

Prospectus supplement
(To prospectus dated August 10, 2021)

11,441,648 shares



Common stock

We are offering 11,441,648 shares of our common stock in this offering.

Our common stock is listed on the Nasdaq Global Select Market under the symbol "CRNX." On September 12, 2023, the last reported sale price of our common stock on the Nasdaq Global Select Market was \$30.59 per share.

	Per share	Total
Public offering price	\$ 30.5900	\$ 350,000,012.32
Underwriting discounts and commissions ⁽¹⁾	\$ 1.8354	\$ 21,000,000.74
Proceeds to Crinetics Pharmaceuticals, Inc., before expenses	\$ 28.7546	\$ 329,000,011.58

(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 1,716,247 shares of our common stock on the same terms as set forth above.

Investing in our common stock involves risks. See "[Risk factors](#)" beginning on page S-7 of this prospectus supplement and the documents incorporated by reference into this prospectus supplement.

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.

The underwriters expect to deliver the shares of common stock to purchasers on or about September 15, 2023.

Joint book-running managers

J.P. Morgan

Morgan Stanley

Leerink Partners

Piper Sandler

Lead manager

LifeSci Capital

September 12, 2023

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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 supplement. All other trademarks, trade names and service marks appearing in this prospectus supplement 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 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 built a highly productive drug discovery and development organization with extensive expertise in endocrine GPCRs. 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 product candidates include paltusotine (formerly CRN00808), which is in clinical development for the treatment of acromegaly and neuroendocrine tumors complicated by carcinoid syndrome, and CRN04894, which is in clinical development for 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 (SST2 agonist program)

Paltusotine, our lead product candidate, establishes a new class of oral selective nonpeptide somatostatin receptor type 2 agonists designed for the treatment of acromegaly and neuroendocrine tumors, or NETs. To date, we have conducted multiple Phase 1 and Phase 2 clinical trials and results have shown that paltusotine was generally well tolerated among healthy adults and patients with acromegaly. Approximately 27,000 people in the United States suffer from acromegaly, and depending on surgical success, we estimate that approximately 11,000 are candidates for chronic pharmacological intervention, of which somatostatin peptide analogs are the primary pharmacotherapy and that there are approximately 10,000 patients currently on endocrine therapy. 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 175,000 adults in the United States. Of these, it is estimated that 33,000 patients have carcinoid syndrome, and there are approximately 10,000 patients currently on endocrine therapy. Based on an average wholesale acquisition cost of injected somatostatin peptide analogs of \$70,000

and \$100,000 per year for acromegaly and carcinoid syndrome, respectively, we estimate the total addressable market for endocrine therapy in the United States is approximately \$800 million for acromegaly (compared to the current market of \$700 million) and \$3.3 billion for carcinoid syndrome (compared to the current market of \$1.0 billion).

We are currently conducting a Phase 3 development program for paltusotine in acromegaly which consists of two placebo-controlled clinical trials. The first of these, the PATHFND-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 somatostatin receptor ligand monotherapy (octreotide LAR or lanreotide depot). We are also conducting a second study, the PATHFND-2 trial, which is designed as a double-blind, placebo-controlled, six-month clinical trial of acromegaly patients with elevated IGF-1 levels who are untreated. Enrollment in PATHFND-1 was completed in 2022, and we announced topline data from the PATHFND-1 study in September 2023. Enrollment in the PATHFND-2 study was completed in August 2023 and a total of 112 subjects were enrolled who were either treatment-naïve (n=46), untreated for at least four months (n=36), or who washed out of prior octreotide or lanreotide monotherapy (n=30). We expect topline data from the PATHFND-2 study in the first quarter of 2024. We believe that, if successful, the two trials could support marketing applications for the use of paltusotine for all acromegaly patients who require pharmacotherapy, including untreated patients and those switching from other therapies, and we would plan to seek regulatory approval for paltusotine for the treatment of acromegaly in the United States with an anticipated submission of a New Drug Application, or NDA, in 2024.

We are also conducting a Phase 2 trial to assess paltusotine in patients with NETs complicated by carcinoid syndrome. The primary objectives for this Phase 2 trial include the evaluation of safety, tolerability, and pharmacokinetics of multiple doses of paltusotine. In addition, exploratory efficacy during the 8-week period will be evaluated including frequency of bowel movements and flushing episodes. We expect preliminary data from this study in the fourth quarter of 2023.

CRN04894 (ACTH antagonist)

CRN04894 is our investigational, oral, nonpeptide product candidate designed to antagonize the ACTH receptor, intended for the treatment of diseases caused by excess ACTH, including Cushing's disease and CAH. We conducted 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. We announced positive topline data from the Phase 1 study. CRN04894 was well tolerated and demonstrated dose-dependent increases in CRN04894 plasma concentrations.

