

PROSPECTUS SUPPLEMENT
(to Prospectus dated October 22, 2020)**Up to \$75,000,000**
Common Shares

We have entered into an amendment, dated March 4, 2021, to our Open Market Sale AgreementSM with Jefferies LLC, or Jefferies, dated December 20, 2018 and previously amended on December 20, 2019 and August 7, 2020, or, as amended, the Sale Agreement, relating to our common shares, without par value per common share, offered by this prospectus supplement. In accordance with the terms of the Sale Agreement, we may offer and sell our common shares having an aggregate offering price of up to \$75,000,000, from time to time through Jefferies, acting as sales agent, pursuant to this prospectus supplement. On August 7, 2020, we filed with the Securities and Exchange Commission a separate prospectus supplement for the offer and sale of up to \$75,000,000 of our common shares pursuant to the Sale Agreement, or the August 2020 Prospectus Supplement, under a shelf registration statement on Form S-3 (Registration Statement No. 333-235674) that was declared effective by the Securities and Exchange Commission on January 10, 2020. As of the date of this prospectus supplement, we have sold \$58,564,835 of our common shares pursuant to the Sale Agreement under the 2020 Prospectus Supplement.

Our common shares trade on the Nasdaq Global Select Market under the symbol "ABUS". On March 3, 2021, the last reported sale price for our common shares on the Nasdaq Global Select Market was \$3.64 per common share.

Sales of our common shares, if any, under this prospectus supplement will be made by any method permitted that is deemed an "at the market offering" as defined in Rule 415(a)(4) promulgated under the Securities Act of 1933, as amended, or the Securities Act. Jefferies is not required to sell any specific amount, but will act as our sales agent using commercially reasonable efforts consistent with its normal trading and sales practices. There is no arrangement for funds to be received in any escrow, trust or similar arrangement.

Jefferies will be entitled to compensation at a commission rate of 3.0% of the gross sales price of the shares sold under the Sale Agreement. See "Plan of Distribution" beginning on page [S-11](#) for additional information regarding the compensation to be paid to Jefferies. In connection with the sale of common shares on our behalf, Jefferies will be deemed to be an "underwriter" within the meaning of the Securities Act and the compensation of Jefferies will be deemed to be underwriting commissions or discounts. We have also agreed to provide indemnification and contribution to Jefferies with respect to certain liabilities, including civil liabilities under the Securities Act.

INVESTING IN OUR COMMON SHARES INVOLVES A HIGH DEGREE OF RISK. YOU SHOULD REVIEW CAREFULLY THE RISKS AND UNCERTAINTIES DESCRIBED UNDER THE HEADING "RISK FACTORS" BEGINNING ON PAGE S-6 OF THIS PROSPECTUS SUPPLEMENT, AS WELL AS THE OTHER INFORMATION CONTAINED IN OR INCORPORATED BY REFERENCE IN THIS PROSPECTUS SUPPLEMENT BEFORE MAKING A DECISION TO INVEST IN OUR SECURITIES.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities, or determined if this prospectus supplement and the accompanying prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

Jefferies

The date of this prospectus supplement is March 4, 2021

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PROSPECTUS

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EXPLANATORY NOTE

On August 7, 2020, we entered into Amendment No. 2 to our Open Market Sale AgreementSM, or Sale Agreement, with Jefferies LLC, or Jefferies, pursuant to which we may issue and sell our common shares having an aggregate offering price of up to \$75.0 million from time to time through Jefferies. The terms of such offering of our common shares are contained in the August 2020 Prospectus Supplement. As of the date of this prospectus supplement, we have sold \$58,564,835 of our common shares pursuant to the Sale Agreement under the August 2020 Prospectus Supplement. Therefore, \$16,435,165 of our common shares remain available for issuance pursuant to the Sale Agreement under the August 2020 Prospectus Supplement. We entered into Amendment No. 3 to the Sale Agreement on March 4, 2021 to provide for an increase in the aggregate offering price under the Sale Agreement. Additional common shares contemplated by Amendment No. 3 to the Sale Agreement are being offered by this prospectus supplement.

ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement relates to the offering of our common shares. Before buying any of the common shares that we are offering, we urge you to carefully read this prospectus supplement, together with the information incorporated by reference as described under the headings “Where You Can Find Additional Information” in the accompanying prospectus, and any free writing prospectus that we have authorized for use in connection with this offering. These documents contain important information that you should consider when making your investment decision.

This prospectus supplement describes the terms of this offering of common shares and also adds to and updates information contained in the documents incorporated by reference into this prospectus supplement. To the extent there is a conflict between the information contained in this prospectus supplement, on the one hand, and the information contained in any document incorporated by reference into this prospectus supplement that was filed with the Securities and Exchange Commission, or SEC, before the date of this prospectus supplement, on the other hand, or the information contained in any free writing prospectus prepared by us or on our behalf that we have authorized for use in connection with this offering, you should rely on the information in this prospectus supplement. If any statement in one of these documents is inconsistent with a statement in another document having a later date — for example, a document incorporated by reference into this prospectus supplement — the statement in the document having the later date modifies or supersedes the earlier statement.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference into this prospectus supplement were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreement, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

You should rely only on the information contained in or incorporated by reference into this prospectus supplement and any free writing prospectus prepared by or on our behalf that we have authorized for use in connection with this offering. We have not, and Jefferies has not, authorized any dealer, salesperson or other person to provide any information or to make any representation other than those contained or incorporated by reference into this prospectus supplement or into any free writing prospectus prepared by or on our behalf or to which we have referred you. If anyone provides you with additional, different or inconsistent information, you should not rely on it. We and Jefferies take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We are not, and Jefferies is not, making an offer to sell the common shares in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing or incorporated by reference into this prospectus supplement and in any free writing prospectus prepared by or on our behalf that we have authorized for use in connection with this offering is accurate only as of the date of each such respective document. Our business, financial condition, results of operations and prospects may have changed since those dates. You should read this prospectus supplement, including the documents incorporated by reference, and any free writing prospectus prepared by or on our behalf that we have authorized for use in connection with this offering, in their entirety before making an investment decision. You should also read and

consider the information in the documents we have referred you to in the sections of this prospectus supplement entitled “Where You Can Find More Information.”

Other than in the United States, no action has been taken by us or Jefferies that would permit a public offering of the common shares offered by this prospectus supplement in any jurisdiction where action for that purpose is required. The common shares offered by this prospectus supplement may not be offered or sold, directly or indirectly, nor may this prospectus supplement or any other offering material or advertisements in connection with the offer and sale of the common shares be distributed or published in any jurisdiction, except under circumstances that will result in compliance with the applicable rules and regulations of that jurisdiction. Persons into whose possession this prospectus supplement comes are advised to inform themselves about and to observe any restrictions relating to this offering and the distribution of this prospectus. This prospectus supplement does not constitute an offer to sell or a solicitation of an offer to buy the common shares offered by this prospectus supplement in any jurisdiction in which such an offer or a solicitation is unlawful.

Unless stated otherwise or the context otherwise requires, references in this prospectus supplement to “Arbutus,” the “Company,” “we,” “us,” or “our” refer to Arbutus Biopharma Corporation and our wholly-owned subsidiary. The Arbutus logo and all other Arbutus product names are trademarks of Arbutus in the United States and in other select countries. The Arbutus logo is a trademark of Arbutus in Canada. We may indicate U.S. trademark registrations and U.S. trademarks with the symbols “®” and “™”, respectively. Other third-party logos and product/trade names are registered trademarks or trade names of their respective owners.

FORWARD-LOOKING STATEMENTS

This prospectus supplement contains “forward-looking statements” or “forward-looking information” within the meaning of applicable securities laws (we collectively refer to these items as “forward-looking statements”). Forward-looking statements are generally identifiable by use of the words “believes,” “may,” “plans,” “will,” “anticipates,” “intends,” “budgets,” “could,” “estimates,” “expects,” “forecasts,” “projects” and similar expressions that are not based on historical fact or that are predictions of or indicate future events and trends, and the negative of such expressions. Forward-looking statements in this prospectus supplement, including the documents incorporated by reference, include statements about, among other things:

- our strategy, future operations, pre-clinical research, pre-clinical studies, clinical trials, prospects and the plans of management;
- the potential impact of the COVID-19 pandemic on our business;
- the discovery, development and commercialization of a curative combination regimen for chronic hepatitis B infection, a disease of the liver caused by the hepatitis B virus (“HBV”);
- our beliefs and development path and strategy to achieve a curative combination regimen for HBV;
- obtaining necessary regulatory approvals;
- obtaining adequate financing through a combination of financing activities and operations;
- using the results from our HBV studies to adaptively design additional clinical trials to test the efficacy of the combination therapy and the duration of the result in patients;
- the expected timing of and amount for payments related to the Enantigen Therapeutics, Inc.’s transaction and its programs;
- the potential of our product candidates to improve upon the standard of care and contribute to a functional curative combination treatment regimen;
- the potential benefits of the reversion of the Ontario Municipal Employees Retirement System (“OMERS”) royalty monetization transaction for our ONPATTRO® (Patisiran) (“ONPATTRO”) royalty interest;
- developing a suite of products that intervene at different points in the viral life cycle, with the potential to reactivate the host immune system;
- using pre-clinical results to adaptively design clinical trials for additional cohorts of patients, testing the combination and the duration of therapy;
- selecting combination therapy regimens and treatment durations to conduct Phase 3 clinical trials intended to ultimately support regulatory filings for marketing approval;
- the potential of substantially increasing diagnosis and treatment rates for people with chronic HBV through the introduction of an HBV curative regimen with a finite duration;
- expanding our HBV product candidate pipeline through internal development, acquisitions and in-licenses;
- our expectation for additional data from ongoing cohorts of the Phase 1a/1b trial of AB-729 to be available late in the first half of 2021 (other than initial data from the 90 mg every 12 week cohort, which is expected in the second half of 2021);
- our expectation that AB-729 could be combined with our lead capsid inhibitor candidate, AB-836, and approved NAs, in our first combination therapy for HBV patients;
- our intention to initiate multiple Phase 2 clinical trials with AB-729, some with one or more investigational agents, in both the first half and second half of 2021;
- our expectations regarding the anticipated trial design, timing, number of patients and dosing of our Phase 2 clinical trial of Assembly Biosciences, Inc.’s investigational HBV core inhibitor candidate, also known as a capsid inhibitor, vebicorvir, in combination with our proprietary GalNAc delivered

RNAi therapeutic candidate, AB-729, and standard-of-care nucleos(t)ide reverse transcriptase inhibitor (NrtI) therapy for the treatment of patients with chronic HBV infection;

- the potential for an oral HBsAg-reducing agent and potential all-oral combination therapy;
- our expectation for AB-836 to progress into a Phase 1a/1b clinical trial in the first half of 2021;
- the potential for AB-836 to have increased potency and an enhanced resistance profile, compared to our previous capsid inhibitor candidate, AB-506;
- the potential for AB-836 to be once-daily dosing;
- our expectation to pursue development of a next generation oral HBV RNA-destabilizer;
- the potential for us to discover and/or develop new molecular entities for treating coronaviruses, including COVID-19;
- payments from the Gritstone Oncology, Inc. licensing agreement;
- the potential for payments from the agreement related to Genevant Sciences Ltd.;
- the expected return from strategic alliances, licensing agreements, and research collaborations;
- statements with respect to revenue and expense fluctuation and guidance;
- having sufficient cash resources to fund our operations through the third quarter of 2022 based on our expectation of a net cash burn between \$70 million and \$75 million in 2021;
- obtaining funding to maintain and advance our business from a variety of sources including public or private equity or debt financing, collaborative arrangements with pharmaceutical companies, other non-dilutive commercial arrangements and government grants and contracts; and
- our use of proceeds from this offering.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this prospectus supplement under the heading “Risk Factors”, and in the documents incorporated by reference into this prospectus supplement, that we believe could cause actual results or events to differ materially from the forward-looking statements that we make.

Moreover, we operate in a very competitive and rapidly changing environment, and new risks emerge from time to time. It is not possible for us to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially and adversely from those contained in any forward-looking statements we may make. In light of these risks, uncertainties and assumptions, the forward-looking events and circumstances discussed in this report may not occur and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements.

You should not rely upon forward-looking statements as predictions of future events. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee that the future results, levels of activity, performance or events and circumstances reflected in the forward-looking statements will be achieved or occur. Moreover, neither we nor any other person assumes responsibility for the accuracy and completeness of the forward-looking statements. Except as required by law, we undertake no obligation to update publicly any forward-looking statements for any reason after the date of this prospectus to conform these statements to actual results or to changes in our expectations.

You should read this prospectus supplement and the documents incorporated by reference in this prospectus supplement with the understanding that our actual future results, levels of activity, performance and events and circumstances may be materially different from what we expect. We qualify all forward-looking statements by these cautionary statements.

SUMMARY

This summary highlights certain information about us, this offering and selected information contained elsewhere in or incorporated by reference into this prospectus supplement. This summary is not complete and does not contain all of the information that you should consider before deciding to invest in our common shares. For a more complete understanding of our company and this offering, you should read carefully this entire prospectus supplement, including the information incorporated by reference into this prospectus supplement, and any free writing prospectus prepared by or on our behalf that we have authorized for use in connection with this offering, including the “Risk Factors” section beginning on page S-6 of this prospectus supplement and the other information included in, or incorporated by reference into, this prospectus supplement.

Company Overview

Arbutus Biopharma Corporation (“Arbutus”, the “Company”, “we”, “us”, and “our”) is a clinical-stage, biopharmaceutical company focused primarily on developing a cure for people with chronic hepatitis B virus (“HBV”) infection. We are advancing multiple product candidates with distinct mechanisms of action and we believe the combination of two or more of these product candidates has the potential to provide a new curative regimen for chronic HBV infection. We have also initiated a drug discovery and development effort for treating coronaviruses, including COVID-19.

