

PROSPECTUS



Up to \$150,000,000

Common Stock

We have entered into an Open Market Sale AgreementSM, or the sales agreement, with Jefferies LLC, or Jefferies, relating to the sale of shares of our common stock offered by this 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. As of March 1, 2022, we have sold \$626,292 of our common stock under the Sales Agreement pursuant to our registration statement on Form S-3 filed with the Securities and Exchange Commission on December 23, 2021 (File No. 333-238851) (the “Prior Registration Statement”). Accordingly, we may now sell up to \$149,373,708 of our common stock under the sales agreement.

Our common stock is listed on the Nasdaq Global Select Market under the symbol “CRTX.” On May 17, 2022, the last reported sale price of our common stock on the Nasdaq Global Select Market was \$3.26 per share.

Sales of our common stock, if any, under this 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 16 of this prospectus for additional information regarding the compensation to be paid to Jefferies.

Investing in our common stock involves risks. See “[Risk Factors](#)” beginning on page 4 of this prospectus 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, 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 is truthful or complete. Any representation to the contrary is a criminal offense.

Jefferies

The date of this prospectus is May 17, 2022.

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ABOUT THIS PROSPECTUS

This prospectus is 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. This prospectus provides you with specific information regarding the terms of this offering and our common stock.

We provide information to you about this offering of shares of our common stock in this prospectus, which describes the specific details regarding this offering. 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—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 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 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 or any free writing prospectus is accurate only as of the date on the front cover of this prospectus. 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. 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 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 must inform themselves about, and observe any restrictions relating to, the offering of our common stock and the distribution of this prospectus outside the United States. This prospectus does 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 by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

This prospectus and the information incorporated herein 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 are the property of their respective owners.

As used in this 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 SUMMARY

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

Overview

We are a clinical stage biopharmaceutical company focused on novel therapeutic approaches to improve the lives of patients diagnosed with Alzheimer’s and other degenerative diseases. Our company was founded on the seminal discovery of the presence of Porphyromonas gingivalis, or P. gingivalis, and its secreted toxic virulence factor proteases, called gingipains, in the relevant brain areas of both Alzheimer’s and Parkinson’s disease patients. Our evidence demonstrates gingipains are tied to neuro degeneration and inflammation in humans and animal models. Our expanding portfolio of gingipain inhibitors are orally administered, brain-penetrating small molecules. Our pipeline includes proprietary drug candidates for the treatment of CNS disorders including Alzheimer’s disease, for the treatment of oncology applications including the prevention of oral squamous cell carcinoma, as well as for the treatment of underserved and chronic conditions like periodontitis. Our pipeline also includes proprietary irreversible protease inhibitors under development for the treatment of coronavirus infection.

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. 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.

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 “Plan of Distribution” on page 16 of this prospectus.
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 4 of this prospectus, and under similar headings in other documents that are incorporated by reference into this 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, 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 33,871,589 shares of our common stock are sold at a price of \$4.41 per share, the last reported sale price of our common stock on the Nasdaq Global Select Market on March 1, 2022, for aggregate gross proceeds of approximately \$149,373,708, and after deducting commissions and estimated offering expenses payable by us, you would experience immediate dilution of \$0.29 per share, representing the difference between our as adjusted net tangible book value per share as of December 31, 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 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.

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 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 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 and the information incorporated by reference herein include, but are not limited to, statements about:

- our use of the net proceeds from this offering;
- our ability to proceed with clinical development of atuzaginstat (COR388) and for potential additional indications that we may pursue beyond Alzheimer’s disease including oncology and periodontal disease, despite the full clinical hold imposed by the FDA;
- future research and development activities, including the scope, success, cost and timing of our development activities, preclinical studies and clinical trials, including clinical trial of COR588 or other pipeline compounds we advance through the drug development process;
- the timing and focus of our future clinical trials, and the reporting of data from those trials,
- our ability and timing of seeking and obtaining FDA, EMA and any other regulatory approval;
- the willingness of the FDA or EMA to accept our completed and planned clinical and preclinical studies and other work, as the basis for review and approval of atuzaginstat (COR 388) or our other compounds for their respective indications;
- success of our clinical development and business strategy, including our ability to realized expected cost saving from our recent reduction in force;
- the ability of our clinical trials to demonstrate safety and efficacy of our drug candidates, and other positive results;
- 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;
- 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, in light of recent management changes and reduction in force;
- 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;
- governmental or regulatory delays, information requests, clinical holds, and 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;