In the fourth quarter of 2022, we entered into a Clinical Trial Agreement with the National Institute of Diabetes and Digestive and Kidney Diseases, or NIDDK, of the National Institutes of Health, or NIH, to collaborate on a company-sponsored multiple-ascending dose exploratory trial of CRN04894 in ACTH dependent Cushing's Syndrome, or ADCS. This open-label study is designed to evaluate safety and pharmacokinetics of increasing doses of CRN04894 in patients with ADCS as well as to measure 24-hour urinary-free cortisol and serum cortisol as indicators of efficacy. Study activities have been initiated and, based on our current projections data is expected from the study in 2024.

In January 2023, we submitted an Investigational New Drug application, or IND, to the FDA for the study of CRN04894 in CAH. In February 2023, we were notified that the IND was allowed to proceed, and we initiated a Phase 2 study in CAH patients. This open-label Phase 2 study is designed to evaluate the safety and

pharmacokinetics of increasing doses of CRN04894. In addition, biomarkers, including serum androstenedione and 17-hydroxyprogesterone, will be measured as we seek to evaluate the potential efficacy of CRN04894. Data from this Phase 2 study is expected in 2024.

Parathyroid hormone antagonist

We are developing antagonists of the parathyroid hormone, or PTH, receptor for the treatment of primary hyperparathyroidism, or PHPT, and humoral hypercalcemia of malignancy, or HHM, and other diseases of excess PTH. We are evaluating a subset of molecules to identify potential development candidates that we believe are suitable for evaluation in human clinical trials, and we expect to select a development candidate in 2023.

Treatment for autosomal dominant polycystic kidney disease

We are developing nonpeptides for the treatment of primary Autosomal Dominant Polycystic Kidney Disease, or ADPKD. We are evaluating a subset of these molecules to identify potential development candidates that we believe are suitable for evaluation in human clinical trials, and we expect to select a development candidate in 2023.

Recent developments

On September 10, 2023, we announced that paltusotine achieved positive results by meeting the primary endpoint and all secondary endpoints of the Phase 3 PATHFNDR-1 study. PATHFNDR-1 was a randomized, double-blind, placebo-controlled 36-week treatment period followed by an optional open label extension study evaluating paltusotine in participants with acromegaly switching from standard-of-care injected depot somatostatin analogs. The study enrolled participants with acromegaly who were biochemically controlled on octreotide or lanreotide depot monotherapy. PATHFNDR-1 is one of two ongoing, placebo-controlled Phase 3 studies of once-daily, oral paltusotine.

The study met statistical significance ($p < 0.0001$) on the primary endpoint, based on the proportion of participants taking paltusotine (83%) who maintained an IGF-1 level ≤ 1.0 times the upper limit of normal (xULN) compared to those taking placebo (4%). All secondary endpoints also met statistical significance: change from baseline in IGF-1 level (xULN) ($p < 0.0001$), change from baseline in Acromegaly Symptoms Diary (ASD) total score ($p = 0.02$) and proportion of participants who maintained a growth hormone (GH) level of $< 1.0 \text{ ng/mL}$ ($p = 0.0003$).

In PATHFNDR-1, paltusotine was well tolerated and no serious or severe adverse events were reported in participants treated with paltusotine. The frequency of participants with at least one treatment emergent adverse event (TEAE) was comparable in the paltusotine (PAL) treatment arm vs. placebo (PBO) arm (80% vs. 100% respectively). The most commonly reported TEAEs in paltusotine included: arthralgia (27% PAL vs. 57% PBO), headache (20% PAL vs. 36% PBO), diarrhea (23% PAL vs. 14% PBO), abdominal pain (17% PAL vs. 11% PBO) and nausea (10% PAL vs. 7% PBO). The frequency of adverse events considered related to acromegaly was notably lower in paltusotine treated participants compared to placebo treated participants (30% vs. 86% respectively).

A full analysis of the PATHFNDR-1 results is underway, which we expect to present at upcoming scientific conferences. PATHFNDR-2, a Phase 3 study of oral paltusotine in participants with acromegaly who are

treatment-naïve or not currently receiving medical therapy, is fully enrolled and topline data are expected in the first quarter of 2024. Pending successful findings from the PATHFINDER-2 study, we plan to submit an NDA to the FDA in 2024 seeking regulatory approval for all acromegaly patients who require pharmacotherapy, including newly diagnosed patients and those switching from other therapies.

The PATHFINDER Program consists of two Phase 3 double-blind, placebo-controlled studies. PATHFINDER-1 enrolled a total of 58 adults with acromegaly who entered with an IGF-1 level $\leq 1.0 \times \text{ULN}$ on octreotide or lanreotide depot monotherapy. They were randomized to receive once-daily, oral paltusotine for 36 weeks or placebo. PATHFINDER-2 enrolled 112 adults with acromegaly who had elevated IGF-1 levels but were medication naïve or were not being treated with pharmacotherapy (untreated patients).

The primary endpoint for both studies is the proportion of patients achieving IGF-1 $\leq 1.0 \times \text{ULN}$ compared to placebo. If successful, we believe these studies 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 standard of care.