Corporate Information

Arbutus was incorporated pursuant to the British Columbia Business Corporations Act, or BCBCA, on October 6, 2005, and commenced active business on April 30, 2007, when Arbutus and its parent company, Inex Pharmaceuticals Corporation, or Inex, were reorganized under a statutory plan of arrangement, or the Plan of Arrangement, completed under the provisions of the BCBCA. The Plan of Arrangement saw Inex’s entire business transferred to and continued by Arbutus.

On March 4, 2015, we completed a business combination pursuant to which OnCore Biopharma, Inc., or OnCore, became our wholly-owned subsidiary. Arbutus Inc. contributed many of the assets in our HBV pipeline. Effective July 31, 2015, our corporate name changed from Tekmira Pharmaceuticals Corporation to Arbutus Biopharma Corporation. Also effective July 31, 2015, the corporate name of our wholly owned subsidiary, OnCore Biopharma, Inc. changed to Arbutus Biopharma, Inc., or Arbutus Inc. We had two wholly owned subsidiaries: Arbutus Inc. and Protiva Biotherapeutics Inc., or Protiva. Effective January 1, 2018, Protiva was amalgamated with Arbutus.

Arbutus’ head office and principal place of business is located at 701 Veterans Circle, Warminster, Pennsylvania 18974 and our telephone number is (267) 469-0914. We maintain a website at www.arbutusbio.com. The information contained on, or that can be accessed through, our website is not a part of this prospectus supplement. We have included our website address in this prospectus supplement solely as an inactive textual reference.

THE OFFERING

Common shares offered by us:	Common shares having an aggregate offering price of up to \$75.0 million.
Common shares to be outstanding following the offering:	Up to 116,060,746 shares (as more fully described in the notes following this table), assuming sales of 20,604,395 of our common shares in this offering at an offering price of \$3.64 per share, which was the last reported sale price of our common shares on the Nasdaq Global Select Market on March 3, 2021. The actual number of shares issued will vary depending on the sales price under this offering.
Plan of Distribution:	“At the market offering” that may be made from time to time on the Nasdaq Global Select Market or other existing trading markets for our common shares through our sales agent, Jefferies. See “Plan of Distribution” on page S-11 of this prospectus supplement
Use of Proceeds:	We currently intend to use the net proceeds from this offering for working capital and general corporate purposes, which may include capital expenditures, research and development expenditures, preclinical study and clinical trial expenditures, acquisitions or new technologies and investments and business combinations. We reserve the right, at the sole discretion of our management, to reallocate the proceeds of this offering in response to developments in our business and other factors. See “Use of Proceeds” on page S-8 of this prospectus supplement.
Risk Factors:	Investing in our common shares involves a high degree of risk. Please read the information contained in and incorporated by reference under the heading “Risk Factors” beginning on page S-6 of this prospectus supplement and the other information included in, or incorporated by reference into, this prospectus supplement for a discussion of certain factors you should carefully consider before deciding to invest in our common shares.
Nasdaq Global Select Market symbol:	“ABUS”

Unless otherwise indicated, the number of common shares to be outstanding after this offering is based on 89,678,722 common shares outstanding as of December 31, 2020, plus 5,777,629 common shares issued under the Sale Agreement from January 1, 2021 to March 4, 2021, and excludes:

- approximately 21 million of our common shares issuable upon the conversion of our Series A participating convertible preferred shares, or the Preferred Shares, outstanding as of December 31, 2020, including accrued dividends thereon as of December 31, 2020;
- 10,669,776 of our common shares issuable upon the exercise of stock options outstanding as of December 31, 2020, at a weighted average exercise price of \$4.50 per common share, of which stock options to purchase 6,662,486 common shares were then exercisable (less 22,647 of our common shares issued upon the exercise of stock options subsequent to December 31, 2020, at a weighted average exercise price of \$4.45 per common share);
- 3,035,021 of our common shares reserved for future grants of stock options (or other similar equity instruments) under the 2016 Share and Omnibus Incentive Plan, or the 2016 Plan, as of December 31, 2020 (less 2,760,900 of our common shares issuable upon the exercise of stock options granted under the 2016 Plan subsequent to December 31, 2020, at a weighted average exercise price of \$4.33 per common share);

- 126,450 of our common shares reserved for future grants of stock options (or other similar equity instruments) under the 2011 Omnibus Share Compensation Plan, or the 2011 Plan, as of December 31 2020 (less 126,450 of our common shares issuable upon the exercise of stock options granted under the 2011 Plan subsequent to December 31, 2020, at a weighted average exercise price of \$4.33 per common share);
- 1,500,000 of our common shares reserved for future issuance under the 2020 Employee Stock Purchase Plan, or 2020 ESPP, as of December 31, 2020 (less 104,917 of our common shares issued under the 2020 ESPP subsequent to December 31, 2020, at a weighted average purchase price of \$2.35 per common share); and
- \$16,435,165 of our common shares available for future issuance pursuant to the Sale Agreement under the August 2020 Prospectus Supplement.

RISK FACTORS

Investing in our common shares is speculative and involves a high degree of risk. Before making an investment decision, you should carefully consider the risks described in this prospectus supplement and the documents incorporated by reference into this prospectus supplement, including the “Risk Factors” section of our Annual Report on Form 10-K for the year ended December 31, 2020, which is incorporated by reference into this prospectus supplement, as updated by annual, quarterly and other reports and documents we file with the SEC after the date of this prospectus supplement and that are incorporated by reference into this prospectus supplement. If any of these risks actually occurs, our business, financial condition or results of operations could be materially adversely affected. These risks and uncertainties are not the only ones faced by us. Additional risks and uncertainties, including those of which we are currently unaware or that are currently deemed immaterial, may also materially and adversely affect our business, financial condition, cash flows, prospects and the price of our common shares.

Risks Related to This Offering

A substantial number of common shares may be sold in the market following this offering, which may depress the market price for our common shares.

Sales of a substantial number of our common shares in the public market following this offering could cause the market price of our common shares to decline. Although there can be no assurance that any of the \$75.0 million worth of common shares being offered under this prospectus supplement will be sold or the price at which any such shares might be sold, assuming that an aggregate of 20,604,395 of our common shares are sold under this prospectus supplement during the term of the Sale Agreement with Jefferies, in each case, for example, at a price of \$3.64 per share, the last reported sale price of our common shares on the Nasdaq Global Select Market on March 3, 2021, upon completion of this offering, based on 89,678,722 shares outstanding as of December 31, 2020 and 5,777,629 common shares issued between January 1, 2021 and March 4, 2021 under the Sale Agreement with Jefferies, we will have outstanding an aggregate of 116,060,746 common shares, assuming no exercise of outstanding options, and no conversion of the Preferred Shares. A substantial majority of our outstanding common shares are, and all of the common shares sold in this offering upon issuance will be, freely tradable without restriction or further registration under the Securities Act, unless these shares are owned or purchased by “affiliates” as that term is defined in Rule 144 under the Securities Act. There is also \$16,435,165 of our common shares that remain available for issuance pursuant to the Sale Agreement under the August 2020 Prospectus Supplement, which, upon issuance, may further depress the market price for our common shares.

In addition, as of December 31, 2020, we had outstanding Preferred Shares convertible for approximately 21 million common shares (including accrued interest thereon) and outstanding stock options exercisable for 10,669,776 common shares at a weighted average exercise price of \$4.50 per share, of which stock options to purchase 6,662,486 common shares were then exercisable. Subsequent to December 31, 2020, we also issued stock options exercisable for an aggregate of 2,887,350 common shares at a weighted average exercise price of \$4.33. Upon conversion of the Preferred Shares or exercise of the stock options, we would issue additional common shares. As a result, our current shareholders as a group would own a substantially smaller interest in us and may have less influence on our management and policies than they now have. Furthermore, the holders may sell these shares in the public markets from time to time, without limitations on the timing, amount or method of sale. Sales of these common shares in the market could cause the market price of our common shares to decline. Moreover, if we issue options to purchase or acquire our common shares in the future and those options are exercised or settled, you may experience further dilution.

Additional dilution may result from the issuance of our common shares in connection with collaborations or other financing efforts.

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

In order to raise additional capital, we may in the future offer additional common shares or other securities convertible into or exchangeable for our common shares at prices that may not be the same as the price per share in this offering. We may sell common shares or other securities convertible into or

exchangeable for our common shares in any other offering at a price per share that is less than the price per share paid by investors in this offering, and investors purchasing common shares or other securities convertible into or exchangeable for our common shares in the future could have rights superior to existing shareholders. The price per share at which we sell additional common shares or other securities convertible or exchangeable into our common shares, in future transactions may be higher or lower than the price per share paid by investors in this offering. There is also \$16,435,165 of our common shares that remain available for issuance pursuant to the Sale Agreement under the August 2020 Prospectus Supplement, which, upon issuance, would result in additional dilution for our existing shareholders.

We have broad discretion in how we use the net proceeds of this offering, and we may not use these proceeds effectively or in ways with which you agree.

We have not designated any portion of the net proceeds from this offering to be used for any particular purpose. Our management will have broad discretion as to the application of the net proceeds of this offering and could use them for purposes other than those contemplated at the time of this offering. Our shareholders may not agree with the manner in which our management chooses to allocate and spend the net proceeds. Moreover, our management may use the net proceeds for corporate purposes that may not increase the market price of our common shares.

Investors in this offering will experience immediate dilution in the pro forma as-adjusted net tangible book value per share of the common shares purchased in the offering.

The common shares sold in this offering, if any, will be sold from time to time at various prices. However, the expected offering price of our common shares will be substantially higher than the pro forma net tangible book value per share of our outstanding common shares. After giving effect to the sale of our common shares in the aggregate amount of \$75.0 million at an assumed offering price of \$3.64 per share, the last reported sale price of our common shares on March 3, 2021 on the Nasdaq Global Select Market, and after deducting estimated commissions and estimated offering expenses, our pro forma as-adjusted net tangible book value as of December 31, 2020, based on 89,678,722 common shares outstanding as of December 31, 2020 plus 5,777,629 common shares issued under the Sale Agreement between January 1, 2021 and March 4, 2021, would have been approximately \$198.8 million, or approximately \$1.71 per common share. This represents an immediate increase in pro forma net tangible book value of approximately \$0.39 per common share to our existing shareholders and an immediate dilution in pro forma as-adjusted net tangible book value of approximately \$1.93 per common share to new investors of our common shares in this offering. See “Dilution” on page S-9 of this prospectus supplement.

It is not possible to predict the aggregate proceeds resulting from sales made under the Sale Agreement.

Subject to certain limitations in the Sale Agreement and compliance with applicable law, we have the discretion to deliver a placement notice to Jefferies at any time throughout the term of the Sale Agreement. The number of shares that are sold through Jefferies after delivering a placement notice will fluctuate based on a number of factors, including the market price of our common shares during the sales period, any limits we may set with Jefferies in any applicable placement notice and the demand for our common shares. Because this offering can be terminated at any time and the price per share of each common share sold pursuant to the Sale Agreement will fluctuate over time, it is not currently possible to predict the aggregate proceeds to be raised in connection with sales under the Sale Agreement.

We do not expect to pay dividends in the foreseeable future. As a result, you must rely on stock appreciation for any return on your investment.

We do not anticipate paying cash dividends on our common shares in the foreseeable future. Any payment of cash dividends will also depend on our financial condition, results of operations, capital requirements and other factors and will be at the discretion of our board of directors. Accordingly, you will have to rely on capital appreciation, if any, to earn a return on your investment in our common shares. Furthermore, we may in the future become subject to additional contractual restrictions on, or prohibitions against, the payment of dividends.

USE OF PROCEEDS

We may issue and sell our common shares having aggregate sales proceeds of up to \$75.0 million from time to time. Because there is no minimum offering amount required as a condition to close this offering, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time. There can be no assurance that, in the future, we will sell any shares under or fully utilize the Sale Agreement with Jefferies as a source of financing.

We currently intend to use the net proceeds from this offering for working capital and general corporate purposes, which may include capital expenditures, research and development expenditures, preclinical study and clinical trial expenditures, acquisitions of new technologies and investments and business combinations.

The precise amount and timing of the application of these net proceeds will depend upon a number of factors, such as the timing and progress of our research and development efforts and the timing and progress of any partnering efforts. As of the date of this prospectus supplement, we cannot specify with certainty all of the particular uses for the net proceeds from this offering. Depending on the outcome of our efforts and other unforeseen events, our plans and priorities may change and we may apply the net proceeds of this offering in different manners than we currently anticipate. Accordingly, our management will have broad discretion in the timing and application of these net proceeds. Pending application of the net proceeds as described above, we intend to temporarily invest the proceeds in short-term, interest-bearing instruments.

DILUTION

If you invest in our common shares in this offering, your ownership interest will be diluted to the extent of the difference between the public offering price per share and our pro forma as adjusted net tangible book value per share after this offering. We calculate net tangible book value per share by dividing our net tangible book value, which is tangible assets less total liabilities, by the number of outstanding common shares.

The net tangible book value of our common shares as of December 31, 2020 was approximately \$102.0 million, or approximately \$1.14 per common share.

Our pro forma net tangible book value as of December 31, 2020 was \$126.3 million, or \$1.32 per common share. Pro forma net tangible book value per share represents pro forma net tangible book value divided by the pro forma number of common shares outstanding, after giving effect to our issuance and sale of 5,777,629 common shares pursuant to the Sale Agreement from January 1, 2021 to March 4, 2021.