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- 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 and the information incorporated by reference herein 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 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 in its 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 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. 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 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 to reflect events or circumstances after the date of this prospectus 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 pursuant to our sales agreement with Jefferies. Of this \$150 million, we have previously sold \$626,292 of our common stock as of March 1, 2022. Accordingly we may now sell the remaining \$149,373,708 of our common stock. 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, 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 December 31, 2021 was \$118.6 million, or \$3.94 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 December 31, 2021.

After giving effect to the sale of 33,871,859 shares of common stock that we are offering at the assumed public offering price of \$4.41 per share, which was the last reported sale price of our common stock on the Nasdaq Global Select Market on March 1, 2022, and after deducting commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of December 31, 2021, would have been approximately \$263.2 million, or approximately \$4.12 per share. This amount represents an immediate increase in as adjusted net tangible book value of \$0.18 per share to our existing stockholders and an immediate dilution in net tangible book value of approximately \$0.29 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	\$4.41
Historical net tangible book value per share as of December 31, 2021	3.94
Increase in as adjusted net tangible book value per share attributable to this offering	0.18
As adjusted net tangible book value per share after this offering	4.12
Dilution per share to new investors in this offering	<u>\$0.29</u>

Each \$1.00 increase in the assumed public offering price of \$4.41 per share, which was the last reported sale price of our common stock on the Nasdaq Global Select Market on March 1, 2022, would increase the as adjusted net tangible book value per share after this offering by approximately \$0.44, and dilution in as adjusted net tangible book value per share to new investors by approximately \$0.56, assuming that the number of shares of common stock offered by us, as set forth on the cover page of this prospectus, 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 \$4.41 per share, which was the last reported sale price of our common stock on the Nasdaq Global Select Market on March 1, 2022, would decrease the as adjusted net tangible book value per share after this offering by approximately \$0.56. New investors would experience no dilution in the as adjusted net tangible book value per share of the Company. The as adjusted net tangible book value per share would increase by approximately \$0.15.

Each increase of 1,000,000 shares in the number of shares of common stock offered by us would have less than \$0.01 increase to our as adjusted net tangible book value per share after this offering and less than \$0.01 decrease in the dilution to investors participating in this offering, 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 \$0.01 per share and increase the dilution to investors participating in this offering by approximately \$0.01 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 30,074,412 shares of our common stock outstanding as of December 31, 2021, and excludes:

- 6,246,293 shares of our common stock issuable upon the exercise of options to purchase shares of our common stock outstanding as of December 31, 2021 (of which 2,232,953 were vested and exercisable), with a weighted-average exercise price of \$28.80 per share;
- 1,065,000 shares of our common stock issuable upon the exercise of outstanding options to purchase shares of our common stock granted after December 31, 2021, with a weighted-average exercise price of \$13.39 per share;
- 138,926 shares of our common stock reserved for future issuance under our 2019 Equity Incentive Plan, which excludes an annual evergreen increase of 1,202,976 shares of common stock effective on January 1, 2022;
- 832,421 shares of our common stock reserved for future issuance under our 2019 Employee Stock Purchase Plan, which excludes an annual evergreen increase of 300,744 shares of common stock effective on January 1, 2022;

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- 1,013,500 shares of our common stock issuable upon the vesting of outstanding restricted stock units granted after December 31, 2021 with a grant date value of \$4.30 per share; and
- 51,769 shares of our common stock sold after December 31, 2021 under the sales agreement with Jeffries and pursuant to the Prior Registration Statement.

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.

