
**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION**
Washington, D.C. 20549

**POST-EFFECTIVE AMENDMENT NO. 2
TO
FORM S-3
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933**

Cortexyme, Inc.

(Exact Name of Registrant as Specified in Its Charter)

Delaware
(State or Other Jurisdiction of
Incorporation or Organization)

90-1024039
(I.R.S. Employer
Identification No.)

**269 East Grand Ave
South San Francisco, California, 94080
(415) 910-5717**

(Address, Including Zip Code, and Telephone Number, Including Area Code, of Registrant's Principal Executive Offices)

Christopher Lowe
Interim Chief Executive Officer, Chief Financial Officer and Chief Operating Officer
Cortexyme, Inc.
269 East Grand Ave.
South San Francisco, CA 94080
(415) 910-5717

(Name, Address, Including Zip Code, and Telephone Number, Including Area Code, of Agent for Service)

Copies to:

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

Approximate date of commencement of proposed sale to the public: From time to time after the effective date of this registration statement.

If the only securities being registered on this form are being offered pursuant to dividend or interest reinvestment plans, please check the following box.

If any of the securities being registered on this form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box.

If this form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this form is a registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box.

If this form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company" and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer

Accelerated filer

Non-accelerated filer

Smaller reporting company

Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 7(a)(2)(B) of the Securities Act.

The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the Registration Statement shall become effective on such date as the Commission acting pursuant to said Section 8(a), may determine.

EXPLANATORY NOTE

This Post-Effective Amendment No. 2 to the Registration Statement on Form S-3 (Commission File No. 333-238851) (the “Automatic Shelf Registration Statement”) of Cortexyme, Inc. (the “Registrant”) is being filed for the purpose of amending the Automatic Shelf Registration Statement to reflect that the Registrant is no longer a well-known seasoned issuer (as such term is defined in Rule 405 of the Securities Act of 1933, as amended) because the Registrant’s worldwide market value of its outstanding voting and non-voting common equity held by non-affiliates was less than \$700 million as of the most recent determination date.

This registration statement contains:

- a base prospectus which covers the offering, issuance and sale by us of the securities identified above from time to time in one or more offerings, with a total value of up to \$150 million; and
- a sales agreement prospectus covering the offering, issuance and sale by us of up to a maximum aggregate offering price of \$150,000,000 of our common stock that may be issued and sold under a sales agreement with Jefferies LLC.

The base prospectus immediately follows this explanatory note. The specific terms of any securities to be offered pursuant to the base prospectus, other than the shares under the Open Market Sale AgreementSM with Jefferies LLC, will be specified in a prospectus supplement to the base prospectus. The specific terms of the securities to be issued and sold under the Open Market Sale AgreementSM are specified in the sales agreement prospectus that immediately follows the base prospectus. The \$150.0 million of common stock that may be offered, issued and sold under the sales agreement prospectus is included in the \$150.0 million of securities that may be offered, issued and sold by us under the base prospectus, and upon termination of the offering under the Open Market Sale AgreementSM, any portion of the \$150.0 million of securities included in the sales agreement prospectus that is not sold pursuant to the Open Market Sale AgreementSM will be available for sale in other offerings pursuant to the base prospectus. As of March 1, 2022, the Registrant has sold \$626,292 of common stock under the sales agreement prospectus pursuant to a 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”).

The information in this preliminary prospectus is not complete and may be changed. We may not sell these securities until the U.S. Securities and Exchange Commission declares our registration statement effective. This preliminary prospectus is not an offer to sell these securities and we are not soliciting offers to buy these securities in any state or jurisdiction where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED MARCH 4, 2022

PROSPECTUS



\$150,000,000

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

From time to time, we may offer and sell any combination of the securities described in this prospectus, with a total value of up to \$150 million, 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.

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 3 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.

We may amend or supplement this prospectus from time to time by filing amendments or supplements as required. We urge you to read the entire prospectus, any amendments or supplements, any free writing prospectuses, and any documents incorporated by reference carefully before you make your investment decision.

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

The date of this prospectus is _____, 2022.

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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) 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 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 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.

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 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.

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 marketable, 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.

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.

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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.

DESCRIPTION OF OUR DEBT SECURITIES

We may issue debt securities from time to time, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. While the terms we have summarized below will apply generally to any debt securities that we may offer under this prospectus, we will describe the particular terms of any debt securities that we may offer in more detail in the applicable prospectus supplement. The terms of any debt securities offered under a prospectus supplement may differ from the terms described below. Unless the context requires otherwise, whenever we refer to the indenture, we also are referring to any supplemental indentures that specify the terms of a particular series of debt securities.

We will issue the debt securities under the indenture that we will enter into with the trustee named in the indenture. The indenture will be qualified under the Trust Indenture Act of 1939, as amended, or the Trust Indenture Act. We have filed the form of indenture as an exhibit to the registration statement of which this prospectus is a part, and supplemental indentures and forms of debt securities containing the terms of the debt securities being offered will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the SEC.

