

## CALCULATION OF REGISTRATION FEE

Title of Securities to be Registered	Proposed Maximum Aggregate Offering Price	Amount of Registration Fee(1)
Common Stock, par value \$0.001 per share	\$150,000,000	\$13,905.00

- (1) Calculated pursuant to Rule 457(o) under the Securities Act of 1933, as amended (the "Securities Act"), based on the proposed maximum aggregate offering price. Payment of the registration fee at the time of filing of the Registrant's registration statement on Form S-3, filed with the Securities and Exchange Commission on June 1, 2020, was deferred pursuant to Rules 456(b) and 457(r) under the Securities Act and is paid herewith.

**PROSPECTUS SUPPLEMENT**  
(TO PROSPECTUS DATED JUNE 1, 2020)



**Up to \$150,000,000**

**Common Stock**

We have entered into an Open Market Sale Agreement<sup>SM</sup>, or the sales agreement, with Jefferies LLC, or Jefferies, relating to the sale of shares of our common stock offered by this prospectus supplement and the accompanying prospectus. In accordance with the terms of the sales agreement, we may offer and sell shares of our common stock, \$0.001 par value per share, having an aggregate offering price of up to \$150,000,000 from time to time through Jefferies acting as our sales agent.

Our common stock is listed on the Nasdaq Global Select Market under the symbol "CRTX." On December 21, 2021, the last reported sale price of our common stock on the Nasdaq Global Select Market was \$12.81 per share.

Sales of our common stock, if any, under this prospectus supplement and the accompanying prospectus will be made in sales deemed to be 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 of securities, but will act as our sales agent using commercially reasonable efforts to sell on our behalf all of the shares of our common stock requested to be sold by us, consistent with its normal trading and sales practices, on mutually-agreed terms between Jefferies and us. 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 proceeds of any shares of common stock sold under the sales agreement. In connection with the sale of the common stock 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 liabilities under the Securities Act or the Securities Exchange Act of 1934, as amended, or the Exchange Act. See "Plan of Distribution" beginning on page S-10 of this prospectus supplement for additional information regarding the compensation to be paid to Jefferies.

**Investing in our common stock involves risks. See "[Risk Factors](#)" beginning on page S-3 of this prospectus supplement and in the reports we file with the Securities and Exchange Commission pursuant to the Securities Exchange Act of 1934, as amended, incorporated by reference in this prospectus supplement and the accompanying prospectus, before making a decision to invest in our common stock.**

**The Securities and Exchange Commission and state securities regulators have not approved or disapproved of these securities, or determined if this prospectus supplement or the accompanying prospectus is truthful or complete. Any representation to the contrary is a criminal offense.**

**Jefferies**

The date of this prospectus supplement is December 23, 2021.

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## ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus are part of a registration statement that we have filed with the Securities and Exchange Commission, or the SEC, utilizing a “shelf” registration process. Under the shelf registration process, we may, from time to time, offer and sell any combination of our securities described in the accompanying prospectus in one or more offerings. We are providing information to you about this offering of our common stock in two parts. The first part is this prospectus supplement, which provides you with specific information regarding the terms of this offering and our common stock, and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference in this prospectus supplement and the accompanying prospectus. The second part is the accompanying prospectus, which provides more general information, some of which does not apply to this offering of our common stock.

We provide information to you about this offering of shares of our common stock in this prospectus supplement, which describes the specific details regarding this offering. This prospectus supplement adds to, updates, and changes information contained in the accompanying prospectus and the information incorporated by reference therein with respect to this offering of our common stock. To the extent that any information in this prospectus supplement is inconsistent with the information in the accompanying prospectus or any information incorporated by reference therein, 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 in this prospectus supplement—the statement in the document having the later date modifies or supersedes the earlier statement as our business, financial condition, results of operations and prospects may have changed since the earlier dates.

Before buying any of the common stock that we are offering, we urge you to carefully read this prospectus supplement and the accompanying prospectus and all of the information incorporated by reference herein and therein, as well as the additional information described under the sections titled “Where You Can Find Additional Information” and “Incorporation of Certain Information by Reference.” These documents contain important information that you should consider when making your investment decision.

We have not, and Jefferies has not, authorized any other person to provide you with any information different from that contained in the prospectus supplement and in the accompanying prospectus or in any free writing prospectus prepared by us or on our behalf. 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 these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus supplement or the accompanying prospectus or any free writing prospectus is accurate only as of the date on the front cover of this prospectus supplement. Our business, financial condition, results of operations and prospects may have changed since that date.

Information contained on our website is not part of this prospectus supplement or the accompanying prospectus. We are offering to sell, and seeking offers to buy, shares of common stock only in jurisdictions where offers and sales are permitted. The distribution of this prospectus supplement and the offering of the common stock in certain jurisdictions may be restricted by law. Persons outside the United States who come into possession of this prospectus supplement and the accompanying prospectus must inform themselves about, and observe any restrictions relating to, the offering of our common stock and the distribution of this prospectus supplement and the accompanying prospectus outside the United States. This prospectus supplement and the accompanying prospectus do not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, any securities offered by this prospectus supplement or the accompanying prospectus by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

This prospectus supplement and the accompanying prospectus and the information incorporated herein and therein by reference include trademarks, service marks and trade names owned by us or other companies. All trademarks, service marks and trade names included or incorporated by reference into this prospectus supplement and the accompanying prospectus are the property of their respective owners.

As used in this prospectus supplement, the accompanying prospectus and the information incorporated by reference herein and therein, unless the context otherwise requires, references to “Cortexyme,” “we,” “us,” “our” and “our company” refer to Cortexyme, Inc.

## PROSPECTUS SUPPLEMENT SUMMARY

*This summary highlights selected information contained elsewhere in this prospectus supplement and the accompanying prospectus and in the documents we incorporate by reference herein and therein. This summary does not contain all of the information you should consider before investing in our common stock. You should read this entire prospectus supplement and the accompanying prospectus carefully, especially the section in this prospectus supplement titled "Risk Factors" and our financial statements and the related notes incorporated by reference into this prospectus supplement and the accompanying prospectus, before making an investment decision.*

### **Overview**

We are a clinical stage biopharmaceutical company with a growing pipeline of therapeutics in Alzheimer's disease and other degenerative diseases. Our approach is based on the seminal discovery of the presence of Porphyromonas gingivalis, or P. gingivalis, and its secreted toxic virulence factor proteases, called gingipains, in the brains of greater than 90% of Alzheimer's patients. Additionally, we and other researchers have observed that P. gingivalis infection causes Alzheimer's and Parkinson's pathology in animal models, and these effects have been successfully treated with a gingipain inhibitor in preclinical studies. Our proprietary lead drug candidate, atuzaginstat (COR388), is an orally administered, brain-penetrating small molecule gingipain protease inhibitor.

### **Corporate information**

We were incorporated in Delaware on June 20, 2012. Our principal executive offices are located at 269 East Grand Avenue, South San Francisco, CA 94080. Our telephone number at that location is (415) 910-5717. Our corporate website address is [www.cortexyme.com](http://www.cortexyme.com). The information contained on our website is not incorporated by reference into this prospectus supplement, and you should not consider any information contained on, or that can be accessed through, our website to be part of this prospectus supplement. We have included our website address only as an inactive textual reference and do not intend it to be an active link to our website.

