PROSPECTUS



Up to \$40,000,000 of Shares

Common Stock

We have entered into a certain Controlled Equity Offering SM Sales Agreement, or sales agreement, with Cantor Fitzgerald & Co., or Cantor Fitzgerald, relating to shares of our common stock offered by this prospectus. Our sales agreement with Cantor Fitzgerald is limited to the sale of up to a number of common shares not to exceed the amount that can be sold under the registration statement of which this prospectus forms a part, which amount, as of the date of this prospectus, is \$40.0 million.

Our common stock is listed on The NASDAQ Capital Market under the symbol "CYTK." On September 15, 2015, the last reported sale price of our common stock on The NASDAQ Capital Market was \$7.76 per share.

Sales of our common stock under this prospectus, if any, may be made in sales deemed to be "at the market offerings" as defined in Rule 415 promulgated under the Securities Act of 1933, as amended, or the Securities Act, including sales made directly on or through The NASDAQ Capital Market, the existing trading market for our common stock, sales made to or through a market maker other than on an exchange or otherwise, in negotiated transactions at market prices prevailing at the time of sale or at prices related to such prevailing market prices, and/or any other method permitted by law. Cantor Fitzgerald will act as a sales agent using commercially reasonable efforts consistent with its normal trading and sales practices, on mutually agreed terms between Cantor Fitzgerald and us. There is no arrangement for funds to be received in any escrow, trust or similar arrangement.

The compensation to Cantor Fitzgerald for sales of common stock sold pursuant to the sales agreement will be an amount equal to 3.0% of the gross proceeds of the sales price per share. In connection with the sale of the common stock on our behalf, Cantor Fitzgerald will be deemed to be an "underwriter" within the meaning of the Securities Act and the compensation of Cantor Fitzgerald will be deemed to be underwriting commissions or discounts. We have also agreed to provide indemnification and contribution to Cantor Fitzgerald with respect to certain liabilities, including liabilities under the Securities Act.

Investing in our common stock involves a high degree of risk. Before making an investment decision, you should carefully consider all of the information set forth in this prospectus and the documents incorporated by reference herein. You should review carefully the risks and uncertainties described under the heading "Risk Factors" beginning on page 4 of this prospectus and under similar headings in the other documents that are incorporated by reference into this prospectus.

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 the prospectus is September 17, 2015.

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You should rely only on the information contained in, or incorporated by reference to, this prospectus and any prospectus supplement or free writing prospectus that we may authorize for use in connection with this offering. You should also read and consider the information in the documents we have referred you to under the headings "Where You Can Find More Information" and "Information Incorporated by Reference." No person has been authorized to give any information or make any representations in connection with this offering other than those contained or incorporated by reference in this prospectus and any related free writing prospectus supplement in connection with the offering described herein and therein, and, if given or made, such information or representations must not be relied upon as having been authorized by us. Neither this prospectus nor any related free writing prospectus or prospectus supplement shall constitute an offer to sell or a solicitation of an offer to buy offered securities in any jurisdiction in which it is unlawful for such person to make such an offering or solicitation. The information contained in this prospectus, the documents and information incorporated by reference in this prospectus and any prospectus supplement or free writing prospectus that we may authorize for use in connection with this offering are accurate only as of their respective dates, regardless of the time of delivery of this prospectus or any sale of our common stock.

SUMMARY

This summary highlights certain information about us, this offering and selected information contained elsewhere or incorporated by reference into this prospectus. This summary is not complete and does not contain all of the information that you should consider before deciding whether to invest in our common stock, and is qualified in its entirety by the more detailed information, including our consolidated financial statements and related notes incorporated in this prospectus by reference. You should carefully consider the information set forth in this entire prospectus and any prospectus supplement or free writing prospectus we may authorize in connection with this offering, including the "Risk Factors" beginning on page 4 of this prospectus, and the other documents we refer to and incorporate by reference. Unless the context otherwise requires, the terms "Cytokinetics," "we," "us" and "our" refer to Cytokinetics, Incorporated, a Delaware corporation.

Cytokinetics, Incorporated

Our Business

We are a clinical stage biopharmaceutical company focused on the discovery and development of novel small molecule therapeutics that modulate muscle function for the potential treatment of serious diseases and medical conditions. Our research and development activities relating to the biology of muscle function have evolved from our knowledge and expertise regarding the cytoskeleton, a complex biological infrastructure that plays a fundamental role within every human cell. Our most advanced research and development programs relate to the biology of muscle function and are directed to small molecule modulators of the contractility of skeletal or cardiac muscle. We are also conducting earlier-stage research directed to other compounds with the potential to modulate muscle contractility and other muscle functions, such as growth, energetics and metabolism.