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	11,441,648 shares
Common stock to be outstanding after this offering	66,124,027 shares (or 67,840,274 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 1,716,247 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 from this offering to fund the development of paltusotine, CRN04894 and our other research and development programs, and for working capital and general corporate purposes. See “Use of proceeds” on page S-9 of this prospectus supplement.
Risk factors	See “Risk factors” beginning on page S-7 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 54,682,379 shares outstanding as of June 30, 2023, and excludes:

- 12,423,014 shares of our common stock issuable upon the exercise of stock options outstanding as of June 30, 2023 under our equity incentive plans, with a weighted-average exercise price of \$18.16 per share;
- 795,307 shares of common stock issuable upon the exercise of stock options granted after June 30, 2023, with a weighted-average exercise price of \$17.90 per share;
- 843,095 shares of common stock issuable upon the vesting and settlement of restricted stock units outstanding as of June 30, 2023 under our 2018 Incentive Award Plan;
- 20,000 shares of common stock issuable upon the vesting and settlement of restricted stock units granted after June 30, 2023 under our 2018 Incentive Award Plan;
- 2,510,587 shares of common stock reserved for future issuance under our 2018 Incentive Award Plan as of June 30, 2023;
- 1,664,012 shares of common stock reserved for future issuance under our 2018 Employee Stock Purchase Plan as of June 30, 2023; and
- 1,240,434 shares of common stock reserved for future issuance under our 2021 Employment Inducement Incentive Award Plan as of June 30, 2023.

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 1,716,247 shares of our common stock.

In addition, the number of shares of our common stock to be outstanding immediately after this offering as shown above does not include the \$138.3 million shares of our common stock that remain available for sale at June 30, 2023 pursuant to our Sales Agreement (the "Sales Agreement") with Leerink Partners LLC and Cantor Fitzgerald & Co. (collectively, the "Sales Agents"). Between June 30, 2023 and the date of this prospectus supplement, we have not sold any shares of our common stock under the Sales Agreement. We have agreed not to make any sales under the Sales Agreement until the expiration or waiver of the 60-day lock-up period applicable to us and described in the section titled "Underwriting."

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, 2022 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.

Sales of a substantial number of shares of our common stock in the public market could occur at any time, including pursuant to the Sales Agreement. 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 \$30.59 per share, new investors will incur immediate dilution of \$21.78 per share based on the net tangible book value as of June 30, 2023. 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 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.

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 the plans and timelines for clinical development of paltusotine and CRN04894, including the therapeutic potential and clinical benefits or safety profile thereof; the expected timing of topline data from the ongoing Phase 3 clinical study of paltusotine in acromegaly and Phase 2 and Phase 3 studies of paltusotine in carcinoid syndrome; plans to submit data from the ongoing Phase 3 clinical studies of paltusotine in acromegaly to regulators in support of applications seeking approval for the use of paltusotine in acromegaly patients and the expected timing of an NDA submission for paltusotine for the treatment for all acromegaly patients who require pharmacotherapy; the expected timing of data from studies of CRN04894 in Cushing's disease and congenital adrenal hyperplasia; the plans to advance our other pipeline product candidates or discovery efforts; our future results of operations and financial position; our business strategy, prospective products, product approvals, research and development costs, timing and likelihood of success, as well as the plans and objectives of management for future operations and future results of anticipated products. 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 \$328.6 million from this offering, or approximately \$378.0 million if the underwriters exercise in full their option to purchase additional 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 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 supplement 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, 2023, our net tangible book value was \$254.1 million, or \$4.65 per share, based on 54,682,379 shares of our common stock outstanding as of June 30, 2023. 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, 2023.

After giving effect to our sale in this offering of 11,441,648 shares of common stock at the public offering price of \$30.59 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, 2023 would have been \$582.7 million, or \$8.81 per share. This represents an immediate increase in net tangible book value of \$4.16 per share to our existing stockholders and immediate dilution of \$21.78 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	\$30.59
Net tangible book value per share as of June 30, 2023	\$4.65
Increase per share attributable to investors purchasing shares in this offering	<u>4.16</u>
As adjusted net tangible book value per share, after giving effect to this offering	<u>8.81</u>
Dilution per share to investors purchasing our common stock in this offering	<u>\$21.78</u>

If the underwriters exercise in full their option to purchase up to an additional 1,716,247 shares of our common stock at the public offering price of \$30.59 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 \$9.32 per share, representing an immediate increase in net tangible book value of \$4.67 per share to our existing stockholders and immediate dilution of \$21.27 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 54,682,379 shares outstanding as of June 30, 2023, and exclude:

- 12,423,014 shares of our common stock issuable upon the exercise of stock options outstanding as of June 30, 2023 under our equity incentive plans, with a weighted-average exercise price of \$18.16 per share;
- 795,307 shares of common stock issuable upon the exercise of stock options granted after June 30, 2023, with a weighted-average exercise price of \$17.90 per share;
- 843,095 shares of common stock issuable upon the vesting and settlement of restricted stock units outstanding as of June 30, 2023 under our 2018 Incentive Award Plan;
- 20,000 shares of common stock issuable upon the vesting and settlement of restricted stock units granted after June 30, 2023 under our 2018 Incentive Award Plan;
- 2,510,587 shares of common stock reserved for future issuance under our 2018 Incentive Award Plan as of June 30, 2023;
- 1,664,012 shares of common stock reserved for future issuance under our 2018 Employee Stock Purchase Plan as of June 30, 2023; and
- 1,240,434 shares of common stock reserved for future issuance under our 2021 Employment Inducement Incentive Award Plan as of June 30, 2023.

