

CALCULATION OF REGISTRATION FEE

TITLE OF EACH CLASS OF SECURITIES TO BE REGISTERED	AMOUNT TO BE REGISTERED	PROPOSED MAXIMUM OFFERING PRICE PER SHARE	PROPOSED MAXIMUM AGGREGATE OFFERING PRICE	AMOUNT OF REGISTRATION FEE(2)
Common Stock, \$0.001 par value per share	8,712,400 ⁽¹⁾	\$19.80	\$172,505,520	\$15,992

- (1) Includes shares of Common Stock that may be purchased by the underwriters pursuant to their option to purchase additional shares of Common Stock.
- (2) The registration fee is calculated and being paid pursuant to Rule 457(r) under the Securities Act of 1933, as amended, and relates to the Registration Statement on Form S-3 (File No. 333-258694) filed by the Registrant on August 10, 2021.

PROSPECTUS SUPPLEMENT
(To Prospectus dated August 10, 2021)

7,576,000 Shares



Common Stock

We are offering 7,576,000 shares of our common stock in this offering.

Our common stock is listed on the Nasdaq Global Select Market under the symbol "CRNX." On October 20, 2021, the last reported sale price of our common stock on the Nasdaq Global Select Market was \$19.80 per share.

Investing in our common stock involves risks. See "[Risk Factors](#)" beginning on page S-6 of this prospectus supplement and the documents incorporated by reference into this prospectus supplement.

	Per Share	Total
Public offering price	\$ 19.800	\$ 150,004,800
Underwriting discounts and commissions ⁽¹⁾	\$ 1.188	\$ 9,000,288
Proceeds, before expenses, to us	\$ 18.612	\$ 141,004,512

(1) See "Underwriting" for additional information regarding total underwriters compensation, including expenses for which we have agreed to reimburse the underwriters.

We have granted the underwriters an option for a period of 30 days to purchase up to an additional 1,136,400 shares of our common stock on the same terms as set forth above.

The underwriters expect to deliver the shares of common stock to purchasers on or about October 25, 2021.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus supplement or the accompanying prospectus. Any representation to the contrary is a criminal offense.

Joint Bookrunning Managers

SVB Leerink

Evercore ISI

Cantor

Lead Manager

H.C. Wainwright & Co.

Co-Manager

JonesTrading

October 20, 2021

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Neither we nor any of the underwriters have authorized anyone to provide information different from that contained in this prospectus supplement. When you make a decision about whether to invest in our common stock, you should not rely upon any information other than the information in this prospectus supplement. Neither the delivery of this prospectus supplement nor the sale of shares of our common stock means that information contained in this prospectus supplement is correct after the date of this prospectus supplement. This prospectus supplement and the accompanying prospectus are not an offer to sell or solicitation of an offer to buy shares of our common stock in any circumstances under which the offer or solicitation is unlawful.

ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus dated August 10, 2021 are part of a registration statement that we filed with the Securities and Exchange Commission, or SEC, as a “well-known seasoned issuer” as defined in Rule 405 under the Securities Act of 1933, as amended, or the Securities Act, utilizing a “shelf” registration process. This prospectus supplement and the accompanying prospectus relate to the offer by us of shares of our common stock to certain investors. We provide information to you about this offering of shares of our common stock in two separate documents that are bound together: (1) this prospectus supplement, which describes the specific details regarding this offering; and (2) the accompanying prospectus, which provides general information, some of which may not apply to this offering. Generally, when we refer to this “prospectus,” we are referring to both documents combined. If information in this prospectus supplement is inconsistent with the accompanying prospectus, you should rely on this prospectus supplement. However, if any statement in one of these documents is inconsistent with a statement in another document having a later date—for example, a document incorporated by reference in this prospectus supplement or the accompanying 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. You should read this prospectus supplement, the accompanying prospectus, the documents and information incorporated by reference in this prospectus supplement and the accompanying prospectus, and any free writing prospectus that we have authorized for use in connection with this offering when making your investment decision. 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; Information Incorporated by Reference.”

You should rely only on information contained in or incorporated by reference into this prospectus supplement and the accompanying prospectus. We have not, and the underwriters have not, authorized anyone to provide you with information that is different. We are offering to sell and seeking offers to buy shares of our common stock only in jurisdictions where offers and sales are permitted. The information contained in this prospectus supplement, the accompanying prospectus, the documents and information incorporated by reference in this prospectus supplement and the accompanying prospectus, and any free writing prospectus that we have authorized for use in connection with this offering are accurate only as of their respective dates, regardless of the time of delivery of this prospectus supplement or of any sale of our common stock.

In this prospectus supplement, unless the context otherwise indicates, the terms “Crinetics,” the “Company,” “we,” “our” and “us” or similar terms refer to Crinetics Pharmaceuticals, Inc., including its subsidiary.

We use our pending trademark Crinetics in this prospectus. All other trademarks, trade names and service marks appearing in this prospectus or the documents incorporated by reference herein are the property of their respective owners. Use or display by us of other parties’ trademarks, trade dress or products is not intended to and does not imply a relationship with, or endorsements or sponsorship of, us by the trademark or trade dress owner. Solely for convenience, trademarks and tradenames referred to in this prospectus appear without the ® and ™ symbols, but those references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or that the applicable owner will not assert its rights, to these trademarks and tradenames.

PROSPECTUS SUPPLEMENT SUMMARY

The items in the following summary are described in more detail later in this prospectus supplement and in the accompanying prospectus. This summary provides an overview of selected information and does not contain all the information you should consider before investing in our common stock. Therefore, you should read the entire prospectus supplement, the accompanying prospectus and any free writing prospectus that we have authorized for use in connection with this offering carefully, including the “Risk Factors” section, and other documents or information included or incorporated by reference in this prospectus supplement and the accompanying prospectus before making any investment decision.

Overview

We are a clinical-stage pharmaceutical company focused on the discovery, development, and commercialization of novel therapeutics for rare endocrine diseases and endocrine-related tumors. Endocrine pathways function to maintain homeostasis and commonly use peptide hormones acting through G protein coupled receptors, or GPCRs, to regulate many aspects of physiology including growth, energy, metabolism, gastrointestinal function, and stress responses. We have assembled a seasoned team with extensive expertise in drug discovery and development in endocrine GPCRs and built a highly productive drug discovery organization. We have discovered a pipeline of oral nonpeptide (small molecule) new chemical entities that target peptide GPCRs to treat a variety of rare endocrine diseases where treatment options have significant efficacy, safety, and/or tolerability limitations. Our lead product candidate, paltusotine (formerly CRN00808), is in clinical development for the treatment of acromegaly and neuroendocrine tumors, or NETs, including NETs complicated by carcinoid syndrome and nonfunctional NETs. Our other product candidates include CRN04777, which is in clinical development for the treatment of congenital hyperinsulinism, or HI, and CRN04894, which is in clinical development for the treatment of diseases of excess adrenocorticotrophic hormone, or ACTH, including Cushing’s Disease and congenital adrenal hyperplasia, or CAH. We are advancing additional product candidates through preclinical discovery and development studies in parallel. Our vision is to build the leading endocrine company which consistently pioneers new therapeutics to help patients better control their disease and improve their daily lives.

We focus on the discovery and development of oral nonpeptide therapeutics that target peptide GPCRs with well understood biological functions, validated biomarkers, and the potential to substantially improve the treatment of endocrine diseases and/or endocrine-related tumors. Our pipeline consists of the following product candidates:

- Paltusotine, our lead product candidate, establishes a new class of oral selective nonpeptide somatostatin receptor type 2, or SST2, agonists designed for the treatment of acromegaly and NETs. Somatostatin is a neuropeptide hormone that broadly inhibits the secretion of other hormones, including growth hormone, or GH, from the pituitary gland. Acromegaly arises from a benign pituitary tumor that secretes excess GH that, in turn, causes excess secretion of insulin-like growth factor-1, or IGF-1, by the liver. This loss of homeostasis in the GH axis results in excess tissue growth and other adverse metabolic effects throughout the body. Approximately 26,000 people in the United States suffer from acromegaly, and depending on surgical success, many are candidates for chronic pharmacological intervention, of which somatostatin peptide analogs are the primary pharmacotherapy. NETs originate from neuroendocrine cells commonly found in the gut, lung, or pancreas. Typically, NETs are only diagnosed at a time of extensive metastatic disease and will often progress to liver failure. NETs are present in approximately 171,000 adults in the United States. Of these, approximately 33,000 patients have carcinoid syndrome, which occurs when the tumors secrete hormones or other chemical substances into the bloodstream that cause severe flushing or diarrhea, among other symptoms. Most NETs overexpress SST2 receptors and injected depots of peptide somatostatin analogs have become the first-line standard of care for many NETs patients. In 2020, injected somatostatin peptide drugs accounted for approximately \$3.2 billion in global sales for the treatment of acromegaly, NETs, and other uses. These drugs require painful monthly or daily injections and, in the case of somatostatin peptide drugs, often fail to fully control the disease in many acromegaly patients.

We have initiated a Phase 3 development program for paltusotine in acromegaly which consists of two placebo-controlled clinical trials. The first of these, the PATHFNDR-1 trial, is designed as a double-blind, placebo-controlled, nine-month clinical trial of paltusotine in acromegaly patients with average IGF-1 levels less than or equal to 1.0 times the upper limit of normal, or ULN, and who are on stable doses of SRL monotherapy (octreotide LAR or lanreotide depot). If successful, we believe the PATHFNDR-1 study could support registration of paltusotine for acromegaly patients switching from other therapies. We also plan to conduct a second study, the PATHFNDR-2 trial, which is designed as a double-blind, placebo-controlled, six-month clinical trial of acromegaly patients with elevated IGF-1 levels. We expect to initiate this trial by the end of 2021. We believe that, if successful, the PATHFNDR-2 trial will support a more expansive registration of paltusotine for untreated acromegaly patients who require pharmacotherapy.

The primary endpoint of both PATHFNDR studies will be the proportion of patients with IGF-1 $\leq 1.0 \times$ ULN at the end of the treatment period on paltusotine as compared to placebo. We expect top line data from both studies in 2023. We believe that, if successful, the two trials could support registration of paltusotine for all acromegaly patients who require pharmacotherapy, including untreated patients and those switching from other therapies. The FDA has granted orphan drug designation for paltusotine for the treatment of acromegaly.

We also plan to initiate a Phase 2 trial with paltusotine in patients with NETs complicated by carcinoid syndrome by the end of 2021.

- CRN04777 is our investigational, oral, nonpeptide somatostatin receptor type 5 agonist designed for the treatment of congenital HI. Congenital HI is a devastating rare genetic disease associated with dysregulated insulin production, in which excess insulin produces life-threatening hypoglycemia (low blood glucose) beginning at birth. This loss of homeostatic control of blood glucose levels can lead to seizures, developmental disorders, learning disabilities, coma, and even death. Congenital HI occurs in approximately 1 in 25,000 to 50,000 new births in the United States. We are currently conducting a double-blind, randomized, placebo-controlled Phase 1 study of CRN04777 in healthy volunteers to assess the safety and tolerability of single and multiple doses of CRN04777. In addition, the study is designed to evaluate the potential mechanism of action of CRN04777 by measuring the suppression of insulin secretion in healthy volunteers following stimulation with either glucose or a sulfonylurea, agents that increase the secretion of insulin. In September 2021, we announced preliminary data from the single ascending dose cohorts of the Phase 1 study. Single doses of CRN04777 were well-tolerated and demonstrated dose-dependent reductions in glucose-stimulated and sulfonylurea-induced insulin secretion. All adverse events reported through the single ascending dose cohorts were considered mild and there were no serious adverse events. We will proceed with the multiple ascending dose cohorts of the Phase 1 study and expect preliminary data in the first quarter of 2022. The FDA has granted rare pediatric disease designation for CRN04777 for the treatment of congenital HI. In addition, the European Medicines Agency has granted orphan drug designation for CRN04777 for the treatment of congenital HI.
- CRN04894 is our investigational, oral, nonpeptide product candidate designed to antagonize ACTH, intended for the treatment of diseases caused by excess ACTH, including Cushing's disease and CAH. Cushing's disease results from a pituitary tumor that secretes excess ACTH which, in turn, causes the downstream synthesis and over-secretion of cortisol by the adrenal glands. Cortisol is the body's main stress hormone and excess amounts can cause significant increases in mortality and morbidity. CAH encompasses a set of disorders that are caused by genetic mutations that result in impaired cortisol synthesis. A lack of cortisol leads to a loss of feedback mechanisms and results in persistently high levels of ACTH, which, in turn, causes overstimulation of the adrenal cortex. The resulting adrenal hyperplasia and over-secretion of other steroids (particularly androgens) and steroid precursors can lead to a variety of effects from improper gonadal development to life-threatening dysregulation of mineralocorticoids. We are currently conducting a double-blind, randomized, placebo-controlled Phase 1 study of CRN04894 in healthy volunteers to assess the safety and tolerability of single and multiple doses of CRN04894. In addition, the study is designed to measure the effect of CRN04894 on suppression of cortisol, cortisol precursors, and adrenal androgens

following exogenous ACTH stimulation. In August 2021, we announced preliminary data from the single ascending dose cohorts of the Phase 1 study. Single doses of CRN04894 were well-tolerated and demonstrated dose-dependent increases in CRN04894 plasma concentrations as well as reductions of both basal cortisol and elevated cortisol following an ACTH challenge. All adverse events reported through the single ascending dose cohorts were considered mild and there were no serious adverse events. We will proceed with the multiple ascending dose cohorts of the Phase 1 study and expect preliminary data in the first quarter of 2022.