DESCRIPTION OF OUR CAPITAL STOCK

Description of Common Stock

Under our amended and restated certificate of incorporation, we have authority to issue 100,000,000 shares of our common stock, par value \$0.001 per share. As of December 31, 2021, 30,074,412 shares of our common stock were issued and outstanding. All shares of our common stock will, when issued, be duly authorized, fully paid and nonassessable.

Voting Rights

The holders of our common stock are entitled to one vote for each share held of record on all matters submitted to a vote of the stockholders. Cumulative voting for the election of directors is not provided for in our restated certificate of incorporation, which means the holders of a majority of our shares of common stock can elect all of the directors then standing for election.

Dividends

Subject to preferences that may be applicable to any then outstanding preferred stock, holders of common stock are entitled to receive dividends, if any, as may be declared from time to time by the board of directors out of legally available funds.

Liquidation

In the event of our liquidation, dissolution or winding up, holders of common stock will be entitled to share ratably in the net assets legally available for distribution to stockholders after the payment of all of our debts and other liabilities and the satisfaction of any liquidation preference granted to the holders of any then outstanding shares of preferred stock.

Rights and Preferences

Holders of common stock have no preemptive, conversion, subscription or other rights, and there are no redemption or sinking fund provisions applicable to the common stock. The rights, preferences and privileges of the holders of common stock are subject to and may be adversely affected by, the rights of the holders of shares of any series of preferred stock that we may designate in the future.

Description of Preferred Stock

Under our amended and restated certificate of incorporation, we have authority, subject to any limitations prescribed by law and without further stockholder approval, to issue from time to time up to 10,000,000 shares of preferred stock, par value \$0.001 per share, in one or more series. As of December 31, 2021, we had no shares of preferred stock issued and outstanding.

Pursuant to our amended and restated certificate of incorporation, our board of directors has the authority to designate the rights, preferences, privileges and restrictions of each such series, including dividend rights, preferences, privileges and restrictions of each such series, including dividend rights, dividend rates, conversion rights, voting rights, terms of redemption, redemption prices, liquidation preferences, sinking fund terms and the number of shares constituting any series.

The issuance of preferred stock may have the effect of delaying, deferring or preventing a change in control of the company without further action by the stockholders. The issuance of redeemable convertible preferred stock with voting and conversion rights may also adversely affect the voting power of the holders of common stock and the likelihood that such holders will receive dividend payments and payments upon liquidation. In certain circumstances, an issuance of preferred stock could have the effect of decreasing the market price of the common stock.

Registration Rights

Under our amended and restated investors' rights agreement, certain holders of shares of our common stock, or their affiliates or transferees, have the right to require us to register their shares under the Securities Act so that those shares may be publicly resold, or to include their shares in any registration statement we file, in each case as described below. The registration rights terminate with respect to the registration rights of an individual holder on the earliest to occur of May 8, 2024 (five years following our initial public offering), 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 with respect to any particular stockholder, such time after the effective date of the registration statement that such stockholder can sell all of its shares under Rule 144 of the Securities Act during any three-month period without registration.

Demand Registration Rights

The holders of at least 35% of the registrable securities may demand that we effect a registration under the Securities Act covering the public offering and sale of at least the number of registrable securities held by such stockholders having an anticipated aggregate offering price of at least \$10,000,000. Upon any such demand we must effect the registration of such registrable securities that have been requested to register together with all other registrable securities that we may have been requested to register by other stockholders pursuant to the incidental registration rights described below. We are only obligated to effect two registrations in response to these demand registration rights.

Piggyback Registration Rights

If we register any securities for public sale, including pursuant to any stockholder-initiated demand registration, 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

We may be obligated to effect a registration on Form S-3 under the Securities Act. At any time after we are qualified to file a registration statement on Form S-3, the holders of registrable securities anticipated to have an aggregate sale price, net of underwriting discounts and commission, of at least \$1,000,000 may request in writing that we effect a registration on Form S-3.