Our lead drug candidate from our skeletal muscle contractility program, tirasemtiv (formerly known as CK-2017357), is a fast skeletal muscle troponin activator. Cytokinetics retains exclusive rights to tirasemtiv and is independently developing this drug candidate for the potential treatment of amyotrophic lateral sclerosis, or ALS. We have conducted a Phase II clinical trials program for tirasemtiv, including a Phase IIb clinical trial in patients with ALS, known as BENEFIT-ALS (Blinded Evaluation of Neuromuscular Effects and Functional Improvement with Tirasemtiv in ALS). In July 2015, based on the findings in BENEFIT-ALS, we started VITALITY-ALS (Ventilatory Investigation of Tirasemtiv and Assessment of Longitudinal Indices after Treatment for a Year in ALS), a Phase III clinical trial designed to assess the effects of tirasemtiv versus placebo on slow vital capacity and other measures of respiratory function in patients with ALS. VITALITY-ALS is designed to confirm and extend the results observed in BENEFIT-ALS. Tirasemtiv has been granted orphan drug designation and fast track status by the FDA and orphan medicinal product designation by the European Medicines Agency, in each case for the potential treatment of ALS.

We are also developing CK-2127107, a structurally distinct fast skeletal muscle troponin activator, under a strategic alliance with Astellas Pharma Inc., or Astellas, established in June 2013 and expanded in December 2014. Astellas holds an exclusive license to develop and commercialize CK-2127107 worldwide, subject to our development and commercialization participation rights. Under this strategic alliance, Cytokinetics conducted Phase I clinical trials of CK-2127107 and plans to initiate a Phase II clinical trial of CK-2127107 in patients with spinal muscular atrophy (SMA) in the second half of 2015. CK-2127107 is also being evaluated for potential use in other indications associated with muscle weakness. We are also conducting joint research with Astellas directed to next-generation skeletal muscle activators.

Our lead drug candidate from our cardiac muscle contractility program, omecamtiv mecarbil (formerly known as CK-1827452), is a novel cardiac muscle myosin activator that is being developed under a strategic alliance with Amgen Inc., or Amgen. In June 2013, we expanded this collaboration to include Japan. As a result, Amgen holds an exclusive license to develop and commercialize omecamtiv mecarbil worldwide, subject to our development and commercialization participation rights. In March 2015, we and Amgen agreed to extend the term of the research program through December 2015. Under the amended Amgen agreement, we are entitled to receive reimbursements of internal costs of certain full-time employee equivalents during 2015, as well as potential additional milestone payments related to the research activities.

A Phase II clinical trial of omecamtiv mecarbil, known as COSMIC-HF (Chronic Oral Study of Myosin Activation to Increase Contractility in Heart Failure), is ongoing. COSMIC-HF is designed to assess the pharmacokinetics and tolerability of omecamtiv mecarbil dosed orally in patients with heart failure and left ventricular systolic dysfunction and its effects on

echocardiographic measures of cardiac function. An intravenous formulation of omecamtiv mecarbil was studied in a Phase IIb clinical trial known as ATOMIC-AHF (Acute Treatment with Omecamtiv Mecarbil to Increase Contractility in Acute Heart Failure), which was designed to evaluate the safety and efficacy of omecamtiv mecarbil in patients with left ventricular systolic dysfunction who are hospitalized with acute heart failure. We expect to continue our joint research with Amgen directed to next-generation compounds in our cardiac muscle contractility program through 2015.

All of our drug candidates have demonstrated evidence of potentially clinically relevant pharmacodynamic activity in humans. For the remainder of 2015, we expect to continue to focus on translating the observed pharmacodynamic activity of these compounds into potentially meaningful clinical benefits for patients.