Patients with many other debilitating endocrine diseases await new therapeutic options. We plan to continue our drug discovery efforts and leverage our expertise in the evaluation of additional conditions including hyperparathyroidism, nonfunctional pituitary adenomas, and polycystic kidney disease, among other indications. All of our product candidates have been discovered, characterized, and developed internally.

Recent Developments

Radionetics

On October 18, 2021, we, together with 5AM Ventures and Frazier Healthcare Partners, announced the formation of an independently operated new company, Radionetics Oncology, Inc., or Radionetics. Radionetics aims to develop a deep pipeline of novel, targeted, nonpeptide radiopharmaceuticals for the treatment of a broad range of oncology indications.

Radionetics' pipeline is based on a broadly enabling platform and intellectual property that will leverage more than a decade of discovery experience within Crinetics. The platform uses nonpeptides as targeting agents designed to deliver therapeutically active radiopharmaceuticals to tumors expressing unique peptide receptors. Radionetics' initial drug development efforts will center on advancing a collection of 10 potent nonpeptide-targeted radiopharmaceutical candidates and leads, discovered at Crinetics, into clinical imaging and efficacy studies. Radionetics will work independently and with us to identify additional novel radiopharmaceutical targets and drug candidates for a range of cancer indications.

Radiation therapy is a common component of many cancer treatment regimens, but can have serious side effects depending on the size and location of the target tumor. The ability to selectively deliver radioactivity to tumor cells through the use of targeted radiopharmaceuticals is an attractive alternative to traditional radiation therapy. Peptide-targeted radiotherapeutics have recently demonstrated important therapeutic benefit for the treatment of neuroendocrine tumors and advanced prostate cancer and are rapidly being integrated into the standard of care for these patients. Their increasing use is expected to drive infrastructure and deployment of additional radiotherapeutics. Radionetics' platform technology is designed to use nonpeptide, small molecule targeting to deliver therapeutic radioisotopes to a broad range of cancers by binding selectively to peptide receptors that are selectively expressed on these tumors. This nonpeptide technology is designed to address many of the significant challenges currently facing peptide and protein targeted radiotherapeutics, particularly in the realm of optimizing drug-like characteristics and manufacturing.

In conjunction with the formation of the company, Radionetics will receive an exclusive world-wide license to the radiotherapeutics technology platform and associated intellectual property from us for use in developing radiotherapeutics and related radio-imaging agents, including exclusive rights to the underlying intellectual property on the preclinical drug candidates and leads targeting 10 different peptide receptors expressed in solid tumors that comprise Radionetics' initial pipeline. In exchange, we received 50,500,000 shares of common stock of Radionetics, which represents an initial majority equity stake in Radionetics, and a warrant to purchase additional shares of common stock designed to maintain a minimum equity interest for us in Radionetics of at least an aggregate of 22% of the fully diluted capitalization of Radionetics in connection with its sale, initial public offering, or SPAC transaction. In addition, we may receive potential sales milestones in excess of \$1 billion and single-digit royalties on net sales. Radionetics also completed a \$30 million private financing with

5AM Ventures and Frazier Healthcare Partners as the sole participants. In addition to the 10 lead candidates, Radionetics and Crinetics will also engage in a research collaboration to identify drug candidates for multiple additional targets.

R. Scott Struthers, Ph.D., our President and Chief Executive Officer, will serve as chairman of the Radionetics board of directors. Our co-founders, Yun-Fei (Frank) Zhu, Ph.D. and Ana K. Kusnetzow, Ph.D., will assume roles with Radionetics as chief research officer and vice president of biology, respectively. While at Crinetics, Dr. Zhu was vice president of chemistry and a co-inventor of our nonpeptide drug candidates, three of which have now demonstrated clinical proof of concept. Dr. Kusnetzow was most recently the senior director of biology and co-leader of our discovery project that gave rise to the nonpeptide targeted radiotherapeutics platform that now forms the basis of the Radionetics pipeline.

Certain Financial Data

We estimate that our cash, cash equivalents and investment securities were approximately \$193.4 million as of September 30, 2021. This amount is unaudited and preliminary and is subject to completion of financial closing procedures. As a result, this amount may differ from the amount that will be reflected in our financial statements as of and for the quarter ended September 30, 2021. Our financial statements for the quarter ended September 30, 2021 will not be available until after this offering is completed, and consequently will not be available to you prior to investing in this offering.

Corporate Information

We were incorporated under the laws of the state of Delaware on November 18, 2008. Our principal executive offices are located at 10222 Barnes Canyon Road, Bldg. #2, San Diego, California 92121, and our telephone number is (858) 450-6464.

THE OFFERING

Common stock offered by us	7,576,000 shares.
Common stock to be outstanding after this offering	45,255,556 shares (or 46,391,956 shares if the underwriters exercise in full their option to purchase additional shares).
Option to purchase additional shares	We have granted the underwriters an option to purchase up to an additional 1,136,400 shares of our common stock. This option is exercisable, in whole or in part, for a period of 30 days from the date of this prospectus supplement.
Use of proceeds	We currently intend to use the net proceeds of this offering to fund the development of paltusotine, CRN04894, CRN04777 and our other research and development programs, and for working capital and general corporate purposes. See “Use of Proceeds”
Risk factors	See “Risk Factors” beginning on page S-6 of this prospectus supplement and in the documents incorporated by reference in this prospectus supplement for a discussion of factors to consider before deciding to invest in our common stock.
Nasdaq Global Select Market symbol	“CRNX”

The number of shares of common stock to be outstanding after this offering is based on 37,679,556 shares outstanding as of June 30, 2021, and excludes:

- 851,306 shares of our common stock issued in a private placement on July 30, 2021;
- 6,144,656 shares of common stock issuable upon the exercise of stock options outstanding as of June 30, 2021 under our equity incentive plans, with a weighted average exercise price of \$14.77 per share;
- 1,833,077 shares of common stock reserved for future issuance under our 2018 Incentive Award Plan as of June 30, 2021; and
- 897,048 shares of common stock reserved for future issuance under our 2018 Employee Stock Purchase Plan as of June 30, 2021.

Except as otherwise indicated, all information in this prospectus supplement assumes no exercise of outstanding options and no exercise by the underwriters of their option to purchase up to an additional 1,136,400 shares of our common stock.

RISK FACTORS

You should consider carefully the risks described below and discussed under the section captioned “Risk Factors” contained in our Annual Report on Form 10-K for the year ended December 31, 2020 as updated by our subsequent filings under the Securities Exchange Act of 1934, as amended, or the Exchange Act, which are incorporated by reference in this prospectus supplement and the accompanying prospectus in their entirety, together with other information in this prospectus supplement, the accompanying prospectus and the information and documents incorporated by reference in this prospectus supplement and the accompanying prospectus, and any free writing prospectus that we have authorized for use in connection with this offering before you make a decision to invest in our common stock. If any of the following events actually occur, our business, operating results, prospects or financial condition could be materially and adversely affected. This could cause the trading price of our common stock to decline and you may lose all or part of your investment. The risks described below are not the only ones that we face. Additional risks not presently known to us or that we currently deem immaterial may also affect our business operations.

Risks Relating to This Offering

If you purchase shares of our common stock sold in this offering, you will experience immediate and substantial dilution in the net tangible book value of your shares. In addition, we may issue additional equity or convertible debt securities in the future, which may result in additional dilution to investors.

The offering price per share of common stock in this offering is considerably more than the net tangible book value per share of our outstanding common stock. As a result, investors purchasing shares of common stock in this offering will pay a price per share that substantially exceeds the value of our tangible assets after subtracting liabilities. Based upon the public offering price of \$19.80 per share, new investors will incur immediate dilution of \$12.24 per share based on the net tangible book value as of June 30, 2021. For a more detailed discussion of the foregoing, see the section entitled “Dilution” below. To the extent outstanding stock options are exercised, there will be further dilution to new investors. In addition, to the extent we need to raise additional capital in the future and we issue additional shares of common stock or securities convertible or exchangeable for our common stock, our then existing stockholders may experience dilution and the new securities may have rights senior to those of our common stock offered in this offering.

Our management team may invest or spend the proceeds of this offering in ways with which you may not agree or in ways which may not yield a significant return.

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 entitled “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. We expect to use the net proceeds from this offering to fund the development of paltusotine, CRN04894, CRN04777 and our other research and development programs, and for working capital and general corporate purposes. 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-term, investment-grade, interest-bearing securities. 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.

Risks Related to our Business Operations and Industry

We may not realize any benefits from our relationship with Radionetics.

In conjunction with formation of Radionetics, we will initially retain a majority equity stake in Radionetics and have the potential to receive future sales milestones and royalties on net sales of any approved products subject and pursuant to the terms of our license agreement. However, Radionetics will need additional capital to advance its pipeline and our ownership interest may be diminished in connection with future capital raising. In addition, our ability to receive milestone or royalty payments from Radionetics will depend on Radionetics ability to advance its pipeline through clinical development, regulatory approval and ultimately commercial sales, all of which will take significant time, will be subject to inherent risks in drug development and may be impacted by changes in regulatory requirements, healthcare reform measures and competitive dynamics. Radionetics will face the same risks associated with preclinical and clinical development that we face as set forth in the “Risk Factors” section contained in our Annual Report on Form 10-K for the year ended December 31, 2020 as updated by our subsequent filings under the Exchange Act. Further, the Radionetics nonpeptide therapeutics platform technology targeting the delivery of therapeutic radioisotopes is novel and unproven and may never lead to approved products of commercial value. As a result, we and our stockholders may never realize future value from our equity interest in or license agreement or research collaboration with Radionetics.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement and the accompanying prospectus, including the documents incorporated by reference herein and therein, and any free writing prospectus that we have authorized for use in connection with this offering contain forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act. All statements other than statements of historical facts contained in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein are forward-looking statements, including statements regarding our future results of operations and financial position, business strategy, the impact of the COVID-19 pandemic, prospective products, product approvals, research and development costs, timing and likelihood of success, plans and objectives of management for future operations and future results of anticipated products, as well as the potential for us and our stockholders to obtain value from our equity interest in Radionetics and our potential to receive future milestone and royalty payments from Radionetics. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. This prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein also contain estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

In some cases, you can identify forward-looking statements by terms such as “may,” “will,” “should,” “expect,” “plan,” “anticipate,” “could,” “intend,” “target,” “project,” “contemplates,” “believes,” “estimates,” “predicts,” “potential” or “continue” or the negative of these terms or other similar expressions. The forward-looking statements in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein are only predictions. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition and results of operations. These forward-looking statements speak only as of the date of this prospectus supplement and are subject to a number of risks, uncertainties and assumptions, which we discuss in greater detail in the documents incorporated by reference herein, including under the heading “Risk Factors.” The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Moreover, we operate in an evolving environment. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties. Given these risks and uncertainties, you should not place undue reliance on these forward-looking statements. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained in this prospectus supplement, the accompanying prospectus or the documents incorporated by reference herein, whether as a result of any new information, future events, changed circumstances or otherwise. For all forward-looking statements, we claim the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995.

USE OF PROCEEDS

We estimate that we will receive net proceeds of approximately \$140.8 million from the sale of 7,576,000 shares of common stock offered by us in this offering, or approximately \$161.9 million if the underwriters exercise in full their option to purchase up to an additional 1,136,400 shares of common stock, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

We currently intend to use the net proceeds of this offering to fund the development of paltusotine, CRN04894, CRN04777 and our other research and development programs, and for working capital and general corporate purposes.

The amounts and timing of our actual expenditures will depend on numerous factors, including the factors described under “Risk Factors” in this prospectus and in the documents incorporated by reference herein, as well as the amount of cash used in our operations. We may find it necessary or advisable to use the net proceeds for other purposes, and we will have broad discretion in the application of the net proceeds. Pending the uses described above, we plan to invest the net proceeds from this offering in short- and intermediate-term, interest-bearing obligations, investment-grade instruments, certificates of deposit or direct or guaranteed obligations of the U.S. government.

DILUTION

If you invest in our common stock in this offering, your interest will be diluted to the extent of the difference between the public offering price per share and the net tangible book value per share of our common stock after this offering. As of June 30, 2021, our net tangible book value was \$201.4 million, or \$5.35 per share, based on 37,679,556 shares of our common stock outstanding as of June 30, 2021. Our net tangible book value per share represents the amount of our total tangible assets reduced by the amount of our total liabilities, divided by the total number of shares of our common stock outstanding as of June 30, 2021. After giving effect to our sale in this offering of 7,576,000 shares of common stock at the public offering price of \$19.80 per share, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us, our net tangible book value as of June 30, 2021 would have been \$342.2 million, or \$7.56 per share. This represents an immediate increase in net tangible book value of \$2.21 per share to our existing stockholders and immediate dilution of \$12.24 per share to new investors purchasing our common stock in this offering. The following table illustrates this per share dilution.