## THE OFFERING

Common stock offered by us	Shares of our common stock having an aggregate offering price of up to \$150.0 million.
Plan of distribution	“At the market offering” that may be made from time to time through the sales agent, Jefferies. See <a href="#">“Plan of Distribution”</a> on page S-10 of this prospectus supplement.
Use of proceeds	We currently intend to use the net proceeds from this offering, if any, together with our existing cash, cash equivalents and investments, to fund the advancement of our product candidates; to fund ongoing research and the potential development of our discovery-stage programs; and for other general corporate purposes, including working capital, operating expenses and capital expenditures. See the section titled “Use of Proceeds” for additional information.
Risk factors	Investing in our common stock involves significant risks. Before making an investment decision, please read the information contained in and incorporated by reference under the heading “Risk Factors” on page S-3 of this prospectus supplement, and under similar headings in other documents that are incorporated by reference into this prospectus supplement and the accompanying prospectus.
The Nasdaq Global Select Market symbol	“CRTX”

## RISK FACTORS

*Investing in our common stock involves a high degree of risk. Before making a decision to invest in our common stock, you should consider carefully the risks and uncertainties described under the heading "Risk Factors" contained or incorporated by reference in this prospectus supplement and the accompanying prospectus, including the risk factors incorporated by reference herein from our most recent Annual Report on Form 10-K, as may be updated by our subsequent Quarterly Reports on Form 10-Q and other filings we make with the SEC. The risks described in these documents are not the only ones we face. There may be other unknown or unpredictable economic, business, competitive, regulatory or other factors that could harm our future results. Past financial performance may not be a reliable indicator of future performance, and historical trends should not be used to anticipate results or trends in future periods. If any of these risks actually occurs, our business, financial condition, results of operations or cash flow could be harmed. This could cause the trading price of our common stock to decline, resulting in a loss of all or part of your investment. Please also read carefully the section below titled "Cautionary Statement Regarding Forward-Looking Statements."*

### **Additional Risks Related to the Offering**

#### ***We have broad discretion in the use of the net proceeds from this offering and may not use them effectively.***

Our management will have broad discretion in the application of the net proceeds from this offering, including for any of the purposes described in the section titled "Use of Proceeds," and you will not have the opportunity as part of your investment decision to assess whether the net proceeds are being used appropriately. Because of the number and variability of factors that will determine our use of the net proceeds from this offering, their ultimate use may vary substantially from their currently intended use. Our management might not apply our net proceeds in ways that ultimately increase the value of your investment. The failure by our management to apply these funds effectively could harm our business. Pending their use, we may invest the net proceeds from this offering in short- and intermediate-term, interest-bearing instruments, certificates of deposit or direct or guaranteed obligations of the United States government or hold the net proceeds as cash. These investments may not yield a favorable return to our stockholders. If we do not invest or apply the net proceeds from this offering in ways that enhance stockholder value, we may fail to achieve expected financial results, which could cause our stock price to decline.

#### ***If you purchase our common stock in this offering, you may experience immediate and substantial dilution in the net tangible book value of your shares.***

The offering price per share in this offering may exceed the net tangible book value per share of our common stock outstanding prior to this offering. Assuming that an aggregate of 11,709,602 shares of our common stock are sold at a price of \$12.81 per share, the last reported sale price of our common stock on the Nasdaq Global Select Market on December 21, 2021, for aggregate gross proceeds of approximately \$150.0 million, and after deducting commissions and estimated offering expenses payable by us, you would experience immediate dilution of \$6.13 per share, representing the difference between our as adjusted net tangible book value per share as of September 30, 2021 after giving effect to this offering and the assumed public offering price. The exercise of outstanding stock options would result in further dilution of your investment. See the section titled "Dilution" below for a more detailed illustration of the dilution you would incur if you participate in this offering. Because the sales of the shares offered hereby will be made directly into the market or in negotiated transactions, the prices at which we sell these shares will vary and these variations may be significant. Purchasers of the shares we sell, as well as our existing stockholders, will experience significant dilution if we sell shares at prices significantly below the price at which they invested.

#### ***Future sales or issuances of our common stock in the public markets, or the perception of such sales, could depress the trading price of our common stock.***

The sale of a substantial number of shares of our common stock or other equity-related securities in the public markets, or the perception that such sales could occur, could depress the market price of our common stock and impair our ability to raise capital through the sale of additional equity securities. We may sell large quantities of our common stock at any time pursuant to this prospectus supplement or in one or more separate offerings. We cannot predict the effect that future sales of common stock or other equity-related securities would have on the market price of our common stock.

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***It is not possible to predict the actual number of shares we will sell under the sales agreement, or the gross proceeds resulting from those sales.***

Subject to certain limitations in the sales agreement and compliance with applicable law, we have the discretion to deliver instruction to Jefferies to sell shares of our common stock at any time throughout the term of the sales agreement. The number of shares, if any, that are sold through Jefferies after our instruction will fluctuate based on a number of factors, including the market price of our common stock during the sales period, the limits we set with Jefferies in any instruction to sell shares, and the demand for our common stock during the sales period. Because the price per share of each share sold, if any, will fluctuate during this offering, it is not currently possible to predict the number of shares that will be sold or the gross proceeds to be raised in connection with those sales.

***The common stock offered hereby will be sold in “at the market offerings”, and investors who buy shares at different times will likely pay different prices.***

Investors who purchase shares in this offering at different times will likely pay different prices, and so may experience different outcomes in their investment results. We will have discretion, subject to market demand, to vary the timing, prices, and numbers of shares sold, and there is no predetermined minimum or maximum sales price. Investors may experience a decline in the value of their shares as a result of share sales made at prices lower than the prices they paid.

## CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus and the information incorporated by reference herein and therein contain forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act about us and our industry that involve substantial risks and uncertainties. All statements other than statements of historical facts contained in this prospectus supplement, the accompanying prospectus and the information incorporated by reference herein and therein, including statements regarding our future results of operations or financial condition, business strategy and plans and objectives of management for future operations, including our statements regarding the benefits and timing of the roll-out of new technology, are forward-looking statements. In some cases, you can identify forward-looking statements because they contain words such as “anticipate,” “believe,” “contemplate,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “should,” “target,” “will,” “would,” “seek,” “grow,” “target” or “if” or the negative of these words or other similar terms or expressions. Forward-looking statements in this prospectus supplement, the accompanying prospectus and the information incorporated by reference herein and therein include, but are not limited to, statements about:

- our use of the net proceeds from this offering;
- our financial performance;
- the sufficiency of our existing cash and cash equivalents to fund our future operating expenses and capital expenditure requirements
- our ability to obtain funding for our operations, including funding necessary to develop and commercialize our drug candidates;
- the ability of our clinical trials to demonstrate safety and efficacy of our drug candidates, and other positive results;
- the success, cost and timing of our development activities, preclinical studies and clinical trials
- the timing and focus of our future clinical trials, and the reporting of data from those trials;
- our plans relating to commercializing our drug candidates, if approved;
- our plans and ability to establish sales, marketing and distribution infrastructure to commercialize any drug candidates for which we obtain approval;
- our ability to attract and retain key scientific and clinical personnel;
- our ability to contract with third-party suppliers and manufacturers and their ability to perform adequately;
- our reliance on third parties to conduct clinical trials of our drug candidates, and for the manufacture of our drug candidates for preclinical studies and clinical trials;
- our ability to expand our drug candidates into additional indications and patient populations;
- the success of competing therapies that are or may become available;
- the beneficial characteristics, safety and efficacy of our drug candidate;
- regulatory developments in the United States and other jurisdictions;
- our ability to obtain and maintain regulatory approval of our drug candidates, and any related restrictions, limitations and/or warnings in the label of any approved drug candidate;
- our plans relating to the further development and manufacturing of our drug candidates, including additional indications for which we may pursue;
- our plans and ability to obtain or protect intellectual property rights, including extensions of existing patent terms where available;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our drug candidates and technology; and
- potential claims relating to our intellectual property.