The following summary of material provisions of the debt securities and the indenture is subject to, and qualified in its entirety by reference to, all of the provisions of the indenture applicable to a particular series of debt securities. We urge you to read the applicable prospectus supplements and any related free writing prospectuses related to the debt securities that we may offer under this prospectus, as well as the complete indenture that contains the terms of the debt securities.

General

The indenture does not limit the amount of debt securities that we may issue. It provides that we may issue debt securities up to the principal amount that we may authorize and may be in any currency or currency unit that we may designate. Except for the limitations on consolidation, merger and sale of all or substantially all of our assets contained in the indenture, the terms of the indenture do not contain any covenants or other provisions designed to give holders of any debt securities protection against changes in our operations, financial condition or transactions involving us.

We may issue the debt securities issued under the indenture as “discount securities,” which means they may be sold at a discount below their stated principal amount. These debt securities, as well as other debt securities that are not issued at a discount, may be issued with “original issue discount,” or OID, for U.S. federal income tax purposes because of interest payment and other characteristics or terms of the debt securities. Material U.S. federal income tax considerations applicable to debt securities issued with OID will be described in more detail in any applicable prospectus supplement.

We will describe in the applicable prospectus supplement the terms of the series of debt securities being offered, including:

- the title of the series of debt securities;
- any limit upon the aggregate principal amount that may be issued;
- the maturity date or dates;
- the form of the debt securities of the series;
- the applicability of any guarantees;
- whether or not the debt securities will be secured or unsecured, and the terms of any secured debt;
- whether the debt securities rank as senior debt, senior subordinated debt, subordinated debt or any combination thereof, and the terms of any subordination;
- if the price (expressed as a percentage of the aggregate principal amount thereof) at which such debt securities will be issued is a price other than the principal amount thereof, the portion of the principal amount thereof payable upon declaration of acceleration of the maturity thereof, or if applicable, the portion of the principal amount of such debt securities that is convertible into another security or the method by which any such portion shall be determined;
- the interest rate or rates, which may be fixed or variable, or the method for determining the rate and the date interest will begin to accrue, the dates interest will be payable and the regular record dates for interest payment dates or the method for determining such dates;
- our right, if any, to defer payment of interest and the maximum length of any such deferral period;

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- if applicable, the date or dates after which, or the period or periods during which, and the price or prices at which, we may, at our option, redeem the series of debt securities pursuant to any optional or provisional redemption provisions and the terms of those redemption provisions;
- the date or dates, if any, on which, and the price or prices at which we are obligated, pursuant to any mandatory sinking fund or analogous fund provisions or otherwise, to redeem, or at the holder's option to purchase, the series of debt securities and the currency or currency unit in which the debt securities are payable;
- the denominations in which we will issue the series of debt securities, if other than denominations of \$1,000 and any integral multiple thereof;
- any and all terms, if applicable, relating to any auction or remarketing of the debt securities of that series and any security for our obligations with respect to such debt securities and any other terms which may be advisable in connection with the marketing of debt securities of that series;
- whether the debt securities of the series shall be issued in whole or in part in the form of a global security or securities; the terms and conditions, if any, upon which such global security or securities may be exchanged in whole or in part for other individual securities; and the depository for such global security or securities;
- if applicable, the provisions relating to conversion or exchange of any debt securities of the series and the terms and conditions upon which such debt securities will be so convertible or exchangeable, including the conversion or exchange price, as applicable, or how it will be calculated and may be adjusted, any mandatory or optional (at our option or the holders' option) conversion or exchange features, the applicable conversion or exchange period and the manner of settlement for any conversion or exchange;
- if other than the full principal amount thereof, the portion of the principal amount of debt securities of the series which shall be payable upon declaration of acceleration of the maturity thereof;
- additions to or changes in the covenants applicable to the particular debt securities being issued, including, among others, the consolidation, merger or sale covenant;
- additions to or changes in the events of default with respect to the securities and any change in the right of the trustee or the holders to declare the principal, premium, if any, and interest, if any, with respect to such securities to be due and payable;
- additions to or changes in or deletions of the provisions relating to covenant defeasance and legal defeasance;
- additions to or changes in the provisions relating to satisfaction and discharge of the indenture;
- additions to or changes in the provisions relating to the modification of the indenture both with and without the consent of holders of debt securities issued under the indenture;
- the currency of payment of debt securities if other than U.S. dollars and the manner of determining the equivalent amount in U.S. dollars;
- whether interest will be payable in cash or additional debt securities at our or the holders' option and the terms and conditions upon which the election may be made;
- the terms and conditions, if any, upon which we will pay amounts in addition to the stated interest, premium, if any and principal amounts of the debt securities of the series to any holder that is not a "United States person" for federal tax purposes;
- any restrictions on transfer, sale or assignment of the debt securities of the series; and
- any other specific terms, preferences, rights or limitations of, or restrictions on, the debt securities, any other additions or changes in the provisions of the indenture, and any terms that may be required by us or advisable under applicable laws or regulations.