After giving effect to the sale of our common shares in the aggregate amount of \$75.0 million at an assumed offering price of \$3.64 per common share, the last reported sale price of our common shares on March 3, 2021 on the Nasdaq Global Select Market, and after deducting estimated commissions and estimated offering expenses, our pro forma as-adjusted net tangible book value as of December 31, 2020 would have been approximately \$198.8 million, or approximately \$1.71 per common share. This represents an immediate increase in pro forma net tangible book value of approximately \$0.39 per common share to our existing shareholders and an immediate dilution in pro forma as-adjusted net tangible book value of approximately \$1.93 per common share to new investors of our common shares in this offering, as illustrated by the following table:

Assumed public offering price per share	\$3.64
Net tangible book value per share as of December 31, 2020	\$1.14
Increase in tangible book value per share attributable to shares sold pursuant to the Sale Agreement from January 1, 2021 to March 4, 2021	<u>\$0.18</u>
Pro forma net tangible book value per share as of December 31, 2020	\$1.32
Increase in pro forma net tangible book value per share after this offering	<u>\$0.39</u>
Pro forma as adjusted net tangible book value per share as of December 31, 2020, after giving effect to this offering	<u>\$1.71</u>
Dilution per share to new investors in this offering ⁽¹⁾⁽²⁾	<u>\$1.93</u>

(1) Calculated as the difference between the assumed public offering price per common share and the pro forma as-adjusted net tangible book value per share after this offering.

(2) The foregoing is based on 89,678,722 common shares outstanding as of December 31, 2020, plus 5,777,629 common shares issued under the Sale Agreement from January 1, 2021 to March 4, 2021, and excludes:

- approximately 21 million of our common shares issuable upon the conversion of Preferred Shares outstanding as of December 31, 2020, including accrued dividends thereon as of December 31, 2020;
- 10,669,776 of our common shares issuable upon the exercise of stock options outstanding as of December 31, 2020, at a weighted average exercise price of \$4.50 per common share, of which stock options to purchase 6,662,486 common shares were then exercisable (less 22,647 of our common shares issued upon the exercise of stock options subsequent to December 31, 2020, at a weighted average exercise price of \$4.45 per common share);
- 3,035,021 of our common shares reserved for future grants of stock options (or other similar equity instruments) under the 2016 Plan as of December 31, 2020 (less 2,760,900 of our common shares issuable upon the exercise of stock options granted under the 2016 Plan subsequent to December 31, 2020, at a weighted average exercise price of \$4.33 per common share);

- 126,450 of our common shares reserved for future grants of stock options (or other similar equity instruments) under the 2011 Plan as of December 31, 2020 (less 126,450 of our common shares issuable upon the exercise of stock options granted under the 2011 Plan subsequent to December 31, 2020, at a weighted average exercise price of \$4.33 per common share);
- 1,500,000 of our common shares reserved for future issuance under the 2020 ESPP as of December 31, 2020 (less 104,917 of our common shares issued under the 2020 ESPP subsequent to December 31, 2020, at a weighted average purchase price of \$2.35 per common share); and
- \$16,435,165 of our common shares available for future issuance pursuant to the Sale Agreement under the August 2020 Prospectus Supplement.

The table above assumes for illustrative purposes that an aggregate of 20,604,395 of our common shares are sold under this prospectus supplement during the term of the Sale Agreement with Jefferies at a price of \$3.64 per share, the last reported sale price of our common shares on the Nasdaq Global Select Market on March 3, 2021, for aggregate net proceeds of approximately \$72.6 million, after deducting commissions and estimated aggregate offering expenses payable by us. The pro forma as adjusted information is illustrative only and will adjust based on the actual price to the public, the actual number of common shares sold and other terms of the offering determined at the time our common shares are sold pursuant to this prospectus supplement. The shares pursuant to the Sale Agreement with Jefferies are being sold from time to time at various prices under this prospectus supplement. An increase of \$1.00 per share in the price at which the shares are sold from the assumed offering price of \$3.64 per share shown in the table above, assuming all of our common shares in the aggregate amount of \$75.0 million during the term of the Sale Agreement with Jefferies is sold at that price under this prospectus supplement, would increase our pro forma as adjusted net tangible book value per share after the offering to \$1.78 per share and would increase the dilution in pro forma as-adjusted net tangible book value per share to new investors in this offering to \$2.86 per share, after deducting commissions and estimated aggregate offering expenses payable by us. A decrease of \$1.00 per share in the price at which the common shares are sold from the assumed offering price of \$3.64 per share shown in the table above, assuming all of our common shares in the aggregate amount of \$75.0 million during the term of the Sale Agreement with Jefferies is sold at that price under this prospectus supplement, would decrease our pro forma as adjusted net tangible book value per share after the offering to \$1.61 per share and would decrease the dilution in pro forma as-adjusted net tangible book value per share to new investors in this offering to \$1.03 per share, after deducting commissions and estimated aggregate offering expenses payable by us. This information is supplied for illustrative purposes only.

To the extent that any options have been or are exercised, preferred shares are converted, new options are issued under our equity incentive plans or as inducement awards or we otherwise issue additional common shares in the future, there will be further dilution to new investors. In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our shareholders.

PLAN OF DISTRIBUTION

We previously entered into the Sale Agreement with Jefferies relating to our common shares. On August 7, 2020, we entered into Amendment No. 2 to the Sale Agreement, pursuant to which we may issue and sell our common shares having an aggregate offering price of up to \$75.0 million from time to time through Jefferies. The terms of such offering of our common shares are contained in the August 2020 Prospectus Supplement. As of the date of this prospectus supplement, we have sold \$58,564,835 of our common shares pursuant to the Sale Agreement under the August 2020 Prospectus Supplement. Therefore, \$16,435,165 of our common shares remain available for issuance pursuant to the Sale Agreement under the August 2020 Prospectus Supplement. We entered into Amendment No. 3 to the Sale Agreement on March 4, 2021 to provide for an increase in the aggregate offering price under the Sale Agreement. Additional common shares contemplated by Amendment No. 3 to the Sale Agreement are being offered by this prospectus supplement.

In accordance with the terms of the Sale Agreement, we may offer and sell up to \$75.0 million of our common shares from time to time through Jefferies, acting as sales agent, under this prospectus supplement. Sales of our common shares, if any, under this prospectus supplement and the accompanying prospectus will be made by any method that is deemed to be an “at the market offering” as defined in Rule 415(a)(4) under the Securities Act including sales made directly on or through the Nasdaq Global Select Market or any other existing trading market for our common shares provided such sales are conducted on a market or exchange outside of Canada or to persons resident outside of Canada.

Each time we wish to issue and sell common shares under the Sale Agreement, we will notify Jefferies of the number of shares to be issued, the dates on which such sales are anticipated to be made, any limitation on the number of shares to be sold in any one day and any minimum price below which sales may not be made. Once we have so instructed Jefferies, unless Jefferies declines to accept the terms of such notice, Jefferies has agreed to use its commercially reasonable efforts consistent with its normal trading and sales practices to sell such shares up to the amount specified on such terms. The obligations of Jefferies under the Sale Agreement to sell our common shares are subject to a number of conditions that we must meet.

The settlement of sales of common shares between us and Jefferies is generally anticipated to occur on the second trading day following the date on which the sale was made. Sales of our common shares as contemplated in this prospectus supplement will be settled through the facilities of The Depository Trust Company or by such other means as we and Jefferies may agree upon. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

We will pay Jefferies a commission equal to 3.0% of the aggregate gross proceeds we receive from each sale of our common shares. Because there is no minimum offering amount required as a condition to close this offering, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time. We estimate that the total expenses for the offering under this prospectus supplement, excluding any commissions or expense reimbursement payable to Jefferies under the terms of the Sale Agreement, will be approximately \$185,000. The remaining sale proceeds, after deducting any other transaction fees, will equal our net proceeds from the sale of such common shares.

Jefferies will provide written confirmation to us before the open on the Nasdaq Global Select Market on the day following each day on which common shares are sold under the Sale Agreement. Each confirmation will include the number of common shares sold on that day, the aggregate gross proceeds of such sales and the proceeds to us.

In connection with the sale of the common shares on our behalf, Jefferies will be deemed to be an “underwriter” within the meaning of the Securities Act, and the compensation of Jefferies will be deemed to be underwriting commissions or discounts. We have agreed to indemnify Jefferies against certain civil liabilities, including liabilities under the Securities Act. We have also agreed to contribute to payments Jefferies may be required to make in respect of such liabilities.

The offering of our common shares pursuant to the Sale Agreement will terminate upon the earlier of (i) the sale of all common shares subject to the Sale Agreement and (ii) the termination of the Sale Agreement as permitted therein.

This summary of the material provisions of the Sale Agreement, does not purport to be a complete statement of its terms and conditions. A copy of the Sale Agreement, and the amendments thereto, are or will be filed as exhibits to our annual report on Form 10-K and a current report on Form 8-K filed under the Securities Exchange Act of 1934, as amended, or the Exchange Act, and incorporated by reference in this prospectus supplement.

Jefferies and its affiliates may in the future provide various investment banking, commercial banking, financial advisory and other financial services for us and our affiliates, for which services they may in the future receive customary fees. In the course of its business, Jefferies may actively trade our securities for its own account or for the accounts of customers, and, accordingly, Jefferies may at any time hold long or short positions in such securities.

This prospectus supplement and the accompanying prospectus in electronic format may be made available on a website maintained by Jefferies, and Jefferies may distribute this prospectus supplement and the accompanying prospectus electronically.

Notwithstanding the above, the securities: (i) have not been qualified for distribution by prospectus in Canada, and (ii) may not be offered or sold in Canada during the course of their distribution except pursuant to a Canadian prospectus or in reliance on an available prospectus exemption.

MATERIAL UNITED STATES FEDERAL INCOME TAX CONSIDERATIONS

The following is a general summary of certain material U.S. federal income tax considerations applicable to a U.S. Holder (as defined below) arising from and relating to the acquisition, ownership, and disposition of common shares acquired pursuant to this prospectus. This section applies only to a U.S. Holder that holds common shares as capital assets for U.S. federal income tax purposes. In addition, it does not set forth all of the U.S. federal income tax consequences that may be relevant in light of the U.S. Holder's particular circumstances, including alternative minimum tax consequences, the potential application of the provisions of the Code known as the Medicare contribution tax and tax consequences applicable to U.S. Holders subject to special rules, such as:

- certain financial institutions;
- dealers or traders in securities who use a mark-to-market method of tax accounting;
- U.S. expatriates and certain former citizens or long-term residents of the United States;
- persons holding common shares as part of a hedging transaction, straddle, wash sale, conversion transaction or other integrated transaction or persons entering into a constructive sale with respect to the common shares;
- persons whose functional currency for U.S. federal income tax purposes is not the U.S. dollar;
- entities classified as partnerships for U.S. federal income tax purposes;
- tax-exempt entities, including an "individual retirement account" or "Roth IRA";
- persons that own or are deemed to own ten percent or more of our shares (by vote or value); or
- persons holding common shares in connection with a trade or business conducted outside of the United States.

If an entity that is classified as a partnership for U.S. federal income tax purposes holds common shares, the U.S. federal income tax treatment of a partner will depend on the status of the partner and the activities of the partnership. Partnerships holding common shares and partners in such partnerships should consult their tax advisers as to the particular U.S. federal income tax consequences of owning and disposing of the common shares.

This section is based on the Code, administrative pronouncements, judicial decisions, final, temporary and proposed Treasury regulations, all as of the date hereof, any of which is subject to change or differing interpretations, possibly with retroactive effect.

A "U.S. Holder" is a holder who, for U.S. federal income tax purposes, is a beneficial owner of common shares, and who is:

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

U.S. Holders should consult their tax advisers concerning the U.S. federal, state, local and non-U.S. tax consequences of owning and disposing of common shares in their particular circumstances.

Passive Foreign Investment Company Rules

Under the Code, we will be a passive foreign investment company, or PFIC, for any taxable year in which, after the application of certain "look-through" rules with respect to subsidiaries, either (i) 75% or more of our gross income consists of "passive income," or (ii) 50% or more of the average quarterly value of

our assets consist of assets that produce, or are held for the production of, “passive income.” For purposes of the above calculations, we will be treated as if we hold our proportionate share of the assets of, and receive directly our proportionate share of the income of, any other corporation in which we directly or indirectly own at least 25%, by value, of the shares of such corporation.

Passive income includes, among other things, interest, dividends, rents, certain non-active royalties and capital gains. Based on the composition of our gross income and assets in 2020, our reasonable estimates of our gross income and assets for 2021, and the nature of our business, we have determined that we were not a PFIC for our 2020 taxable year and we do not expect to be a PFIC for our taxable year ending December 31, 2021. Nevertheless, whether we are a PFIC in 2021 or any future taxable year is uncertain because, among other things, (i) we currently own, and will own after the closing of this offering, a substantial amount of passive assets, including cash, (ii) the valuation of our assets that generate non-passive income for PFIC purposes is uncertain and may vary substantially over time, and (iii) the composition of our income may vary substantially over time. If we are a PFIC for any year during which a U.S. Holder holds common shares, we will continue to be treated as a PFIC with respect to that U.S. Holder for all succeeding years during which the U.S. Holder holds common shares, even if we ceased to meet the threshold requirements for PFIC status, unless the U.S. Holder makes a valid deemed sale or deemed dividend election under the applicable Treasury regulations with respect to its common shares.

If we are a PFIC for any taxable year during which a U.S. Holder holds common shares (assuming such U.S. Holder has not made a timely mark-to-market election, as described below), gain recognized by a U.S. Holder on a sale or other disposition (including certain pledges) of the common shares would be allocated ratably over the U.S. Holder’s holding period for the common shares. The amounts allocated to the taxable year of the sale or other disposition and to any year before we became a PFIC would be taxed as ordinary income. The amount allocated to each other taxable year would be subject to tax at the highest rate in effect for individuals or corporations, as appropriate, for that taxable year, and an interest charge would be imposed on the amount allocated to that taxable year. Further, to the extent that any distribution received by a U.S. Holder on its common shares exceeds 125% of the average of the annual distributions on the common shares received during the preceding three years or the U.S. Holder’s holding period, whichever is shorter, that distribution would be subject to taxation in the same manner as gain, described immediately above.