Public offering price per share	\$19.80
Net tangible book value per share at June 30, 2021	\$5.35
Increase per share attributable to investors purchasing shares in this offering	<u>2.21</u>
As adjusted net tangible book value per share, after giving effect to this offering	<u>7.56</u>
Dilution per share to investors purchasing our common stock in this offering	<u>\$12.24</u>

If the underwriters exercise in full their option to purchase up to an additional 1,136,400 shares of our common stock at the public offering price of \$19.80 per share, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value after this offering would be \$7.83 per share, representing an immediate increase in net tangible book value of \$2.48 per share to our existing stockholders and immediate dilution of \$11.97 per share to new investors purchasing common stock in this offering.

The foregoing tables and calculations (other than net tangible book value calculations) are based on 37,679,556 shares outstanding as of June 30, 2021, and exclude:

- 851,306 shares of our common stock issued in a private placement on July 30, 2021;
- 6,144,656 shares of common stock issuable upon the exercise of stock options outstanding as of June 30, 2021 under our equity incentive plans, with a weighted average exercise price of \$14.77 per share;
- 1,833,077 shares of common stock reserved for future issuance under our 2018 Incentive Award Plan as of June 30, 2021; and
- 897,048 shares of common stock reserved for future issuance under our 2018 Employee Stock Purchase Plan as of June 30, 2021.

To the extent that outstanding options are exercised, you may 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 we raise additional capital by issuing equity or convertible debt securities, your ownership will be further diluted.

UNDERWRITING

SVB Leerink LLC, Evercore Group L.L.C. and Cantor Fitzgerald & Co. are acting as representatives, or the Representatives, of each of the underwriters named below and SVB Leerink LLC, Evercore Group L.L.C. and Cantor Fitzgerald & Co. are acting as joint bookrunning managers for this offering. Subject to the terms and conditions set forth in the underwriting agreement among us and the underwriters, we have agreed to sell to the underwriters, and each of the underwriters has agreed, severally and not jointly, to purchase from us, the number of shares of common stock set forth opposite its name below.

Underwriter	Number of Shares
SVB Leerink LLC	2,878,880
Evercore Group L.L.C.	2,272,800
Cantor Fitzgerald & Co.	1,515,200
H.C. Wainwright & Co., LLC	606,080
JonesTrading Institutional Services, LLC	303,040
Total	<u>7,576,000</u>

Subject to the terms and conditions set forth in the underwriting agreement, the underwriters have agreed, severally and not jointly, to purchase all of the shares sold under the underwriting agreement if any of the shares are purchased. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the non-defaulting underwriters may be increased or the underwriting agreement may be terminated.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act, or to contribute to payments the underwriters may be required to make in respect of those liabilities.

The underwriters are offering the shares, subject to prior sale, when, as and if issued to and accepted by them, subject to approval of legal matters by their counsel, including the validity of the shares, and subject to other conditions contained in the underwriting agreement, such as the receipt by the underwriters of officers' certificates and legal opinions. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Discounts and Commissions

The Representatives advised us that the underwriters propose initially to offer the shares to the public at the initial public offering price set forth on the cover page of this prospectus supplement and to dealers at that price less a concession not in excess of \$0.7128 per share. After the initial offering of the shares, the public offering price, concession or any other term of this offering may be changed by the Representatives.

The following table shows the public offering price, underwriting discounts and commissions and proceeds, before expenses, to us. The information assumes either no exercise or full exercise by the underwriters of their option to purchase additional shares of our common stock.

	Per Share	Total	
		Without Option	With Option
Public offering price	\$ 19.800	\$ 150,004,800	\$ 172,505,520
Underwriting discounts and commissions	\$ 1.188	\$ 9,000,288	\$ 10,350,331
Proceeds, before expenses, to us	\$ 18.612	\$ 141,004,512	\$ 162,155,189

We estimate expenses payable by us in connection with this offering, other than the underwriting discounts and commissions referred to above, will be approximately \$250,000. We also have agreed to reimburse the underwriters for up to \$10,000 for their FINRA counsel fee. In accordance with FINRA Rule 5110, this reimbursed fee is deemed underwriting compensation for this offering.

Option to Purchase Additional Shares

We have granted an option to the underwriters, exercisable for 30 days after the date of this prospectus supplement, to purchase up to 1,136,400 additional shares at the public offering price, less underwriting discounts and commissions. If the underwriters exercise this option, each underwriter will be obligated, subject to the conditions contained in the underwriting agreement, to purchase a number of additional shares proportionate to that underwriter's initial amount reflected in the above table.

No Sales of Similar Securities

We have agreed that we will not (1) offer, pledge, announce the intention to sell, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, hedge, lend or otherwise transfer or dispose of, directly or indirectly, or submit to or file with the SEC a registration statement under the Securities Act relating to, any shares of our common stock or securities convertible into or exchangeable or exercisable for any shares of our common stock, (2) enter into any swap, hedging or other arrangement that transfers all or a portion of the economic consequences associated with the ownership of any shares of common stock or any such other securities (regardless of whether any of these transactions are to be settled by the delivery of shares of common stock or such other securities, in cash or otherwise), in each case without the prior written consent of SVB Leerink LLC and Evercore Group L.L.C. for a period of 90 days after the date of this prospectus, subject to certain exceptions, or (3) publicly disclose the intention to do any of the foregoing.

Our directors and executive officers have entered into lock-up agreements with the underwriter prior to the commencement of this offering pursuant to which each of these persons or entities, for a period of 90 days after the date of this prospectus, may not, and may not cause any direct or indirect affiliate to, subject to certain exceptions, without the prior written consent of SVB Leerink LLC and Evercore Group L.L.C., (1) lend, offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, hedge, lend or otherwise transfer or dispose of, directly or indirectly, any shares of common stock or any securities convertible into or exercisable or exchangeable for common stock (including, without limitation, common stock or such other securities which may be deemed to be beneficially owned by the undersigned in accordance with the rules and regulations of the SEC and securities which may be issued upon exercise of a stock option or warrant), (2) enter into any hedging, swap or other agreement or transaction that transfers, in whole or in part, any of the economic consequences of ownership of the common stock or such other securities, whether any such transaction described in clause (1) or (2) above is to be settled by delivery of common stock or such other securities, in cash or otherwise, (3) make any demand for or exercise any right with respect to the registration of any shares of common stock or any security convertible into or exercisable or exchangeable for common stock (and, for the avoidance of doubt, the undersigned hereby waives any and all notice requirements and rights with respect to the registration of any securities pursuant to any agreement, instrument, understanding or otherwise, including any stockholders or registration rights agreement or similar agreement, to which the undersigned is a party or under which the undersigned is entitled to any right or benefit) or (4) publicly disclose the intention to do any of the foregoing.

The lock-up provisions apply to common stock and to securities owned now or acquired later by the person executing the lock-up agreement or for which the person executing the lock-up agreement later acquires the power of disposition.

Nasdaq Global Select Market Listing

Our common stock is listed on the Nasdaq Global Select Market under the symbol "CRNX".

Price Stabilization, Short Positions and Penalty Bids

Until the distribution of the shares is completed, SEC rules may limit underwriters and selling group members from bidding for and purchasing our common stock. However, the Representatives may engage in transactions that stabilize the price of the common stock, such as bids or purchases to peg, fix or maintain that price.

In connection with this offering, the underwriters may purchase and sell our common stock in the open market. These transactions may include short sales, purchases on the open market to cover positions created by short sales and stabilizing transactions. Short sales involve the sale by the underwriters of a greater number of shares than they are required to purchase in this offering. "Covered" short sales are sales made in an amount not greater than the underwriters' option to purchase additional shares described above. The underwriters may close out any covered short position by either exercising their option to purchase additional shares or purchasing shares in the open market. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the option to purchase additional shares granted to them under the underwriting agreement described above. "Naked" short sales are sales in excess of such option. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of our common stock in the open market after pricing that could adversely affect investors who purchase in this offering. Stabilizing transactions consist of various bids for or purchases of shares of common stock made by the underwriters in the open market prior to the closing of this offering.

The underwriters may also impose a penalty bid. This occurs when a particular underwriter repays to the underwriters a portion of the underwriting discount received by it because the Representatives have repurchased shares sold by or for the account of such underwriter in stabilizing or short covering transactions.

Similar to other purchase transactions, the underwriters' purchases to cover the syndicate short sales may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock may be higher than the price that might otherwise exist in the open market. The underwriters may conduct these transactions on the Nasdaq Global Select Market, in the over-the-counter market or otherwise.

Neither we nor any of the underwriters make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our common stock. In addition, neither we nor any of the underwriters make any representation that the Representatives will engage in these transactions or that these transactions, once commenced, will not be discontinued without notice.

Electronic Distribution

In connection with this offering, certain of the underwriters or securities dealers may distribute prospectuses by electronic means, such as e-mail.

Other Relationships

The underwriters and certain of their affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. Some of the underwriters and certain of their affiliates have provided in the past to us and may in the future engage in investment banking and other commercial dealings in the ordinary course of business with us and our affiliates, for which they may in the future receive customary fees, commissions and expenses. For example, certain of the underwriters served as underwriters in our previous common stock offerings. In addition, we are party to a Sales Agreement with SVB Leerink LLC and Cantor Fitzgerald & Co., pursuant to which up to \$75.0 million of our common stock is available for sale.

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In addition, in the ordinary course of their business activities, the underwriters and their affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers. Such investments and securities activities may involve securities and/or instruments of ours or our affiliates. The underwriters and their affiliates may also make investment recommendations and/or publish or express independent research views in respect of such securities or financial instruments and may hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

Selling Restrictions

Notice to Prospective Investors in the European Economic Area

In relation to each member state of the European Economic Area (each a “Relevant State”), no shares have been offered or will be offered pursuant to the offering to the public in that Relevant State prior to the publication of a prospectus in relation to the shares which has been approved by the competent authority in that Relevant State or, where appropriate, approved in another Relevant State and notified to the competent authority in that Relevant State, all in accordance with the Prospectus Regulation, except that the shares may be offered to the public in that Relevant State at any time:

- (a) to any legal entity which is a qualified investor as defined under Article 2 of the Prospectus Regulation;
- (b) to fewer than 150 natural or legal persons (other than qualified investors as defined under Article 2 of the Prospectus Regulation), subject to obtaining the prior consent of the Representatives for any such offer; or
- (c) in any other circumstances falling within Article 1(4) of the Prospectus Regulation,

provided that no such offer of the shares shall require us or any of the Representatives to publish a prospectus pursuant to Article 3 of the Prospectus Regulation or supplement a prospectus pursuant to Article 23 of the Prospectus Regulation.

For the purposes of this provision, the expression an “offer to the public” in relation to the shares in any Relevant State means the communication in any form and by any means of sufficient information on the terms of the offer and any shares to be offered so as to enable an investor to decide to purchase or subscribe for any shares, and the expression “Prospectus Regulation” means Regulation (EU) 2017/1129.

Notice to Prospective Investors in the United Kingdom

No shares have been offered or will be offered pursuant to the offering to the public in the United Kingdom prior to the publication of a prospectus in relation to the Shares which has been approved by the Financial Conduct Authority, except that the shares may be offered to the public in the United Kingdom at any time:

- (a) to any legal entity which is a qualified investor as defined under Article 2 of the UK Prospectus Regulation;
- (b) to fewer than 150 natural or legal persons (other than qualified investors as defined under Article 2 of the UK Prospectus Regulation), subject to obtaining the prior consent of the underwriter for any such offer; or
- (c) in any other circumstances falling within Section 86 of the FSMA.

provided that no such offer of the shares shall require us or any underwriter to publish a prospectus pursuant to Section 85 of the FSMA or supplement a prospectus pursuant to Article 23 of the UK Prospectus Regulation. For the purposes of this provision, the expression an “offer to the public” in relation to the shares in the United Kingdom means the communication in any form and by any means of sufficient information on the terms of the

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offer and any shares to be offered so as to enable an investor to decide to purchase or subscribe for any shares and the expression “UK Prospectus Regulation” means Regulation (EU) 2017/1129 as it forms part of domestic law by virtue of the European Union (Withdrawal) Act 2018.

Notice to Prospective Investors in Canada

The shares may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 Prospectus Exemptions or subsection 73.3(1) of the Securities Act (Ontario), and are permitted clients, as defined in National Instrument 31-103 Registration Requirements, Exemptions and Ongoing Registrant Obligations. Any resale of the shares must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus supplement (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser’s province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser’s province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 of National Instrument 33-105 Underwriting Conflicts (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

LEGAL MATTERS

The validity of the issuance of the securities offered hereby will be passed upon by our counsel, Latham & Watkins LLP, San Diego, California. The underwriters are being represented in connection with this offering by Cooley LLP, San Francisco, California.

EXPERTS

The financial statements as of December 31, 2020 and 2019 and for each of the three years in the period ended December 31, 2020 incorporated by reference in this prospectus supplement have been so incorporated in reliance on the report of BDO USA, LLP, an independent registered public accounting firm, incorporated herein by reference, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION; INFORMATION INCORPORATED BY REFERENCE

Available Information

We have filed with the SEC a registration statement on Form S-3ASR under the Securities Act, of which this prospectus supplement forms a part. The rules and regulations of the SEC allow us to omit from this prospectus supplement and the accompanying prospectus certain information included in the registration statement. For further information about us and the securities we are offering under this prospectus supplement, you should refer to the registration statement and the exhibits and schedules filed with the registration statement. With respect to the statements contained in this prospectus supplement and the accompanying prospectus regarding the contents of any agreement or any other document, in each instance, the statement is qualified in all respects by the complete text of the agreement or document, a copy of which has been filed as an exhibit to the registration statement.