Conversion or Exchange Rights

We will set forth in the applicable prospectus supplement the terms on which a series of debt securities may be convertible into or exchangeable for our common stock or our other securities. We will include provisions as to settlement upon conversion or exchange and whether conversion or exchange is mandatory, at the option of the holder or at our option. We may include provisions pursuant to which the number of shares of our common stock or our other securities that the holders of the series of debt securities receive would be subject to adjustment.

Consolidation, Merger or Sale

Unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, the indenture will not contain any covenant that restricts our ability to merge or consolidate, or sell, convey, transfer or otherwise dispose of our assets as an entirety or substantially as an entirety. However, any successor to or acquirer of such assets (other than a subsidiary of ours) must assume all of our obligations under the indenture or the debt securities, as appropriate.

Events of Default under the Indenture

Unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, the following are events of default under the indenture with respect to any series of debt securities that we may issue:

- if we fail to pay any installment of interest on any series of debt securities, as and when the same shall become due and payable, and such default continues for a period of 90 days; provided, however, that a valid extension of an interest payment period by us in accordance with the terms of any indenture supplemental thereto shall not constitute a default in the payment of interest for this purpose;
- if we fail to pay the principal of, or premium, if any, on any series of debt securities as and when the same shall become due and payable whether at maturity, upon redemption, by declaration or otherwise, or in any payment required by any sinking or analogous fund established with respect to such series; provided, however, that a valid extension of the maturity of such debt securities in accordance with the terms of any indenture supplemental thereto shall not constitute a default in the payment of principal or premium, if any;
- if we fail to observe or perform any other covenant or agreement contained in the debt securities or the indenture, other than a covenant specifically relating to another series of debt securities, and our failure continues for 90 days after we receive written notice of such failure, requiring the same to be remedied and stating that such is a notice of default thereunder, from the trustee or holders of at least 25% in aggregate principal amount of the outstanding debt securities of the applicable series; and
- if specified events of bankruptcy, insolvency or reorganization occur.

If an event of default with respect to debt securities of any series occurs and is continuing, other than an event of default specified in the last bullet point above, the trustee or the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series, by notice to us in writing, and to the trustee if notice is given by such holders, may declare the unpaid principal of, premium, if any, and accrued interest, if any, due and payable immediately. If an event of default specified in the last bullet point above occurs with respect to us, the principal amount of and accrued interest, if any, of each issue of debt securities then outstanding shall be due and payable without any notice or other action on the part of the trustee or any holder.

The holders of a majority in principal amount of the outstanding debt securities of an affected series may waive any default or event of default with respect to the series and its consequences, except defaults or events of default regarding payment of principal, premium, if any, or interest, unless we have cured the default or event of default in accordance with the indenture. Any waiver shall cure the default or event of default.

Subject to the terms of the indenture, if an event of default under an indenture shall occur and be continuing, the trustee will be under no obligation to exercise any of its rights or powers under such indenture at the request or direction of any of the holders of the applicable series of debt securities, unless such holders have offered the trustee reasonable indemnity. The holders of a majority in principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the trustee, or exercising any trust or power conferred on the trustee, with respect to the debt securities of that series, provided that:

- the direction so given by the holder is not in conflict with any law or the applicable indenture; and
- subject to its duties under the Trust Indenture Act, the trustee need not take any action that might involve it in personal liability or might be unduly prejudicial to the holders not involved in the proceeding.

A holder of the debt securities of any series will have the right to institute a proceeding under the indenture or to appoint a receiver or trustee, or to seek other remedies only if:

- the holder has given written notice to the trustee of a continuing event of default with respect to that series;
- the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series have made written request;

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- such holders have offered to the trustee indemnity satisfactory to it against the costs, expenses and liabilities to be incurred by the trustee in compliance with the request; and
- the trustee does not institute the proceeding, and does not receive from the holders of a majority in aggregate principal amount of the outstanding debt securities of that series other conflicting directions within 90 days after the notice, request and offer.

These limitations do not apply to a suit instituted by a holder of debt securities if we default in the payment of the principal, premium, if any, or interest on, the debt securities.

We will periodically file statements with the trustee regarding our compliance with specified covenants in the indenture.

Modification of Indenture; Waiver

We and the trustee may change an indenture without the consent of any holders with respect to specific matters:

- to cure any ambiguity, defect or inconsistency in the indenture or in the debt securities of any series;
- to comply with the provisions described above under “Description of Debt Securities—Consolidation, Merger or Sale;”
- to provide for uncertificated debt securities in addition to or in place of certificated debt securities;
- to add to our covenants, restrictions, conditions or provisions such new covenants, restrictions, conditions or provisions for the benefit of the holders of all or any series of debt securities, to make the occurrence, or the occurrence and the continuance, of a default in any such additional covenants, restrictions, conditions or provisions an event of default or to surrender any right or power conferred upon us in the indenture;
- to add to, delete from or revise the conditions, limitations, and restrictions on the authorized amount, terms, or purposes of issue, authentication and delivery of debt securities, as set forth in the indenture;
- to make any change that does not adversely affect the interests of any holder of debt securities of any series in any material respect;
- to provide for the issuance of and establish the form and terms and conditions of the debt securities of any series as provided above under “Description of Debt Securities—General” to establish the form of any certifications required to be furnished pursuant to the terms of the indenture or any series of debt securities, or to add to the rights of the holders of any series of debt securities;
- to evidence and provide for the acceptance of appointment under any indenture by a successor trustee; or
- to comply with any requirements of the SEC in connection with the qualification of any indenture under the Trust Indenture Act.