Beyond Muscle Contractility

We have developed preclinical expertise in the mechanics of skeletal, cardiac and smooth muscle that extends from proteins to tissues to intact animal models. Our translational research in muscle contractility has enabled us to better understand the potential impact of small molecule compounds that increase skeletal or cardiac muscle contractility and to apply those findings to the further evaluation of our drug candidates in clinical populations. In addition to contractility, the other major functions of muscle include metabolism, growth and energetics, with each of these functions playing a role in certain diseases that could benefit from novel mechanism treatments. Accordingly, our knowledge of muscle contractility may serve as an entry point to the discovery of novel treatments for disorders involving muscle functions other than muscle contractility. We are leveraging our current understandings of muscle biology to investigate new ways of modulating these other aspects of muscle function for other potential therapeutic applications. For example, we are conducting research with compounds that affect muscle growth and that may have applications for serious diseases and medical conditions such as cachexia. Cachexia is a condition that can be associated with cancer, heart failure, chronic obstructive pulmonary disease or other conditions. This syndrome is characterized by the loss of muscle mass and may lead to weakness and disability. We are performing research on compounds that may increase muscle mass and which may impact patient functionality or potentially alter the course of diseases associated with muscle wasting.

Company Information

We were incorporated in Delaware in August 1997 as Cytokinetics, Incorporated. We conduct our administration, finance, business development, clinical development, commercial development, quality assurance and regulatory affairs activities primarily from our headquarters located at 280 East Grand Avenue, South San Francisco, CA. Our general telephone number at that address is (650) 624-3000 and our website is located at www.cytokinetics.com. The information on, or that can be accessed through, our website is not incorporated by reference in this prospectus, and you should not consider it to be a part of this prospectus. Our website address is included as an inactive textual reference only.

CYTOKINETICS and our logo used alone and with the mark CYTOKINETICS are our registered service marks and trademarks. Other service marks, trademarks and trade names referred to in this prospectus are the property of their respective owners.

The Offering

Common Stock Offered by Us Shares of our common stock having an aggregate offering price of up to

\$40.0 million.

Manner of Offering "At-the-market" offering that may be made from time to time through our

sales agent, Cantor Fitzgerald. See "Plan of Distribution" on page 9.

Use of Proceeds We currently intend to use the net proceeds, if any, from the sale of

shares of our common stock for general corporate purposes, which may include research and development, including clinical trials for our drug candidates, capital expenditures, working capital and other general corporate purposes. See "Use of Proceeds" on page 7 of this prospectus.

Risk Factors Investing in our securities involves a high degree of risk. See the

information contained in or incorporated by reference under the heading "Risk Factors" beginning on page 4 of this prospectus and under similar headings in the documents incorporated by reference into this

prospectus.

NASDAQ Capital Market Listing Our common stock is listed on The NASDAQ Capital Market under the

symbol "CYTK."

RISK FACTORS

Investing in our securities involves a high degree of risk. You should carefully review the risks and uncertainties described below and under the heading "Risk Factors" in our most recent Annual Report on Form 10-K, as revised and supplemented by our Quarterly Reports on Form 10-Q filed since the filing of our most recent Annual Report on Form 10-K, each of which is incorporated by reference herein, and any subsequent reports we file after the date of this prospectus, all other information contained or incorporated by reference into this prospectus and any prospectus supplement or free writing prospectus with respect to this offering filed by us with the Securities and Exchange Commission, or the SEC, before deciding whether to purchase any of the common stock being offered under this prospectus. Each of the risk factors could adversely affect our business, operating results and financial condition, as well as adversely affect the value of an investment in our securities, and the occurrence of any of these risks might cause you to lose all or part of your investment. Moreover, the risks described are not the only ones that we face. Additional risks not presently known to us or that we currently believe are immaterial may also significantly impair our business operations. Please also read carefully the section below titled "Special Note Regarding Forward-Looking Statements."

Risks Relating to This Offering

We will have broad discretion over the use of the net proceeds to us from this offering and may apply them to uses that do not improve our operating results or the value of your securities.

We will have broad discretion to use the net proceeds to us from this offering, including for any of the purposes described in the section titled "Use of Proceeds," and investors will be relying solely on the judgment of our board of directors and management regarding the application of these proceeds. Investors will not have the opportunity, as part of their investment decision, to assess whether the proceeds are being used appropriately. Our use of the proceeds may not improve our operating results or increase the value of the securities being offered hereby. 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. The failure of our management to use these funds effectively could have a material adverse effect on our business, cause the market price of our common stock to decline or delay the development of our product candidates.

If you purchase shares of common stock in this offering, you will 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 5,154,639 shares of our common stock are sold at a price of \$7.76 per share, the last reported sale price of our common stock on The NASDAQ Capital Market on September 15, 2015, for aggregate gross proceeds of \$40.0 million, and after deducting commissions and estimated aggregate offering expenses payable by us, you will experience immediate dilution of \$5.18 per share, representing the difference between our as adjusted net tangible book value per share as of June 30, 2015 after giving effect to this offering and the assumed offering price. The exercise of outstanding stock options and warrants will 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.