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.crinetics.com. The information on, or accessible through, our website is not part of, and is not incorporated into, this prospectus supplement or the accompanying prospectus and should not be considered part of this prospectus supplement or the accompanying prospectus.

Incorporation by Reference

The SEC's rules allow us to "incorporate by reference" information into this prospectus supplement, which means that we can disclose important information to you by referring you to another document filed separately with the SEC. The information incorporated by reference is deemed to be part of this prospectus supplement and the accompanying prospectus, and subsequent information that we file with the SEC will automatically update and supersede that information. Any statement contained in a previously filed document incorporated by reference will be deemed to be modified or superseded for purposes of this prospectus supplement and the accompanying prospectus to the extent that a statement contained in this prospectus supplement or the accompanying prospectus modifies or replaces that statement.

We incorporate by reference our documents listed below and any future filings made by us with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act between the date of this prospectus supplement and the termination of the offering of the securities described in this prospectus supplement. We are not, however, incorporating by reference any documents or portions thereof, whether specifically listed below or filed in the

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future, that are not deemed “filed” with the SEC, including our Compensation Committee report and performance graph or any information furnished pursuant to Items 2.02 or 7.01 of Form 8-K or related exhibits furnished pursuant to Item 9.01 of Form 8-K.

This prospectus supplement and the accompanying prospectus incorporate by reference the documents set forth below that have previously been filed with the SEC:

- our Annual Report on [Form 10-K](#) for the year ended December 31, 2020, filed with the SEC on March 30, 2021;
- our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2021 and June 30, 2021, filed with the SEC on [May 6, 2021](#) and [August 10, 2021](#), respectively;
- our Current Reports on Form 8-K filed with the SEC on [January 6, 2021](#), [February 3, 2021](#), [February 4, 2021](#), [April 8, 2021](#), [June 23, 2021](#), [June 28, 2021](#), [July 29, 2021](#), [August 10, 2021](#), [September 2, 2021](#), [September 15, 2021](#), [September 27, 2021](#) and [October 18, 2021](#);
- our Definitive Proxy Statement on [Schedule 14A](#) (other than information furnished rather than filed), filed with the SEC on April 30, 2021; and
- the description of our Common Stock contained in our registration statement on [Form 8-A](#), filed with the SEC on July 12, 2018 and any amendment or report filed with the SEC for the purpose of updating the description.

All reports and other documents we subsequently file pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act prior to the termination of this offering, including, but excluding any information furnished to, rather than filed with, the SEC, will also be incorporated by reference into this prospectus supplement and the accompanying prospectus and deemed to be part of this prospectus supplement and the accompanying prospectus from the date of the filing of such reports and documents.

You may request a free copy of any of the documents incorporated by reference in this prospectus supplement and the accompanying prospectus (other than exhibits, unless they are specifically incorporated by reference in the documents) by writing or telephoning us at the following address:

Crinetics Pharmaceuticals, Inc.
Attention: Corporate Secretary
10222 Barnes Canyon Road, Bldg. #2
San Diego, CA 92121
(858) 450-6464

PROSPECTUS



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

**Common Stock
Offered by the Selling Securityholders**

We may offer and sell the securities identified above, and the selling securityholders may offer and sell common stock, in each case from time to time in one or more offerings. This prospectus provides you with a general description of the securities. We will not receive any proceeds from the sale of our common stock by the selling securityholders.

Each time we or any of the selling securityholders offer and sell securities, we or such selling securityholders will provide a supplement to this prospectus that contains specific information about the offering and, if applicable, the selling securityholders, as well as the amounts, prices and terms of the securities. The supplement may also add, update or change information contained in this prospectus with respect to that offering. You should carefully read this prospectus and the applicable prospectus supplement before you invest in any of our securities.

We may offer and sell the securities described in this prospectus and any prospectus supplement to or through one or more underwriters, dealers and agents, or directly to purchasers, or through a combination of these methods. In addition, the selling securityholders may offer and sell shares of our common stock from time to time, together or separately. If any underwriters, dealers or agents are involved in the sale of any of the securities, their names and any applicable purchase price, fee, commission or discount arrangement between or among them will be set forth, or will be calculable from the information set forth, in the applicable prospectus supplement. See the sections of this prospectus entitled "About this Prospectus" and "Plan of Distribution" for more information. No securities may be sold without delivery of this prospectus and the applicable prospectus supplement describing the method and terms of the offering of such securities.

INVESTING IN OUR SECURITIES INVOLVES RISKS. SEE THE "[RISK FACTORS](#)" ON PAGE 7 OF THIS PROSPECTUS AND ANY SIMILAR SECTION CONTAINED IN THE APPLICABLE PROSPECTUS SUPPLEMENT CONCERNING FACTORS YOU SHOULD CONSIDER BEFORE INVESTING IN OUR SECURITIES.

Our common stock is listed on The Nasdaq Global Select Market under the symbol "CRNX." On August 9, 2021, the last reported sale price of our common stock on The Nasdaq Global Select Market was \$16.88 per share.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

The date of this prospectus is August 10, 2021.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the U.S. Securities and Exchange Commission, or the SEC, as a “well-known seasoned issuer” as defined in Rule 405 under the Securities Act of 1933, as amended, or the Securities Act, using a “shelf” registration process. By using a shelf registration statement, we may sell securities from time to time and in one or more offerings and the selling securityholders to be named in a supplement to this prospectus may, from time to time, sell shares of common stock from time to time in one or more offerings, as described in this prospectus. Each time that we or the selling securityholders offer and sell securities, we or the selling securityholders will provide a prospectus supplement to this prospectus that contains specific information about the securities being offered and sold and the specific terms of that offering. We may also authorize one or more free writing prospectuses to be provided to you that may contain material information relating to these offerings. The prospectus supplement or free writing prospectus may also add, update or change information contained in this prospectus with respect to that offering. If there is any inconsistency between the information in this prospectus and the applicable prospectus supplement or free writing prospectus, you should rely on the prospectus supplement or free writing prospectus, as applicable. Before purchasing any securities, you should carefully read both this prospectus and the applicable prospectus supplement (and any applicable free writing prospectuses), together with the additional information described under the heading “Where You Can Find More Information; Incorporation by Reference.”

Neither we, nor the selling securityholders, have authorized anyone to provide you with any information or to make any representations other than those contained in this prospectus, any applicable prospectus supplement or any free writing prospectuses prepared by or on behalf of us or to which we have referred you. We and the selling securityholders take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We and the selling securityholders will not make 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 and the applicable prospectus supplement to this prospectus is accurate only as of the date on its respective cover, that the information appearing in any applicable free writing prospectus is accurate only as of the date of that free writing prospectus, and that any information incorporated by reference is accurate only as of the date of the document incorporated by reference, unless we indicate otherwise. Our business, financial condition, results of operations and prospects may have changed since those dates. 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. Although we are not aware of any misstatements regarding the market and industry data presented in this prospectus and the documents incorporated herein by reference, these estimates involve 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.

When we refer to “Crinetics,” “we,” “our,” “us” and the “Company” in this prospectus, we mean Crinetics Pharmaceuticals, Inc., unless otherwise specified. When we refer to “you,” we mean the potential holders of the applicable series of securities.

We use our pending trademark, Crinetics, in this prospectus. This prospectus also includes trademarks, tradenames and service marks that are the property of other organizations. Solely for convenience, trademarks and tradenames referred to in this prospectus appear without the ® and ™ symbols, but those references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or that the applicable owner will not assert its rights, to these trademarks and tradenames.

WHERE YOU CAN FIND MORE INFORMATION; INCORPORATION BY REFERENCE

Available 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 <http://www.sec.gov>.

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

This prospectus and any prospectus supplement are part of a registration statement that we filed with the SEC and do not contain all of the information in the registration statement. The full registration statement may be obtained from the SEC or us, as provided below. Forms of the indenture and other documents establishing the terms of the offered securities are or may be filed as exhibits to the registration statement or documents incorporated by reference in the registration statement. Statements in this prospectus or any prospectus supplement 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 by Reference

The SEC's rules allow us to "incorporate by reference" information into this prospectus, which means that we can disclose important information to you by referring you to another document filed separately with the SEC. The information incorporated by reference is deemed to be part of this prospectus, and subsequent information that we file with the SEC will automatically update and supersede that information. Any statement contained in this prospectus or a previously filed document incorporated by reference will be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus or a subsequently filed document incorporated by reference modifies or replaces that statement.

We incorporate by reference our documents listed below and any future filings made by us with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, which we refer to as the "Exchange Act," in this prospectus, between the date of this prospectus and the termination of the offering of the securities described in this prospectus. We are not, however, incorporating by reference any documents or portions thereof, whether specifically listed below or filed in the future, that are not deemed "filed" with the SEC, including our Compensation Committee report and performance graph or any information furnished pursuant to Items 2.02 or 7.01 of Form 8-K or related exhibits furnished pursuant to Item 9.01 of Form 8-K.

This prospectus and any accompanying prospectus supplement incorporate by reference the documents set forth below that have previously been filed with the SEC:

- our Annual Report on Form 10-K for the year ended December 31, 2020, filed with the SEC on [March 30, 2021](#);
- our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2021 and June 30, 2021, filed with the SEC on [May 6, 2021](#) and [August 10, 2021](#), respectively;
- the information specifically incorporated by reference into our Annual Report on Form 10-K from our Definitive Proxy Statement on Schedule 14A, filed with the SEC on [April 30, 2021](#);
- our Current Reports on Form 8-K, filed with the SEC on [January 6, 2021](#), [February 3, 2021](#), [February 4, 2021](#), [April 8, 2021](#), [June 23, 2021](#), [June 28, 2021](#), [July 29, 2021](#) and [August 10, 2021](#); and

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- the description of our common stock contained in our registration statement on Form 8-A, filed with the SEC on [July 12, 2018](#) and any amendment or report filed with the SEC for the purpose of updating the description.

All reports and other documents we subsequently file pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act prior to the termination of this offering, but excluding any information furnished to, rather than filed with, the SEC, will also be incorporated by reference into this prospectus and deemed to be part of this prospectus from the date of the filing of such reports and documents.

You may request a free copy of any of the documents incorporated by reference in this prospectus (other than exhibits, unless they are specifically incorporated by reference in the documents) by writing or telephoning us at the following address:

Crinetics Pharmaceuticals, Inc.
Attention: Corporate Secretary
10222 Barnes Canyon Road, Bldg. #2
San Diego, CA 92121
(858) 450-6464

Exhibits to the filings will not be sent, however, unless those exhibits have specifically been incorporated by reference in this prospectus or any accompanying prospectus supplement.

THE COMPANY

We are a clinical-stage pharmaceutical company focused on the discovery, development, and commercialization of novel therapeutics for rare endocrine diseases and endocrine-related tumors. Endocrine pathways function to maintain homeostasis and commonly use peptide hormones acting through G protein coupled receptors, or GPCRs, to regulate many aspects of physiology including growth, energy, metabolism, gastrointestinal function, and stress responses. We have assembled a seasoned team with extensive expertise in drug discovery and development in endocrine GPCRs and built a highly productive drug discovery organization. We have discovered a pipeline of oral nonpeptide (small molecule) new chemical entities that target peptide GPCRs to treat a variety of rare endocrine diseases where treatment options have significant efficacy, safety, and/or tolerability limitations. Our lead product candidate, paltusotine (formerly CRN00808), is in clinical development for the treatment of acromegaly and neuroendocrine tumors, or NETs, including NETs complicated by carcinoid syndrome and nonfunctional NETs. Our other product candidates include CRN04777, which is in clinical development for the treatment of congenital hyperinsulinism, or HI, and CRN04894, which is in clinical development for the treatment of diseases of excess adrenocorticotrophic hormone, or ACTH, including Cushing's Disease and congenital adrenal hyperplasia, or CAH. We are advancing additional product candidates through preclinical discovery and development studies in parallel. Our vision is to build the leading endocrine company which consistently pioneers new therapeutics to help patients better control their disease and improve their daily lives.

We focus on the discovery and development of oral nonpeptide therapeutics that target peptide GPCRs with well understood biological functions, validated biomarkers, and the potential to substantially improve the treatment of endocrine diseases and/or endocrine-related tumors. Our pipeline consists of the following product candidates:

- Paltusotine, our lead product candidate, establishes a new class of oral selective nonpeptide somatostatin receptor type 2, or SST2, agonists designed for the treatment of acromegaly and NETs. Somatostatin is a neuropeptide hormone that broadly inhibits the secretion of other hormones, including growth hormone, or GH, from the pituitary gland. Acromegaly arises from a benign pituitary tumor that secretes excess GH that, in turn, causes excess secretion of insulin-like growth factor-1, or IGF-1, by the liver. This loss of homeostasis in the GH axis results in excess tissue growth and other adverse metabolic effects throughout the body. Approximately 26,000 people in the United States suffer from acromegaly, and depending on surgical success, many are candidates for chronic pharmacological intervention, of which somatostatin peptide analogs are the primary pharmacotherapy. NETs originate from neuroendocrine cells commonly found in the gut, lung, or pancreas. Typically, NETs are only diagnosed at a time of extensive metastatic disease and will often progress to liver failure. NETs are present in approximately 171,000 adults in the United States. Of these, approximately 33,000 patients have carcinoid syndrome, which occurs when the tumors secrete hormones or other chemical substances into the bloodstream that cause severe flushing or diarrhea, among other symptoms. Most NETs overexpress SST2 receptors and injected depots of peptide somatostatin analogs have become the first-line standard of care for many NETs patients. In 2020, injected somatostatin peptide drugs accounted for approximately \$3.2 billion in global sales for the treatment of acromegaly, NETs, and other uses. These drugs require painful monthly or daily injections and, in the case of somatostatin peptide drugs, often fail to fully control the disease in many acromegaly patients.