In addition, under the indenture, the rights of holders of a series of debt securities may be changed by us and the trustee with the written consent of the holders of at least a majority in aggregate principal amount of the outstanding debt securities of each series that is affected. However, unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, we and the trustee may make the following changes only with the consent of each holder of any outstanding debt securities affected:

- extending the fixed maturity of any debt securities of any series;
- reducing the principal amount, reducing the rate of or extending the time of payment of interest, or reducing any premium payable upon the redemption of any series of any debt securities; or
- reducing the percentage of debt securities, the holders of which are required to consent to any amendment, supplement, modification or waiver.

Discharge

Each indenture provides that we can elect to be discharged from our obligations with respect to one or more series of debt securities, except for specified obligations, including obligations to:

- provide for payment;
- register the transfer or exchange of debt securities of the series;
- replace stolen, lost or mutilated debt securities of the series;
- pay principal of and premium and interest on any debt securities of the series;
- maintain paying agencies;
- hold monies for payment in trust;
- recover excess money held by the trustee;
- compensate and indemnify the trustee; and
- appoint any successor trustee.

In order to exercise our rights to be discharged, we must deposit with the trustee money or government obligations sufficient to pay all the principal of, any premium, if any, and interest on, the debt securities of the series on the dates payments are due.

Form, Exchange and Transfer

We will issue the debt securities of each series only in fully registered form without coupons and, unless we provide otherwise in the applicable prospectus supplement, in denominations of \$1,000 and any integral multiple thereof. The indenture provides that we may issue debt securities of a series in temporary or permanent global form and as book-entry securities that will be deposited with, or on behalf of, The Depository Trust Company, or DTC, or another depository named by us and identified in the applicable prospectus supplement with respect to that series. To the extent the debt securities of a series are issued in global form and as book-entry, a description of terms relating to any book-entry securities will be set forth in the applicable prospectus supplement.

At the option of the holder, subject to the terms of the indenture and the limitations applicable to global securities described in the applicable prospectus supplement, the holder of the debt securities of any series can exchange the debt securities for other debt securities of the same series, in any authorized denomination and of like tenor and aggregate principal amount.

Subject to the terms of the indenture and the limitations applicable to global securities set forth in the applicable prospectus supplement, holders of the debt securities may present the debt securities for exchange or for registration of transfer, duly endorsed or with the form of transfer endorsed thereon duly executed if so required by us or the security registrar, at the office of the security registrar or at the office of any transfer agent designated by us for this purpose. Unless otherwise provided in the debt securities that the holder presents for transfer or exchange, we will impose no service charge for any registration of transfer or exchange, but we may require payment of any taxes or other governmental charges.

We will name in the applicable prospectus supplement the security registrar, and any transfer agent in addition to the security registrar, that we initially designate for any debt securities. We may at any time designate additional transfer agents or rescind the designation of any transfer agent or approve a change in the office through which any transfer agent acts, except that we will be required to maintain a transfer agent in each place of payment for the debt securities of each series.

If we elect to redeem the debt securities of any series, we will not be required to:

- issue, register the transfer of, or exchange any debt securities of that series during a period beginning at the opening of business 15 days before the day of mailing of a notice of redemption of any debt securities that may be selected for redemption and ending at the close of business on the day of the mailing; or
- register the transfer of or exchange any debt securities so selected for redemption, in whole or in part, except the unredeemed portion of any debt securities we are redeeming in part.

Information Concerning the Trustee

The trustee, other than during the occurrence and continuance of an event of default under an indenture, undertakes to perform only those duties as are specifically set forth in the applicable indenture. Upon an event of default under an indenture, the trustee must use the same degree of care as a prudent person would exercise or use in the conduct of his or her own affairs. Subject to this provision, the trustee is under no obligation to exercise any of the powers given it by the indenture at the request of any holder of debt securities unless it is offered reasonable security and indemnity against the costs, expenses and liabilities that it might incur.

Payment and Paying Agents

Unless we otherwise indicate in the applicable prospectus supplement, we will make payment of the interest on any debt securities on any interest payment date to the person in whose name the debt securities, or one or more predecessor securities, are registered at the close of business on the regular record date for the interest.