A U.S. Holder can avoid certain of the adverse rules described above by making a mark-to-market election with respect to its common shares, provided that the common shares are “marketable.” Common shares will be marketable if they are “regularly traded” on a “qualified exchange” or other market within the meaning of applicable Treasury regulations. The common shares will be treated as “regularly traded” in any calendar year in which more than a de minimis quantity of the common shares are traded on a qualified exchange on at least 15 days during each calendar quarter (subject to the rule that trades that have as one of their principal purposes the meeting of the trading requirement as disregarded). The Nasdaq Global Select Market is a qualified exchange for this purpose and, consequently, if the common shares are regularly traded, the mark-to-market election will be available to a U.S. Holder. If a U.S. Holder makes the mark-to-market election, it will recognize as ordinary income any excess of the fair market value of the common shares at the end of each taxable year over their adjusted tax basis, and will recognize an ordinary loss in respect of any excess of the adjusted tax basis of the common shares over their fair market value at the end of the taxable year (but only to the extent of the net amount of income previously included as a result of the mark-to-market election). If a U.S. Holder makes the election, the U.S. Holder’s tax basis in the common shares will be adjusted to reflect the income or loss amounts recognized. Any gain recognized on the sale or other disposition of common shares in a year when we are a PFIC will be treated as ordinary income and any loss will be treated as an ordinary loss (but only to the extent of the net amount of income previously included as a result of the mark-to-market election).

However, a mark-to-market election generally cannot be made for equity interests in any lower-tier PFICs that we own, unless shares of such lower-tier PFIC are themselves “marketable.” As a result, even if a U.S. Holder validly makes a mark-to-market election with respect to our common shares, the U.S. Holder may continue to be subject to the PFIC rules (described above) with respect to its indirect interest in any of our investments that are treated as an equity interest in a PFIC for U.S. federal income tax purposes. U.S. Holders should consult their tax advisors as to the availability and desirability of a mark-to-market election, as well as the impact of such election on interests in any lower-tier PFICs.

Alternatively, a U.S. Holder can make an election, if we provide the necessary information, to treat us and each lower-tier PFIC as a qualified electing fund, or a QEF Election, in the first taxable year we (and our relevant subsidiaries) are treated as a PFIC with respect to the U.S. Holder. If a U.S. Holder makes a QEF Election with respect to a PFIC, the U.S. Holder will be currently taxable on its pro rata share of the PFIC's ordinary earnings and net capital gain (at ordinary income and capital gain rates, respectively) for each taxable year that the entity is classified as a PFIC and will not be required to include such amounts in income when actually distributed by the PFIC. We intend to provide the information necessary for a U.S. Holder to make a QEF Election with respect to us and to cause each lower-tier PFIC which we control to provide such information with respect to such lower-tier PFIC. If such election remains in place while we and any lower-tier PFIC subsidiaries are PFICs, we and our subsidiaries will not be treated as PFICs with respect to such U.S. Holder. A U.S. Holder must make the QEF Election for us and for each of our subsidiaries that is a PFIC by attaching a separate properly completed IRS Form 8621 for each such PFIC to the U.S. Holder's timely filed U.S. federal income tax return.

In addition, if we are a PFIC or, with respect to a particular U.S. Holder, are treated as a PFIC for the taxable year in which we paid a dividend or for the prior taxable year, the preferential dividend rates discussed above with respect to dividends paid to certain non-corporate U.S. Holders would not apply.

If a U.S. Holder owns common shares during any year in which we are a PFIC, the U.S. Holder must file annual reports, containing such information as the U.S. Treasury may require on IRS Form 8621 (or any successor form) with respect to us, with the U.S. Holder's federal income tax return for that year, unless otherwise specified in the instructions with respect to such form.

U.S. Holders should consult their tax advisers concerning our PFIC status and the application of the PFIC rules.

General Rules Applicable to the Ownership and Disposition of Common Shares

The following discussion describes the general rules applicable to the ownership and disposition of the common shares but is subject in its entirety to the special rules described above under the heading "Passive Foreign Investment Company Rules."

Distributions on Common Shares

A U.S. Holder that receives a distribution with respect to a common share will be required to include the amount of such distribution in gross income as a dividend (without reduction for any Canadian income tax withheld from such distribution) to the extent of our current and accumulated "earnings and profits," as computed for U.S. federal income tax purposes. Subject to the passive foreign investment company rules described above, a distribution generally will be treated as a dividend to the extent paid out of our current or accumulated earnings and profits (as determined under U.S. federal income tax principles). To the extent that a distribution exceeds our current and accumulated "earnings and profits," such distribution will be treated first as a tax-free return of capital to the extent of a U.S. Holder's tax basis in the common shares and thereafter as gain from the sale or exchange of such common shares. (See "Sale or Other Taxable Disposition of Common Shares" below). However, we may not maintain the calculations of our earnings and profits in accordance with U.S. federal income tax principles, and each U.S. Holder may have to assume that any distribution by us with respect to the common shares will constitute ordinary dividend income. Dividends paid by a "qualified foreign corporation" to certain non-corporate U.S. Holders may be eligible for taxation at a reduced capital gains rate rather than the marginal tax rates generally applicable to ordinary income provided that a holding period requirement (more than 60 days of ownership, without protection from the risk of loss, during the 121-day period beginning 60 days before the ex-dividend date) and certain other requirements are met. Each U.S. Holder is advised to consult its tax advisors regarding the availability of the reduced tax rate on dividends to its particular circumstances. However, if we are a PFIC for the taxable year in which the dividend is paid or the preceding taxable year, we will not be treated as a qualified foreign corporation, and therefore the reduced capital gains tax rate described above will not apply. Dividends received on common shares by corporate U.S. Holders generally will not be eligible for the "dividends received deduction." The dividend rules are complex, and each U.S. Holder should consult its own tax advisors regarding the application of such rules.

Sale or Other Taxable Disposition of Common Shares

Upon the sale or other taxable disposition of common shares, a U.S. Holder generally will recognize capital gain or loss in an amount equal to the difference between the U.S. dollar value of cash received plus the fair market value of any property received and such U.S. Holder's tax basis in such common shares sold or otherwise disposed of. A U.S. Holder's tax basis in common shares generally will be such holder's U.S. dollar cost for such common shares. Gain or loss recognized on such sale or other disposition generally will be long-term capital gain or loss if, at the time of the sale or other disposition, the common shares have been held for more than one year.

Subject to the PFIC rules discussed above, preferential tax rates currently apply to long-term capital gain of a U.S. Holder that is an individual, estate, or trust. There are currently no preferential tax rates for long-term capital gain of a U.S. Holder that is a corporation. Deductions for capital losses are subject to significant limitations under the Code.

Receipt of Foreign Currency

The amount of any distribution paid to a U.S. Holder in foreign currency, or on the sale, exchange or other taxable disposition of common shares, generally will be equal to the U.S. dollar value of such foreign currency based on the exchange rate applicable on the date of receipt (regardless of whether such foreign currency is converted into U.S. dollars at that time). A U.S. Holder will have a basis in the foreign currency equal to its U.S. dollar value on the date of receipt. Any U.S. Holder who converts or otherwise disposes of the foreign currency after the date of receipt may have a foreign currency exchange gain or loss that would be treated as ordinary income or loss, and generally will be U.S. source income or loss for foreign tax credit purposes. Different rules apply to U.S. Holders who use the accrual method. Each U.S. Holder should consult its own U.S. tax advisors regarding the U.S. federal income tax consequences of receiving, owning, and disposing of foreign currency.

Foreign Tax Credit

Subject to the PFIC rules discussed above, a U.S. Holder that pays (whether directly or through withholding) Canadian income tax with respect to dividends paid on the common shares generally will be entitled, at the election of such U.S. Holder, to receive either a deduction or a credit for such Canadian income tax. Generally, a credit will reduce a U.S. Holder's U.S. federal income tax liability on a dollar-for-dollar basis, whereas a deduction will reduce a U.S. Holder's income that is subject to U.S. federal income tax. This election is made on a year-by-year basis and applies to all foreign taxes paid (whether directly or through withholding) by a U.S. Holder during a year.

Complex limitations apply to the foreign tax credit, including the general limitation that the credit cannot exceed the proportionate share of a U.S. Holder's U.S. federal income tax liability that such U.S. Holder's "foreign source" taxable income bears to such U.S. Holder's worldwide taxable income. In applying this limitation, a U.S. Holder's various items of income and deduction must be classified, under complex rules, as either "foreign source" or "U.S. source." Generally, dividends paid by a foreign corporation should be treated as foreign source for this purpose, and gains recognized on the sale of stock of a foreign corporation by a U.S. Holder should be treated as U.S. source for this purpose. However, the amount of a distribution with respect to the common shares that is treated as a "dividend" may be lower for U.S. federal income tax purposes than it is for Canadian federal income tax purposes, resulting in a reduced foreign tax credit allowance to a U.S. Holder. In addition, this limitation is calculated separately with respect to specific categories of income. The foreign tax credit rules are complex, and each U.S. Holder should consult its own U.S. tax advisors regarding the foreign tax credit rules.

Backup Withholding and Information Reporting

Payments made within the U.S., or by a U.S. payor or U.S. middleman, of dividends on, and proceeds arising from the sale or other taxable disposition of, common shares will generally be subject to information reporting and backup withholding if a U.S. Holder (a) fails to furnish such U.S. Holder's correct U.S. taxpayer identification number (generally on Form W-9), (b) furnishes an incorrect U.S. taxpayer identification number, (c) is notified by the IRS that such U.S. Holder has previously failed to properly report items

subject to backup withholding tax, or (d) fails to certify, under penalty of perjury, that such U.S. Holder has furnished its correct U.S. taxpayer identification number and that the IRS has not notified such U.S. Holder that it is subject to backup withholding tax. However, certain exempt persons generally are excluded from these information reporting and backup withholding rules. Backup withholding is not an additional tax. Any amounts withheld under the U.S. backup withholding tax rules will be allowed as a credit against a U.S. Holder's U.S. federal income tax liability, if any, or will be refunded, if such U.S. Holder furnishes required information to the IRS in a timely manner.

THE ABOVE SUMMARY IS NOT INTENDED TO CONSTITUTE A COMPLETE ANALYSIS OF ALL TAX CONSIDERATIONS APPLICABLE TO U.S. HOLDERS WITH RESPECT TO THE ACQUISITION, OWNERSHIP, AND DISPOSITION OF COMMON SHARES. U.S. HOLDERS SHOULD CONSULT THEIR OWN TAX ADVISORS AS TO THE TAX CONSIDERATIONS APPLICABLE TO THEM IN THEIR OWN PARTICULAR CIRCUMSTANCES.

CERTAIN CANADIAN FEDERAL INCOME TAX CONSIDERATIONS

The following is a general summary of the principal Canadian federal income tax considerations under the *Income Tax Act* (Canada) and the regulations thereunder (collectively, the “Tax Act”) generally applicable to a Non-Canadian Holder (as defined below) arising from and relating to the acquisition, ownership, and disposition of common shares acquired pursuant to this prospectus.

This summary is applicable to a purchaser who acquires common shares pursuant to this offering and who, for the purposes of the Tax Act and any applicable tax treaty at all relevant times: (i) is not (and is not deemed to be) a resident in Canada, (ii) holds such common shares as capital property, (iii) deals at arm’s length and is not affiliated with the Company or the underwriter, (iv) does not use or hold (and will not use or hold) and is not deemed to use or hold the common shares in, or in the course of, carrying on a business in Canada, (v) does not carry on an insurance business in Canada and elsewhere, and (vi) is not an “authorized foreign bank” as defined in the Tax Act (each, a “Non-Canadian Holder”).

This summary does not apply to a Non-Canadian Holder (i) that is a “financial institution”, as defined in the Tax Act for purposes of the “mark-to-market property” rules; (ii) an interest in which is or would constitute a “tax shelter investment” as defined in the Tax Act; (iii) that is a “specified financial institution” as defined in the Tax Act; or (iv) that has or will enter into a “synthetic disposition arrangement” or a “derivative forward agreement”, as those terms are defined in the Tax Act, in respect of common shares pursuant to this offering. All such Non-Canadian Holders should consult their own tax advisors with respect to an investment in common shares.

This summary is based on the current provisions of the Tax Act, our understanding of the current published administrative policies and assessing practices of the Canada Revenue Agency (the “CRA”), all specific proposals to amend the Tax Act announced by or on behalf of the Minister of Finance (Canada) prior to the date hereof (the “Tax Proposals”), and the current provisions of the Canada-US Tax Convention (1980) (the “Canada-US Tax Treaty”). This summary assumes that the Tax Proposals will be enacted in the current form proposed and does not otherwise take into account or anticipate any changes in the law or in the administrative policies and assessing practices of the CRA, whether by judicial, administrative, or legislative decisions or action, and whether prospective or retroactive in effect, nor does it take into account tax legislation or considerations of any province or territory of Canada or any jurisdiction other than Canada.

The summary is of a general nature only, is not exhaustive of all Canadian federal income tax considerations, and is not intended to be, and should not be construed to be, legal or tax advice to any particular Non-Canadian Holder of the common shares and no representation with respect to the Canadian tax consequences to any particular Non-Canadian Holder is made. The relevant tax considerations applicable to the acquiring, holding and disposing of common shares pursuant to this offering may vary according to the status of the holder, the jurisdiction in which the holder resides or carries on business and the holder’s own particular circumstances. Accordingly, each Non-Canadian Holder should consult with their own tax advisors with respect to the Canadian federal income tax consequences to them of acquiring, holding or disposing of the common shares.