We have initiated a Phase 3 development program for paltusotine in acromegaly which consists of two placebo-controlled clinical trials. The first of these, the PATHFNDR-1 trial, is designed as a double-blind, placebo-controlled, nine-month clinical trial of paltusotine in 52 acromegaly patients with average IGF-1 levels less than or equal to 1.0 times the upper limit of normal, or ULN, and who are on stable doses of SRL monotherapy (octreotide LAR or lanreotide depot). If successful, the PATHFNDR-1 study could support registration of paltusotine for acromegaly patients switching from other therapies.

We also plan to conduct a second study, the PATHFNDR-2 trial, which is designed as a double-blind, placebo-controlled, trial of acromegaly patients with elevated IGF-1 levels. In July 2021, we held a Type C meeting with the U.S. Food and Drug Administration, or FDA, to better understand the FDA's expectations regarding key aspects of the PATHFNDR-2 study design. We are awaiting the FDA's final minutes from the Type C meeting in order to finalize the PATHFNDR-2 study protocol and initiate recruitment. We believe that, if successful, the PATHFNDR-2 trial will support a more expansive registration of paltusotine for untreated acromegaly patients who require pharmacotherapy.

The primary endpoint of both PATHFNDR studies will be the proportion of patients with IGF-1 $\leq 1.0 \times$ ULN at the end of the treatment period on paltusotine as compared to placebo. We expect top line data from both studies in 2023. We believe that, if successful, the two trials could support registration of paltusotine in the United States and Europe for all acromegaly patients who require pharmacotherapy, including untreated patients and those switching from other therapies. The FDA has granted orphan drug designation for paltusotine for the treatment of acromegaly.

We also plan to initiate a Phase 2 trial with paltusotine in patients with NETs complicated by carcinoid syndrome in 2021.

- CRN04777 is our investigational, oral, nonpeptide somatostatin receptor type 5 agonist designed for the treatment of congenital HI. Congenital HI is a devastating rare genetic disease associated with dysregulated insulin production, in which excess insulin produces life-threatening hypoglycemia (low blood glucose) beginning at birth. This loss of homeostatic control of blood glucose levels can lead to seizures, developmental disorders, learning disabilities, coma, and even death. Congenital HI occurs in approximately 1 in 25,000 to 50,000 new births in the United States. We are currently conducting a double-blind, randomized, placebo-controlled Phase 1 study of CRN04777 in healthy volunteers to assess the safety and tolerability of single and multiple doses of CRN04777. In addition, the study is designed to evaluate the potential mechanism of action of CRN04777 by measuring the suppression of insulin secretion in healthy volunteers following stimulation with either glucose or a sulfonylurea, agents that increase the secretion of insulin. We expect preliminary data from the single ascending dose cohorts in September 2021 and from the multiple ascending dose cohorts in the second half of 2021. The FDA has granted rare pediatric disease designation for CRN04777 for the treatment of congenital HI. In addition, the European Medicines Agency has granted orphan drug designation for CRN04777 for the treatment of congenital HI.
- CRN04894 is our investigational, oral, nonpeptide product candidate designed to antagonize ACTH, intended for the treatment of diseases caused by excess ACTH, including Cushing's disease and CAH. Cushing's disease results from a pituitary tumor that secretes excess ACTH which, in turn, causes the downstream synthesis and over-secretion of cortisol by the adrenal glands. Cortisol is the body's main stress hormone and excess amounts can cause significant increases in mortality and morbidity. CAH encompasses a set of disorders that are caused by genetic mutations that result in impaired cortisol synthesis. A lack of cortisol leads to a loss of feedback mechanisms and results in persistently high levels of ACTH, which, in turn, causes overstimulation of the adrenal cortex. The resulting adrenal hyperplasia and over-secretion of other steroids (particularly androgens) and steroid precursors can lead to a variety of effects from improper gonadal development to life-threatening dysregulation of mineralocorticoids. We are currently conducting a double-blind, randomized, placebo-controlled Phase 1 study of CRN04894 in healthy volunteers to assess the safety and tolerability of single and multiple doses of CRN04894. In addition, the study is designed to measure the effect of CRN04894 on suppression of cortisol, cortisol precursors, and adrenal androgens following exogenous ACTH stimulation. In August 2021, we announced preliminary data from the single ascending dose cohorts of the Phase 1 study. Single doses of CRN04894 were well-tolerated and demonstrated dose-dependent increases in CRN04894 plasma concentrations as well as reductions of both basal cortisol and

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elevated cortisol following an ACTH challenge. All adverse events reported through the single ascending dose cohorts were considered mild and there were no serious adverse events. We will proceed with the multiple ascending dose cohorts of the Phase 1 study and expect preliminary data in the second half of 2021.

Patients with many other debilitating endocrine diseases await new therapeutic options. We plan to continue our drug discovery efforts and leverage our expertise in the evaluation of additional conditions including hyperparathyroidism, nonfunctional pituitary adenomas and polycystic kidney disease, among other indications. All our product candidates have been discovered, characterized, and developed internally and are the subject of composition of matter patent applications, including issued U.S. patents covering paltusotine extending to 2037. We have retained worldwide rights to commercialize our product candidates and do not have any royalty obligations. Over time, we intend to sell our products, if approved, through our own commercial organization, which we believe can be of modest size to cover the relatively small number of specialty endocrinologists who treat patients with rare endocrine diseases and endocrine-related tumors.

We were founded by a team of scientists with a track record of drug discovery and development to create important new therapeutic options for patients with rare endocrine diseases. Prior to founding the company, our Chief Executive Officer, Scott Struthers, Ph.D., was Senior Director and Head of Endocrinology and Metabolism at Neurocrine Biosciences, Inc. There, Dr. Struthers and his fellow co-founders, Stephen Betz, Ph.D. and Frank Zhu, Ph.D., as well as our VP of Development Ajay Madan, Ph.D., D.A.B.T., held key leadership roles in the discovery and development of ORLISSA (elagolix), a nonpeptide product candidate designed for the treatment of endometriosis and uterine fibroids that received marketing approval from the FDA in July 2018. In addition, Dr. Madan held a key leadership role in the discovery and development of INGREZZA (valbenazine), which was approved by the FDA in 2017 for tardive dyskinesia. Our Chief Medical Officer, Alan Krasner, served as the Global Development Lead at Shire Pharmaceuticals for Natpara, the first recombinant human intact parathyroid hormone treatment for hypoparathyroidism.

We were incorporated under the laws of the state of Delaware on November 18, 2008. Our principal executive offices are located at 10222 Barnes Canyon Road, Bldg. #2, San Diego, California 92121, and our telephone number is (858) 450-6464.

RISK FACTORS

Investment in any securities offered pursuant to this prospectus and the applicable prospectus supplement involves risks. You should carefully consider the risk factors incorporated by reference to our most recent Annual Report on Form 10-K and any subsequent Quarterly Reports on Form 10-Q or Current Reports on Form 8-K we file after the date of this prospectus, and all other information contained or incorporated by reference into this prospectus, as updated by our subsequent filings under the Exchange Act, and the risk factors and other information contained in the applicable prospectus supplement and any applicable free writing prospectus before acquiring any of such securities. The occurrence of any of these risks might cause you to lose all or part of your investment in the offered securities.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and the documents incorporated by reference herein contain forward-looking statements within the meaning of Section 21E of the Exchange Act. All statements other than statements of historical facts contained in this prospectus and the documents incorporated by reference herein, including statements regarding our future results of operations and financial position, business strategy, prospective products, product approvals, research and development costs, timing and likelihood of success, plans and objectives of management for future operations and future results of anticipated products, are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. This prospectus and the documents incorporated by reference herein also contain estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

In some cases, you can identify forward-looking statements by terms such as “may,” “will,” “should,” “expect,” “plan,” “anticipate,” “could,” “intend,” “target,” “project,” “contemplates,” “believes,” “estimates,” “predicts,” “potential” or “continue” or the negative of these terms or other similar expressions. The forward-looking statements in this prospectus and the documents incorporated by reference herein are only predictions. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition and results of operations. These forward-looking statements speak only as of the date of this prospectus and are subject to a number of risks, uncertainties and assumptions, which we discuss in greater detail in the documents incorporated by reference herein, including under the heading “Risk Factors” and elsewhere in this prospectus. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Moreover, we operate in an evolving environment. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties. Given these risks and uncertainties, you should not place undue reliance on these forward-looking statements. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained in this prospectus or the documents incorporated by reference herein, whether as a result of any new information, future events, changed circumstances or otherwise. For all forward-looking statements, we claim the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995.

USE OF PROCEEDS

We intend to use the net proceeds from the sale of the securities as set forth in the applicable prospectus supplement. We will not receive any of the proceeds from the sale of common stock being offered by any of the selling securityholders.

DIVIDEND POLICY

We have never declared or paid any cash dividends on our capital stock. We intend to retain future earnings, if any, to finance the operation of our business and do not anticipate paying any cash dividends in the foreseeable future. Any future determination related to our dividend policy will be made at the discretion of our board of directors after considering our financial condition, results of operations, capital requirements, business prospects and other factors our board of directors deems relevant, and subject to the restrictions contained in any future financing instruments.

DESCRIPTION OF CAPITAL STOCK

The following description of our capital stock is not complete and may not contain all the information you should consider before investing in our capital stock. This description is summarized from, and qualified in its entirety by reference to, our amended and restated certificate of incorporation, which has been publicly filed with the SEC. See “Where You Can Find More Information; Incorporation by Reference.”

Our authorized capital stock consists of:

- 200,000,000 shares of common stock, \$0.001 par value; and
- 10,000,000 shares of preferred stock, \$0.001 par value.

Common Stock

As of August 3, 2021, there were 38,563,765 shares of our common stock outstanding and held of record by 10 stockholders. Under the terms of our amended and restated certificate of incorporation, holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders, including the election of directors, and do not have cumulative voting rights. Holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders, including the election of directors, and do not have cumulative voting rights. Accordingly, the holders of a majority of the outstanding shares of common stock entitled to vote in any election of directors can elect all of the directors standing for election, if they so choose, other than any directors that holders of any preferred stock we may issue may be entitled to elect. Subject to the supermajority votes for some matters, other matters shall be decided by the affirmative vote of our stockholders having a majority in voting power of the votes cast by the stockholders present or represented and voting on such matter. Our amended and restated certificate of incorporation and amended and restated bylaws also provide that our directors may be removed only for cause and only by the affirmative vote of the holders of at least two-thirds in voting power of the outstanding shares of capital stock entitled to vote thereon. In addition, the affirmative vote of the holders of at least two-thirds in voting power of the outstanding shares of capital stock entitled to vote thereon is required to amend or repeal, or to adopt any provision inconsistent with, several of the provisions of our amended and restated certificate of incorporation.

Subject to preferences that may be applicable to any then outstanding preferred stock, holders of common stock are entitled to receive ratably those dividends, if any, as may be declared by the board of directors out of legally available funds. In the event of our liquidation, dissolution or winding up, the holders of common stock will be entitled to share ratably in the assets legally available for distribution to stockholders after the payment of or provision for all of our debts and other liabilities, subject to the prior rights of any preferred stock then outstanding. Holders of common stock have no preemptive or conversion rights or other subscription rights and there are no redemption or sinking funds provisions applicable to the common stock. All outstanding shares of common stock are, and the common stock to be outstanding upon the closing of this offering will be, duly authorized, validly issued, fully paid and nonassessable. The rights, preferences and privileges of 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 and issue in the future.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Computershare Trust Company, N.A.

Preferred Stock

We currently have no outstanding shares of preferred stock. Under the terms of our amended and restated certificate of incorporation, our board of directors has the authority, without further action by our stockholders, to issue up to 10,000,000 shares of preferred stock in one or more series, to establish from time to time the number

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of shares to be included in each such series, to fix the dividend, voting and other rights, preferences and privileges of the shares of each wholly unissued series and any qualifications, limitations or restrictions thereon, and to increase or decrease the number of shares of any such series, but not below the number of shares of such series then outstanding. Our board of directors may authorize the issuance of preferred stock with voting or conversion rights that could adversely affect the voting power or other rights of the holders of the common stock. The issuance of preferred stock, while providing flexibility in connection with possible acquisitions and other corporate purposes, could, among other things, have the effect of delaying, deferring or preventing a change in our control and may adversely affect the market price of the common stock and the voting and other rights of the holders of common stock. We have no current plans to issue any shares of preferred stock.

Prior to the issuance of shares of each series, the board of directors is required by the General Corporation Law of the State of Delaware, or the DGCL, and our amended and restated certificate of incorporation to adopt resolutions and file a certificate of designation with the Secretary of State of the State of Delaware. The certificate of designation fixes for each class or series the designations, powers, preferences, rights, qualifications, limitations and restrictions, including dividend rights, conversion rights, redemption privileges and liquidation preferences.