We will pay principal of and any premium and interest on the debt securities of a particular series at the office of the paying agents designated by us, except that unless we otherwise indicate in the applicable prospectus supplement, we will make interest payments by check that we will mail to the holder or by wire transfer to certain holders. Unless we otherwise indicate in the applicable prospectus supplement, we will designate the corporate trust office of the trustee as our sole paying agent for payments with respect to debt securities of each series. We will name in the applicable prospectus supplement any other paying agents that we initially designate for the debt securities of a particular series. We will maintain a paying agent in each place of payment for the debt securities of a particular series.

All money we pay to a paying agent or the trustee for the payment of the principal of or any premium or interest on any debt securities that remains unclaimed at the end of two years after such principal, premium or interest has become due and payable will be repaid to us, and the holder of the debt security thereafter may look only to us for payment thereof.

Governing Law

The indenture and the debt securities will be governed by and construed in accordance with the internal laws of the State of New York, except to the extent that the Trust Indenture Act of 1939 is applicable.

LEGAL OWNERSHIP OF SECURITIES

We can issue securities in registered form or in the form of one or more global securities. We describe global securities in greater detail below. We refer to those persons who have securities registered in their own names on the books that we or any applicable trustee, depositary or warrant agent maintain for this purpose as the “holders” of those securities. These persons are the legal holders of the securities. We refer to those persons who, indirectly through others, own beneficial interests in securities that are not registered in their own names, as “indirect holders” of those securities. As we discuss below, indirect holders are not legal holders, and investors in securities issued in book-entry form or in street name will be indirect holders.

Book-Entry Holders

We may issue securities in book-entry form only, as we will specify in the applicable prospectus supplement. This means securities may be represented by one or more global securities registered in the name of a financial institution that holds them as depositary on behalf of other financial institutions that participate in the depositary’s book-entry system. These participating institutions, which are referred to as participants, in turn, hold beneficial interests in the securities on behalf of themselves or their customers.

Only the person in whose name a security is registered is recognized as the holder of that security. Securities issued in global form will be registered in the name of the depositary or its participants. Consequently, for securities issued in global form, we will recognize only the depositary as the holder of the securities, and we will make all payments on the securities to the depositary. The depositary passes along the payments it receives to its participants, which in turn pass the payments along to their customers who are the beneficial owners. The depositary and its participants do so under agreements they have made with one another or with their customers; they are not obligated to do so under the terms of the securities.

As a result, investors in a book-entry security will not own securities directly. Instead, they will own beneficial interests in a global security, through a bank, broker or other financial institution that participates in the depositary’s book-entry system or holds an interest through a participant. As long as the securities are issued in global form, investors will be indirect holders, and not holders, of the securities.

Street Name Holders

We may terminate a global security or issue securities in non-global form. In these cases, investors may choose to hold their securities in their own names or in “street name.” Securities held by an investor in street name would be registered in the name of a bank, broker or other financial institution that the investor chooses, and the investor would hold only a beneficial interest in those securities through an account he or she maintains at that institution.

For securities held in street name, we will recognize only the intermediary banks, brokers and other financial institutions in whose names the securities are registered as the holders of those securities, and we will make all payments on those securities to them. These institutions pass along the payments they receive to their customers who are the beneficial owners, but only because they agree to do so in their customer agreements or because they are legally required to do so. Investors who hold securities in street name will be indirect holders, not holders, of those securities.

Legal Holders

Our obligations, as well as the obligations of any applicable trustee and of any third parties employed by us or a trustee, run only to the legal holders of the securities. We do not have obligations to investors who hold beneficial interests in global securities, in street name or by any other indirect means. This will be the case whether an investor chooses to be an indirect holder of a security or has no choice because we are issuing the securities only in global form.

For example, once we make a payment or give a notice to the holder, we have no further responsibility for the payment or notice even if that holder is required, under agreements with depositary participants or customers or by law, to pass it along to the indirect holders but does not do so. Similarly, we may want to obtain the approval of the holders to amend an indenture, to relieve us of the consequences of a default or of our obligation to comply with a particular provision of the indenture or for other purposes. In such an event, we would seek approval only from the registered holders, and not the indirect holders, of the securities. Whether and how the holders contact the indirect holders is up to the holders.

Special Considerations for Indirect Holders

If you hold securities through a bank, broker or other financial institution, either in book-entry form or in street name, you should check with your own institution to find out:

- how it handles securities payments and notices;
- whether it imposes fees or charges;
- how it would handle a request for the holders' consent, if ever required;
- whether and how you can instruct it to send you securities registered in your own name so you can be a holder, if that is permitted in the future;
- how it would exercise rights under the securities if there were a default or other event triggering the need for holders to act to protect their interests; and
- if the securities are in book-entry form, how the depository's rules and procedures will affect these matters.

Global Securities

A global security is a security that represents one or any other number of individual securities held by a depository. Generally, all securities represented by the same global securities will have the same terms.