Actual events or results may differ from those expressed in forward-looking statements. You should not rely on forward-looking statements as predictions of future events. We have based the forward-looking statements contained in this prospectus supplement, the accompanying prospectus and the information incorporated by reference herein

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and therein primarily on our current expectations and projections about future events and trends that we believe may affect our business, financial condition and operating results. The outcome of the events described in these forward-looking statements is subject to risks, uncertainties and other factors described in the section titled "Risk Factors" and elsewhere in this prospectus supplement, the accompanying prospectus and in our most recent Annual Report on Form 10-K, as may be updated by our subsequent Quarterly Reports on Form 10-Q and other filings we make with the SEC, which are incorporated by reference into this prospectus supplement and the accompanying prospectus in their entirety. Moreover, we operate in a very competitive and rapidly changing environment. New risks and uncertainties emerge from time to time, and it is not possible for us to predict all risks and uncertainties that could have an impact on the forward-looking statements contained in this prospectus supplement, the accompanying prospectus and the information incorporated by reference herein. The results, events and circumstances reflected in the forward-looking statements may not be achieved or occur, and actual results, events or circumstances could differ materially from those described in the forward-looking statements.

In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based on information available to us as of the date of this prospectus supplement. While we believe that information provides a reasonable basis for these statements, that information may be limited or incomplete. Our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all relevant information. These statements are inherently uncertain, and investors are cautioned not to unduly rely on these statements.

The forward-looking statements made in this prospectus supplement relate only to events as of the date on which the statements are made. We undertake no obligation to update any forward-looking statements made in this prospectus supplement to reflect events or circumstances after the date of this prospectus supplement or to reflect new information or the occurrence of unanticipated events, except as required by law. 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. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments.

## USE OF PROCEEDS

We may issue and sell shares of our common stock having aggregate sales proceeds of up to \$150.0 million from time to time. Because there is no minimum offering price for the shares that we may offer from time to time, 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 we will sell any shares under or fully utilize the sales agreement with Jefferies as a source of financing.

We currently intend to use the net proceeds from this offering, if any, together with our existing cash, cash equivalents and investments, to fund the advancement of our product candidates; to fund ongoing research and the potential development of our discovery-stage programs; and for other general corporate purposes, including working capital, operating expenses and capital expenditures.

This expected use of the net proceeds from this offering represents our intentions based on our current plans and business conditions, which could change in the future as our plans and business conditions evolve. Further, due to the uncertainties inherent in the product development process, it is difficult to estimate with certainty the exact amounts of the net proceeds from this offering that may be used for the above purposes. We cannot specify with certainty all of the particular uses for the remaining net proceeds to us from this offering. We may also use a portion of the net proceeds for acquisitions or strategic investments in complementary businesses, products, services or technologies. However, we do not have agreements or commitments to enter into any such acquisitions or investments at this time. We will have broad discretion over how to use the net proceeds to us from this offering, and our investors will be relying on the judgment of our management regarding the application of the net proceeds of this offering. The amounts and timing of our expenditures will depend upon numerous factors including the results of our research and development efforts, the timing and success of preclinical studies and any clinical trials we may commence in the future, the timing of regulatory submissions, and the amount of cash obtained through any future collaborations.

As of the date of this prospectus supplement, we cannot predict with certainty all of the particular uses for the net proceeds from this offering or the amounts that we will actually spend on the uses set forth above. As a result, our management will have broad discretion regarding the timing and application of the net proceeds from this offering. We intend to invest the net proceeds to us from this offering that are not used as described above in short- and intermediate-term, interest-bearing obligations, investment-grade instruments, certificates of deposit or direct or guaranteed obligations of the United States government or hold the net proceeds as cash.

## DILUTION

Our historical net tangible book value as of September 30, 2021 was \$132.7 million, or \$4.44 per share of our common stock. Our historical net tangible book value represents the amount of our total tangible assets less our total liabilities. Historical net tangible book value per share represents historical net tangible book value divided by the number of shares of our common stock outstanding as of September 30, 2021.

After giving effect to the sale of 11,709,602 shares of common stock that we are offering at the assumed public offering price of \$12.81 per share, which was the last reported sale price of our common stock on the Nasdaq Global Select Market on December 21, 2021, and after deducting commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of September 30, 2021, would have been approximately \$277.6 million, or approximately \$6.68 per share. This amount represents an immediate increase in as adjusted net tangible book value of \$2.24 per share to our existing stockholders and an immediate dilution in net tangible book value of approximately \$6.13 per share to new investors purchasing shares of common stock in this offering.

Dilution per share to new investors is determined by subtracting as adjusted net tangible book value per share after this offering from the price per share paid by new investors. The following table illustrates this dilution:

Assumed public offering price per share	\$12.81
Historical net tangible book value per share as of September 30, 2021	\$4.44
Increase in as adjusted net tangible book value per share attributable to this offering	<u>2.24</u>
As adjusted net tangible book value per share after this offering	<u>6.68</u>
Dilution per share to new investors in this offering	<u>\$ 6.13</u>

Each \$1.00 increase in the assumed public offering price of \$12.81 per share, which was the last reported sale price of our common stock on the Nasdaq Global Select Market on December 21, 2021, would increase the as adjusted net tangible book value per share after this offering by approximately \$0.14, and dilution in as adjusted net tangible book value per share to new investors by approximately \$0.86, assuming that the number of shares of common stock offered by us, as set forth on the cover page of this prospectus supplement, remains the same and after deducting commissions and estimated offering expenses payable by us. Each \$1.00 decrease in the assumed public offering price of \$12.81 per share, which was the last reported sale price of our common stock on the Nasdaq Global Select Market on December 21, 2021, would decrease the as adjusted net tangible book value per share after this offering by approximately \$0.16, and dilution in as adjusted net tangible book value per share to new investors by approximately \$0.84.

Each increase of 1,000,000 shares in the number of shares of common stock offered by us would increase our as adjusted net tangible book value per share after this offering by approximately \$0.13 per share and decrease the dilution to investors participating in this offering by approximately \$0.13 per share, assuming that the assumed public offering price remains the same, and after deducting commissions and estimated offering expenses payable by us. Each decrease of 1,000,000 shares in the number of shares of common stock offered by us would decrease our as adjusted net tangible book value per share after this offering by approximately \$0.15 per share and increase the dilution to investors participating in this offering by approximately \$0.15 per share, assuming that the assumed public offering price remains the same, and after deducting commissions and estimated offering expenses payable by us. The as adjusted information is illustrative only, and we will adjust this information based on the actual public offering price and other terms of this offering determined at pricing.