In addition, the number of shares of our common stock to be outstanding immediately after this offering as shown above does not include the \$138.3 million shares of our common stock that remain available for sale at June 30, 2023 pursuant to the Sales Agreement. Between June 30, 2023 and the date of this prospectus supplement, we have not sold any shares of our common stock under the Sales Agreement.

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

We are offering the shares of common stock described in this prospectus supplement through a number of underwriters. J.P. Morgan Securities LLC, Morgan Stanley & Co. LLC, Leerink Partners LLC and Piper Sandler & Co. are acting as joint book-running managers of the offering and as representatives of the underwriters. We have entered into an underwriting agreement with the underwriters. Subject to the terms and conditions of the underwriting agreement, we have agreed to sell to the underwriters, and each underwriter has severally agreed to purchase, at the public offering price less the underwriting discounts and commissions set forth on the cover page of this prospectus supplement, the number of shares of common stock listed next to its name in the following table:

Name	Number of shares
J.P. Morgan Securities LLC	4,004,578
Morgan Stanley & Co. LLC	3,203,661
Leerink Partners LLC	2,345,538
Piper Sandler & Co.	1,544,622
LifeSci Capital LLC	343,249
Total	11,441,648

The underwriters are committed to purchase all the shares of common stock offered by us if they purchase any shares. The underwriting agreement also provides that if an underwriter defaults, the purchase commitments of non-defaulting underwriters may also be increased or the offering may be terminated.

The underwriters propose to offer the common stock directly to the public at the public offering price set forth on the cover page of this prospectus supplement and to certain dealers at that price less a concession not in excess of \$1.10124 per share. After the initial offering of the shares to the public, if all of the shares of common stock are not sold at the public offering price, the underwriters may change the offering price and the other selling terms. Sales of any shares made outside of the United States may be made by affiliates of the underwriters.

The underwriters have an option to buy up to 1,716,247 additional shares of common stock from us to cover sales of shares by the underwriters which exceed the number of shares specified in the table above. The underwriters have 30 days from the date of this prospectus supplement to exercise this option to purchase additional shares. If any shares are purchased with this option to purchase additional shares, the underwriters will purchase shares in approximately the same proportion as shown in the table above. If any additional shares of common stock are purchased, the underwriters will offer the additional shares on the same terms as those on which the shares are being offered.

The underwriting fee is equal to the public offering price per share of common stock less the amount paid by the underwriters to us per share of common stock. The underwriting fee is \$1.8354 per share. The following table shows the per share and total underwriting discounts and commissions to be paid to the underwriters assuming both no exercise and full exercise of the underwriters' option to purchase additional shares.

	Without exercise of option to purchase additional shares	With exercise of full option to purchase additional shares
Per share	\$ 1.8354	\$ 1.8354
Total	\$ 21,000,000.74	\$ 24,150,000.48

We estimate that the total expenses of this offering, including registration, filing and listing fees, printing fees and legal and accounting expenses, but excluding the underwriting discounts and commissions, will be approximately \$400,000. We have agreed to reimburse the underwriters for expenses relating to the clearance of this offering with the Financial Industry Regulatory Authority, Inc. in an amount up to \$10,000.

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A prospectus supplement and the accompanying prospectus in electronic format may be made available on the web sites maintained by one or more underwriters, or selling group members, if any, participating in the offering. The underwriters may agree to allocate a number of shares to underwriters and selling group members for sale to their online brokerage account holders. Internet distributions will be allocated by the representatives to underwriters and selling group members that may make Internet distributions on the same basis as other allocations.

We have agreed that we will not, subject to certain exceptions, (i) 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, or file with, or submit to, the SEC a registration statement under the Securities Act relating to, any shares of our common stock or securities convertible into or exercisable or exchangeable for any shares of our common stock, or publicly disclose the intention to undertake any of the foregoing, or (ii) enter into any swap, hedging, or other agreement that transfers, in whole or in part, any 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 J.P. Morgan Securities LLC, Morgan Stanley & Co. LLC, Leerink Partners LLC and Piper Sandler & Co. for a period of 60 days after the date of this prospectus supplement.