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

In order to raise additional capital, we may in the future offer additional shares of our common stock or other securities convertible into or exchangeable for our common stock at prices that may not be the same as the price per share paid by any investor in this offering. We may sell shares or other securities in any other offering at a price per share that is less than the price per share paid by any investor in this offering, and investors purchasing shares or other securities in the future could have rights superior to you. The price per share at which we sell additional shares of our common stock, or securities convertible or exchangeable into common stock, in future transactions may be higher or lower than the price per share paid by any investor in this offering.

We do not intend to pay dividends in the foreseeable future.

We have never paid cash dividends on our common stock and currently do not plan to pay any cash dividends in the foreseeable future.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and the documents we incorporate by reference in this prospectus include "forward-looking statements" within the meaning of Section 27A of the Securities Act and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. These statements relate to future events or to our future operating or financial performance and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performances or achievements expressed or implied by such forward-looking statements. Examples of such forward-looking statements include, but are not limited to, statements about or relating to:

- · guidance concerning revenues, research and development expenses and general and administrative expenses;
- the sufficiency of existing resources to fund our operations;
- our capital requirements and needs for additional financing;
- the initiation, design, conduct, enrollment, progress, timing and scope of clinical trials and development activities for our drug candidates conducted by ourselves or our partners, Amgen and Astellas, including the anticipated timing for initiation of clinical trials, anticipated rates of enrollment for clinical trials and anticipated timing of results becoming available or being announced from clinical trials;
- the results from the clinical trials and non-clinical and preclinical studies of our drug candidates and other compounds, and the significance and utility of such results;
- the potential further development of tirasemtiv for the potential treatment of ALS;
- the expected acceptability by regulatory authorities of the effects of tirasemtiv on Slow Vital Capacity or other measures of clinical benefit related to respiratory function in patients with ALS as a Phase 3 clinical trial endpoint to support the registration of tirasemtiv as a treatment for ALS;
- · our and our partners' plans or ability to conduct the continued research and development of our drug candidates and other compounds;
- · our expected roles in research, development or commercialization under our strategic alliances with Amgen and Astellas;
- the properties and potential benefits of, and the potential market opportunities for, our drug candidates and other compounds, including the potential indications for which they may be developed;
- the sufficiency of the clinical trials conducted with our drug candidates to demonstrate that they are safe and efficacious;
- our receipt of milestone payments, royalties, reimbursements and other funds from current or future partners under strategic alliances, such as with Amgen or Astellas;
- our ability to continue to identify additional potential drug candidates that may be suitable for clinical development;
- our plans or ability to commercialize drugs with or without a partner, including our intention to develop sales and marketing capabilities;
- the focus, scope and size of our research and development activities and programs;
- the utility of our focus on the biology of muscle function, and our ability to leverage our experience in muscle contractility to other muscle functions:
- · our ability to protect our intellectual property and to avoid infringing the intellectual property rights of others;
- expected future sources of revenue and capital;
- losses, costs, expenses and expenditures;
- future payments under loan and lease obligations;
- potential competitors and competitive products;
- retaining key personnel and recruiting additional key personnel;
- expected timing for recognition of compensation cost related to unvested stock options; and

• the potential impact of recent accounting pronouncements on our financial position or results of operations.

In some cases, you can identify forward-looking statements by terms such as "may," "will," "should," "could," "would," "expects," "plans," "anticipates," "believes," "estimates," "projects," "predicts," "potential" and similar expressions intended to identify forward-looking statements. These statements reflect our current views with respect to future events and are based on assumptions and are subject to risks and uncertainties. Given these uncertainties, you should not place undue reliance on these forward-looking statements. We discuss in greater detail many of these risks under the heading "Risk Factors" contained in this prospectus or in any prospectus supplement or free writing prospectuses we may authorize for use in connection with a specific offering, and in our most recent annual report on Form 10-K and in our most recent quarterly report on Form 10-Q, as well as any amendments thereto reflected in subsequent filings with the SEC, which are incorporated by reference into this prospectus in their entirety. Also, these forward-looking statements represent our estimates and assumptions only as of the date of the document containing the applicable statement. Unless required by law, we undertake no obligation to update or revise any forward-looking statements to reflect new information or future events or developments. Thus, you should not assume that our silence over time means that actual events are bearing out as expressed or implied in such forward-looking statements. You should read this prospectus together with the documents we have filed with the SEC that are incorporated by reference and any prospectus supplement or free writing prospectus that we may authorize for use in connection with this offering completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of the forward-looking statements in the foregoing documents by these cautionary statements.