Dividends

Dividends paid or credited (or deemed to be paid or credited, including on a repurchase or redemption of the common shares by the Company) on the common shares to a Non-Canadian Holder will generally be subject to withholding tax under the Tax Act at a rate of 25%, subject to reduction under the provisions of any applicable tax treaty that the Non-Canadian Holder is entitled to the benefits of, which withholding tax will be withheld and remitted by the Company for the account of the Non-Canadian Holder as required by law. For Non-Canadian Holders who are resident in the U.S. for purposes of, and are entitled to the benefits of, the Canada-U.S. Tax Treaty (a “U.S. Holder”), and are the beneficial owner of such dividends paid on the common shares, the Canadian withholding tax may generally be reduced to the rate of 15%, or if such Non-Canadian Holder owns at least 10% of our voting shares, to the rate of 5%. Not all persons who are resident of the U.S. for purposes of the Canada-US Tax Treaty will be qualified for the benefits of the Canada-US Tax Treaty. **Non-Canadian Holders who may be eligible for a reduced rate of withholding tax on dividends (if any) pursuant to any applicable tax treaty should consult with their own tax**

advisors with respect to taking all appropriate steps to obtain the benefit of a reduced withholding rate, including the execution and delivery to us of CRA Form NR301, NR302, or NR303.

Disposition of common shares

A Non-Canadian Holder will not be subject to tax under the Tax Act in respect of any capital gain realized upon the disposition or deemed disposition of common shares (other than on a repurchase or redemption of the common shares by the Company) unless the common shares are “taxable Canadian property” (as defined in the Tax Act) of the Non-Canadian Holder, and the gain is not otherwise exempt from tax in Canada pursuant to the terms of an applicable tax treaty that the Non-Canadian Holder is entitled to the benefits of.

Provided the common shares are listed on a “designated stock exchange” within the meaning of the Tax Act (which currently includes Nasdaq) at the time of disposition, the common shares generally will not constitute “taxable Canadian property” of a Non-Canadian Holder, unless at any time during the 60-months immediately preceding the disposition, (i) one or any combination of (a) the Non-Canadian Holder, (b) persons with whom the Non-Canadian Holder does not deal at arm’s length for purposes of the Tax Act, or (c) partnerships in which the Non-Canadian Holder or persons referred to in (b) hold a membership interest directly or indirectly through one or more partnerships, owned at least 25% of the issued shares of any class or series of the Company’s capital stock, and (ii) more than 50% of the fair market value of the common shares was derived directly or indirectly from one or any combination of (a) real or immovable property situated in Canada, (b) “Canadian resource properties” (as defined in the Tax Act), (c) “timber resource properties” (as defined in the Tax Act), or (d) an option, interest or right in any such property described in (a) to (c), whether or not such property exists. For a U.S. Holder, even if the common shares are taxable Canadian property to such holder at the time of disposition, the Canada-US Tax Treaty will generally exempt a disposition of common shares from Canadian federal income taxes unless the value of the common shares at that time is derived principally from real property situated in Canada. Common shares may also be deemed to be “taxable Canadian property” in certain other circumstances as set out in the Tax Act.

In the event the common shares are (or are deemed to be) taxable Canadian property to a Non-Canadian Holder at the time of disposition and the gain, if any, realized on the disposition of such common shares is not exempt from tax under the Tax Act by virtue of the terms of an applicable tax treaty, such Non-Canadian Holder will realize a capital gain (or capital loss) equal to the amount by which such Non-Canadian Holder’s proceeds of disposition in respect of the common share exceeds (or is exceeded by) the aggregate of the adjusted cost base of such common share to the Non-Canadian Holder and any reasonable expenses associated with the disposition. The cost to such Non-Canadian Holder of a common share acquired pursuant to this offering generally will be averaged with the adjusted cost base of any other common shares owned by the Non-Canadian Holder as capital property for the purposes of determining the adjusted cost base of each such common share to that Non-Canadian Holder.

Such Non-Canadian Holder whose common shares are taxable Canadian property at the time of disposition is generally required to comply with certain reporting and notification obligations under the Tax Act in respect of the disposition of such common shares including the requirement to file a Canadian income tax return reporting the disposition of such common shares. Non-Canadian Holders whose common shares are taxable Canadian property should consult their own tax advisors for advice having regard to their particular circumstances.

LEGAL MATTERS

Certain United States legal matters in connection with this offering will be passed upon on our behalf by Hogan Lovells US LLP. Certain Canadian legal matters in connection with this offering will be passed upon on our behalf by Farris LLP, Vancouver, British Columbia. Jefferies LLC is being represented in connection with this offering by Cooley LLP, New York, New York, for certain United States legal matters and Bennett Jones LLP, Vancouver, British Columbia, for certain Canadian legal matters.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2020, as set forth in their reports, which are incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP's reports, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND ADDITIONAL INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC. The SEC maintains an Internet website at <http://www.sec.gov> that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC. Our reports on Forms 10-K, 10-Q and 8-K, and amendments to those reports, are also available for download, free of charge, as soon as reasonably practicable after these reports are filed with, or furnished to, the SEC, at our website at www.arbutusbio.com. Information contained on or accessible through our website is not a part of this prospectus supplement, and the inclusion of our website address in this prospectus supplement is an inactive textual reference only.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to “incorporate by reference” into this prospectus supplement the information in other documents that we file with it. This means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be a part of this prospectus supplement, and information in documents that we file later with the SEC will automatically update and supersede information contained in documents filed earlier with the SEC or contained in this prospectus supplement. We incorporate by reference in this prospectus supplement (i) the documents listed below, (ii) all documents that we file with the SEC under Section 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of the initial filing of the registration statement of which this prospectus supplement is included and prior to the effectiveness of such registration statement, and (iii) any future filings that we may make with the SEC under Sections 13(a), 13(c), 14, or 15(d) of the Exchange Act prior to the termination of the offerings under this prospectus supplement; provided, however, that we are not incorporating, in each case, any documents or information deemed to have been furnished and not filed, including any information that we disclose under Items 2.02 or 7.01 of any Current Report on Form 8-K, in accordance with SEC rules:

- [our Annual Report on Form 10-K for the year ended December 31, 2020, filed with the SEC on March 4, 2021](#);
- our Current Reports on Form 8-K as filed with the SEC on [January 25, 2021](#) (other than the portions thereof that are furnished and not filed), [February 1, 2021](#) and [February 26, 2021](#);
- [our Definitive Proxy Statement on Schedule 14A, filed with the SEC on April 24, 2020 \(other than the portions thereof that are furnished and not filed\)](#); and
- [the description of our common shares contained in our registration statement on Form 8-A filed with the SEC on November 4, 2010, including any amendment or report filed for purposes of updating such description](#).

You may request, orally or in writing, a copy of any or all of the documents incorporated herein by reference. These documents will be provided to you at no cost, by contacting: Arbutus Biopharma Corporation, Attn: Corporate Secretary, 701 Veterans Circle, Warminster, Pennsylvania 18974. In addition,

copies of any or all of the documents incorporated herein by reference may be accessed at our website at www.arbutusbio.com. The information on such website is not incorporated by reference and is not a part of this prospectus supplement.

PROSPECTUS



\$200,000,000
Common Shares
Preferred Shares
Warrants
Debt Securities
Units

We may offer and issue from time to time common shares, preferred shares, warrants, debt securities, or any combination of those securities, either individually or in units, up to an aggregate initial offering price of \$200,000,000, in one or more transactions under this prospectus. The securities may be offered in amounts, at prices and on terms to be determined based on market conditions at the time of sale and set forth in an accompanying prospectus supplement.

This prospectus provides you with a general description of the securities that we may offer. Each time we offer securities, we will provide you with a prospectus supplement that describes specific information about the particular securities being offered and may add, update or change information contained or incorporated by reference in this prospectus. You should read both this prospectus and the applicable prospectus supplement, together with the additional information that is incorporated by reference into this prospectus and the applicable prospectus supplement.

The securities may be sold by us to or through underwriters or dealers, directly to purchasers or through agents designated from time to time. For additional information on the methods of sale, you should refer to the section entitled "Plan of Distribution" in this prospectus and the comparable section of any applicable prospectus supplement. If any underwriters are involved in the sale of the securities with respect to which this prospectus is being delivered, the names of such underwriters and any applicable discounts or commissions and options will be set forth in the applicable prospectus supplement.

Our common shares are listed on the Nasdaq Global Select Market under the ticker symbol "ABUS." On August 27, 2020, the last reported sale price per share of our common shares on the Nasdaq Global Select Market was \$2.92 per share. We have not yet determined whether the other securities that may be offered by this prospectus will be listed on any exchange, interdealer quotation system or over-the-counter market. If we decide to seek the listing of any such securities upon issuance, the prospectus supplement relating to those securities will disclose the exchange, quotation system or market on which those securities will be listed.

INVESTING IN OUR SECURITIES INVOLVES A HIGH DEGREE OF RISK. RISKS ASSOCIATED WITH AN INVESTMENT IN OUR SECURITIES WILL BE DESCRIBED IN THE APPLICABLE PROSPECTUS SUPPLEMENT AND CERTAIN OF OUR FILINGS WITH THE SECURITIES AND EXCHANGE COMMISSION INCORPORATED BY REFERENCE INTO THIS PROSPECTUS, AS DESCRIBED UNDER "RISK FACTORS" ON PAGE 5.

You should read this prospectus and any applicable prospectus supplement together with additional information described under the heading "Where You Can Find Additional Information" before you make your investment decision.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus is October 22, 2020.

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ABOUT THIS PROSPECTUS

This prospectus is a part of a registration statement that we filed with the Securities and Exchange Commission, or the SEC, using a “shelf” registration process. Under this shelf registration process, we may offer to sell any of the securities, or any combination of the securities, described in this prospectus, in each case, in one or more offerings, up to a total dollar amount of \$200,000,000.

This prospectus provides you only with a general description of the securities that we may offer. Each time securities are sold under this registration statement, we will provide an accompanying prospectus supplement that will contain specific information about the terms of those securities and the terms of that offering. The accompanying prospectus supplement may also add, update or change information contained in this prospectus. If there is any inconsistency between the information in this prospectus and any accompanying prospectus supplement, you should rely on the information in the accompanying prospectus supplement. You should read both this prospectus and any accompanying prospectus supplement, including all documents incorporated by reference herein and therein, together with the additional information described under “Where You Can Find Additional Information” below.

The information contained in this prospectus is not complete and may be changed. You should rely only on the information provided in or incorporated by reference in this prospectus or in any accompanying prospectus supplement, or documents to which we otherwise refer you. We have not authorized anyone else to provide you with different information.

We have not authorized any dealer, agent or other person to give any information or to make any representation other than those contained or incorporated by reference in this prospectus and any accompanying prospectus supplement. You must not rely upon any information or representation not contained or incorporated by reference in this prospectus or an accompanying prospectus supplement. This prospectus and the accompanying prospectus supplement, if any, do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the registered securities to which they relate, nor do this prospectus and any accompanying prospectus supplement, if any, constitute an offer to sell or the solicitation of an offer to buy securities in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation in such jurisdiction. You should not assume that the information contained in this prospectus and any accompanying prospectus supplement is accurate on any date subsequent to the date set forth on the front of such document or that any information we have incorporated by reference is correct on any date subsequent to the date of the document incorporated by reference, even though this prospectus and any accompanying prospectus supplement is delivered or securities are sold on a later date.

As used in this prospectus, unless the context otherwise requires, the terms “Arbutus,” the “Company,” “we,” “us,” and “our” refer to Arbutus Biopharma Corporation, and, unless the context requires otherwise, the subsidiaries through which it conducts business. The Arbutus logo and all other Arbutus product names are trademarks of Arbutus in the United States and in other select countries. The Arbutus logo is a trademark of Arbutus in Canada. We may indicate U.S. trademark registrations and U.S. trademarks with the symbols “®” and “™”, respectively. Other third-party logos and product/trade names are registered trademarks or trade names of their respective owners.

FORWARD-LOOKING STATEMENTS

This prospectus, including the documents incorporated by reference into this prospectus, contains “forward-looking statements” or “forward-looking information” within the meaning of applicable U.S. and Canadian securities laws (we collectively refer to these items as “forward-looking statements”). Forward-looking statements are generally identifiable by use of the words “believes,” “may,” “plans,” “will,” “anticipates,” “intends,” “budgets,” “could,” “estimates,” “expects,” “forecasts,” “projects” and similar expressions that are not based on historical fact or that are predictions of or indicate future events and trends, and the negative of such expressions. Forward-looking statements in this prospectus, including the documents incorporated by reference, include statements about, among other things:

- our strategy, future operations, pre-clinical research, pre-clinical studies, clinical trials, prospects and the plans of management;
- the potential impact of the COVID-19 pandemic on our business;
- our expectations regarding the technology that we licensed to Genevant Sciences Ltd.;
- the discovery, development and commercialization of a cure for chronic hepatitis B infection, a disease of the liver caused by the hepatitis B virus, or HBV;
- our beliefs and development path and strategy to achieve a cure for HBV;
- obtaining necessary regulatory approvals;
- obtaining adequate financing through a combination of financing activities and operations;
- using the results from our HBV studies to adaptively design additional clinical trials to test the efficacy of the combination therapy and the duration of the result in patients;
- the expected timing of and amount for payments related to Enantigen Therapeutics, Inc.’s transaction and its programs;
- the potential of our drug candidates to improve upon the standard of care and contribute to a curative combination treatment regimen;
- the potential benefits of the reversion of the Ontario Municipal Employees Retirement System, or OMERS, royalty monetization transaction for our ONPATPRO™ (Patisiran) royalty interest;
- developing a suite of products that intervene at different points in the viral life cycle, with the potential to reactivate the host immune system;
- using pre-clinical results to adaptively design clinical trials for additional cohorts of patients, testing the combination and the duration of therapy;
- selecting combination therapy regimens and treatment durations to conduct Phase 3 clinical trials intended to ultimately support regulatory filings for marketing approval;
- expanding our HBV drug candidate pipeline through internal development, acquisitions and in-licenses;
- our expectation for AB-729 for preliminary results from a single-dose 90 mg cohort and multi-dose 60 mg cohorts in our Phase 1a/1b trial to be available in the second half of 2020;
- our expectation for AB-729 for preliminary results from a 90 mg single-dose cohort in HBV DNA positive subjects to be available in the second half of 2020;
- our expectation that AB-729 could be combined with our lead capsid inhibitor candidate, AB-836, and approved NAs, in our first combination therapy for HBV patients;
- our expectations regarding the dose interval for the planned AB-729 90 mg multi-dose cohorts;
- expectations regarding our proposed Phase 2 clinical trial to explore the safety, pharmacokinetics, and antiviral activity of the triple combination of ABI-H0731, AB-729 and a standard-of-care nucleos(t)ide reverse transcriptase inhibitor therapy pursuant to our clinical collaboration agreement with Assembly Biosciences, Inc.;

- the potential for an oral HBsAg-reducing agent and potential all-oral combination therapy;
- our objective to complete IND/CTA-enabling studies for AB-836 by the end of 2020;
- the potential for AB-836 to be low-dose regimen with a wide therapeutic window and to address known capsid resistant variants T33N and 1105T;
- the potential for AB-836 to have increased potency and an enhanced resistance profile, compared to our previous capsid inhibitor candidate, AB-506;
- the potential for AB-836 to be once-daily dosing;
- our expectation to pursue development of a next generation oral HBV RNA-destabilizer;
- our expectations regarding our ability to develop a potential COVID-19 therapy;
- payments from the Gritstone Oncology, Inc. licensing agreement;
- the expected return from strategic alliances, licensing agreements, and research collaborations;
- statements with respect to revenue and expense fluctuation and guidance;
- having sufficient cash resources to fund our operations through mid-2022; and
- obtaining funding to maintain and advance our business from a variety of sources including public or private equity or debt financing, collaborative arrangements with pharmaceutical companies and government grants and contracts.