The restrictions on our actions, as described above, do not apply to certain transactions, including (A) the shares of our common stock to be sold in this offering, (B) any shares of common stock issued upon the exercise of options granted under our and our subsidiaries' stock-based compensation plans described in this prospectus supplement, or Company Stock Plans, (C) any options and other awards granted under a Company Stock Plan described in this prospectus supplement, (D) our filing of any registration statement on Form S-8 or a successor form thereto relating to a Company Stock Plan described in this prospectus supplement and (E) any shares of our common stock, or any securities convertible into or exercisable or exchangeable for shares of our common stock, or the entry into any agreement to issue shares of our common stock, or any securities convertible into or exercisable or exchangeable for, shares of our common stock, issued in connection with any merger, joint venture, strategic alliances, commercial or other collaborative transaction or the acquisition or license of the business, property, technology or other assets of another individual or entity or the assumption of an employee benefit plan in connection with a merger or acquisition; provided, however, that the aggregate number of shares of our common stock, or any securities convertible into or exercisable or exchangeable for our common stock, that we may issue or agree to issue pursuant to this clause (E) shall not exceed 5% of the total outstanding shares of our common stock immediately following the issuance of the shares of common stock offered by this prospectus supplement and provided, further, that (i) each newly appointed director or executive officer that is a recipient of any such shares of our common stock or securities issued pursuant to clauses (B) or (C) and (ii) the recipient of any such shares of our common stock or securities issued pursuant to clause (E) during the 60-day restricted period described above, shall enter into a lock-up agreement with the underwriters.

Our directors and executive officers, and certain of our securityholders (such persons, the lock-up parties) have entered into lock-up agreements with the underwriters prior to the commencement of this offering pursuant to which each lock-up party, with limited exceptions, for a period of 60 days after the date of this prospectus supplement (such period, the restricted period), may not (and may not cause any of their direct or indirect affiliates to (and will cause any spouse or immediate family member of the spouse or the lock-up party living in the lock-up party's household not to)), without the prior written consent of J.P. Morgan Securities LLC, Morgan Stanley & Co. LLC, Leerink Partners LLC and Piper Sandler & Co., (1) 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 our common

stock or any securities convertible into or exercisable or exchangeable for our common stock (including, without limitation, common stock or such other securities which may be deemed to be beneficially owned by such lock-up parties in accordance with the rules and regulations of the SEC and securities which may be issued upon exercise of a stock option or warrant (collectively with the common stock, the lock-up securities)), (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 lock-up securities, whether any such transaction described in clause (1) or (2) above is to be settled by delivery of lock-up securities, in cash or otherwise, (3) make any demand for or exercise any right with respect to the registration of any lock-up securities (and, for the avoidance of doubt, the lock-up party 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 lock-up party is a party or under which the lock-up party is entitled to any right or benefit), or (4) publicly disclose the intention to do any of the foregoing. Such persons or entities have further acknowledged that these undertakings preclude them from engaging in any hedging or other transactions or arrangements (including, without limitation, any short sale or the purchase or sale of, or entry into, any put or call option, or combination thereof, forward, swap or any other derivative transaction or instrument, however described or defined) designed or intended, or which could reasonably be expected to lead to or result in, a sale or disposition or transfer (whether by the lock-up party or any other person) of any economic consequences of ownership, in whole or in part, directly or indirectly, of any lock-up securities, whether any such transaction or arrangement (or instrument provided for thereunder) would be settled by delivery of lock-up securities, in cash or otherwise.

The restrictions described in the immediately preceding paragraph and contained in the lock-up agreements between the underwriters and the lock-up parties do not apply, subject in certain cases to various conditions, to certain transactions, including:

- (i) transfers or dispositions of lock-up securities:
 - (A) by the lock-up party pursuant to the underwriting agreement for this offering,
 - (B) as a bona fide gift or gifts,
 - (C) to limited or general partners, members or stockholders of the lock-up party,
 - (D) to an immediate family member or trust for the direct or indirect benefit of the lock-up party or an immediate family member,
 - (E) to any corporation, partnership, limited liability company or other entity all of the beneficial ownership interests of which are held by the lock-up party,
 - (F) by will, other testamentary document or intestate succession to the legal representative, heir, beneficiary or a member of the immediate family of the lock-up party,
 - (G) pursuant to a court or regulatory agency order, a qualified domestic order or in connection with a divorce settlement,
 - (H) to us in connection with the “net” or “cashless” exercise of options or other rights to purchase shares of our common stock granted pursuant to an equity incentive plan, stock purchase plan or other arrangement described in this prospectus supplement (including the documents incorporated by reference) in satisfaction of any tax withholding obligations through cashless surrender or otherwise, provided, that, any shares of our common stock issued upon exercise of such option or other rights shall continue to be subject to the restrictions in the immediately preceding paragraph until the expiration of the restricted period,