USE OF PROCEEDS

We may issue and sell shares of our common stock having aggregate sales proceeds of up to \$40,000,000 million from time to time. Because there is no minimum offering amount required as a condition to close this offering, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time. There can be no assurance that we will sell any shares under or fully utilize the sales agreement with Cantor Fitzgerald as a source of financing.

We will retain broad discretion over the use of the net proceeds from the sale of the securities offered hereby. Except as described in any prospectus supplement or free writing prospectus related to this offering that we may authorize to be provided to you, we currently intend to use the net proceeds from the sale of the securities offered hereby for general corporate purposes, which may include research and development, including clinical trials for our drug candidates, capital expenditures, working capital and general and administrative expenses. We may also use a portion of the net proceeds to acquire or invest in businesses, products and technologies that are complementary to our own, although we have no commitments or agreements with respect to any acquisitions as of the date of this prospectus.

Pending the application of the net proceeds, we intend to invest the net proceeds in a variety of capital preservation instruments, including direct or guaranteed obligations of the U.S. government, certificates of deposit and money market funds, in accordance with our investment policy.

DILUTION

If you invest in this offering, your ownership interest will be diluted to the extent of the difference between the public offering price per share and the as adjusted net tangible book value per share after giving effect to this offering. We calculate net tangible book value per share by dividing the net tangible book value, which is tangible assets less total liabilities, by the number of outstanding shares of our common stock. Dilution represents the difference between the amount per share paid by purchasers of shares in this offering and the as adjusted net tangible book value per share of our common stock immediately after giving effect to this offering. Our net tangible book value as of June 30, 2015 was approximately \$74.9 million, or \$1.93 per share.

After giving effect to the sale of our common stock in the aggregate amount of \$40.0 million at an assumed offering price of \$7.76 per share, the last reported sale price of our common stock on The NASDAQ Capital Market on September 15, 2015, and after deducting estimated offering commissions and expenses payable by us, our net tangible book value as of June 30, 2015 would have been \$113.3 million, or \$2.58 per share of common stock. This represents an immediate increase in the net tangible book value of \$0.65 per share to our existing stockholders and an immediate dilution in net tangible book value of \$5.18 per share to new investors. The following table illustrates this per share dilution:

| Assumed public offering price per share | | \$7.76 |
|--|--------|--------|
| Net tangible book value per share as of June 30, 2015 | \$1.93 | |
| Increase in net tangible book value per share attributable to this offering | \$0.65 | |
| As adjusted net tangible book value per share as of June 30, 2015, after giving effect to this | ' | |
| offering | | \$2.58 |
| Dilution per share to new investors purchasing shares in this offering | | \$5.18 |

The table above assumes for illustrative purposes that an aggregate of 5,154,639 shares of our common stock are sold at a price of \$7.76 per share, the last reported sale price of our common stock on The NASDAQ Capital Market on September 15, 2015, for aggregate gross proceeds of \$40.0 million. The shares sold in this offering, if any, will be sold from time to time at various prices. This information is supplied for illustrative purposes only.

The above discussion and table are based on 38,728,921 shares of our common stock issued and outstanding as of June 30, 2015 and excludes the following, all as of June 30, 2015:

- 4,121,471 shares of our common stock issuable upon exercise of outstanding stock options under our stock option plans, at a weighted average exercise price of \$11.01;
- 71,752 units of restricted stock outstanding;
- 5,576,048 shares of our common stock issuable upon exercise of outstanding warrants at a weighted average price of \$5.28 per share; and
- 4,147,779 shares of our common stock reserved for future awards under our stock option plans and employee stock purchase plans.

To the extent that options or warrants are exercised, or other shares are issued, investors purchasing shares in this offering could experience further dilution. In addition, we may choose to raise additional capital due to market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

PLAN OF DISTRIBUTION

We have entered into a Controlled Equity Offering SM sales agreement with Cantor Fitzgerald, under which we may offer and sell shares of our common stock having an aggregate gross sales price of up to \$40,000,000 from time to time through Cantor Fitzgerald acting as agent. The sales agreement has been filed as an exhibit to a Current Report on Form 8-K and incorporated by reference into this prospectus.