We cannot guarantee that the results and other expectations expressed, anticipated or implied in any forward-looking statement will be realized. The risks set forth under Item 1A of our Form 10-K for the year ended December 31, 2019, as revised or supplemented by our Quarterly Reports on Form 10-Q and other documents we file with the SEC, describe material risks to our business, and you should read and interpret any forward-looking statements together with these risks. A variety of factors, including these risks, could cause our actual results and other expectations to differ materially from the anticipated results or other expectations expressed, anticipated or implied in our forward-looking statements. Should known or unknown risks materialize, or should underlying assumptions prove inaccurate, actual results could differ materially from past results and those anticipated, estimated or projected in the forward-looking statements. You should bear this in mind as you consider any forward-looking statements.

You should read this prospectus, any prospectus supplement and the documents that we incorporate by reference herein and therein completely and with the understanding that our actual future results may be materially different from what we expect. The forward-looking statements contained in this prospectus are made as of the date of this prospectus and we do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by applicable law.

This prospectus and any applicable prospectus supplement and the documents incorporated by reference herein and therein contain estimates, projections, market research and other information concerning, among other things, our industry, our business, markets and our product candidates. Unless otherwise expressly stated, we obtain this information from reports, research surveys, studies and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources as well as from our own internal estimates and research and from publications, research, surveys and studies conducted by third parties on our behalf. Information that is based on estimates, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances that are reflected in this information. As a result, you are cautioned not to give undue weight to such information.

THE COMPANY

Company Overview

Arbutus Biopharma Corporation (“Arbutus”, the “Company”, “we”, “us”, and “our”) is a publicly traded (Nasdaq Global Select Market: ABUS) clinical-stage biopharmaceutical company primarily focused on developing a cure for people with HBV infection. We are advancing multiple drug product candidates that may be combined into a potentially curative regimen for chronic HBV infection. Arbutus has also initiated a drug discovery and development effort for treating coronaviruses, including COVID-19.

Our focus is on developing new HBV treatment regimens with finite treatment durations and higher cure rates. We define a cure as a functional cure where HBV DNA replication and hepatitis B surface antigen expression are reduced to undetectable levels and this level of expression is sustained six months after a finite duration of therapy. Our HBV product pipeline includes RNA interference therapeutics, oral capsid inhibitors, oral compounds that inhibit PD-L1 and oral HBV RNA destabilizers. We believe a combination of these product candidates could lead to a curative treatment regimen with a finite duration for patients with chronic HBV infection.

Corporate Information

Arbutus was incorporated pursuant to the British Columbia Business Corporations Act, or BCBCA, on October 6, 2005, and commenced active business on April 30, 2007, when Arbutus and its parent company, Inex Pharmaceuticals Corporation, or Inex, were reorganized under a statutory plan of arrangement, or the Plan of Arrangement, completed under the provisions of the BCBCA. The Plan of Arrangement saw Inex’s entire business transferred to and continued by Arbutus.

On March 4, 2015, we completed a business combination pursuant to which OnCore Biopharma, Inc., or OnCore, became our wholly-owned subsidiary. Arbutus Inc. contributed many of the assets in our HBV pipeline.

Effective July 31, 2015, our corporate name changed from Tekmira Pharmaceuticals Corporation to Arbutus Biopharma Corporation. Also effective July 31, 2015, the corporate name of our wholly owned subsidiary, OnCore Biopharma, Inc. changed to Arbutus Biopharma, Inc., or Arbutus Inc. We had two wholly owned subsidiaries: Arbutus Inc. and Protiva Biotherapeutics Inc., or Protiva. Effective January 1, 2018, Protiva was amalgamated with Arbutus.

Arbutus’ head office and principal place of business is located at 701 Veterans Circle, Warminster, Pennsylvania 18974 and our telephone number is (267) 469-0914. We maintain a website at www.arbutusbio.com. The information contained on, or that can be accessed through, our website is not a part of this prospectus or any accompanying prospectus supplement. We have included our website address in this prospectus solely as an inactive textual reference.

RISK FACTORS

Investing in our securities involves a high degree of risk. The prospectus supplement applicable to each offering of our securities will contain a discussion of the risks applicable to an investment in our securities. Prior to making a decision about investing in our securities, you should carefully consider the specific factors discussed under the heading “Risk Factors” in the applicable prospectus supplement, together with all of the other information contained or incorporated by reference in the prospectus supplement or appearing or incorporated by reference in this prospectus. You should also consider the risks, uncertainties and assumptions discussed under the heading “Risk Factors” in our most recent Annual Report on Form 10-K and our Quarterly Reports on Form 10-Q and other documents that we file with the SEC, which are incorporated herein by reference as described in this prospectus under the heading “Where You Can Find Additional Information”. The risks and uncertainties we have described in such documents are not the only risks that we face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also affect our operations.

USE OF PROCEEDS

Except as otherwise provided in the applicable prospectus supplement relating to a specific offering, we intend to use the net proceeds from the sale of securities by us under this prospectus and any applicable prospectus supplement for general corporate purposes, which may include working capital, capital expenditures, research and development expenditures, clinical trial expenditures, acquisitions of new technologies, products or businesses, and investments. Additional information on the use of net proceeds from the sale of securities by us under this prospectus may be set forth in the accompanying prospectus supplement relating to the specific offering.

GENERAL DESCRIPTION OF OUR SECURITIES

We may offer and sell, at any time and from time to time:

- common shares;
- preferred shares;
- warrants to purchase common shares;
- debt securities consisting of debentures, notes or other evidences of indebtedness;
- units consisting of a combination of the foregoing securities; or
- any combination of these securities.

The terms of any securities we offer will be determined at the time of sale. We may issue debt securities that are exchangeable for and/or convertible into common shares or any of the other securities that may be sold under this prospectus. When particular securities are offered by us, a supplement to this prospectus will be filed with the SEC, which will describe the terms of the offering and sale of the offered securities.

The descriptions below of our share capital, warrants, debt securities and related information are summaries and are qualified by reference to documents incorporated by reference to the registration statement of which this prospectus is a part. Please refer to “Where You Can Find Additional Information” below for directions on obtaining these documents.

DESCRIPTION OF OUR CAPITAL STOCK

Authorized and Outstanding Shares

Our authorized share capital consists of an unlimited number of common shares, without par value, and an unlimited number of preferred shares, without par value. As of August 27, 2020, there were (a) 82,909,259 common shares outstanding and (b) 1,164,000 preferred shares outstanding. None of our common shares or preferred shares are held by us or on behalf of us.

Voting Rights

The holders of our common shares are entitled to receive notice of any meeting of our shareholders and to attend and vote thereat, except those meetings at which only the holders of shares of another class or of a particular series are entitled to vote. Each common share entitles its holder to one vote. There are no cumulative voting rights.

Dividends

Subject to the rights of the holders of preferred shares, the holders of common shares are entitled to receive on a pro rata basis such dividends as our board of directors may declare out of funds legally available for payment of dividends. In the event of the dissolution, liquidation, winding-up or other distribution of our assets, those holders are entitled to receive on a pro rata basis all of our assets remaining after payment of all of our liabilities, subject to the rights of holders of preferred shares. Our common shares carry no pre-emptive or conversion rights.

Series A Participating Convertible Preferred Shares

In October 2017, we entered into a subscription agreement with Roivant Sciences Ltd., or Roivant, for the sale of 1,164,000 Series A participating convertible preferred shares, or the Preferred Shares, for gross proceeds of \$116.4 million. These Preferred Shares are non-voting and accrue an 8.75% per annum coupon in the form of additional Preferred Shares, compounded annually, until October 16, 2021, at which time all the Preferred Shares will be subject to mandatory conversion into common shares (subject to limited exceptions in the event of certain fundamental corporate transactions relating to our capital structure or assets, which would permit earlier conversion at Roivant's option). The conversion price is \$7.13 per share, which will result in the Preferred Shares being converted into approximately 23 million common shares. After conversion of the Preferred Shares into common shares, based on the number of common shares outstanding as of August 1, 2020, Roivant would hold approximately 37% of our common shares. Roivant agreed to a four year lock-up period for this investment and its existing holdings in us. Roivant also agreed to a four year standstill whereby Roivant will not acquire greater than 49.99% of our common shares or securities convertible into common shares. The initial investment of \$50.0 million closed in October 2017, and the remaining amount of \$66.4 million closed in January 2018 following regulatory and shareholder approvals.

Registration Rights

On January 11, 2015, we entered into an Agreement and Plan of Merger and Reorganization, or the Merger Agreement, with OnCore pursuant to which OnCore became our wholly-owned subsidiary. In connection with the Merger Agreement, we entered into a Registration Rights Agreement, or the Registration Rights Agreement, with certain of OnCore's shareholders. On October 16, 2017, we entered into an Amending Agreement pursuant to which the common shares underlying the Preferred Shares purchased by Roivant were included as registrable securities under the Registration Rights Agreement.

Pursuant to the Registration Rights Agreement, certain holders of our common shares have registration rights. After registration of these common shares pursuant to these rights, these shares will become freely tradable without restriction under the Securities Act. The registration rights will terminate with respect to each shareholder on the date on which such shareholder ceases to beneficially own more than three percent of our common shares then outstanding, if such shares may be sold pursuant to Rule 144 of the Securities Act.

An aggregate of 19,111,583 common shares are entitled to these registration rights. We have complied with all of our other obligations under the Registration Rights Agreement in connection with the filing of this registration statement.

Director Nomination Rights

Pursuant to the terms of the Amended and Restated Governance Agreement, dated October 16, 2017, between us and Roivant and Part 28 of our Notice of Articles and Articles, or our Articles, for so long as Roivant has “beneficial ownership” (as defined pursuant Rule 13d-3 under the Securities Exchange Act of 1934, as amended, or the Exchange Act), or Beneficial Ownership, or exercises control or direction over not less than:

- thirty percent (30%) of our issued and outstanding common shares calculated on a partially diluted basis as of a particular date, Roivant has the right to nominate three (3) individuals for election to our Board of Directors at each shareholder meeting, one (1) of whom must satisfy the applicable independence standards;
- twenty percent (20%) of our issued and outstanding common shares calculated on a partially diluted basis as of a particular date, Roivant has the right to nominate two (2) individuals for election to our Board of Directors at each shareholder meeting; and
- ten percent (10%) of our issued and outstanding common shares calculated on a partially diluted basis as of a particular date, Roivant has the right to nominate one (1) individual for election to our Board of Directors at each shareholder meeting.

Upon Roivant having Beneficial Ownership or exercising control or direction over less than ten percent (10%) of our outstanding common shares calculated on a partially diluted basis as of a particular date, the nomination rights provided above will be of no further force and effect. The total number of common shares underlying the Preferred Shares beneficially owned by Roivant are included in the Beneficial Ownership calculations described above.

Limitations to Control due to Certain Provisions of Canadian and British Columbian Law and our Articles

Unless such offer constitutes an exempt transaction, an offer made by a person, or an offeror, to acquire outstanding shares of a Canadian entity that, when aggregated with the offeror’s holdings (and those of persons or companies acting jointly with the offeror), would constitute 20% or more of the outstanding shares, would be subject to the take-over provisions of Canadian securities laws. The foregoing is a limited and general summary of certain aspects of applicable securities law in the provinces and territories of Canada, all in effect as of the date hereof.

In addition to the take-over bid requirements noted above, the acquisition of shares may trigger the application of additional statutory regimes including amongst others, the Investment Canada Act (Canada) and the Competition Act (Canada).

This summary is not a comprehensive description of relevant or applicable considerations regarding such requirements and, accordingly, is not intended to be, and should not be interpreted as, legal advice to any prospective purchaser and no representation with respect to such requirements to any prospective purchaser is made. Prospective investors should consult their own Canadian legal advisors with respect to any questions regarding securities law in the provinces and territories of Canada.

As well, under the Business Corporations Act (British Columbia), unless otherwise stated in the Articles, certain corporate actions require the approval of a special majority of shareholders, meaning holders of shares representing 66 $\frac{2}{3}$ % of those votes cast in respect of a shareholder vote addressing such matter. Those items requiring the approval of a special majority generally relate to fundamental changes with respect to our business, and include amongst others, resolutions: (i) removing a director prior to the expiry of his or her term; (ii) altering the Articles, (iii) approving an amalgamation; (iv) approving a plan of arrangement; and (v) providing for a sale of all or substantially all of our assets.