Each security issued in book-entry form will be represented by a global security that we deposit with and register in the name of a financial institution or its nominee that we select. The financial institution that we select for this purpose is called the depository. Unless we specify otherwise in the applicable prospectus supplement, The Depository Trust Company, New York, New York, known as DTC, will be the depository for all securities issued in book-entry form.

A global security may not be transferred to or registered in the name of anyone other than the depository, its nominee or a successor depository, unless special termination situations arise. We describe those situations below under the section captioned "Special Situations When a Global Security Will Be Terminated" in this prospectus. As a result of these arrangements, the depository, or its nominee, will be the sole registered owner and holder of all securities represented by a global security, and investors will be permitted to own only beneficial interests in a global security. Beneficial interests must be held by means of an account with a broker, bank or other financial institution that in turn has an account with the depository or with another institution that does. Thus, an investor whose security is represented by a global security will not be a holder of the security, but only an indirect holder of a beneficial interest in the global security.

If the prospectus supplement for a particular security indicates that the security will be issued in global form only, then the security will be represented by a global security at all times unless and until the global security is terminated. If termination occurs, we may issue the securities through another book-entry clearing system or decide that the securities may no longer be held through any book-entry clearing system.

Special Considerations for Global Securities

The rights of an indirect holder relating to a global security will be governed by the account rules of the investor's financial institution and of the depository, as well as general laws relating to securities transfers. We do not recognize an indirect holder as a holder of securities and instead deal only with the depository that holds the global security.

If securities are issued only in the form of a global security, an investor should be aware of the following:

- an investor cannot cause the securities to be registered in his or her name, and cannot obtain non-global certificates for his or her interest in the securities, except in the special situations we describe below;
- an investor will be an indirect holder and must look to his or her own bank or broker for payments on the securities and protection of his or her legal rights relating to the securities, as we describe above;
- an investor may not be able to sell interests in the securities to some insurance companies and to other institutions that are required by law to own their securities in non-book-entry form;
- an investor may not be able to pledge his or her interest in a global security in circumstances where certificates representing the securities must be delivered to the lender or other beneficiary of the pledge in order for the pledge to be effective;

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- the depositary's policies, which may change from time to time, will govern payments, transfers, exchanges and other matters relating to an investor's interest in a global security;
- we and any applicable trustee have no responsibility for any aspect of the depositary's actions or for its records of ownership interests in a global security, nor do we or any applicable trustee supervise the depositary in any way;
- the depositary may, and we understand that DTC will, require that those who purchase and sell interests in a global security within its book-entry system use immediately available funds, and your broker or bank may require you to do so as well; and
- financial institutions that participate in the depositary's book-entry system, and through which an investor holds its interest in a global security, may also have their own policies affecting payments, notices and other matters relating to the securities.

There may be more than one financial intermediary in the chain of ownership for an investor. We do not monitor and are not responsible for the actions of any of those intermediaries.

Special Situations When a Global Security Will Be Terminated

In a few special situations described below, the global security will terminate and interests in it will be exchanged for physical certificates representing those interests. After that exchange, the choice of whether to hold securities directly or in street name will be up to the investor. Investors must consult their own banks or brokers to find out how to have their interests in securities transferred to their own name, so that they will be direct holders. We have described the rights of holders and street name investors above.

Unless we provide otherwise in the applicable prospectus supplement, the global security will terminate when the following special situations occur:

- if the depositary notifies us that it is unwilling, unable or no longer qualified to continue as depositary for that global security and we do not appoint another institution to act as depositary within 90 days;
- if we notify any applicable trustee that we wish to terminate that global security; or
- if an event of default has occurred with regard to securities represented by that global security and has not been cured or waived.

The applicable prospectus supplement may also list additional situations for terminating a global security that would apply only to the particular series of securities covered by the applicable prospectus supplement. When a global security terminates, the depositary, and not we or any applicable trustee, is responsible for deciding the names of the institutions that will be the initial direct holders.

DESCRIPTION OF OUR WARRANTS

We may issue warrants to purchase common stock, preferred stock or debt securities. We may offer warrants separately or together with one or more additional warrants, common stock, preferred stock or debt securities, or any combination of those securities in the form of units, as described in the applicable prospectus supplement. If we issue warrants as part of a unit, the accompanying prospectus supplement will specify whether those warrants may be separated from the other securities in the unit prior to the expiration date of the warrants. The applicable prospectus supplement will also describe the following terms of any warrants:

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

DESCRIPTION OF OUR UNITS

We may issue units comprised of one or more of the other securities that may be offered under this prospectus, in any combination. The following, together with the additional information we may include in the applicable prospectus supplement, summarizes the material terms and provisions of the units that we may offer under this prospectus. While the terms summarized below will apply generally to any units we may offer, we will describe the particular terms of any series of units in more detail in the applicable prospectus supplement.

Each unit will be issued so that the holder of the unit is also the holder of each security included in the unit. Thus, the holder of a unit will have the rights and obligations of a holder of each included security. The unit agreement under which a unit is issued may provide that the securities included in the unit may not be held or transferred separately at any time, or at any time before a specified date.