Upon delivery of a placement notice and subject to the terms and conditions of the sales agreement, Cantor Fitzgerald may sell shares of our common stock by any method permitted by law deemed to be an "at the market offering" as defined in Rule 415 promulgated under the Securities Act, including sales made directly on The NASDAQ Capital Market, on any other existing trading market for our common stock or to or through a market maker. Cantor Fitzgerald may also sell our common stock by any other method permitted by law, including in privately negotiated transactions. We may instruct Cantor Fitzgerald not to sell our common stock if the sales cannot be effected at or above the price designated by us from time to time. We or Cantor Fitzgerald may suspend the offering of our common stock upon notice and subject to other conditions.

We will pay Cantor Fitzgerald commissions, in cash, for its services in acting as agent in the sale of our common stock. Cantor Fitzgerald will be entitled to compensation at a commission rate of 3.0% of the gross sales price per share sold. Because there is no minimum offering amount required as a condition to close this offering, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time. We have also agreed to reimburse Cantor Fitzgerald for certain specified expenses, including the fees and disbursements of its legal counsel in an amount not to exceed \$50,000. We estimate that the total expenses for the offering, excluding compensation and reimbursements payable to Cantor Fitzgerald under the terms of the sales agreement, will be approximately \$350,000.

Settlement for sales of common stock will occur on the third business day following the date on which any sales are made, or on some other date that is agreed upon by us and Cantor Fitzgerald in connection with a particular transaction, in return for payment of the net proceeds to us. Sales of our 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 Cantor Fitzgerald may agree upon. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

Cantor Fitzgerald will use its commercially reasonable efforts, consistent with its sales and trading practices, to solicit offers to purchase the common stock shares under the terms and subject to the conditions set forth in the sales agreement. In connection with the sale of the common stock on our behalf, Cantor Fitzgerald will be deemed to be an "underwriter" within the meaning of the Securities Act and the compensation of Cantor Fitzgerald will be deemed to be underwriting commissions or discounts. We have agreed to provide indemnification and contribution to Cantor Fitzgerald against certain civil liabilities, including liabilities under the Securities Act.

The offering of our common stock pursuant to the sales agreement will terminate upon the earlier of (1) the sale of all shares of our common stock subject to the sales agreement, or (2) termination of the sales agreement as permitted therein. We and Cantor Fitzgerald may each terminate the sales agreement at any time upon five days' and ten days' prior notice, respectively.

Cantor Fitzgerald and its affiliates may in the future provide various investment banking, commercial banking and other financial services for us and our affiliates, for which services they may in the future receive customary fees. To the extent required by Regulation M, Cantor Fitzgerald will not engage in any market making activities involving our common stock while the offering is ongoing under this prospectus.

This prospectus in electronic format may be made available on a website maintained by Cantor Fitzgerald, and Cantor Fitzgerald may distribute this prospectus electronically.

DESCRIPTION OF CAPITAL STOCK

As of the date of this prospectus, our authorized capital stock consists of 91,500,000 shares. Those shares consist of 81,500,000 shares designated as common stock, \$0.001 par value, and 10,000,000 shares designated as preferred stock, \$0.001 par value. As of September 15, 2015, there were 38,756,313 shares of common stock issued and outstanding.

The following description summarizes the material terms of our capital stock. This summary is, however, subject to the provisions of our restated certificate of incorporation and any applicable certificate of designations for a series of preferred stock, and the provisions of applicable law.

Common Stock

Holders of common stock are entitled to one vote for each share held of record on all matters submitted to a vote of stockholders. Upon any liquidation, dissolution or winding up of our business, the holders of common stock are entitled to share equally in all assets available for distribution after payment of all liabilities and provision for liquidation preference of shares of preferred stock then outstanding. Holders of common stock have no preemptive rights or rights to convert their common stock into any other securities. There are no redemption or sinking fund provisions applicable to the common stock. Holders of common stock are entitled to receive dividends declared by the board of directors, out of funds legally available for the payment of dividends, subject to the rights of holders of preferred stock. Currently, we are not paying dividends.

Our common stock is listed on The NASDAQ Capital Market under the symbol "CYTK." The transfer agent and registrar for our common stock is Computershare. Computershare's address is 330 N Brand Blvd., Suite 701, Glendale, CA 91203.

All outstanding shares of common stock are fully paid and non-assessable, and all shares of common stock offered by this prospectus, or issuable upon conversion or exercise of securities, will, when issued, be validly issued and fully paid and non-assessable.