Outstanding Stock Options

As of August 27, 2020, we had outstanding options to purchase 9,747,637 of our common shares at a weighted-average exercise price of \$4.87 per share, pursuant to our 2011 Omnibus Share Compensation Plan and our 2016 Omnibus Share and Incentive Plan.

As of August 27, 2020, we had outstanding options to purchase 99,991 of our common shares at a weighted-average exercise price of \$0.58 per share, pursuant to the OnCore Option Plan.

As of August 27, 2020, we had outstanding options to purchase 1,112,000 of our common shares at a weighted-average exercise price of \$2.18 per share, which options were issued outside of our equity compensation plans.

The Nasdaq Global Select Market

Our common shares are listed on the Nasdaq Global Select Market under the symbol “ABUS.”

Transfer Agent and Registrar

The transfer agent and registrar for our common shares is AST Trust Company (Canada).

DESCRIPTION OF OUR WARRANTS

We may issue warrants to purchase our common shares with other securities or separately, as described in each applicable prospectus supplement. Below is a description of certain general terms and provisions of the warrants that we may offer. Particular terms of the warrants will be described in the applicable warrant agreements and the applicable prospectus supplement for the warrants.

The applicable prospectus supplement will contain, where applicable, the following terms of and other information relating to the warrants:

- the specific designation and aggregate number of, and the price at which we will issue, the warrants;
- the currency or currency units in which the offering price, if any, and the exercise price are payable;
- the designation, amount and terms of the securities purchasable upon exercise of the warrants;
- if applicable, the exercise price for our common shares and the number of common shares to be received upon exercise of the warrants;
- the date on which the right to exercise the warrants will begin and the date on which that right will expire or, if the warrants may not be continuously exercised throughout that period, the specific date or dates on which the warrants may be exercised;
- whether the warrants will be issued in fully registered form or bearer form, in definitive or global form or in any combination of these forms, although, in any case, the form of a warrant included in a unit will correspond to the form of the unit and of any security included in that unit;
- any applicable material U.S. federal income tax or foreign tax consequences;
- the identity of the warrant agent for the warrants, if any, and of any other depositaries, execution or paying agents, transfer agents, registrars or other agents;
- the proposed listing, if any, of the warrants or any securities purchasable upon exercise of the warrants on any securities exchange or market;
- if applicable, the date from and after which the warrants and the common shares;
- if applicable, the minimum or maximum amount of the warrants that may be exercised at any one time;
- information with respect to book-entry procedures, if any
- the anti-dilution provisions of the warrants, if any;
- any redemption, put or call provisions;
- whether the warrants are to be sold separately or with other securities as parts of units; and
- any additional terms of the warrants, including terms, procedures and limitations relating to the exchange and exercise of the warrants.

Before the exercise of their warrants, holders of warrants will not have any of the rights of holders of common shares. Therefore, holders of warrants will not be entitled, by virtue of being such holders, to vote, consent, receive dividends, receive notice as shareholders with respect to any meeting of shareholders for the election of our directors or any other matter, or to exercise any rights whatsoever as our shareholders. We reserve the right to include in an applicable prospectus supplement specific terms of the warrants that are not within the options and parameters described in this prospectus. In addition, to the extent that any particular terms of the warrants described in an applicable prospectus supplement differ from any of the terms described in this prospectus, the description of those terms included in this prospectus shall be deemed to have been superseded by the description of the differing terms set forth in such applicable prospectus supplement with respect to such warrants.

Transfer Agent and Registrar

The transfer agent and registrar for any warrants will be set forth in the applicable prospectus supplement.

DESCRIPTION OF OUR DEBT SECURITIES

This section describes the general terms and provisions of the debt securities that we may offer under this prospectus, any of which may be issued as convertible or exchangeable debt securities. We will set forth the particular terms of the debt securities we offer in an applicable prospectus supplement. The extent, if any, to which the following general provisions apply to particular debt securities will be described in the applicable prospectus supplement. The following description of general terms relating to the debt securities and the indenture under which the debt securities will be issued are summaries only and therefore are not complete. You should read the indenture and the applicable prospectus supplement regarding any particular issuance of debt securities.

We will issue the debt securities offered by this prospectus and any accompanying prospectus supplement under an indenture to be entered into between us and the trustee identified in the applicable prospectus supplement. The terms of the debt securities will include those stated in the indenture and those made part of the indenture by reference to the Trust Indenture Act of 1939, as in effect on the date of the indenture. We have filed or will file a copy of the form of indenture as an exhibit to the registration statement in which this prospectus is included. The indenture will be subject to and governed by the terms of the Trust Indenture Act of 1939.

We may offer under this prospectus up to an aggregate principal amount of \$200,000,000 in debt securities, or if debt securities are issued at a discount, or in a foreign currency, foreign currency units or composite currency, the principal amount as may be sold for an aggregate initial public offering price of up to \$200,000,000. Unless otherwise specified in the applicable prospectus supplement, the debt securities will represent direct, unsecured obligations of the Company and will rank equally with all of our other unsecured indebtedness.

The following statements relating to the debt securities and the indenture are summaries, qualified in their entirety by reference to the detailed provisions of the indenture and the final form indenture as may be filed with an applicable prospectus supplement.

General

We may issue the debt securities in one or more series with the same or various maturities, at par, at a premium, or at a discount. We will describe the particular terms of each series of debt securities in an applicable prospectus supplement relating to that series, which we will file with the SEC.

The applicable prospectus supplement will set forth, to the extent required, the following terms of the debt securities in respect of which such prospectus supplement is delivered:

- the title of the series;
- the aggregate principal amount;
- the issue price or prices, expressed as a percentage of the aggregate principal amount of the debt securities;
- any limit on the aggregate principal amount;
- the date or dates on which principal is payable;
- the interest rate or rates (which may be fixed or variable) or, if applicable, the method used to determine such rate or rates;
- the date or dates from which interest, if any, will be payable and any regular record date for the interest payable;
- the place or places where principal and, if applicable, premium and interest, is payable;
- the terms and conditions upon which we may, or the holders may require us to, redeem or repurchase the debt securities;
- the denominations in which such debt securities may be issuable, if other than denominations of \$1,000 or any integral multiple of that number;

- whether the debt securities are to be issuable in the form of certificated debt securities (as described below) or global debt securities (as described below);
- the portion of principal amount that will be payable upon declaration of acceleration of the maturity date if other than the principal amount of the debt securities;
- the currency of denomination;
- the designation of the currency, currencies or currency units in which payment of principal and, if applicable, premium and interest, will be made;
- if payments of principal and, if applicable, premium or interest, on the debt securities are to be made in one or more currencies or currency units other than the currency of denomination, the manner in which the exchange rate with respect to such payments will be determined;
- if amounts of principal and, if applicable, premium and interest may be determined by reference to an index based on a currency or currencies or by reference to a commodity, commodity index, stock exchange index or financial index, then the manner in which such amounts will be determined;
- the provisions, if any, relating to any collateral provided for such debt securities;
- any addition to or change in the covenants and/or the acceleration provisions described in this prospectus or in the indenture;
- any events of default, if not otherwise described below under “Events of Default”;
- the terms and conditions, if any, for conversion into or exchange for shares of our common or preferred shares;
- any depositaries, interest rate calculation agents, exchange rate calculation agents or other agents; and
- the terms and conditions, if any, upon which the debt securities shall be subordinated in right of payment to other indebtedness of the Company.

We may issue discount debt securities that provide for an amount less than the stated principal amount to be due and payable upon acceleration of the maturity of such debt securities in accordance with the terms of the indenture. We may also issue debt securities in bearer form, with or without coupons. If we issue discount debt securities or debt securities in bearer form, we will describe material U.S. federal income tax considerations and other material special considerations that apply to these debt securities in the applicable prospectus supplement.

We may issue debt securities denominated in or payable in a foreign currency or currencies or a foreign currency unit or units. If we do, we will describe the restrictions, elections, and general tax considerations relating to the debt securities and the foreign currency or currencies or foreign currency unit or units in the applicable prospectus supplement.

Exchange and/or Conversion Rights

We may issue debt securities which can be exchanged for or converted into our common or preferred shares. If we do, we will describe the terms of exchange or conversion in the prospectus supplement relating to these debt securities.

Transfer and Exchange

We may issue debt securities that will be represented by either:

- “book-entry securities,” which means that there will be one or more global securities registered in the name of a depositary or a nominee of a depositary; or
- “certificated securities,” which means that they will be represented by a certificate issued in definitive registered form.

We will specify in the prospectus supplement applicable to a particular offering whether the debt securities offered will be book-entry or certificated securities.

Certificated Debt Securities

If you hold certificated debt securities issued under an indenture, you may transfer or exchange such debt securities in accordance with the terms of the indenture. You will not be charged a service charge for any transfer or exchange of certificated debt securities but may be required to pay an amount sufficient to cover any tax or other governmental charge payable in connection with such transfer or exchange.

Global Securities

The debt securities of a series may be issued in the form of one or more global securities that will be deposited with a depositary or its nominees identified in the prospectus supplement relating to the debt securities. In such a case, one or more global securities will be issued in a denomination or aggregate denominations equal to the portion of the aggregate principal amount of outstanding debt securities of the series to be represented by such global security or securities.

Unless and until it is exchanged in whole or in part for debt securities in definitive registered form, a global security may not be registered for transfer or exchange except as a whole by the depositary for such global security to a nominee of the depositary and except in the circumstances described in the applicable prospectus supplement relating to the debt securities. The specific terms of the depositary arrangement with respect to a series of debt securities will be described in the applicable prospectus supplement relating to such series.

Protection in the Event of Change of Control

Any provision in an indenture that governs our debt securities covered by this prospectus that includes any covenant or other provision providing for a put or increased interest or otherwise that would afford holders of our debt securities additional protection in the event of a recapitalization transaction, a change of control of the Company, or a highly leveraged transaction will be described in the applicable prospectus supplement.

Covenants

Unless otherwise indicated in this prospectus or the applicable prospectus supplement, our debt securities may not have the benefit of any covenant that limits or restricts our business or operations, the pledging of our assets or the incurrence by us of indebtedness. We will describe in the applicable prospectus supplement any material covenants in respect of a series of debt securities.

Consolidation, Merger and Sale of Assets

We may agree in any indenture that governs the debt securities of any series covered by this prospectus that we will not consolidate with or merge into any other person or convey, transfer, sell or lease our properties and assets substantially as an entirety to any person, unless such person and such proposed transaction meets various criteria, which we will describe in detail in the applicable prospectus supplement.

Defaults and Notice

The debt securities of any series will contain events of default to be specified in the applicable prospectus supplement, which may include, without limitation:

- failure to pay the principal of, or premium or make-whole amount, if any, on any debt security of such series when due and payable (whether at maturity, by call for redemption, through any mandatory sinking fund, by redemption at the option of the holder, by declaration or acceleration or otherwise);
- failure to make a payment of any interest on any debt security of such series when due;
- our failure to perform or observe any other covenants or agreements in the indenture with respect to the debt securities of such series;
- certain events relating to our bankruptcy, insolvency or reorganization; and
- certain cross defaults, if and as applicable.

If an event of default with respect to debt securities of any series shall occur and be continuing, we may agree that the trustee or the holders of at least 25% in aggregate principal amount of the then outstanding debt securities of such series may declare the principal amount (or, if the debt securities of such series are issued at an original issue discount, such portion of the principal amount as may be specified in the terms of the debt securities of such series) of all debt securities of such series or such other amount or amounts as the debt securities or supplemental indenture with respect to such series may provide, to be due and payable immediately. Any provisions pertaining to events of default and any remedies associated therewith will be described in the applicable prospectus supplement.

Any indenture that governs our debt securities covered by this prospectus may require that the trustee under such indenture shall, within 90 days after the occurrence of a default, give to holders of debt securities of any series notice of all uncured defaults with respect to such series known to it. However, in the case of a default that results from the failure to make any payment of the principal of, premium or make-whole amount, if any, or interest on the debt securities of any series, or in the payment of any mandatory sinking fund installment with respect to debt securities of such series, if any, the trustee may withhold such notice if it in good faith determines that the withholding of such notice is in the interest of the holders of debt securities of such series. Any terms and provisions relating to the foregoing types of provisions will be described in further detail in the applicable prospectus supplement.

Any indenture that governs our debt securities covered by this prospectus will contain a provision entitling the trustee to be indemnified by holders of debt securities before proceeding to exercise any trust or power under the indenture at the request of such holders. Any such indenture may provide that the holders of at least a majority in aggregate principal amount of the then outstanding debt securities of any series may direct the time, method and place of conducting any proceedings for any remedy available to the trustee, or of exercising any trust or power conferred upon the trustee with respect to the debt securities of such series. However, the trustee under any such indenture may decline to follow any such direction if, among other reasons, the trustee determines in good faith that the actions or proceedings as directed may not lawfully be taken, would involve the trustee in personal liability or would be unduly prejudicial to the holders of the debt securities of such series not joining in such direction.

Any indenture that governs our debt securities covered by this prospectus may endow the holders of such debt securities to institute a proceeding with respect to such indenture, subject to certain conditions, which will be specified in the applicable prospectus supplement and which may include, that the holders of at least a majority in aggregate principal amount of the debt securities of such series then outstanding make a written request upon the trustee to exercise its power under the indenture, indemnify the trustee and afford the trustee reasonable opportunity to act. Even so, such holders may have an absolute right to receipt of the principal of, premium or make-whole amount, if any, and interest when due, to require conversion or exchange of debt securities if such indenture provides for convertibility or exchangeability at the option of the holder and to institute suit for the enforcement of such rights. Any terms and provisions relating to the foregoing types of provisions will be described in further detail in the applicable prospectus supplement.