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- (I) if the undersigned is an investment company registered under the Investment Company Act of 1940, as amended, or Mutual Fund, transfers pursuant to a merger or reorganization with or into another Mutual Fund that shares the same investment adviser registered pursuant to the requirements of the Investment Advisers Act of 1940, as amended, and
 - (J) to any affiliate (as defined in Rule 405 promulgated under the Securities Act) of the lock-up party or any investment fund or other entity controlled or managed by the lock-up party or under common management or control with the lock-up party;
- (ii) transfers of our common stock to us in connection with any contractual arrangement in effect on the date of this prospectus supplement that provides for the repurchase of the lock-up party's shares by us in connection with the termination of the lock-up party's employment or other services with us is permitted, provided that no public filing, report or announcement reporting a reduction in beneficial ownership of shares of our common stock shall be voluntarily made and if the lock-up party is required to file a report under Section 16 of the Exchange Act reporting a reduction in beneficial ownership of shares of our common stock during the restricted period, the lock-up party shall clearly indicate in the footnotes thereto that the filing relates to the termination of the lock-up party's employment or other services;
- (iii) transfers of our common stock pursuant to a bona fide third-party tender offer, merger, consolidation or other similar transaction made to all of our stockholders involving a change in control, in each case that is approved by the independent members of our board of directors, provided that if such transaction is not completed, all such securities held by the lock-up party shall remain subject to the restrictions on transfer set forth in the immediately preceding paragraph;
- (iv) the establishment by lock-up parties of trading plans under Rule 10b5-1 under the Exchange Act, or 10b5-1 Trading Plan, for the transfer of shares of our common stock, provided that (1) such 10b5-1 Trading Plan does not provide for the transfer of shares of our common stock during the restricted period, (2) if the establishment of such 10b5-1 Trading Plan is required to be reported in any public report or filing with the SEC, or otherwise, such report or filing shall indicate that no transfers under such trading plans will take place during the restricted period and (3) the lock-up party does not otherwise voluntarily effect any public filing or report or any public announcement regarding the establishment of such 10b5-1 Trading Plan;
- (v) sales of shares of our common stock made pursuant to a 10b5-1 Trading Plan that has been entered into by the lock-up party prior to the date of the lock-up agreement and disclosed to the representatives, or an Existing 10b5-1 Plan; provided that if the lock-up party reports any such sale on a Form 4 filed with the SEC, the lock-up party shall cause such Form 4 to include a statement that such sale was effected pursuant to such Existing 10b5-1 Plan; or
- (vi) sales of shares of our common stock purchased in this offering or in the open market following the date of this prospectus supplement if and only if (1) such securities are not required to be reported in any public report or filing with the SEC, or otherwise and (ii) the lock-up party does not otherwise voluntarily effect any public filing or report regarding such sales.

Notwithstanding the foregoing, and subject to the conditions above, the lock-up party may transfer the lock-up securities without the prior written consent of J.P. Morgan Securities LLC, Morgan Stanley & Co. LLC, Leerink Partners LLC and Piper Sandler & Co., provided that in the case of any transfer or distribution pursuant to clauses (i)(B), (i)(C), (i)(D), (i)(E), (i)(F), (i)(G), (i)(I) or (i)(J), each transferee, donee or distributee shall execute and deliver to the representatives a lock-up agreement; provided, further, that in the case of any transfer or distribution pursuant to clauses (i)(B), (i)(C), (i)(D), (i)(E), (i)(F), (i)(G) and (i)(J), such transfer shall not involve a disposition for value; and provided, further, that in the case of any transfer or distribution pursuant to clauses (i)(B) through (i)(J), no filing by any party (donor, donee, transferor or transferee) under the Exchange

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Act, or other public announcement shall be required or shall be made voluntarily in connection with such transfer or distribution (other than a required filing on Form 4 or Form 5 with respect to clauses (B), (D), (F) or (H); provided any such filing shall indicate (in the notes thereto or otherwise) that the filing relates to the circumstances set forth in such clauses).

J.P. Morgan Securities LLC, Morgan Stanley & Co. LLC, Leerink Partners LLC and Piper Sandler & Co., in their sole discretion, may release the securities subject to any of the lock-up agreements with the underwriters described above, in whole or in part at any time.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act.

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

In connection with this offering, the underwriters may engage in stabilizing transactions, which involves making bids for, purchasing and selling shares of common stock in the open market for the purpose of preventing or retarding a decline in the market price of the common stock while this offering is in progress. These stabilizing transactions may include making short sales of common stock, which involves the sale by the underwriters of a greater number of shares of common stock than they are required to purchase in this offering, and purchasing shares of common stock on the open market to cover positions created by short sales. Short sales may be "covered" shorts, which are short positions in an amount not greater than the underwriters' option to purchase additional shares referred to above, or may be "naked" shorts, which are short positions in excess of that amount. The underwriters may close out any covered short position either by exercising their option to purchase additional shares, in whole or in part, or by purchasing shares in the open market. In making this determination, the underwriters will consider, among other things, the price of shares available for purchase in the open market compared to the price at which the underwriters may purchase shares through the option to purchase additional shares. 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 the common stock in the open market that could adversely affect investors who purchase in this offering. To the extent that the underwriters create a naked short position, they will purchase shares in the open market to cover the position.