Preferred Stock

Pursuant to our restated certificate of incorporation, our board of directors has the authority, without further approval by our stockholders, to designate and issue up to 10,000,000 shares of preferred stock in one or more series. Our board of directors previously designated 8,070 of the authorized shares of preferred stock as Series A convertible preferred stock, and 23,026 of the authorized shares of preferred stock as Series B convertible preferred stock, none of which are currently outstanding. Our board of directors may designate the powers, preferences and rights, and the qualifications, limitations or restrictions of each series of preferred stock, including dividend rights, dividend rate, conversion rights, voting rights, rights and terms of redemption (including sinking fund provisions), redemption price or prices, and liquidation preferences, any or all of which may be greater than the rights of the common stock. Thus, without stockholder approval, our board of directors could authorize the issuance of preferred stock with voting, conversion and other rights that could dilute the voting power and other rights of holders of our common stock, and may have the effect of decreasing the market price of the common stock.

Anti-Takeover Effects of Some Provisions of Delaware Law

Provisions of Delaware law and our amended and restated certificate of incorporation and amended bylaws could make the acquisition of our company through a tender offer, a proxy contest or other means more difficult and could make the removal of incumbent officers and directors more difficult. We expect these provisions to discourage coercive takeover practices and inadequate takeover bids and to encourage persons seeking to acquire control of our company to first negotiate with our board of directors. We believe that the benefits provided by our ability to negotiate with the proponent of an unfriendly or unsolicited proposal outweigh the disadvantages of discouraging these proposals. We believe the negotiation of an unfriendly or unsolicited proposal could result in an improvement of its terms.

We are subject to Section 203 of the Delaware General Corporation Law, an anti-takeover law. In general, Section 203 prohibits a publicly held Delaware corporation from engaging 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 time the stockholder become an interested stockholder, the board of directors of the corporation approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;

- upon consummation of the transaction which resulted in the stockholder becoming an interested stockholder, the stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding those shares owned (a) by persons who are directors and also officers, and (b) employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or
- at or subsequent to such time the stockholder become an interested stockholder, the business combination is approved by the 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 66 2/3% 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 securities. 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 also 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.

Anti-Takeover Effects of Provisions of Our Charter Documents

Our amended and restated certificate of incorporation provides for our board of directors to be divided into three classes serving staggered terms. Approximately one-third of the board of directors will be elected each year. The provision for a classified board could prevent a party who acquires control of a majority of the outstanding voting stock from obtaining control of the board of directors until the second annual stockholders meeting following the date the acquirer obtains the controlling stock interest. The classified board provision could discourage a potential acquirer from making a tender offer or otherwise attempting to obtain control of our company and could increase the likelihood that incumbent directors will retain their positions. Our amended and restated certificate of incorporation provides that directors may be removed with cause by the affirmative vote of the holders of the outstanding shares of common stock.

Our amended and restated bylaws establish an advance notice procedure for stockholder proposals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to the board of directors. At an annual meeting, stockholders may only consider proposals or nominations specified in the notice of meeting or brought before the meeting by or at the direction of the board of directors. Stockholders may also consider a proposal or nomination by a person who was a stockholder of record on the record date for the meeting, who is entitled to vote at the meeting and who has given to our Secretary timely written notice, in proper form, of his or her intention to bring that business before the meeting. The amended bylaws do not give the board of directors the power to approve or disapprove stockholder nominations of candidates or proposals regarding other business to be conducted at a special or annual meeting of the stockholders. However, our bylaws may have the effect of precluding the conduct of 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.

Under Delaware law, a special meeting of stockholders may be called by the board of directors or by any other person authorized to do so in the amended and restated certificate of incorporation or the amended bylaws. Our amended bylaws authorize a majority of our board of directors, the chairperson of the board, the chief executive officer or the president to call a special meeting of stockholders.

Because our stockholders do not have the right to call a special meeting, a stockholder could not force stockholder consideration of a proposal over the opposition of the board of directors by calling a special meeting of stockholders prior to such time as a majority of the board of directors believed or the chief executive officer believed the matter should be considered or until the next annual meeting provided that the requestor met the notice requirements. The restriction on the ability of stockholders to call a special meeting means that a proposal to replace the board also could be delayed until the next annual meeting.

Delaware law provides that stockholders may execute an action by written consent in lieu of a stockholder meeting. However, Delaware law also allows us to eliminate stockholder actions by written consent. Elimination of written consents of stockholders may lengthen the amount of time required to take stockholder actions since actions by written consent are not

subject to the minimum notice requirement of a stockholder's meeting. However, we believe that the elimination of stockholders' written consents may deter hostile takeover attempts. Without the availability of stockholder's actions by written consent, a holder controlling a majority of our capital stock would not be able to amend our bylaws or remove directors without holding a stockholders' meeting. The holder would have to obtain the consent of a majority of the board of directors, the chairperson of the board or the chief executive officer to call a stockholders' meeting and satisfy the notice periods determined by the board of directors. Our amended and restated certificate of incorporation provides for the elimination of actions by written consent of stockholders.