Any applicable prospectus supplement will describe:

- any material provisions relating to the issuance, payment, settlement, transfer or exchange of the units or of the securities comprising the units; and
- any material provisions of the governing unit agreement that differ from those described above.

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 Cooley LLP, Palo Alto, 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, 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 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.

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, 2021, filed with the SEC on March 1, 2022;
- our Current Reports on Form 8-K (other than information furnished rather than filed) filed with the SEC on [January 26, 2022](#) and [February 2, 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 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 or on the “Investor Relations” page of our website at 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.

The information in this preliminary prospectus is not complete and may be changed. We may not sell these securities until the U.S. Securities and Exchange Commission declares our registration statement effective. This preliminary prospectus is not an offer to sell these securities and we are not soliciting offers to buy these securities in any state or jurisdiction where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED MARCH 4, 2022

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 March 1, 2022, the last reported sale price of our common stock on the Nasdaq Global Select Market was \$4.41 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 _____, 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;

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- 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;
- 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.

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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	<u>0.18</u>
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.

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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;
- 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;
- our Current Reports on Form 8-K (other than information furnished rather than filed) filed with the SEC on [January 26, 2022](#) and [February 2, 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

, 2022

PART II**INFORMATION NOT REQUIRED IN THE PROSPECTUS****Item 14. Other Expenses of Issuance and Distribution**

The following is a statement of the estimated expenses (other than underwriting discounts and commissions) to be incurred by our company in connection with the issuance and distribution of the securities registered under this registration statement.

SEC registration fee	\$13,905*
FINRA filing fee	**
Accounting fees and expenses	**
Legal fees and expenses (including Blue Sky fees)	**
Transfer agent, trustee and warrant agent fees and expenses	**
Printing fees	**
Miscellaneous	**
Total	\$**

* The registrant previously paid the fee related to \$150,000,000 of the registrant's common stock that may be issued and sold under a certain sales agreement with Jefferies LLC and that may be issued and sold pursuant to the registration statement, as amended.

** These fees and expenses depend on the securities offered and the number of issuances and accordingly cannot be estimated at this time and will be provided as applicable by amendment or in a filing with the SEC pursuant to the Exchange Act and incorporated herein by reference.

Item 15. Indemnification of Directors and Officers

Section 145 of the Delaware General Corporation Law authorizes a court to award, or a corporation's board of directors to grant, indemnity to directors and officers in terms sufficiently broad to permit such indemnification under certain circumstances for liabilities (including reimbursement for expenses incurred) arising under the Securities Act. Article VI of our amended and restated bylaws provides for indemnification of our directors, officers, employees and other agents to the maximum extent permitted by the Delaware General Corporation Law. In addition, we have entered into indemnification agreements with our officers and directors, whereby we have agreed to indemnify our directors and officers to the fullest extent permitted by law. These indemnification agreements also generally require us to advance any expenses incurred by the directors or officers as a result of any proceeding against them as to which they could be indemnified. In addition, we have purchased a policy of directors' and officers' liability insurance that insures our directors and officers against the cost of defense, settlement or payment of a judgment in some circumstances. The underwriters will be obligated, under certain circumstances, pursuant to any underwriting agreements we enter into in connection with the sale of any securities being registered hereby, to indemnify us and our officers and directors against certain liabilities under the Securities Act.

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Item 16. Exhibits

Filing Fee Table.

The Filing Fee Table and related disclosure is filed herewith as Exhibit 107.

Exhibit No.	Exhibit title	Incorporated by reference			Filed or furnished herewith
		Form	File No.	Exhibit No. Filing date	
1.1*	Form of Underwriting Agreement				
1.2	Open Market Sale AgreementSM dated December 23, 2021, by and between Cortexyme, Inc. and Jefferies LLC.	8-K	001-38890	10.1	12/23/2021
4.1	Amended and Restated Certificate of Incorporation	8-K	001-38890	3.1	5/13/2019
4.2	Amended and Restated Bylaws	8-K	001-38890	3.2	5/13/2019
4.3	Form of Specimen Common Stock Certificate	S-1/A	333-230853	4.1	4/29/2019
4.4	Amended and Restated Investors' Rights Agreement, dated May 23, 2018, by and among the Registrant and certain of its stockholders	S-1	333-230853	4.2	4/12/2019
4.5*	Form of any certificate of designation with respect to any preferred stock issued hereunder and the related form of preferred stock certificate				
4.6*	Form of any warrant agreement with respect to each particular series of warrants issued hereunder				
4.7*	Form of any unit agreement with respect to any unit issued hereunder				
4.8	Form of indenture	POSASR	333-238851	4.8	2/7/2022
4.9*	Form of note				
5.1	Opinion of Cooley LLP	POSASR	333-238851	5.1	2/7/2022
23.1	Consent of Cooley LLP (included in Exhibit 5.1)	POSASR	333-238851	5.1	2/7/2022
23.2	Consent of Independent Registered Public Accounting Firm				X
24.1	Power of Attorney (previously filed with the SEC)				
25.1**	Form T-1 Statement of Eligibility under the Trust Indenture Act of 1939, as amended, of Debt Trustee				
107	Filing Fee Table	POSASR	333-238851	107	2/7/2022

* To be filed, if necessary, subsequent to the effectiveness of this registration statement by an amendment to this registration statement or incorporation by reference pursuant to a Current Report on Form 8-K in connection with an offering of securities.