Modification of the Indenture

We and the trustee may modify any indenture that governs our debt securities of any series covered by this prospectus with or without the consent of the holders of such debt securities, under certain circumstances to be described in an applicable prospectus supplement.

Defeasance; Satisfaction and Discharge

The applicable prospectus supplement will outline the conditions under which we may elect to have certain of our obligations under the indenture discharged and under which the indenture obligations will be deemed to be satisfied.

Regarding the Trustee

We will identify the trustee and any relationship that we may have with such trustee, with respect to any series of debt securities, in the applicable prospectus supplement relating to the applicable debt securities. You should note that if the trustee becomes a creditor of the Company, the indenture and the Trust Indenture

Act of 1939 limit the rights of the trustee to obtain payment of claims in certain cases, or to realize on certain property received in respect of any such claim, as security or otherwise. The trustee and its affiliates may engage in, and will be permitted to continue to engage in, other transactions with us and our affiliates. If, however, the trustee acquires any “conflicting interest” within the meaning of the Trust Indenture Act of 1939, it must eliminate such conflict or resign.

Governing Law

The law governing the indenture and the debt securities will be identified in the applicable prospectus supplement relating to the applicable indenture and debt securities.

DESCRIPTION OF OUR UNITS

The following description, together with the additional information we include in any applicable prospectus supplement, summarizes the material terms and provisions of the units that we may offer under this prospectus. Units may be offered independently or together with common shares, preferred shares, warrants or debt securities offered by any prospectus supplement, and may be attached to or separate from those securities. While the terms we have summarized below will generally apply to any future units that we may offer under this prospectus, we will describe the particular terms of any series of units that we may offer in more detail in the applicable prospectus supplement. The terms of any units offered under an applicable prospectus supplement may differ from the terms described below.

We will incorporate by reference into the registration statement of which this prospectus forms a part the form of unit agreement, including a form of unit certificate, if any, that describes the terms of the series of units we are offering before the issuance of the related series of units. The following summaries of material provisions of the units, and the unit agreements, are subject to, and qualified in their entirety by reference to, all the provisions of the unit agreement applicable to a particular series of units. We urge you to read the applicable prospectus supplements related to the units that we sell under this prospectus, as well as the complete unit agreements that contain the terms of the units.

We may issue units comprised of one or more of the 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, if any, under which a unit is issued may provide that the securities comprising 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 an applicable prospectus supplement, and the extent to which the general terms and provisions described below may apply thereto, will be described in the applicable prospectus supplement filed in respect of such units. This description will include, where applicable:

- the designation and aggregate number of units offered;
- the price at which the units will be offered;
- the rights and obligations of the unit agent, if any;
- the currency or currencies in which the units are denominated;
- any provisions of the governing unit agreement that differ from those described below;
- the 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;
- the number of securities that may be purchased upon exercise of each unit and the price at which the currency or currencies in which that amount of securities may be purchased upon exercise of each unit;
- any provisions for the issuance, payment, settlement, transfer, adjustment or exchange of the units or of the securities comprising the units; and
- any other material terms of the units.

We reserve the right to set forth in an applicable prospectus supplement specific terms of the units that are not within the options and parameters set forth in this prospectus. In addition, to the extent that any particular terms of the units described in an applicable 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 the differing terms set forth in such prospectus supplement with respect to such units.

PLAN OF DISTRIBUTION

We may sell the securities, from time to time, to or through underwriters or dealers, through agents or remarketing firms, or directly to one or more purchasers pursuant to:

- underwritten public offerings;
- negotiated transactions;
- block trades;
- “At the Market Offerings,” within the meaning of Rule 415(a)(4) of the Securities Act of 1933, as amended, or the Securities Act, into an existing trading market, at prevailing market prices; or
- through a combination of these methods.

We may sell the securities to or through one or more underwriters or dealers (acting as principal or agent), through agents, or directly to one or more purchasers.

We may distribute securities from time to time in one or more transactions:

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

A prospectus supplement or supplements (and any related free writing prospectus that we may authorize to be provided to you) will describe the terms of the offering of the securities, including, to the extent applicable:

- the name or names of the underwriters, dealers or agents, if any;
- if the securities are to be offered through the selling efforts of brokers or dealers, the plan of distribution and the terms of any agreement, arrangement, or understanding entered into with broker(s) or dealer(s) prior to the effective date of the registration statement, and, if known, the identity of any broker(s) or dealer(s) who will participate in the offering and the amount to be offered through each;
- the purchase price of the securities or other consideration therefor, and the proceeds, if any, we will receive from the sale;
- if any of the securities being registered are to be offered otherwise than for cash, the general purposes of the distribution, the basis upon which the securities are to be offered, the amount of compensation and other expenses of distribution, and by whom they are to be borne;
- any delayed delivery arrangements;
- any over-allotment or other options under which underwriters may purchase additional securities from us;
- any agency fees or underwriting discounts and other items constituting agents’ or underwriters’ compensation;
- any public offering price;
- any discounts, commissions or concessions allowed or reallocated or paid to dealers;
- the identity and relationships of any finders, if applicable; and
- any securities exchange or market on which the securities may be listed.

In compliance with the guidelines of the Financial Industry Regulatory Authority, the maximum compensation to the underwriters or dealers in connection with the sale by the Company of its securities pursuant to this prospectus and the accompanying supplement to this prospectus may not exceed 8% of the aggregate offering price of the securities as set forth on the cover page of any prospectus supplement.

Only underwriters named in the prospectus supplement will be underwriters of the securities offered by the prospectus supplement.

If underwriters are used in the sale, they will acquire the securities for their own account and may resell the securities from time to time in one or more transactions at a fixed public offering price or at varying prices determined at the time of sale. The obligations of the underwriters to purchase the securities will be subject to the conditions set forth in the applicable underwriting agreement. We may offer the securities to the public through underwriting syndicates represented by managing underwriters or by underwriters without a syndicate. Unless otherwise indicated in the prospectus supplement, subject to certain conditions, the underwriters will be obligated to purchase all of the securities offered by the prospectus supplement, other than securities covered by any underwriter's option. Any public offering price and any discounts or concessions allowed or reallocated or paid to dealers may change from time to time. We may use underwriters, dealers or agents with whom we have a material relationship. We will describe in the prospectus supplement, naming the underwriter, dealer or agent, the nature of any such relationship.

We may use a remarketing firm to offer the securities in connection with a remarketing arrangement upon their purchase. Remarketing firms will act as principals for their own account or as agents for us. These remarketing firms will offer or sell the securities pursuant to the terms of the securities. A prospectus supplement will identify any remarketing firm and the terms of its agreement, if any, with us and will describe the remarketing firm's compensation. Remarketing firms may be deemed to be underwriters in connection the securities they remarket.

If we offer and sell securities through a dealer, we or an underwriter will sell the securities to the dealer, as principal. The dealer may then resell the securities to the public at varying prices to be determined by the dealer at the time of resale. The name of the dealer and the terms of the transaction will be set forth in the applicable prospectus supplement.

We may sell securities directly or through agents we designate from time to time. We will name any agent involved in the offering and sale of securities and we will describe any commissions payable to the agent in the prospectus supplement. Unless the prospectus supplement states otherwise, the agent will act on a best-efforts basis for the period of its appointment.

Dealers and agents participating in the distribution of the securities may be deemed to be underwriters, and compensation received by them on resale of the securities may be deemed to be underwriting discounts. If such dealers or agents were deemed to be underwriters, they may be subject to statutory liabilities under the Securities Act.

We may sell securities directly to one or more purchasers without using underwriters or agents. Underwriters, dealers and agents that participate in the distribution of the securities may be underwriters as defined in the Securities Act, and any discounts or commissions they receive from us and any profit on their resale of the securities may be treated as underwriting discounts and commissions under the Securities Act.

We may authorize agents or underwriters to solicit offers by certain types of institutional investors to purchase securities from us at the public offering price set forth in the prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. We will describe the conditions to these contracts and the commissions we must pay for solicitation of these contracts in the prospectus supplement.

We may provide agents, underwriters and dealers with indemnification against civil liabilities, including liabilities under the Securities Act, or contribution with respect to payments that the agents, underwriters or dealers may make with respect to these liabilities. Agents, underwriters and dealers, or their respective affiliates, may engage in transactions with, or perform services for, us in the ordinary course of business.

The securities we offer may be new issues of securities and may have no established trading market. The securities may or may not be listed on a securities exchange. Underwriters may make a market in these securities, but will not be obligated to do so and may discontinue any market making at any time without notice. We can make no assurance as to the liquidity of, or the existence of trading markets for, any of the securities.

Any underwriter may engage in over-allotment, stabilizing transactions, short-covering transactions and penalty bids in accordance with Regulation M under the Securities Exchange Act of 1934, as amended, or the Exchange Act. Over-allotment involves sales in excess of the offering size, which create a short position. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum price. Syndicate-covering or other short-covering transactions involve purchases of the securities, either through exercise of the over-allotment option or in the open market after the distribution is completed, to cover short positions. Penalty bids permit the underwriters to reclaim a selling concession from a dealer when the securities originally sold by the dealer are purchased in a stabilizing or covering transaction to cover short positions. Those activities may cause the price of the securities to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of the activities at any time.

Any underwriters that are qualified market makers on the Nasdaq Stock Market LLC may engage in passive market making transactions in the common shares on the Nasdaq Stock Market LLC in accordance with Regulation M under the Exchange Act, during the business day prior to the pricing of the offering, before the commencement of offers or sales of the common shares. Passive market makers must comply with applicable volume and price limitations and must be identified as passive market makers. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for such security; if all independent bids are lowered below the passive market maker's bid, however, the passive market maker's bid must then be lowered when certain purchase limits are exceeded. Passive market making may stabilize the market price of the securities at a level above that which might otherwise prevail in the open market and, if commenced, may be discontinued at any time.

Notwithstanding the above, the securities: (i) have not been qualified for distribution by prospectus in Canada, and (ii) may not be offered or sold in Canada during the course of their distribution except pursuant to a Canadian prospectus or in reliance on an available prospectus exemption.

LEGAL MATTERS

Unless otherwise specified in a prospectus supplement, certain legal matters relating to the securities will be passed upon for us by Hogan Lovells US LLP with respect to matters of United States law, and Farris LLP, Vancouver, B.C., Canada, with respect to matters of Canadian law. As appropriate, legal counsel representing the underwriters, dealers or agents will be named in the accompanying prospectus supplement and may opine to certain legal matters.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our [Annual Report on Form 10-K for the year ended December 31, 2019](#) and the effectiveness of our internal control over financial reporting as of December 31, 2019, as set forth in their reports, which are incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP's reports, given on their authority as experts in accounting and auditing.

The consolidated financial statements of Arbutus Biopharma Corporation as of December 31, 2018 appearing in Arbutus Biopharma Corporation's Annual Report on Form 10-K, have been incorporated by reference herein in reliance upon the report of KPMG LLP, independent registered public accounting firm, also incorporated by reference herein, and upon their authority as experts in accounting and auditing.

WHERE YOU CAN FIND ADDITIONAL INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC. The SEC maintains an Internet website at <http://www.sec.gov> that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC. Our reports on Forms 10-K, 10-Q and 8-K, and amendments to those reports, are also available for download, free of charge, as soon as reasonably practicable after these reports are filed with, or furnished to, the SEC, at our website at www.arbutusbio.com. Information contained on or accessible through our website is not a part of this prospectus or any prospectus supplement, and the inclusion of our website address in this prospectus is an inactive textual reference only.

The SEC allows us to "incorporate by reference" into this prospectus the information in other documents that we file with it. This means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be a part of this prospectus, and information in documents that we file later with the SEC will automatically update and supersede information contained in documents filed earlier with the SEC or contained in this prospectus. We incorporate by reference in this prospectus (i) the documents listed below, (ii) all documents that we file with the SEC under Section 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of the initial filing of the registration statement of which this prospectus is included and prior to the effectiveness of such registration statement, and (iii) and any future filings that we may make with the SEC under Sections 13(a), 13(c), 14, or 15(d) of the Exchange Act prior to the termination of the offerings under this prospectus; provided, however, that we are not incorporating, in each case, any documents or information deemed to have been furnished and not filed, including any information that we disclose under Items 2.02 or 7.01 of any Current Report on Form 8-K, in accordance with SEC rules:

- our Annual Report on Form 10-K for the year ended December 31, 2019, filed with the SEC on [March 5, 2020](#), as amended by our Annual Report on Form 10-K/A, filed with the SEC on [March 6, 2020](#);
- our Quarterly Reports on Form 10-Q for the fiscal quarters ended March 31, 2020 and June 30, 2020, filed with the SEC on [May 11, 2020](#) and [August 7, 2020](#), respectively;
- our Current Reports on Form 8-K as filed with the SEC on [January 13, 2020](#) (other than the portions thereof that are furnished and not filed), [February 10, 2020](#), [February 19, 2020](#), [March 26, 2020](#), [May 18, 2020](#), [June 1, 2020](#), [July 24, 2020](#), [August 7, 2020](#), [August 10, 2020](#) and [August 27, 2020](#);
- our Definitive Proxy Statement on Schedule 14A, filed with the SEC on [April 24, 2020](#) (other than the portions thereof that are furnished and not filed); and

- the description of our common shares contained in our registration statement on Form 8-A filed with the SEC on [November 4, 2010](#), including any amendment or report filed for purposes of updating such description.

You may request, orally or in writing, a copy of any or all of the documents incorporated herein by reference. These documents will be provided to you at no cost, by contacting: Arbutus Biopharma Corporation, Attn: Corporate Secretary, 701 Veterans Circle, Warminster, Pennsylvania 18974. In addition, copies of any or all of the documents incorporated herein by reference may be accessed at our website at www.arbutusbio.com. The information on such website is not incorporated by reference and is not a part of this prospectus.



**Up to \$75,000,000
Common Shares**

PROSPECTUS SUPPLEMENT

Jefferies

March 4, 2021
