance by the Corporation of its obligations under the terms and conditions thereunder do not and will not conflict with and do not and will not result in a breach of or default under, and do not and will not create a state of facts which, after notice or lapse of time or both, will conflict with or result in a breach of or default under any of the terms or conditions of the notice of articles or articles of the Corporation, any resolutions of the board of directors or shareholders of the Corporation, any agreement or obligation of the Corporation, or applicable law;
10. the authorization, creation, authentication, sale, delivery and issuance of the Securities and the Corporation's performance of its obligations under the terms and conditions of the Securities do not and will not conflict with and do not and will not result in a breach of or default under, and do not and will not create a state of facts which, after notice or lapse of time or both, will conflict with or result in a breach of or default under any of the terms or conditions of the notice of articles or articles of the Corporation, any resolutions of the board of directors or shareholders of the Corporation, any agreement or obligation of the Corporation, or applicable law; and
11. the terms of the offering of the Securities and related matters do not and will not conflict with and do not and will not result in a breach of or default under, and do not and will not create a state of facts which, after notice or lapse of time or both, will conflict with or result in a breach of or default under any of the terms or conditions of the notice of articles or articles of the Corporation, any resolutions of the board of directors or shareholders of the Corporation, any agreement or obligation of the Corporation, or applicable law.

Based upon the foregoing, and subject to the qualifications, assumptions and limitations stated herein, we are of the opinion that, upon payment for the applicable Securities provided for in the applicable Agreement and when issued, sold and delivered in accordance with such Agreement, (i) the Common Shares and the First Preferred Shares will be validly issued, fully paid and non-assessable shares in the capital of the Corporation, and (ii) the Subscription Receipts, the Warrants and the Units will be validly created and issued securities of the Corporation and will be binding obligations of the Corporation.

This opinion letter is furnished solely for the benefit of the addressee in connection with the filing of the Registration Statement with the Commission and is not to be transmitted to any other person, nor is it to be relied upon by any other person or used for any other purpose or referred to in any public document or filed with any government agency or other person without our prior express consent. Our opinions are given as of the date of this opinion letter. Among other things, our opinions do not take into account any circumstance (including changes in law or facts or the conduct of any of the relevant parties) that may occur after that date. We assume no obligation to update or supplement any of the opinions set forth herein to reflect any changes of law or fact that may occur.

We hereby consent to the filing of this opinion letter as Exhibit 5.1 to the Registration Statement and to the use of our name on the cover page and under the captions "Legal Matters" and "Enforceability of Civil Liabilities" in the Prospectus. In giving such consent, we do not thereby admit that we come within the category of persons whose consent is required by the Act or the rules and regulations promulgated thereunder.

Yours very truly,

/s/ Baker & McKenzie LLP

Consent of Independent Registered Public Accounting Firm

We consent to the reference to our firm under the caption "Experts" in this Registration Statement (Form S-3) and related Prospectus of Trillium Therapeutics Inc., for the registration of common shares, first preferred shares, subscription receipts, warrants and units, and to the incorporation by reference therein of our report dated March 18, 2021, with respect to the consolidated financial statements of Trillium Therapeutics Inc. included in its Annual Report (Form 10-K) for the year ended December 31, 2020, filed with the Securities and Exchange Commission.

Toronto, Canada
March 18 2021

/s/ Ernst & Young LLP
Chartered Professional Accountants
Licensed Public Accountants