The outstanding share information in the table above is based on 29,867,263 shares of our common stock outstanding as of September 30, 2021, and excludes:

- 5,017,442 shares of our common stock issuable upon the exercise of options to purchase shares of our common stock outstanding as of September 30, 2021 (of which 2,144,364 were vested and exercisable), with a weighted-average exercise price of \$30.34 per share;

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- 761,000 shares of our common stock issuable upon the exercise of options to purchase shares of our common stock granted after September 30, 2021, with a weighted-average exercise price of \$11.42 per share;
- 899,925 shares of our common stock reserved for future issuance under our 2019 Equity Incentive Plan, which includes an annual evergreen increase; and
- 832,421 shares of our common stock reserved for future issuance under our 2019 Employee Stock Purchase Plan, which includes an annual evergreen increase.

To the extent any outstanding options are exercised, new options or other equity awards are issued under our equity incentive plans, or we issue additional equity or convertible debt securities in the future, there will be further dilution to new investors.

## PLAN OF DISTRIBUTION

We have entered into a sales agreement with Jefferies, under which we may offer and sell up to \$150.0 million of our shares of common stock from time to time through Jefferies acting as agent. Sales of our shares of common stock, 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.

Each time we wish to issue and sell our shares of common stock under the sales 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 sales agreement to sell our shares of common stock are subject to a number of conditions that we must meet.

The settlement of sales of 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 shares of common stock 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 stock. 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. In addition, we have agreed to reimburse Jefferies for the fees and disbursements of its counsel, payable upon execution of the sales agreement, in an amount not to exceed \$75,000, in addition to certain ongoing disbursements of its legal counsel. We estimate that the total expenses for the offering, excluding any commissions or expense reimbursement payable to Jefferies under the terms of the sales agreement, will be approximately \$250,000. The remaining sale proceeds, after deducting any other transaction fees, will equal our net proceeds from the sale of such 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 our shares of common stock are sold under the sales agreement. Each confirmation will include the number of shares sold on that day, the aggregate gross proceeds of such sales and the proceeds to us.

In connection with the sale of our shares of common stock 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 shares of common stock pursuant to the sales agreement will terminate upon the earlier of (i) the sale of all shares of common stock subject to the sales agreement and (ii) the termination of the sales agreement as permitted therein. We and Jefferies may each terminate the sales agreement at any time upon ten days' prior notice.

This summary of the material provisions of the sales agreement does not purport to be a complete statement of its terms and conditions. A copy of the sales agreement is filed as an exhibit to a Current Report on Form 8-K that will be filed under 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.

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

**LEGAL MATTERS**

The validity of the shares of common stock offered by this prospectus supplement will be passed upon for us by Cooley LLP, Palo Alto, California. Jefferies LLC is being represented in connection with this offering by Latham & Watkins LLP, San Diego, California.

**EXPERTS**

The financial statements as of December 31, 2020 and 2019 and for each of the three years in the period ended December 31, 2020 and management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2020 incorporated by reference in this prospectus supplement and in the registration statement have been so incorporated in reliance on the reports of BDO USA, LLP, an independent registered public accounting firm, incorporated herein by reference given on the authority of said firm as experts in accounting and auditing.

## WHERE YOU CAN FIND ADDITIONAL INFORMATION

We file reports, proxy statements and other information with the SEC. The SEC maintains a website that contains reports, proxy and information statements and other information about issuers, such as us, who file electronically with the SEC. The address of that website is [www.sec.gov](http://www.sec.gov).

Our website address is [www.cortexyme.com](http://www.cortexyme.com). The information on our website, however, is not, and should not be deemed to be, a part of this prospectus supplement or the accompanying prospectus.

This prospectus supplement and the accompanying prospectus are part of a registration statement that we filed with the SEC and do not contain all of the information in the registration statement. The full registration statement may be obtained from the SEC or us, as provided below. Forms of the indenture and other documents establishing the terms of the offered securities are or may be filed as exhibits to the registration statement or documents incorporated by reference in the registration statement. Statements in this prospectus supplement and the accompanying prospectus about these documents are summaries and each statement is qualified in all respects by reference to the document to which it refers. You should refer to the actual documents for a more complete description of the relevant matters. You may inspect a copy of the registration statement through the SEC's website, as provided above.

## INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to “incorporate by reference” information from other documents that we file with it, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus supplement and the accompanying prospectus. Information in this prospectus supplement supersedes information incorporated by reference that we filed with the SEC prior to the date of this prospectus supplement, while information that we file later with the SEC will automatically update and supersede the information in this prospectus supplement. We incorporate by reference into this prospectus supplement and the accompanying prospectus the information or documents listed below that we have filed with the SEC:

- our Annual Report on [Form 10-K](#) for the year ended December 31, 2020, filed with the SEC on March 1, 2021;
- the information specifically incorporated by reference into our Annual Report on [Form 10-K](#) for the year ended December 31, 2020 from our Definitive Proxy Statement on [Schedule 14A](#), filed with the SEC on April 30, 2021;
- our Quarterly Reports on Form 10-Q for the quarters ended on [March 31, 2021](#), [June 30, 2021](#) and [September 30, 2021](#), filed with the SEC on May 6, 2021, August 6, 2021 and October 29, 2021, respectively;
- our Current Reports on Form 8-K (other than information furnished rather than filed) filed with the SEC on [January 25, 2021](#), [January 26, 2021](#), [February 10, 2021](#), [February 16, 2021](#), [May 18, 2021](#), [June 21, 2021](#) and [October 26, 2021](#); and
- the description of our common stock contained in our registration statement on [Form 8-A](#), filed with the SEC on May 1, 2019, as updated by [Exhibit 4.3](#) to our Annual Report on [Form 10-K](#) for the year ended December 31, 2020, and any amendment or report filed with the SEC for the purpose of updating the description.

Any documents we file with the SEC pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of this prospectus supplement and prior to the termination of the offering of our common stock to which this prospectus supplement relates will automatically be deemed to be incorporated by reference into this prospectus supplement and to be part hereof from the date of filing those documents. We are not, however, incorporating by reference any documents or portions thereof that are not deemed “filed” with the SEC, including any information furnished pursuant to Item 2.02 or Item 7.01 of Form 8-K or related exhibits furnished pursuant to Item 9.01 of Form 8-K. Any statements in any such future filings will automatically be deemed to modify and supersede any information in any document we previously filed with the SEC that is incorporated or deemed to be incorporated herein by reference to the extent that statements in the later filed document modify or replace such earlier statements.

You can request a copy of these filings, at no cost, by writing or telephoning us at the following address or telephone number:

Cortexyme, Inc.  
269 East Grand Avenue  
South San Francisco, CA 94080  
(415) 910-5717

PROSPECTUS



**Common Stock  
Preferred Stock  
Debt Securities  
Warrants  
Units**

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From time to time, we may offer and sell any combination of the securities described in this prospectus in one or more offerings. The securities we may offer may be convertible into or exercisable or exchangeable for other securities. We may offer the securities separately or together, in separate classes, series and in amounts, at prices and on terms that will be determined at the time the securities are offered.