All shares of preferred stock offered by this prospectus will, when issued, be fully paid and nonassessable and will not have any preemptive or similar rights. Our board of directors may authorize the issuance of preferred stock with voting or conversion rights that could adversely affect the voting power or other rights of the holders of the common stock. The issuance of preferred stock, while providing flexibility in connection with possible acquisitions and other corporate purposes, could, among other things, have the effect of delaying, deferring or preventing a change in our control and may adversely affect the market price of the common stock and the voting and other rights of the holders of common stock.

We will describe in a prospectus supplement relating to the class or series of preferred stock being offered the following terms:

- the title and stated value of the preferred stock;
- the number of shares of the preferred stock offered, the liquidation preference per share and the offering price of the preferred stock;
- the dividend rate(s), period(s) or payment date(s) or method(s) of calculation applicable to the preferred stock;
- whether dividends are cumulative or non-cumulative and, if cumulative, the date from which dividends on the preferred stock will accumulate;
- the procedures for any auction and remarketing, if any, for the preferred stock;
- the provisions for a sinking fund, if any, for the preferred stock;
- the provision for redemption, if applicable, of the preferred stock;
- any listing of the preferred stock on any securities exchange;
- the terms and conditions, if applicable, upon which the preferred stock will be convertible into common stock, including the conversion price or manner of calculation and conversion period;
- voting rights, if any, of the preferred stock;
- a discussion of any material or special U.S. federal income tax considerations applicable to the preferred stock;
- the relative ranking and preferences of the preferred stock as to dividend rights and rights upon the liquidation, dissolution or winding up of our affairs;

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- any limitations on issuance of any class or series of preferred stock ranking senior to or on a parity with the class or series of preferred stock as to dividend rights and rights upon liquidation, dissolution or winding up of our affairs; and
- any other specific terms, preferences, rights, limitations or restrictions of the preferred stock.

Unless we specify otherwise in the applicable prospectus supplement, the preferred stock will rank, relating to dividends and upon our liquidation, dissolution or winding up:

- senior to all classes or series of our common stock and to all of our equity securities ranking junior to the preferred stock;
- on a parity with all of our equity securities the terms of which specifically provide that the equity securities rank on a parity with the preferred stock; and
- junior to all of our equity securities the terms of which specifically provide that the equity securities rank senior to the preferred stock.

The term equity securities does not include convertible debt securities.

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

Some provisions of Delaware law, our amended and restated certificate of incorporation and our amended and restated bylaws contain provisions that could make the following transactions more difficult: an acquisition of us by means of a tender offer; an acquisition of us by means of a proxy contest or otherwise; or the removal of our incumbent officers and directors. It is possible that these provisions could make it more difficult to accomplish or could deter transactions that stockholders may otherwise consider to be in their best interest or in our best interests, including transactions which provide for payment of a premium over the market price for our shares.

These provisions, summarized below, are intended to discourage coercive takeover practices and inadequate takeover bids. These provisions are also designed to encourage persons seeking to acquire control of us to first negotiate with our board of directors. We believe that the benefits of the increased protection of our potential ability to negotiate with the proponent of an unfriendly or unsolicited proposal to acquire or restructure us outweigh the disadvantages of discouraging these proposals because negotiation of these proposals could result in an improvement of their terms.

Undesignated Preferred Stock

The ability of our board of directors, without action by the stockholders, to issue up to 10,000,000 shares of undesignated preferred stock with voting or other rights or preferences as designated by our board of directors could impede the success of any attempt to change control of us. These and other provisions may have the effect of deferring hostile takeovers or delaying changes in control or management of our company.

Stockholder Meetings

Our amended and restated bylaws provide that a special meeting of stockholders may be called only by our chairman of the board of directors, chief executive officer or president, or by a resolution adopted by a majority of our board 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 to be brought before a stockholder meeting and the nomination of candidates for election as directors, other than nominations made by or at the direction of the board of directors or a committee of the board of directors.

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Elimination of Stockholder Action by Written Consent

Our amended and restated certificate of incorporation and amended and restated bylaws eliminate the right of stockholders to act by written consent without a meeting.

Staggered Board of Directors

Our board of directors is divided into three classes. The directors in each class will serve for a three-year term, one class being elected each year by our stockholders. This system of electing and removing directors may tend to discourage a third party from making a tender offer or otherwise attempting to obtain control of us, because it generally makes it more difficult for stockholders to replace a majority of the directors.

Removal of Directors

Our amended and restated certificate of incorporation provides that no member of our board of directors may be removed from office by our stockholders except for cause and, in addition to any other vote required by law, upon the approval of not less than two thirds of the total voting power of all of our outstanding voting stock then entitled to vote in the election of directors.

Stockholders Not Entitled to Cumulative Voting

Our amended and restated certificate of incorporation does not permit stockholders to cumulate their votes in the election of directors. Accordingly, the holders of a majority of the outstanding shares of our common stock entitled to vote in any election of directors can elect all of the directors standing for election, if they choose, other than any directors that holders of our preferred stock may be entitled to elect.

Delaware Anti-Takeover Statute

We are subject to Section 203 of the Delaware General Corporation Law, which prohibits persons deemed to be “interested stockholders” from engaging in a “business combination” with a publicly held Delaware corporation for three years following the date these persons become interested stockholders unless the business combination is, or the transaction in which the person became an interested stockholder was, approved in a prescribed manner or another prescribed exception applies. Generally, 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 voting stock. Generally, a “business combination” includes a merger, asset or stock sale, or other transaction resulting in a financial benefit to the interested stockholder. The existence of this provision may have an anti-takeover effect with respect to transactions not approved in advance by the board of directors.

Choice of Forum

Our amended and restated certificate of incorporation provides that, unless we consent in writing to the selection of an alternative form, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for: (1) any derivative action or proceeding brought on our behalf; (2) any action asserting a claim of breach of a fiduciary duty or other wrongdoing by any of our directors, officers, employees or agents to us or our stockholders, creditors or other constituents; (3) any action asserting a claim against us arising pursuant to any provision of the General Corporation Law of the State of Delaware or our amended and restated certificate of incorporation or amended and restated bylaws; (4) any action to interpret, apply, enforce or determine the validity of our certificate of incorporation or bylaws; or (5) any action asserting a claim governed by the internal affairs doctrine. This exclusive forum provision would not apply to suits brought to enforce any liability or duty created by the Securities Act or the Exchange Act or any other claim for which the federal courts have exclusive jurisdiction. To the extent that any such claims may be based upon federal law claims, Section 27 of the Exchange Act creates exclusive federal jurisdiction over all suits brought to enforce any duty or liability created

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by the Exchange Act or the rules and regulations thereunder. Furthermore, Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all suits brought to enforce any duty or liability created by the Securities Act or the rules and regulations thereunder. Our amended and restated bylaws provide that unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States shall be the exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act. Our amended and restated certificate of incorporation also provides that any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock will be deemed to have notice of and to have consented to this choice of forum provision. It is possible that a court of law could rule that the choice of forum provisions contained in our restated certificate of incorporation or amended and restated bylaws are inapplicable or unenforceable if they are challenged in a proceeding or otherwise.

Amendment of Charter Provisions

The amendment of any of the above provisions, except for the provision making it possible for our board of directors to issue preferred stock, would require approval by holders of at least two thirds of the total voting power of all of our outstanding voting stock.

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

DESCRIPTION OF DEBT SECURITIES

The following description, together with the additional information we include in any applicable prospectus supplement or free writing prospectus, summarizes certain general terms and provisions of the debt securities that we may offer under this prospectus. When we offer to sell a particular series of debt securities, we will describe the specific terms of the series in a supplement to this prospectus. We will also indicate in the supplement to what extent the general terms and provisions described in this prospectus apply to a particular series of debt securities. To the extent the information contained in the prospectus supplement differs from this summary description, you should rely on the information in the prospectus supplement.

We may issue debt securities either separately, or together with, or upon the conversion or exercise of or in exchange for, other securities described in this prospectus. Debt securities may be our senior, senior subordinated or subordinated obligations and, unless otherwise specified in a supplement to this prospectus, the debt securities will be our direct, unsecured obligations and may be issued in one or more series.

The debt securities will be issued under an indenture between us and a trustee named in the prospectus supplement. We have summarized select portions of the indenture below. The summary is not complete. The form of the indenture has been filed as an exhibit to the registration statement and you should read the indenture for provisions that may be important to you. In the summary below, we have included references to the section numbers of the indenture so that you can easily locate these provisions. Capitalized terms used in the summary and not defined herein have the meanings specified in the indenture.

General

The terms of each series of debt securities will be established by or pursuant to a resolution of our board of directors and set forth or determined in the manner provided in a resolution of our board of directors, in an officer's certificate or by a supplemental indenture. (Section 2.2) The particular terms of each series of debt securities will be described in a prospectus supplement relating to such series (including any pricing supplement or term sheet).

We can issue an unlimited amount of debt securities under the indenture that may be in one or more series with the same or various maturities, at par, at a premium, or at a discount. (Section 2.1) We will set forth in a prospectus supplement (including any pricing supplement or term sheet) relating to any series of debt securities being offered, the aggregate principal amount and the following terms of the debt securities, if applicable:

- the title and ranking of the debt securities (including the terms of any subordination provisions);
- the price or prices (expressed as a percentage of the principal amount) at which we will sell the debt securities;
- any limit on the aggregate principal amount of the debt securities;
- the date or dates on which the principal on a particular series of debt securities is payable;
- the rate or rates (which may be fixed or variable) per annum or the method used to determine the rate or rates (including any commodity, commodity index, stock exchange index or financial index) at which the debt securities will bear interest, the date or dates from which interest will accrue, the date or dates on which interest will commence and be payable and any regular record date for the interest payable on any interest payment date;
- the place or places where principal of, and interest, if any, on the debt securities will be payable (and the method of such payment), where the debt securities of such series may be surrendered for registration of transfer or exchange, and where notices and demands to us in respect of the debt securities may be delivered;
- the period or periods within which, the price or prices at which and the terms and conditions upon which we may redeem the debt securities;

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- any obligation we have to redeem or purchase the debt securities pursuant to any sinking fund or analogous provisions or at the option of a holder of debt securities and the period or periods within which, the price or prices at which and the terms and conditions upon which the debt securities of a particular series shall be redeemed or purchased, in whole or in part, pursuant to such obligation;
- the dates on which and the price or prices at which we will repurchase debt securities at the option of the holders of debt securities and other detailed terms and provisions of these repurchase obligations;
- the denominations in which the debt securities will be issued, if other than denominations of \$1,000 and any integral multiple thereof;
- whether the debt securities will be issued in the form of certificated debt securities or global debt securities;
- the portion of principal amount of the debt securities payable upon declaration of acceleration of the maturity date, if other than the principal amount;
- the currency of denomination of the debt securities, which may be U.S. dollars or any foreign currency, and if such currency of denomination is a composite currency, the agency or organization, if any, responsible for overseeing such composite currency;
- the designation of the currency, currencies or currency units in which payment of principal of, and premium and interest on, the debt securities will be made;
- if payments of principal of, or premium or interest on, the debt securities will be made in one or more currencies or currency units other than that or those in which the debt securities are denominated, the manner in which the exchange rate with respect to these payments will be determined;
- the manner in which the amounts of payment of principal of, and premium, if any, and interest on, the debt securities will be determined, if these amounts may be determined by reference to an index based on a currency or currencies or by reference to a commodity, commodity index, stock exchange index or financial index;
- any provisions relating to any security provided for the debt securities;
- any addition to, deletion of or change in the Events of Default described in this prospectus or in the indenture with respect to the debt securities and any change in the acceleration provisions described in this prospectus or in the indenture with respect to the debt securities;
- any addition to, deletion of or change in the covenants described in this prospectus or in the indenture with respect to the debt securities;
- any depositaries, interest rate calculation agents, exchange rate calculation agents or other agents with respect to the debt securities;
- the provisions, if any, relating to conversion or exchange of any debt securities of such series, including if applicable, the conversion or exchange price and period, provisions as to whether conversion or exchange will be mandatory, the events requiring an adjustment of the conversion or exchange price and provisions affecting conversion or exchange;
- any other terms of the debt securities, which may supplement, modify or delete any provision of the indenture as it applies to that series, including any terms that may be required under applicable law or regulations or advisable in connection with the marketing of the securities; and
- whether any of our direct or indirect subsidiaries will guarantee the debt securities of that series, including the terms of subordination, if any, of such guarantees. (Section 2.2)

We may issue debt securities that provide for an amount less than their stated principal amount to be due and payable upon declaration of acceleration of their maturity pursuant to the terms of the indenture. We will provide you with information on the federal income tax considerations and other special considerations applicable to any of these debt securities in the applicable prospectus supplement.

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If we denominate the purchase price of any of the debt securities in a foreign currency or currencies or a foreign currency unit or units, or if the principal of, and premium, if any, and interest on, any series of debt securities is payable in a foreign currency or currencies or a foreign currency unit or units, we will provide you with information on the restrictions, elections, general tax considerations, specific terms and other information with respect to that issue of debt securities and such foreign currency or currencies or foreign currency unit or units in the applicable prospectus supplement.

Transfer and Exchange

Each debt security will be represented by either one or more global securities registered in the name of The Depository Trust Company (DTC or the Depository) or a nominee of the Depository (we will refer to any debt security represented by a global debt security as a “book-entry debt security”), or a certificate issued in definitive registered form (we will refer to any debt security represented by a certificated security as a “certificated debt security”) as set forth in the applicable prospectus supplement. Except as set forth under the heading “Global Debt Securities and Book-Entry System” below, book-entry debt securities will not be issuable in certificated form.