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 Amended and Restated Certificate of Incorporation and Amended and Restated 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 have 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 will 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 permit 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 will require 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 our amended and restated bylaws will require approval by the holders of at least two thirds of our outstanding capital stock entitled to vote generally in the election of directors.

Delaware Anti-Takeover Statute

We are subject to the provisions of Section 203 of the DGCL 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.

The provisions of Delaware law and the provisions 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.

Authorized but Unissued Shares

Our authorized but unissued shares of common stock and preferred stock will be available for future issuances without stockholder approval, except as required by the listing standards of the Nasdaq Global Select Market, and could be utilized for a variety of corporate purposes, including future offerings to raise additional capital, acquisitions and employee benefit plans. The existence of authorized but unissued and unreserved common stock and preferred stock could render more difficult or discourage an attempt to obtain control of the company by means of a proxy contest, tender offer, merger or otherwise.

Choice of Forum

Our amended and restated certificate of incorporation provides that, unless we consent to the selection of an alternative forum, to the fullest extent permitted by law, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for: (i) any derivative action or proceeding brought on behalf of us; (ii) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or other employees or agents to us or our stockholders; (iii) any action asserting a claim against us arising pursuant to any provision of the Delaware General Corporation Law or our amended and restated certificate of incorporation or amended and restated bylaws; or (iv) any action asserting a claim against us governed by the internal affairs doctrine; provided that, the exclusive forum provision will 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; and provided further that, if and only if the Court of Chancery of the State of Delaware dismisses any such action for lack of subject matter jurisdiction, such action may be brought in another state or federal court sitting in the State of Delaware. Our amended and restated certificate of incorporation also provides that the federal district courts of the United States of America will be the exclusive forum for the resolution of any complaint asserting a cause of action against us or any of our directors, officers, employees or agents and arising under the Securities Act. 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 Securities Act against us, our directors, officers, employees or agents in a venue other than in the federal district courts of the United States of America. In such instance, we would expect to vigorously assert the validity and enforceability of the exclusive forum provisions of our amended and restated certificate of incorporation, and this may require significant additional costs associated with resolving such action in other jurisdictions.

Listing. Our common stock is listed on the Nasdaq Global Select Market under the symbol “CRTX.”

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

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. As of March 1, 2022, we have sold \$626,292 of our common Stock under the sales agreement with Jefferies and pursuant to the Prior Registration Statement. Accordingly, we may now sell up to \$149,373,708 of our common stock under the sales agreement. Sales of our shares of common stock, if any, under this 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 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 \$230,000. 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 was filed under the Exchange Act, and incorporated by reference in this prospectus.

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

LEGAL MATTERS

The validity of the shares of common stock offered by this prospectus 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, 2021 and 2020 and for each of the three years in the period ended December 31, 2021 and management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2021 incorporated by reference in this prospectus 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.

Our website address is www.cortexyme.com. The information on our website, however, is not, and should not be deemed to be, a part of this prospectus.

This prospectus is 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 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. Information in this prospectus supersedes information incorporated by reference that we filed with the SEC prior to the date of this prospectus, while information that we file later with the SEC will automatically update and supersede the information in this prospectus. We incorporate by reference into this 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, 2021, filed with the SEC on March 1, 2022;
- the information specifically incorporated by reference into our Annual Report on [Form 10-K](#) for the fiscal year ended December 31, 2021, from our Definitive Proxy Statement on [Schedule 14A](#), filed with the SEC on April 27, 2022;
- our Quarterly Report on [Form 10-Q](#) for the fiscal quarter ended March 31, 2022, filed with the SEC on May 10, 2022;
- our Current Reports on Form 8-K (other than information furnished rather than filed) filed with the SEC on [January 26, 2022](#), [February 2, 2022](#), [March 15, 2022](#), [May 2, 2022](#), [May 10, 2022](#) and [May 12, 2022](#); 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 and prior to the termination of the offering of our common stock to which this prospectus relates will automatically be deemed to be incorporated by reference into this prospectus 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



Up to \$150,000,000

Common Stock

PROSPECTUS

Jefferies

May 17, 2022