In addition, from time to time, the selling securityholders to be named in a prospectus supplement may offer our securities. We will not receive any of the proceeds from the sale of securities by the selling securityholders.

This prospectus describes some of the general terms that may apply to these securities. Each time securities are sold, the specific terms and amounts of the securities being offered, and any other information relating to the specific offering and, if applicable, the selling securityholders, will be set forth in a supplement to this prospectus. We may also authorize one or more free writing prospectuses to be provided to you in connection with these offerings. The prospectus supplement and any related free writing prospectus may also add, update or change information contained in this prospectus. You should carefully read this prospectus, the applicable prospectus supplement and any related free writing prospectus, as well as any documents incorporated by reference, before you invest in any of the securities being offered. This prospectus may not be used to sell our securities unless accompanied by a prospectus supplement.

Our common stock is traded on the Nasdaq Global Select Market under the symbol "CRTX." The applicable prospectus supplement will contain information, where applicable, as to any other listing, if any, of the securities covered by the applicable prospectus supplement.

We or any selling securityholders may offer and sell our securities to or through one or more underwriters, dealers and agents, or directly to purchasers, on a continuous or delayed basis. The names of any underwriters, dealers or agents and the terms of the arrangements with such entities will be stated in the accompanying prospectus supplement. See the sections of this prospectus entitled "About this Prospectus" and "Plan of Distribution" for more information.

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**Investing in our securities involves a high degree of risk. You should review carefully the risks and uncertainties referenced under the heading "[RISK FACTORS](#)" on page 4 of this prospectus as well as those contained in the applicable prospectus supplement and any related free writing prospectus, and in the other documents that are incorporated by reference into this prospectus or the applicable prospectus supplement.**

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 June 1, 2020.

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We are responsible for the information contained and incorporated by reference in this prospectus, in any accompanying prospectus supplement, and in any related free writing prospectus we prepare or authorize. We have not authorized anyone to give you any other information, and we take no responsibility for any other information that others may give you. If you are in a jurisdiction where offers to sell, or solicitations of offers to purchase, the securities offered by this documentation are unlawful, or if you are a person to whom it is unlawful to direct these types of activities, then the offer presented in this document does not extend to you. The information contained in this document speaks only as of the date of this document, unless the information specifically indicates that another date applies. Neither the delivery of this prospectus or any accompanying prospectus supplement, nor any sale of securities made under these documents, will, under any circumstances, create any implication that there has been no change in our affairs since the date of this prospectus, any accompanying prospectus supplement or any free writing prospectus we may provide you in connection with an offering or that the information contained or incorporated by reference is correct as of any time subsequent to the date of such information. You should assume that the information in this prospectus or any accompanying prospectus supplement, as well as the information incorporated by reference in this prospectus or any accompanying prospectus supplement, is accurate only as of the date of the documents containing the information, unless the information specifically indicates that another date applies. Our business, financial condition, results of operations and prospects may have changed since those dates

## ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement we filed with the Securities and Exchange Commission (SEC), as a “well-known seasoned issuer” as defined in Rule 405 under the Securities Act of 1933, as amended (the Securities Act), using a “shelf” registration process. Under this process, we and/or the selling securityholders to be named in a prospectus supplement may sell any combination of the securities described in this prospectus from time to time in one or more offerings. Before purchasing any securities, you should read this prospectus and any applicable prospectus supplement together with the additional information described under the heading “Where You Can Find Additional Information” and “Incorporation of Certain Information by Reference.”

This prospectus only provides you with a general description of the securities we may offer. Each time we or the selling securityholders sell a type or series of securities under this prospectus, we or the selling securityholders, as the case may be, will provide a prospectus supplement that will contain more specific information about the terms of the offering, including the specific amounts, prices and terms of the securities offered, and, if applicable, the selling securityholders. We may also authorize one or more free writing prospectuses to be provided to you that may contain material information relating to these offerings. This prospectus may not be used to sell our securities unless accompanied by a prospectus supplement. Each such prospectus supplement and any free writing prospectus that we may authorize to be provided to you may also add, update or change information contained in this prospectus or in documents incorporated by reference into this prospectus. If this prospectus is inconsistent with the prospectus supplement, you should rely upon the prospectus supplement.

This prospectus contains summaries of certain provisions contained in some of the documents described herein, but reference is made to the actual documents for complete information. All of the summaries are qualified in their entirety by the actual documents. Copies of some of the documents referred to herein have been filed, will be filed or will be incorporated by reference as exhibits to the registration statement of which this prospectus is a part, and you may obtain copies of those documents as described below under the heading “Where You Can Find Additional Information.”

This prospectus incorporates by reference, and any prospectus supplement or free writing prospectus may contain and incorporate by reference, market data and industry statistics and forecasts that are based on independent industry publications and other publicly available information. Although we believe these sources are reliable, we do not guarantee the accuracy or completeness of this information and we have not independently verified this information. In addition, the market and industry data and forecasts that may be included or incorporated by reference in this prospectus, any prospectus supplement or any applicable free writing prospectus may involve estimates, assumptions and other risks and uncertainties and are subject to change based on various factors, including those discussed under the heading “Risk Factors” contained in this prospectus, the applicable prospectus supplement and any applicable free writing prospectus, and under similar headings in other documents that are incorporated by reference into this prospectus. Accordingly, investors should not place undue reliance on this information.

Unless otherwise mentioned or unless the context requires otherwise, throughout this prospectus, any applicable prospectus supplement and any related free writing prospectus, the words “Cortexyme”, “we”, “us”, “our”, the “company” or similar references refer to Cortexyme, Inc.; and the term “securities” refers collectively to our common stock, preferred stock, warrants, debt securities, or any combination of the foregoing securities.

We own various U.S. federal trademark registrations and applications and unregistered trademarks, including our corporate logo. This prospectus and the information incorporated herein by reference contains references to trademarks, service marks and trade names owned by us or other companies. Solely for convenience, trademarks, service marks and trade names referred to in this prospectus and the information incorporated herein, including logos, artwork, and other visual displays, may appear without the ® or TM symbols, but such references are not intended to indicate, in any way, that we will not assert, to the fullest extent

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under applicable law, our rights or the rights of the applicable licensor to these trademarks, service marks and trade names. We do not intend our use or display of other companies' trade names, service marks or trademarks to imply a relationship with, or endorsement or sponsorship of us by, any other companies. All trademarks, service marks and trade names included or incorporated by reference into this prospectus, any applicable prospectus supplement or any related free writing prospectus are the property of their respective owners.