Certificated Debt Securities. You may transfer or exchange certificated debt securities at any office we maintain for this purpose in accordance with the terms of the indenture. (Section 2.4) No service charge will be made for any transfer or exchange of certificated debt securities, but we may require payment of a sum sufficient to cover any tax or other governmental charge payable in connection with a transfer or exchange. (Section 2.7)

You may effect the transfer of certificated debt securities and the right to receive the principal of, premium and interest on certificated debt securities only by surrendering the certificate representing those certificated debt securities and either reissuance by us or the trustee of the certificate to the new holder or the issuance by us or the trustee of a new certificate to the new holder.

Global Debt Securities and Book-Entry System. Each global debt security representing book-entry debt securities will be deposited with, or on behalf of, the Depository, and registered in the name of the Depository or a nominee of the Depository. Please see the section entitled “Global Securities” for more information.

Covenants

We will set forth in the applicable prospectus supplement any restrictive covenants applicable to any issue of debt securities. (Article IV)

No Protection in the Event of a Change of Control

Unless we state otherwise in the applicable prospectus supplement, the debt securities will not contain any provisions that may afford holders of the debt securities protection in the event we have a change in control or in the event of a highly leveraged transaction (whether or not such transaction results in a change in control) that could adversely affect holders of debt securities.

Consolidation, Merger and Sale of Assets

We may not consolidate with or merge with or into, or convey, transfer or lease all or substantially all of our properties and assets to, any person (a “successor person”) unless:

- we are the surviving corporation or the successor person (if other than Crinetics) is a corporation organized and validly existing under the laws of any U.S. domestic jurisdiction and expressly assumes our obligations on the debt securities and under the indenture;
- immediately after giving effect to the transaction, no Default or Event of Default, shall have occurred and be continuing; and

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- certain other conditions are met.

Notwithstanding the above, any of our subsidiaries may consolidate with, merge into or transfer all or part of its properties to us. (Section 5.1)

Events of Default

“Event of Default” means with respect to any series of debt securities, any of the following:

- default in the payment of any interest upon any debt security of that series when it becomes due and payable, and continuance of such default for a period of 30 days (unless the entire amount of the payment is deposited by us with the trustee or with a paying agent prior to the expiration of the 30-day period);
- default in the payment of principal of any debt security of that series at its maturity;
- default in the performance or breach of any other covenant or warranty by us in the indenture or any debt security (other than a covenant or warranty that has been included in the indenture solely for the benefit of a series of debt securities other than that series), which default continues uncured for a period of 60 days after we receive written notice from the trustee or Crinetics and the trustee receive written notice from the holders of not less than 25% in principal amount of the outstanding debt securities of that series as provided in the indenture;
- certain voluntary or involuntary events of bankruptcy, insolvency or reorganization of Crinetics; or
- any other Event of Default provided with respect to debt securities of that series that is described in the applicable prospectus supplement. (Section 6.1)

No Event of Default with respect to a particular series of debt securities (except as to certain events of bankruptcy, insolvency or reorganization) necessarily constitutes an Event of Default with respect to any other series of debt securities. (Section 6.1) The occurrence of certain Events of Default or an acceleration under the indenture may constitute an event of default under certain indebtedness of ours or our subsidiaries outstanding from time to time.

We will provide the trustee written notice of any Default or Event of Default within 30 days of becoming aware of the occurrence of such Default or Event of Default, which notice will describe in reasonable detail the status of such Default or Event of Default and what action we are taking or propose to take in respect thereof. (Section 6.1)

If an Event of Default with respect to debt securities of any series at the time outstanding occurs and is continuing, then the trustee or the holders of not less than 25% in principal amount of the outstanding debt securities of that series may, by a notice in writing to us (and to the trustee if given by the holders), declare to be due and payable immediately the principal of (or, if the debt securities of that series are discount securities, that portion of the principal amount as may be specified in the terms of that series) and accrued and unpaid interest, if any, on all debt securities of that series. In the case of an Event of Default resulting from certain events of bankruptcy, insolvency or reorganization, the principal (or such specified amount) of and accrued and unpaid interest, if any, on all outstanding debt securities will become and be immediately due and payable without any declaration or other act on the part of the trustee or any holder of outstanding debt securities. At any time after a declaration of acceleration with respect to debt securities of any series has been made, but before a judgment or decree for payment of the money due has been obtained by the trustee, the holders of a majority in principal amount of the outstanding debt securities of that series may rescind and annul the acceleration if all Events of Default, other than the non-payment of accelerated principal and interest, if any, with respect to debt securities of that series, have been cured or waived as provided in the indenture. (Section 6.2) We refer you to the prospectus supplement relating to any series of debt securities that are discount securities for the particular provisions relating to acceleration of a portion of the principal amount of such discount securities upon the occurrence of an Event of Default.

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The indenture provides that the trustee may refuse to perform any duty or exercise any of its rights or powers under the indenture, unless the trustee receives indemnity satisfactory to it against any cost, liability or expense that might be incurred by it in performing such duty or exercising such right or power. (Section 7.1(e)) Subject to certain rights of the trustee, 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. (Section 6.12)

No holder of any debt security of any series will have any right to institute any proceeding, judicial or otherwise, with respect to the indenture or for the appointment of a receiver or trustee, or for any remedy under the indenture, unless:

- that holder has previously given to the trustee written notice of a continuing Event of Default with respect to debt securities of that series; and
- the holders of not less than 25% in principal amount of the outstanding debt securities of that series have made written request, and offered indemnity or security satisfactory to the trustee, to the trustee to institute the proceeding as trustee, and the trustee has not received from the holders of not less than a majority in principal amount of the outstanding debt securities of that series a direction inconsistent with that request and has failed to institute the proceeding within 60 days. (Section 6.7)

Notwithstanding any other provision in the indenture, the holder of any debt security will have an absolute and unconditional right to receive payment of the principal of, and premium and any interest on, that debt security on or after the due dates expressed in that debt security and to institute suit for the enforcement of payment. (Section 6.8)

The indenture requires us, within 120 days after the end of our fiscal year, to furnish to the trustee a statement as to compliance with the indenture. (Section 4.3) If a Default or Event of Default occurs and is continuing with respect to the securities of any series and if it is known to a responsible officer of the trustee, the trustee shall mail to each holder of the securities of that series notice of a Default or Event of Default within 90 days after it occurs or, if later, after a responsible officer of the trustee has knowledge of such Default or Event of Default. The indenture provides that the trustee may withhold notice to the holders of debt securities of any series of any Default or Event of Default (except in payment on any debt securities of that series) with respect to debt securities of that series if the trustee determines in good faith that withholding notice is in the interest of the holders of those debt securities. (Section 7.5)

Modification and Waiver

We and the trustee may modify, amend or supplement the indenture or the debt securities of any series without the consent of any holder of any debt security:

- to cure any ambiguity, defect or inconsistency;
- to comply with covenants in the indenture described above under the heading "Consolidation, Merger and Sale of Assets;"
- to provide for uncertificated securities in addition to or in place of certificated securities;
- to add guarantees with respect to debt securities of any series or secure debt securities of any series;
- to surrender any of our rights or powers under the indenture;
- to add covenants or Events of Default for the benefit of the holders of debt securities of any series;
- to comply with the applicable procedures of the applicable depositary;
- to make any change that does not adversely affect the rights of any holder of debt securities;

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- to provide for the issuance of and establish the form and terms and conditions of debt securities of any series as permitted by the indenture;
- to effect the appointment of a successor trustee with respect to the debt securities of any series and to add to or change any of the provisions of the indenture to provide for or facilitate administration by more than one trustee; or
- to comply with requirements of the SEC in order to effect or maintain the qualification of the indenture under the Trust Indenture Act. (Section 9.1)

We may also modify and amend the indenture with the consent of the holders of at least a majority in principal amount of the outstanding debt securities of each series affected by the modifications or amendments. We may not make any modification or amendment without the consent of the holders of each affected debt security then outstanding if that amendment will:

- reduce the amount of debt securities whose holders must consent to an amendment, supplement or waiver;
- reduce the rate of or extend the time for payment of interest (including default interest) on any debt security;
- reduce the principal of or premium on or change the fixed maturity of any debt security or reduce the amount of, or postpone the date fixed for, the payment of any sinking fund or analogous obligation with respect to any series of debt securities;
- reduce the principal amount of discount securities payable upon acceleration of maturity;
- waive a Default or Event of Default in the payment of the principal of, or premium or interest on, any debt security (except a rescission of acceleration of the debt securities of any series by the holders of at least a majority in aggregate principal amount of the then outstanding debt securities of that series and a waiver of the payment default that resulted from such acceleration);
- make the principal of, or premium or interest on, any debt security payable in currency other than that stated in the debt security;
- make any change to certain provisions of the indenture relating to, among other things, the right of holders of debt securities to receive payment of the principal of, and premium and interest on, those debt securities and to institute suit for the enforcement of any such payment and to waivers or amendments; or
- waive a redemption payment with respect to any debt security. (Section 9.3)

Except for certain specified provisions, the holders of at least a majority in principal amount of the outstanding debt securities of any series may on behalf of the holders of all debt securities of that series waive our compliance with provisions of the indenture. (Section 9.2) The holders of a majority in principal amount of the outstanding debt securities of any series may on behalf of the holders of all the debt securities of such series waive any past default under the indenture with respect to that series and its consequences, except a default in the payment of the principal of, or any interest on, any debt security of that series; provided, however, that the holders of a majority in principal amount of the outstanding debt securities of any series may rescind an acceleration and its consequences, including any related payment default that resulted from the acceleration. (Section 6.13)

Defeasance of Debt Securities and Certain Covenants in Certain Circumstances

Legal Defeasance. The indenture provides that, unless otherwise provided by the terms of the applicable series of debt securities, we may be discharged from any and all obligations in respect of the debt securities of any series (subject to certain exceptions). We will be so discharged upon the deposit with the trustee, in trust, of money and/or U.S. government obligations or, in the case of debt securities denominated in a single currency

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other than U.S. dollars, government obligations of the government that issued or caused to be issued such currency, that, through the payment of interest and principal in accordance with their terms, will provide money or U.S. government obligations in an amount sufficient in the opinion of a nationally recognized firm of independent public accountants or investment bank to pay and discharge each installment of principal of, premium and interest on, and any mandatory sinking fund payments in respect of, the debt securities of that series on the stated maturity of those payments in accordance with the terms of the indenture and those debt securities.

This discharge may occur only if, among other things, we have delivered to the trustee an opinion of counsel stating that we have received from, or there has been published by, the U.S. Internal Revenue Service a ruling or, since the date of execution of the indenture, there has been a change in the applicable U.S. federal income tax law, in either case to the effect that, and based thereon such opinion shall confirm that, the holders of the debt securities of that series will not recognize income, gain or loss for U.S. federal income tax purposes as a result of the deposit, defeasance and discharge and will be subject to U.S. federal income tax on the same amounts and in the same manner and at the same times as would have been the case if the deposit, defeasance and discharge had not occurred. (Section 8.3)

Defeasance of Certain Covenants. The indenture provides that, unless otherwise provided by the terms of the applicable series of debt securities, upon compliance with certain conditions:

- we may omit to comply with the covenant described under the heading “Consolidation, Merger and Sale of Assets” and certain other covenants set forth in the indenture, as well as any additional covenants that may be set forth in the applicable prospectus supplement; and
- any omission to comply with those covenants will not constitute a Default or an Event of Default with respect to the debt securities of that series (“covenant defeasance”).

The conditions include:

- depositing with the trustee money and/or U.S. government obligations or, in the case of debt securities denominated in a single currency other than U.S. dollars, government obligations of the government that issued or caused to be issued such currency, that, through the payment of interest and principal in accordance with their terms, will provide money in an amount sufficient in the opinion of a nationally recognized firm of independent public accountants or investment bank to pay and discharge each installment of principal of, premium and interest on, and any mandatory sinking fund payments in respect of, the debt securities of that series on the stated maturity of those payments in accordance with the terms of the indenture and those debt securities; and
- delivering to the trustee an opinion of counsel to the effect that the holders of the debt securities of that series will not recognize income, gain or loss for U.S. federal income tax purposes as a result of the deposit and related covenant defeasance and will be subject to U.S. federal income tax on the same amounts and in the same manner and at the same times as would have been the case if the deposit and related covenant defeasance had not occurred. (Section 8.4)

No Personal Liability of Directors, Officers, Employees or Securityholders

None of our past, present or future directors, officers, employees or securityholders, as such, will have any liability for any of our obligations under the debt securities or the indenture or for any claim based on, or in respect or by reason of, such obligations or their creation. By accepting a debt security, each holder waives and releases all such liability. This waiver and release is part of the consideration for the issue of the debt securities. However, this waiver and release may not be effective to waive liabilities under U.S. federal securities laws, and it is the view of the SEC that such a waiver is against public policy.

Governing Law

The indenture and the debt securities, including any claim or controversy arising out of or relating to the indenture or the debt securities, will be governed by the laws of the State of New York.

The indenture will provide that we, the trustee and the holders of the debt securities (by their acceptance of the debt securities) irrevocably waive, to the fullest extent permitted by applicable law, any and all right to trial by jury in any legal proceeding arising out of or relating to the indenture, the debt securities or the transactions contemplated thereby.