** To be filed as an exhibit to a Current Report on Form 8-K or pursuant to Section 305(b)(2) of the Trust Indenture Act of 1939 and incorporated herein by reference.

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Item 17. Undertakings

The undersigned Registrant hereby undertakes:

(1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:

(i) To include any prospectus required by Section 10(a)(3) of the Securities Act;

(ii) To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the SEC pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20 percent change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement;

(iii) To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement;

provided, however, that paragraphs (1)(i), (1)(ii) and (1)(iii) above do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the SEC by the Registrant pursuant to Section 13 or Section 15(d) of the Exchange Act that are incorporated by reference in the registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of the registration statement.

(2) That, for the purpose of determining any liability under the Securities Act, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

(3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

(4) That, for the purpose of determining liability under the Securities Act to any purchaser:

(i) Each prospectus filed by the Registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and

(ii) Each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5) or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii) or (x) for the purpose of providing the information required by Section 10(a) of the Securities Act shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which the prospectus relates, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof. *Provided, however*, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such effective date.

(5) That, for the purpose of determining liability of the Registrant under the Securities Act to any purchaser in the initial distribution of the securities, the undersigned Registrant undertakes that in a primary offering of securities of the undersigned Registrant pursuant to this registration statement, regardless of the underwriting method used to sell the securities to the purchaser, if the securities are offered or sold to such purchaser by means of any of the following communications, the undersigned Registrant will be a seller to the purchaser and will be considered to offer or sell such securities to such purchaser:

(i) Any preliminary prospectus or prospectus of the undersigned Registrant relating to the offering required to be filed pursuant to Rule 424;

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(ii) Any free writing prospectus relating to the offering prepared by or on behalf of the undersigned Registrant or used or referred to by the undersigned Registrant;

(iii) The portion of any other free writing prospectus relating to the offering containing material information about the undersigned Registrant or its securities provided by or on behalf of the undersigned Registrant; and

(iv) Any other communication that is an offer in the offering made by the undersigned Registrant to the purchaser.

(6) That, for purposes of determining any liability under the Securities Act, each filing of the Registrant's annual report pursuant to Section 13(a) or 15(d) of the Exchange Act (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Exchange Act) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

(7) To file an application for the purpose of determining the eligibility of the trustee to act under subsection (a) of Section 310 of the Trust Indenture Act in accordance with the rules and regulations prescribed by the SEC under Section 305(b)(2) of the Trust Indenture Act.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the Registrant pursuant to the foregoing provisions, or otherwise, the Registrant has been advised that in the opinion of the SEC such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Registrant of expenses incurred or paid by a director, officer or controlling person of the Registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the Registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this Post-Effective Amendment No. 2 to the Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of South San Francisco, State of California, on the 4th day of March, 2022.

CORTEXYME, INC.

By: /s/ Christopher Lowe
Christopher Lowe
Interim Chief Executive Officer, Chief Financial
Officer and Chief Operating Officer

Pursuant to the requirements of the Securities Act of 1933, this Post-Effective Amendment No. 2 to the Registration Statement has been signed by the following persons in the capacities and on the dates indicated.

Signature	Title	Date
<u>/s/ Christopher Lowe</u> Christopher Lowe	Interim Chief Executive Officer, Chief Financial Officer and Chief Operating Officer, Director (principal executive officer and principal financial officer)	March 4, 2022
<u>/s/ Ted Monohon</u> Ted Monohon	Chief Accounting Officer and Vice President, Finance (principal accounting officer)	March 4, 2022
<u>*</u> David A. Lamond	Director	March 4, 2022
<u>*</u> Margaret McLoughlin, Ph.D.	Director	March 4, 2022
<u>*</u> Una Ryan, OBE, Ph.D.	Director	March 4, 2022
<u>*</u> Christopher J. Senner	Director	March 4, 2022

* By: /s/ Christopher Lowe
Christopher Lowe
Attorney-In-Fact

Consent of Independent Registered Public Accounting Firm

Cortexyme, Inc.
South San Francisco, California

We hereby consent to the incorporation by reference in the Prospectus constituting a part of this Registration Statement of our reports dated March 1, 2022, relating to the financial statements and the effectiveness of Cortexyme Inc.'s internal control over financial reporting appearing in the Company's Annual Report on Form 10-K for the year ended December 31, 2021.

We also consent to the reference to us under the caption "Experts" in the Prospectus.

/s/ BDO USA, LLP
San Jose, CA

March 4, 2022