**CORTEXYME, INC.**

We are a clinical stage biopharmaceutical company pioneering a novel disease-modifying therapeutic approach to treat what we believe to be a key underlying cause of Alzheimer's and other degenerative diseases. Our approach is based on the seminal discovery of the presence of *Porphyromonas gingivalis*, or *P. gingivalis*, and its secreted toxic virulence factor proteases, called gingipains, in the brains of greater than 90% of more than 100 Alzheimer's patients observed across multiple studies to date. Additionally, we have observed that *P. gingivalis* infection causes Alzheimer's pathology in animal models, and these effects have been successfully treated with a gingipain inhibitor in preclinical studies. Our proprietary lead drug candidate, COR388, is an orally administered, brain-penetrating small molecule gingipain protease inhibitor. COR388 was well-tolerated with no concerning safety signals in our Phase 1a and Phase 1b clinical trials conducted to date, which enrolled a total of 67 subjects, including nine patients with mild to moderate Alzheimer's disease. We initiated a global Phase 2/3 clinical trial of COR388, called the GAIN trial, in mild to moderate Alzheimer's patients in April 2019 in the United States and in September 2019 in Europe. We plan to conduct the interim analysis by the end of 2020 after approximately 100 patients in each of the GAIN trial's three arms complete six months of treatment and expect top-line results by the end of 2021.

We were incorporated in Delaware on June 20, 2012. Our principal executive offices are located at 269 East Grand Avenue, South San Francisco, CA 94080. Our telephone number at that location is (415) 910-5717. Our corporate website address is [www.cortexyme.com](http://www.cortexyme.com). The information contained on our website is not incorporated by reference into this prospectus, and you should not consider any information contained on, or that can be accessed through, our website to be part of this prospectus. We have included our website address only as an inactive textual reference and do not intend it to be an active link to our website.

## **RISK FACTORS**

Investing in our securities involves a high degree of risk. Before making a decision to invest in our securities, you should carefully consider the risks described under the heading “Risk Factors” in the applicable prospectus supplement and any related free writing prospectus, and discussed under “Part I, Item 1A. Risk Factors” contained in our most recent annual report on Form 10-K and in “Part II, Item 1A. Risk Factors” in our most recent quarterly report on Form 10-Q filed subsequent to such Form 10-K, as well as any amendments thereto, which are incorporated by reference into this prospectus and the applicable prospectus supplement in their entirety, together with other information in this prospectus and the applicable prospectus supplement, the documents incorporated by reference herein and therein, and any free writing prospectus that we may authorize for use in connection with a specific offering. See “Where You Can Find Additional Information.”

## CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, any prospectus supplement and any related free writing prospectus, including the information incorporated by reference herein and therein, contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. Any statements about our expectations, beliefs, plans, objectives, assumptions or future events or performance are not historical facts and may be forward-looking. These statements are often, but are not always, made through the use of words or phrases such as “anticipate,” “believe,” “contemplate,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “seek,” “should,” “target,” “will,” “would,” or the negative of these words or other comparable terminology. Accordingly, these statements involve estimates, assumptions and uncertainties which could cause actual results to differ materially from those expressed in them.

Given these uncertainties, you should not place undue reliance on these forward-looking statements as actual events or results may differ materially from those projected in the forward-looking statements due to various factors, including, but not limited to, those set forth under the heading “Risk Factors” in any applicable prospectus supplement, the documents incorporated by reference therein or any free writing prospectus that we authorized. Our actual future results may be materially different from what we expect. We qualify all of the forward-looking statements contained in this prospectus, in the documents incorporated by reference herein and in any prospectus supplement by these cautionary statements. These forward-looking statements speak only as of the date on which the statements were made and are not guarantees of future performance. Although we undertake no obligation to revise or update any forward-looking statements, whether as a result of new information, future events or otherwise, you are advised to review any additional disclosures we make in the documents we subsequently file with the SEC that are incorporated by reference in this prospectus and any prospectus supplement. See “Where You Can Find Additional Information.”

## **USE OF PROCEEDS**

Unless otherwise indicated in a prospectus supplement, we intend to use the net proceeds from the sale of securities offered by this prospectus and any applicable prospectus supplement for general corporate purposes. Until we apply the proceeds from a sale of securities to their intended purposes, we may invest those proceeds in short-term, interest-bearing, investment-grade, securities or hold as cash. We will not receive any of the proceeds from the sale of securities by selling securityholders, where applicable.

## **SELLING SECURITYHOLDERS**

Information about selling securityholders, where applicable, will be set forth in a prospectus supplement, in an amendment to the registration statement of which this prospectus is a part, or in filings we make with the SEC under the Exchange Act, which are incorporated by reference.

## DESCRIPTION OF OUR CAPITAL STOCK

### General

The following is a summary of the rights of our common stock and preferred stock and certain provisions of our amended and restated certificate of incorporation and amended and restated bylaws as they are currently in effect, which we refer to in this section as our certificate of incorporation and bylaws, respectively. This summary does not purport to be complete and is qualified in its entirety by the provisions of our certificate of incorporation and bylaws, copies of which have been filed with the SEC.

Our authorized capital stock consists of 110,000,000 shares, of which 100,000,000 shares, par value \$0.001 per share, are designated as common stock, and 10,000,000 shares, par value \$0.001 per share, are designated as preferred stock.

### Common Stock

The holders of our common stock are entitled to one vote per share on all matters to be voted on by our stockholders. Holders of common stock are entitled to receive such dividends as may be declared by the board of directors out of funds legally available therefor. In the event of our liquidation, dissolution or winding up, holders of common stock are entitled to share ratably in all assets remaining after payment of liabilities and distribution of the liquidation preferences of any then outstanding shares of preferred stock. There are no redemption or sinking fund provisions applicable to the common stock.

### Stock Exchange Listing

Our common stock is listed on the Nasdaq Global Select Market and trades under the symbol "CRTX."

### Transfer Agent and Registrar

The Transfer Agent and Registrar for our common stock is American Stock Transfer & Trust Company, LLC. Its address is 6201 15th Avenue, Brooklyn, NY 11219.

### Preferred Stock

Our board of directors has the authority, without further action by our stockholders, to designate and issue up to the total number of authorized shares of preferred stock in one or more series and to fix the rights, preferences, privileges and restrictions granted to or imposed upon each such series of preferred stock, including dividend rights, dividend rate, conversion rights, voting rights, rights and terms of redemption, redemption prices, liquidation preference and sinking fund terms, any or all of which may be greater than or senior to the rights of the common stock. The issuance of preferred stock could adversely affect the voting power of holders of common stock and reduce the likelihood that such holders will receive dividend payments or payments upon liquidation. Such issuance could have the effect of decreasing the market price of the common stock. The issuance of preferred stock or even the ability to issue preferred stock could also have the effect of delaying, deterring or preventing a change of control or other corporate action.

### Registration Rights

Certain holders of shares of our common stock, including all of our former preferred stockholders prior to our initial public offering and certain holders of more than five percent of our capital stock and entities affiliated with certain of our directors, are entitled to certain rights with respect to the registration of their respective shares of common stock under the Securities Act. These shares are referred to as registrable securities. The holders of these registrable securities possess registration rights pursuant to the terms of our amended and restated registration rights agreement and are described in additional detail below.

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The registration rights terminate with respect to the registration rights of an individual holder on the earliest to occur of (i) May 8, 2024 (five years following our initial public offering), (ii) the liquidation, dissolution or indefinite cessation of the business operations of our company, or the closing of a deemed liquidation, dissolution or winding up of our company pursuant to our amended and restated certificate of incorporation, or (iii) such time as Rule 144 or another similar exemption under the Securities Act is available for the sale of such stockholder's shares.