The indenture will provide that any legal suit, action or proceeding arising out of or based upon the indenture or the transactions contemplated thereby may be instituted in the federal courts of the United States of America located in the City of New York or the courts of the State of New York in each case located in the City of New York, and we, the trustee and the holder of the debt securities (by their acceptance of the debt securities) irrevocably submit to the non-exclusive jurisdiction of such courts in any such suit, action or proceeding. The indenture will further provide that service of any process, summons, notice or document by mail (to the extent allowed under any applicable statute or rule of court) to such party's address set forth in the indenture will be effective service of process for any suit, action or other proceeding brought in any such court. The indenture will further provide that we, the trustee and the holders of the debt securities (by their acceptance of the debt securities) irrevocably and unconditionally waive any objection to the laying of venue of any suit, action or other proceeding in the courts specified above and irrevocably and unconditionally waive and agree not to plead or claim any such suit, action or other proceeding has been brought in an inconvenient forum. (Section 10.10)

DESCRIPTION OF OTHER SECURITIES

We will set forth in the applicable prospectus supplement a description of any warrants or units issued by us that may be offered and sold pursuant to this prospectus.

GLOBAL SECURITIES

Book-Entry, Delivery and Form

Unless we indicate differently in any applicable prospectus supplement or free writing prospectus, the securities initially will be issued in book-entry form and represented by one or more global notes or global securities, or, collectively, global securities. The global securities will be deposited with, or on behalf of DTC and registered in the name of Cede & Co., the nominee of DTC. Unless and until it is exchanged for individual certificates evidencing securities under the limited circumstances described below, a global security may not be transferred except as a whole by the depository to its nominee or by the nominee to the depository, or by the depository or its nominee to a successor depository or to a nominee of the successor depository.

DTC has advised us that it is:

- a limited-purpose trust company organized under the New York Banking Law;
- a “banking organization” within the meaning of the New York Banking Law;
- a member of the Federal Reserve System;
- a “clearing corporation” within the meaning of the New York Uniform Commercial Code; and
- a “clearing agency” registered pursuant to the provisions of Section 17A of the Exchange Act.

DTC holds securities that its participants deposit with DTC. DTC also facilitates the settlement among its participants of securities transactions, such as transfers and pledges, in deposited securities through electronic computerized book-entry changes in participants’ accounts, thereby eliminating the need for physical movement of securities certificates. “Direct participants” in DTC include securities brokers and dealers, including underwriters, banks, trust companies, clearing corporations and other organizations. DTC is a wholly-owned subsidiary of The Depository Trust & Clearing Corporation, or DTCC. DTCC is the holding company for DTC, National Securities Clearing Corporation and Fixed Income Clearing Corporation, all of which are registered clearing agencies. DTCC is owned by the users of its regulated subsidiaries. Access to the DTC system is also available to others, which we sometimes refer to as indirect participants, that clear through or maintain a custodial relationship with a direct participant, either directly or indirectly. The rules applicable to DTC and its participants are on file with the SEC.

Purchases of securities under the DTC system must be made by or through direct participants, which will receive a credit for the securities on DTC’s records. The ownership interest of the actual purchaser of a security, which we sometimes refer to as a beneficial owner, is in turn recorded on the direct and indirect participants’ records. Beneficial owners of securities will not receive written confirmation from DTC of their purchases. However, beneficial owners are expected to receive written confirmations providing details of their transactions, as well as periodic statements of their holdings, from the direct or indirect participants through which they purchased securities. Transfers of ownership interests in global securities are to be accomplished by entries made on the books of participants acting on behalf of beneficial owners. Beneficial owners will not receive certificates representing their ownership interests in the global securities, except under the limited circumstances described below.

To facilitate subsequent transfers, all global securities deposited by direct participants with DTC will be registered in the name of DTC’s partnership nominee, Cede & Co., or such other name as may be requested by an authorized representative of DTC. The deposit of securities with DTC and their registration in the name of Cede & Co. or such other nominee will not change the beneficial ownership of the securities. DTC has no knowledge of the actual beneficial owners of the securities. DTC’s records reflect only the identity of the direct participants to whose accounts the securities are credited, which may or may not be the beneficial owners. The participants are responsible for keeping account of their holdings on behalf of their customers.

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So long as the securities are in book-entry form, you will receive payments and may transfer securities only through the facilities of the depositary and its direct and indirect participants. We will maintain an office or agency in the location specified in the prospectus supplement for the applicable securities, where notices and demands in respect of the securities and the indenture may be delivered to us and where certificated securities may be surrendered for payment, registration of transfer or exchange.

Conveyance of notices and other communications by DTC to direct participants, by direct participants to indirect participants and by direct participants and indirect participants to beneficial owners will be governed by arrangements among them, subject to any legal requirements in effect from time to time.

Redemption notices will be sent to DTC. If less than all of the securities of a particular series are being redeemed, DTC's practice is to determine by lot the amount of the interest of each direct participant in the securities of such series to be redeemed.

Neither DTC nor Cede & Co. (or such other DTC nominee) will consent or vote with respect to the securities. Under its usual procedures, DTC will mail an omnibus proxy to us as soon as possible after the record date. The omnibus proxy assigns the consenting or voting rights of Cede & Co. to those direct participants to whose accounts the securities of such series are credited on the record date, identified in a listing attached to the omnibus proxy.

So long as securities are in book-entry form, we will make payments on those securities to the depositary or its nominee, as the registered owner of such securities, by wire transfer of immediately available funds. If securities are issued in definitive certificated form under the limited circumstances described below and unless if otherwise provided in the description of the applicable securities herein or in the applicable prospectus supplement, we will have the option of making payments by check mailed to the addresses of the persons entitled to payment or by wire transfer to bank accounts in the United States designated in writing to the applicable trustee or other designated party at least 15 days before the applicable payment date by the persons entitled to payment, unless a shorter period is satisfactory to the applicable trustee or other designated party.

Redemption proceeds, distributions and dividend payments on the securities will be made to Cede & Co., or such other nominee as may be requested by an authorized representative of DTC. DTC's practice is to credit direct participants' accounts upon DTC's receipt of funds and corresponding detail information from us on the payment date in accordance with their respective holdings shown on DTC records. Payments by participants to beneficial owners will be governed by standing instructions and customary practices, as is the case with securities held for the account of customers in bearer form or registered in "street name." Those payments will be the responsibility of participants and not of DTC or us, subject to any statutory or regulatory requirements in effect from time to time. Payment of redemption proceeds, distributions and dividend payments to Cede & Co., or such other nominee as may be requested by an authorized representative of DTC, is our responsibility; disbursement of payments to direct participants is the responsibility of DTC; and disbursement of payments to the beneficial owners is the responsibility of direct and indirect participants.

Except under the limited circumstances described below, purchasers of securities will not be entitled to have securities registered in their names and will not receive physical delivery of securities. Accordingly, each beneficial owner must rely on the procedures of DTC and its participants to exercise any rights under the securities and the indenture.

The laws of some jurisdictions may require that some purchasers of securities take physical delivery of securities in definitive form. Those laws may impair the ability to transfer or pledge beneficial interests in securities.

DTC may discontinue providing its services as securities depositary with respect to the securities at any time by giving reasonable notice to us. Under such circumstances, in the event that a successor depositary is not obtained, securities certificates are required to be printed and delivered.

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As noted above, beneficial owners of a particular series of securities generally will not receive certificates representing their ownership interests in those securities. However, if:

- DTC notifies us that it is unwilling or unable to continue as a depository for the global security or securities representing such series of securities or if DTC ceases to be a clearing agency registered under the Exchange Act at a time when it is required to be registered and a successor depository is not appointed within 90 days of the notification to us or of our becoming aware of DTC's ceasing to be so registered, as the case may be;
- we determine, in our sole discretion, not to have such securities represented by one or more global securities; or
- an Event of Default has occurred and is continuing with respect to such series of securities,

we will prepare and deliver certificates for such securities in exchange for beneficial interests in the global securities. Any beneficial interest in a global security that is exchangeable under the circumstances described in the preceding sentence will be exchangeable for securities in definitive certificated form registered in the names that the depository directs. It is expected that these directions will be based upon directions received by the depository from its participants with respect to ownership of beneficial interests in the global securities.

Euroclear and Clearstream

If so provided in the applicable prospectus supplement, you may hold interests in a global security through Clearstream Banking S.A., which we refer to as "Clearstream," or Euroclear Bank S.A./N.V., as operator of the Euroclear System, which we refer to as "Euroclear," either directly if you are a participant in Clearstream or Euroclear or indirectly through organizations which are participants in Clearstream or Euroclear. Clearstream and Euroclear will hold interests on behalf of their respective participants through customers' securities accounts in the names of Clearstream and Euroclear, respectively, on the books of their respective U.S. depositories, which in turn will hold such interests in customers' securities accounts in such depositories' names on DTC's books.

Clearstream and Euroclear are securities clearance systems in Europe. Clearstream and Euroclear hold securities for their respective participating organizations and facilitate the clearance and settlement of securities transactions between those participants through electronic book-entry changes in their accounts, thereby eliminating the need for physical movement of certificates.

Payments, deliveries, transfers, exchanges, notices and other matters relating to beneficial interests in global securities owned through Euroclear or Clearstream must comply with the rules and procedures of those systems. Transactions between participants in Euroclear or Clearstream, on one hand, and other participants in DTC, on the other hand, are also subject to DTC's rules and procedures.

Investors will be able to make and receive through Euroclear and Clearstream payments, deliveries, transfers and other transactions involving any beneficial interests in global securities held through those systems only on days when those systems are open for business. Those systems may not be open for business on days when banks, brokers and other institutions are open for business in the United States.

Cross-market transfers between participants in DTC, on the one hand, and participants in Euroclear or Clearstream, on the other hand, will be effected through DTC in accordance with the DTC's rules on behalf of Euroclear or Clearstream, as the case may be, by their respective U.S. depositories; however, such cross-market transactions will require delivery of instructions to Euroclear or Clearstream, as the case may be, by the counterparty in such system in accordance with the rules and procedures and within the established deadlines (European time) of such system. Euroclear or Clearstream, as the case may be, will, if the transaction meets its settlement requirements, deliver instructions to its U.S. depository to take action to effect final settlement on its behalf by delivering or receiving interests in the global securities through DTC, and making or receiving payment in accordance with normal procedures for same-day fund settlement. Participants in Euroclear or Clearstream may not deliver instructions directly to their respective U.S. depositories.

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Due to time zone differences, the securities accounts of a participant in Euroclear or Clearstream purchasing an interest in a global security from a direct participant in DTC will be credited, and any such crediting will be reported to the relevant participant in Euroclear or Clearstream, during the securities settlement processing day (which must be a business day for Euroclear or Clearstream) immediately following the settlement date of DTC. Cash received in Euroclear or Clearstream as a result of sales of interests in a global security by or through a participant in Euroclear or Clearstream to a direct participant in DTC will be received with value on the settlement date of DTC but will be available in the relevant Euroclear or Clearstream cash account only as of the business day for Euroclear or Clearstream following DTC's settlement date.

Other

The information in this section of this prospectus concerning DTC, Clearstream, Euroclear and their respective book-entry systems has been obtained from sources that we believe to be reliable, but we do not take responsibility for this information. This information has been provided solely as a matter of convenience. The rules and procedures of DTC, Clearstream and Euroclear are solely within the control of those organizations and could change at any time. Neither we nor the trustee nor any agent of ours or of the trustee has any control over those entities and none of us takes any responsibility for their activities. You are urged to contact DTC, Clearstream and Euroclear or their respective participants directly to discuss those matters. In addition, although we expect that DTC, Clearstream and Euroclear will perform the foregoing procedures, none of them is under any obligation to perform or continue to perform such procedures and such procedures may be discontinued at any time. Neither we nor any agent of ours will have any responsibility for the performance or nonperformance by DTC, Clearstream and Euroclear or their respective participants of these or any other rules or procedures governing their respective operations.

SELLING SECURITYHOLDERS

Information about selling securityholders, where applicable, will be set forth in a prospectus supplement, in a post-effective amendment or in filings we make with the SEC under the Exchange Act that are incorporated by reference.

PLAN OF DISTRIBUTION

We or any of the selling securityholders may sell the offered securities from time to time:

- through underwriters or dealers;
- through agents;
- directly to one or more purchasers; or
- through a combination of any of these methods of sale.

We will identify the specific plan of distribution, including any underwriters, dealers, agents or direct purchasers and their compensation in the applicable prospectus supplement.

LEGAL MATTERS

Latham & Watkins LLP, San Diego, California, will pass upon certain legal matters relating to the issuance and sale of the securities offered hereby on behalf of Crinetics Pharmaceuticals, Inc. Additional legal matters may be passed upon for us, the selling securityholders or any underwriters, dealers or agents, by counsel that we will name in the applicable prospectus supplement.

EXPERTS

The consolidated financial statements as of December 31, 2020 and 2019 and for each of the three years in the period ended December 31, 2020 incorporated by reference in this Prospectus have been so incorporated in reliance on the report of BDO USA, LLP, an independent registered public accounting firm, incorporated herein by reference, given on the authority of said firm as experts in auditing and accounting.

7,576,000 Shares



Common Stock

SVB Leerink

Evercore ISI

Cantor

H.C. Wainwright & Co.

JonesTrading

October 20, 2021