LEGAL MATTERS

Cooley LLP, Palo Alto, California, will pass upon the validity of the securities offered by this prospectus. Latham & Watkins LLP, San Diego, California, is counsel for Cantor Fitzgerald in connection with this offering.

EXPERTS

The audited financial statements and management's assessment of the effectiveness of internal control over financial reporting (which is included in Management's Report on Internal Control over Financial Reporting) incorporated in this Prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2014 have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC. We have filed with the SEC a Registration Statement on Form S-3 under the Securities Act with respect to the shares of common stock we are offering under this prospectus. This prospectus does not contain all of the information set forth in the Registration Statement and the exhibits to the Registration Statement. For further information with respect to us and the securities we are offering under this prospectus, we refer you to the Registration Statement and the exhibits and schedules filed as a part of the Registration Statement. You may read and copy the Registration Statement, as well as our reports, proxy statements and other information, at the SEC's public reference room at 100 F Street, N.E., Room 1580, Washington, D.C. 20549-0102. You can request copies of these documents by writing to the SEC and paying a fee for the copying cost. You may obtain further information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. Our SEC filings are also available on the SEC Internet site at www.sec.gov, which contains periodic reports and other information regarding issuers that file electronically.

We also maintain a website at www.cytokinetics.com, through which you can access our filings with the SEC. The information contained in, or accessible through, our website is not a part of this prospectus.

INFORMATION INCORPORATED BY REFERENCE

The SEC allows us to "incorporate by reference" information into this prospectus, which means that we can disclose important information to you by referring you to other documents that we have filed or will file with the SEC. We are incorporating by reference in this prospectus the information or documents below that we have filed with the SEC (Commission File No. 000-50633):

- The Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2014, filed on March 6, 2015;
- The information specifically incorporated by reference into the Company's Annual Report on Form 10-K for the ended December 31, 2014 from the Company's definitive proxy statement relating to the Company's 2015 annual meeting of stockholders, which was filed with the SEC on March 30, 2015;
- The Company's Quarterly Report on Form 10-Q for the fiscal quarter ended March 31, 2015, filed on May 4, 2015;
- The Company's Quarterly Report on Form 10-Q for the fiscal quarter ended June 30, 2015, filed on August 5, 2015;
- The Company's Current Reports on Form 8-K filed on February 10, 2015, March 2, 2015, March 13, 2015, May 21, 2015, July 14, 2015 and September 4, 2015; and
- The Company's Current Reports on Form 8-K filed on February 12, 2015, April 30, 2015 and July 29, 2015 (in each case, as to information therein explicitly filed with the SEC only).

All future documents that we file with the SEC pursuant to Section 13(a), 13(c) or 15(d) of the Exchange Act, including those made after the date of the initial filing of the registration statement of which this prospectus is a part and prior to effectiveness of such registration statement, until the termination or completion of this offering of common stock shall be deemed to be incorporated by reference in this prospectus and to be a part of it from the filing dates of such documents (except in each case the information contained in such documents to the extent "furnished" and not "filed"). Certain statements in and portions of

this prospectus update and replace information in the above listed documents incorporated by reference. Likewise, statements in or portions of a future document incorporated by reference in this prospectus may update and replace statements in and portions of this prospectus or the above listed documents. To the extent there is a conflict between the information contained in this prospectus, on the one hand, and the information contained in any document incorporated by reference into this prospectus that was filed with the SEC before the date of this prospectus, on the other hand, you should rely on the information in this prospectus. If any statement in one of these documents is inconsistent with a statement in another document having a later date, the statement in the document having the later date modifies or supersedes the earlier statement.

We will provide without charge to each person, including any beneficial owner, to whom a copy of this prospectus is delivered, upon written or oral request of any such person, a copy of any or all of the documents that are incorporated herein by reference. Requests should be directed to:

Cytokinetics, Incorporated 280 East Grand Avenue South San Francisco, California 94080 United States of America Attn: Investor Relations (650) 624-3000



Up to \$40,000,000 of Shares

Common Stock

Prospectus

CANTOR Litzgerald

September 17, 2015