### ***Demand Registration Rights***

The holders of the registrable securities are entitled to certain demand registration rights. At any time, the holders of at least 35% of the registrable securities then outstanding may make a written request that we register all or a portion of their shares, subject to certain specified exceptions. Such request for registration must cover securities that have an anticipated aggregate offering price, net of underwriting discounts and commissions, of at least \$10,000,000. We are only obligated to effect two registrations in response to these demand registration rights.

### ***Piggyback Registration Rights***

In connection with this registration statement, the holders of registrable securities were entitled to, and the necessary percentage of holders waived, their rights to notice of this registration statement and to include their shares of registrable securities in this registration statement. If we propose to register for offer and sale any of our securities under the Securities Act on another registration statement, either for our own account or for the account of other securityholders, including pursuant to any stockholder-initiated demand registration, the holders of such registrable securities will have the right to include their shares in the registration statement for such offering, subject to certain exceptions. The underwriters of any underwritten offering will have the right to limit the number of registrable securities to be included in the registration statement, subject to certain restrictions.

### ***Form S-3 Registration Rights***

The holders of the registrable securities are entitled to certain Form S-3 registration rights. Holders of the registrable securities may request that we register for offer and sale their shares on Form S-3 if we are qualified to file a registration statement on Form S-3, subject to certain specified exceptions. Such request for registration on Form S-3 must cover securities anticipated to have an aggregate sale price, net of underwriting discounts and commission, of at least \$1,000,000.

### ***Expenses of Registration***

We will pay all registration expenses related to any demand, piggyback or Form S-3 registration, including reasonable fees and disbursements of one special counsel for the holders of such registrable securities, other than underwriting fees, discounts or commissions (if any), which will be borne by the holders of such registrable securities.

## **Anti-Takeover Effects of Delaware Law and Our Certificate of Incorporation and Bylaws**

Our amended and restated certificate of incorporation and our amended and restated bylaws contain certain provisions that could have the effect of delaying, deterring or preventing another party from acquiring control of us. These provisions and certain provisions of Delaware law, which are summarized below, are expected to discourage coercive takeover practices and inadequate takeover bids. These provisions are also designed, in part, to encourage persons seeking to acquire control of us to negotiate first with our board of directors. We believe that the benefits of increased protection of our potential ability to negotiate more favorable terms with an unfriendly or unsolicited acquirer outweigh the disadvantages of discouraging a proposal to acquire us.

### ***Undesignated Preferred Stock***

As discussed above, our board of directors has the ability to issue preferred stock with voting or other rights or preferences that could impede the success of any attempt to change control of us. These and other provisions may have the effect of deterring hostile takeovers or delaying changes in control or management of our company.

### ***Limits on Ability of Stockholders to Act by Written Consent or Call a Special Meeting***

Our amended and restated certificate of incorporation provides that our stockholders may not act by written consent, which may lengthen the amount of time required to take stockholder actions. As a result, a holder controlling a majority of our capital stock would not be able to amend our amended and restated bylaws or remove directors without holding a meeting of our stockholders called in accordance with our amended and restated bylaws.

In addition, our amended and restated bylaws provides that special meetings of the stockholders may be called only by the chairperson of the board, the chief executive officer, the lead independent director, or at the request of a majority of our board of directors. Stockholders may not call a special meeting, which may delay the ability of our stockholders to force consideration of a proposal or for holders controlling a majority of our capital stock to take any action, including the removal of directors.

### ***Requirements for Advance Notification of Stockholder Nominations and Proposals***

Our amended and restated bylaws establish advance notice procedures with respect to stockholder proposals and the nomination of candidates for election as directors, other than nominations made by or at the direction of our board of directors or a committee of our board of directors. These provisions may have the effect of precluding the conduct of certain business at a meeting if the proper procedures are not followed. These provisions may also discourage or deter a potential acquirer from conducting a solicitation of proxies to elect the acquirer's own slate of directors or otherwise attempting to obtain control of our company.

### ***Board Classification***

Our board of directors is divided into three classes, one class of which is elected each year by our stockholders. The directors in each class serve three-year terms. A third party may be discouraged from making a tender offer or otherwise attempting to obtain control of us as it is more difficult and time-consuming for stockholders to replace a majority of the directors on a classified board.

### ***No Cumulative Voting***

Our amended and restated certificate of incorporation and amended and restated bylaws do not provide for cumulative voting in the election of directors. Cumulative voting allows a stockholder to vote a portion or all of its shares for one or more candidates for seats on the board of directors. Without cumulative voting, a minority stockholder may not be able to gain as many seats on our board of directors as the stockholder would be able to gain if cumulative voting were permitted. The absence of cumulative voting makes it more difficult for a minority stockholder to gain a seat on our board of directors to influence our board's decision regarding a takeover.

### ***Amendment of Charter and Bylaws Provisions***

The amendment of the above provisions of our amended and restated certificate of incorporation requires approval by holders of at least two thirds of our outstanding capital stock entitled to vote generally in the election of directors. The amendment of certain provisions of our amended and restated bylaws also requires approval by the holders of at least two thirds of our outstanding capital stock entitled to vote generally in the election of directors.

### ***Delaware Takeover Statutes***

We are subject to the provisions of Section 203 of the Delaware General Corporation Law regulating corporate takeovers. In general, Section 203 prohibits a publicly held Delaware corporation from engaging, under certain circumstances, in a business combination with an interested stockholder for a period of three years following the date the person became an interested stockholder, unless:

- prior to the date of the transaction, our board of directors approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;
- upon completion of the transaction that resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, calculated as provided under Section 203; or
- at or subsequent to the date of the transaction, the business combination is approved by our board of directors and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder.

Generally, a business combination includes a merger, asset or stock sale, or other transaction resulting in a financial benefit to the interested stockholder. An interested stockholder is a person who, together with affiliates and associates, owns or, within three years prior to the determination of interested stockholder status, did own 15% or more of a corporation's outstanding voting stock. We expect the existence of this provision to have an anti-takeover effect with respect to transactions our board of directors does not approve in advance. We anticipate that Section 203 may also discourage attempts that might result in a premium over the market price for the shares of common stock held by stockholders.

These provisions of Delaware law and of our amended and restated certificate of incorporation and amended and restated bylaws, could have the effect of discouraging others from attempting hostile takeovers and, as a consequence, they might also inhibit temporary fluctuations in the market price of our common stock that often result from actual or rumored hostile takeover attempts. These provisions might also have the effect of preventing changes in our management. It is possible that these provisions could make it more difficult to accomplish transactions that stockholders might otherwise deem to be in their best interests.

### ***Choice of Forum***

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware is the sole and exclusive forum for any derivative action or proceeding brought on our behalf, any action asserting a breach of fiduciary duty owed by any of our directors, officers or other employees to us or our stockholders, any action asserting a claim against us arising pursuant to any provisions of the Delaware General Corporation Law, our amended and restated certificate of incorporation or our amended and restated bylaws, any action or proceeding asserting a claim as to which the Delaware General Corporation Law confers jurisdiction upon the Court of Chancery of the State of Delaware or any action asserting a claim against us that is governed by the internal affairs doctrine, subject in each case to the Court of Chancery having personal jurisdiction over the parties named as defendants therein. The exclusive forum provision does not apply to suits brought to enforce any liability or duty created by the Exchange Act or any other claim for which the federal courts have exclusive jurisdiction.