The underwriters have advised us that, pursuant to Regulation M of the Securities Act, they may also engage in other activities that stabilize, maintain or otherwise affect the price of the common stock, including the imposition of penalty bids. This means that if the representatives of the underwriters purchase common stock in the open market in stabilizing transactions or to cover short sales, the representatives can require the underwriters that sold those shares as part of this offering to repay the underwriting discount received by them.

These activities may have the effect of raising or maintaining the market price of the common stock or preventing or retarding a decline in the market price of the common stock, and, as a result, the price of the common stock may be higher than the price that otherwise might exist in the open market. If the underwriters commence these activities, they may discontinue them at any time. The underwriters may carry out these transactions on Nasdaq, in the over-the-counter market or otherwise.

Other relationships

Certain of the underwriters and their affiliates have provided in the past to us and our affiliates and may provide from time to time in the future certain commercial banking, financial advisory, investment banking and other services for us and such affiliates in the ordinary course of their business, for which they have received and may continue to receive customary fees and commissions. In addition, from time to time, certain of the

underwriters and their affiliates may effect transactions for their own account or the account of customers, and hold on behalf of themselves or their customers, long or short positions in our debt or equity securities or loans, and may do so in the future. For example, certain of the underwriters also serve as Sales Agents pursuant to the Sales Agreement.

Selling restrictions

Other than in the United States, no action has been taken by us or the underwriters that would permit a public offering of the securities offered by this prospectus supplement and the accompanying prospectus in any jurisdiction where action for that purpose is required. The securities offered by this prospectus supplement and the accompanying prospectus may not be offered or sold, directly or indirectly, nor may this prospectus supplement and the accompanying prospectus or any other offering material or advertisements in connection with the offer and sale of any such securities be distributed or published in any jurisdiction, except under circumstances that will result in compliance with the applicable rules and regulations of that jurisdiction. Persons into whose possession this prospectus supplement and the accompanying prospectus comes are advised to inform themselves about and to observe any restrictions relating to the offering and the distribution of this prospectus supplement and the accompanying prospectus. This prospectus supplement and the accompanying prospectus do not constitute an offer to sell or a solicitation of an offer to buy any securities offered by this prospectus supplement and the accompanying prospectus in any jurisdiction in which such an offer or a solicitation is unlawful.

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 of our common stock 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 of our common stock 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 of our common stock may be made under the following exemptions under the Prospectus Regulation:

- (i) to any legal entity which is a qualified investor as defined under Article 2 of the Prospectus Regulation;
- (ii) 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
- (iii) in any other circumstances falling within Article 1(4) of the Prospectus Regulation,

provided that no such offer of shares shall require us or any of the representatives to publish a prospectus provided that no such offer of the shares of our common stock shall require us or any underwriter to publish a prospectus pursuant to Article 3 of the Prospectus Regulation or supplement a prospectus pursuant to Article 23 of the Prospectus Regulation, and each person who initially acquires any shares of our common stock or to whom any offer is made will be deemed to have represented, acknowledged and agreed to and with each of the underwriters and the Company that it is a “qualified investor” within the meaning of Article 2[©] of the Prospectus Regulation. In the case of any shares of our common stock being offered to a financial intermediary as that term is used in the Prospectus Regulation, each such financial intermediary will be deemed to have represented, acknowledged and agreed that the shares of our common stock acquired by it in the offer have not been acquired on a non-discretionary basis on behalf of, nor have they been acquired with a view to their offer or resale to, persons in circumstances which may give rise to an offer of any shares of our common stock to the public other than their offer or resale in a Relevant State to qualified investors as so defined or in circumstances in which the prior consent of the underwriters have been obtained to each such proposed offer or resale.

For the purposes of this provision, the expression an “offer to the public” in relation to the shares of our common stock 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 of our common stock to be offered so as to enable an investor to decide to purchase or subscribe for any shares of our common stock, and the expression “Prospectus Regulation” means Regulation (EU) 2017/1129.

Notice to prospective investors in the United Kingdom

No shares of our common stock 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 of our common stock which has been approved by the Financial Conduct Authority, except that the shares of our common stock may be offered to the public in the United Kingdom at any time:

- (i) to any legal entity which is a qualified investor as defined under Article 2 of the UK Prospectus Regulation;
- (ii) 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 representatives for any such offer; or
- (iii) in any other circumstances falling within Section 86 of the FSMA.

Provided that no such offer of the shares shall require the Issuer or any Manager 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 of our common stock in the United Kingdom means the communication in any form and by any means of sufficient information on the terms of the offer and any shares of our common stock to be offered so as to enable an investor to decide to purchase or subscribe for any shares of our common stock and the expression “UK Prospectus Regulation” means Regulation (EU) 2017/1129 as it forms part of domestic law in the United Kingdom by virtue of the European Union (Withdrawal) Act 2018.