In addition, our certificate of incorporation provides that the U.S. federal district courts are the exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act. Our exclusive forum provision will not relieve us of our duties to comply with the federal securities laws and the rules and regulations thereunder, and our stockholders will not be deemed to have waived our compliance with these laws, rules and regulations. While the Delaware Supreme Court recently determined that such choice of forum provisions are facially valid, a stockholder may nevertheless seek to bring such a claim arising under the

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Securities Act against us, our directors, officers, or other employees in a venue other than in the U.S. federal district courts. In such instance, we would expect to vigorously assert the validity and enforceability of the exclusive forum provisions of our certificate of incorporation, and this may require significant additional costs associated with resolving such action in other jurisdictions.

#### **DESCRIPTION OF OUR DEBT SECURITIES**

The debt securities will constitute either senior or subordinated debt of Cortexyme, Inc. The debt securities that are sold may be exchangeable for and/or convertible into shares of common stock or any of the other securities that may be sold under this prospectus. The debt securities will be issued under one or more separate indentures between us and a designated trustee. We will include in a prospectus supplement the specific terms of each series of senior or subordinated debt securities being offered, including the terms, if any, on which a series of senior or subordinated debt securities may be convertible into or exchangeable for other securities. In addition, the material terms of any indenture, which will govern the rights of the holders of our senior or subordinated debt securities will be set forth in the applicable prospectus supplement.

#### **DESCRIPTION OF OUR WARRANTS**

We may issue warrants to purchase our debt or equity securities or securities of third parties or other rights, including rights to receive payment in cash or securities based on the value, rate or price of one or more specified commodities, currencies, securities or indices, or any combination of the foregoing. Warrants may be issued independently or together with any other securities and may be attached to, or separate from, such securities. Each series of warrants will be issued under a separate warrant agreement to be entered into between us and a warrant agent. The terms of any warrants to be issued and a description of the material provisions of the applicable warrant agreement will be set forth in the applicable prospectus supplement.

#### **DESCRIPTION OF OUR UNITS**

As specified in the applicable prospectus supplement, we may issue units consisting of one or more shares of common stock, shares of preferred stock, debt securities or warrants or any combination of such securities.

## PLAN OF DISTRIBUTION

We and any selling securityholder, as applicable, may offer and sell the securities being offered hereby in one or more of the following ways from time to time:

- to or through underwriters;
- on any national securities exchange or quotation service on which the securities may be listed or quoted at the time of sale;
- in the over-the-counter market;
- in transactions other than on these exchanges or systems or in the over-the-counter market;
- in “at the market offerings,” within the meaning of Rule 415(a)(4) of the Securities Act, to or through market makers or into an existing market for the securities;
- through the writing or settlement of options or other hedging transactions, whether through an options exchange or otherwise;
- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- block trades in which the broker-dealer will attempt to sell the shares as agent but may position and resell a portion of the block as principal to facilitate the transaction;
- purchases by a broker-dealer as principal and resale by the broker-dealer for its account;
- an exchange distribution in accordance with the rules of the applicable exchange;
- privately negotiated transactions;
- a combination of any of these methods of sale; and
- any other method permitted pursuant to applicable law.

We will identify the specific plan of distribution, including any underwriters, dealers, agents or other purchasers, persons or entities, and any applicable compensation, in a prospectus supplement, in an amendment to the registration statement of which this prospectus is a part, or in other filings we make with the SEC under the Exchange Act, which are incorporated by reference.

## **LEGAL MATTERS**

Unless the applicable prospectus supplement indicates otherwise, the validity of the securities being offered by this prospectus will be passed upon by Orrick, Herrington & Sutcliffe LLP, Menlo Park, California. Additional legal matters may be passed upon for us or any underwriters, dealers or agents, by counsel that we will name in the applicable prospectus supplement.

## **EXPERTS**

The financial statements as of December 31, 2019 and 2018 and for the years then ended incorporated by reference in this prospectus have been so incorporated in reliance on the report of BDO USA, LLP, an independent registered public accounting firm, incorporated herein by reference, given on the authority of said firm as experts in auditing and accounting.

## **WHERE YOU CAN FIND ADDITIONAL INFORMATION**

We file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public at the SEC's website at [www.sec.gov](http://www.sec.gov).

We have filed with the SEC a registration statement on Form S-3 relating to the securities covered by this prospectus. This prospectus is a part of the registration statement and does not contain all the information in the registration statement. Other documents establishing the terms of the offered securities are or may be filed as exhibits to the registration statement or documents incorporated by reference in the registration statement. Whenever a reference is made in this prospectus to a contract or other document of ours, the reference is only a summary and you should refer to the exhibits that are a part of the registration statement for a copy of the contract or other document. You may review a copy of the registration statement through the SEC's website, as provided above.

## INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to “incorporate by reference” the information from other documents we file with the SEC, which means that we can disclose important information to you by referring you to those documents instead of having to repeat the information in this prospectus. The information incorporated by reference is considered to be part of this prospectus, and later information that we file with the SEC will automatically update and supersede this information. We incorporate by reference the documents listed below and any future filings we make with the SEC under Sections 13(a), 13(c), 14, or 15(d) of the Exchange Act on or after the date of this prospectus (other than, in each case, documents or information deemed to have been furnished and not filed in accordance with SEC rules) until the termination of the registration statement of which this prospectus is a part:

- Our Annual Report on Form 10-K for the year ended December 31, 2019, filed with the SEC on [March 16, 2020](#);
- Our Quarterly Report on Form 10-Q for the quarter ended March 31, 2020, filed with the SEC on [May 12, 2020](#);
- Our Current Reports on Form 8-K filed with the SEC on [February 6, 2020](#), [April 30, 2020](#) and [May 21, 2020](#);
- The description of our common stock contained in the Registration Statement on Form 8-A filed with the SEC on [May 1, 2019](#), including any amendment or report filed for the purpose of updating such description.

Any statement contained in this prospectus, or in a document all or a portion of which is incorporated by reference, shall be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus, any applicable prospectus supplement and any related free writing prospectus or any document incorporated by reference modifies or supersedes such statement. Any such statement so modified or superseded shall not, except as so modified or superseded, constitute a part of this prospectus.

Upon request, we will provide, without charge, to each person, including any beneficial owner, to whom a copy of this prospectus is delivered a copy of the documents incorporated by reference into this prospectus. You may request a copy of these filings, and any exhibits we have specifically incorporated by reference as an exhibit in this prospectus, at no cost by writing or telephoning us at the following:

Cortexyme, Inc.  
269 East Grand Avenue  
South San Francisco, CA 94080  
(415) 910-5717

You may also access these documents, free of charge on the SEC’s website at [www.sec.gov](http://www.sec.gov) or on the “Investor Relations” page of our website at [www.cortexyme.com](http://www.cortexyme.com). Information contained on our website is not incorporated by reference into this prospectus, and you should not consider any information on, or that can be accessed from, our website as part of this prospectus or any accompanying prospectus supplement.



**Up to \$150,000,000**

**Common Stock**

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**PROSPECTUS SUPPLEMENT**

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**Jefferies**

December 23, 2021

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