In addition, in the United Kingdom, this document is being distributed only to, and is directed only at, and any offer subsequently made may only be directed at persons who are “qualified investors” (as defined in the Prospectus Regulation) (i) who have professional experience in matters relating to investments falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended (Order) and/or (ii) who are high net worth companies (or persons to whom it may otherwise be lawfully communicated) falling within Article 49(2)(a) to (d) of the Order (all such persons together being referred to as “relevant persons”) or otherwise in circumstances which have not resulted and will not result in an offer to the public of the shares in the United Kingdom within the meaning of the Financial Services and Markets Act 2000.

Any person in the United Kingdom that is not a relevant person should not act or rely on the information included in this document or use it as basis for taking any action. In the United Kingdom, any investment or investment activity that this document relates to may be made or taken exclusively by relevant persons.

Notice to prospective investors in Canada

The shares of our common stock 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 of our common stock 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.

Notice to prospective investors in Switzerland

The shares may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange, or SIX, or on any other stock exchange or regulated trading facility in Switzerland. This document does not constitute a prospectus within the meaning of, and has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this document nor any other offering or marketing material relating to the shares or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this document nor any other offering or marketing material relating to the offering, the Company, the shares have been or will be filed with or approved by any Swiss regulatory authority. In particular, this document will not be filed with, and the offer of shares will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA, or FINMA, and the offer of shares has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes, or CIS. The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of shares.

Notice to prospective investors in the Dubai International Financial Centre

This document relates to an Exempt Offer in accordance with the Markets Rules 2012 of the Dubai Financial Services Authority, or DFSA. This document is intended for distribution only to persons of a type specified in the Markets Rules 2012 of the DFSA. It must not be delivered to, or relied on by, any other person. The DFSA has no responsibility for reviewing or verifying any documents in connection with Exempt Offers. The DFSA has not approved this prospectus supplement nor taken steps to verify the information set forth herein and has no responsibility for this document. The securities to which this document relates may be illiquid and/or subject to restrictions on their resale. Prospective purchasers of the securities offered should conduct their own due diligence on the securities. If you do not understand the contents of this document you should consult an authorized financial advisor.

In relation to its use in the DIFC, this document is strictly private and confidential and is being distributed to a limited number of investors and must not be provided to any person other than the original recipient, and may not be reproduced or used for any other purpose. The interests in the securities may not be offered or sold directly or indirectly to the public in the DIFC.

Notice to prospective investors in the United Arab Emirates

The shares have not been, and are not being, publicly offered, sold, promoted or advertised in the United Arab Emirates (including the Dubai International Financial Centre) other than in compliance with the laws of the

United Arab Emirates (and the Dubai International Financial Centre) governing the issue, offering and sale of securities. Further, this prospectus supplement does not constitute a public offer of securities in the United Arab Emirates (including the Dubai International Financial Centre) and is not intended to be a public offer. This prospectus supplement has not been approved by or filed with the Central Bank of the United Arab Emirates, the Securities and Commodities Authority or the Dubai Financial Services Authority.

Notice to prospective investors in Australia

This prospectus supplement:

- does not constitute a disclosure document or a prospectus under Chapter 6D.2 of the Corporations Act 2001 (Cth), or the “Corporations Act”;
- has not been, and will not be, lodged with the Australian Securities and Investments Commission, or the ASIC, as a disclosure document for the purposes of the Corporations Act and does not purport to include the information required of a disclosure document for the purposes of the Corporations Act; and
- may only be provided in Australia to select investors who are able to demonstrate that they fall within one or more of the categories of investors, available under section 708 of the Corporations Act, or the Exempt Investors.

The shares of our common stock may not be directly or indirectly offered for subscription or purchased or sold, and no invitations to subscribe for or buy the shares of our common stock may be issued, and no draft or definitive offering memorandum, advertisement or other offering material relating to any shares of our common stock may be distributed in Australia, except where disclosure to investors is not required under Chapter 6D of the Corporations Act or is otherwise in compliance with all applicable Australian laws and regulations. By submitting an application for the shares of our common stock, you represent and warrant to us that you are an Exempt Investor.

As any offer of shares of our common stock under this prospectus supplement will be made without disclosure in Australia under Chapter 6D.2 of the Corporations Act, the offer of those securities for resale in Australia within 12 months may, under section 707 of the Corporations Act, require disclosure to investors under Chapter 6D.2 if none of the exemptions in section 708 applies to that resale. By applying for the shares of our common stock you undertake to us that you will not, for a period of 12 months from the date of issue of the shares, offer, transfer, assign or otherwise alienate those shares of our common stock to investors in Australia except in circumstances where disclosure to investors is not required under Chapter 6D.2 of the Corporations Act or where a compliant disclosure document is prepared and lodged with ASIC.

Notice to prospective investors in Japan

The shares of our common stock have not been and will not be registered pursuant to Article 4, Paragraph 1 of the Financial Instruments and Exchange Act. Accordingly, none of the shares of our common stock nor any interest therein may be offered or sold, directly or indirectly, in Japan or to, or for the benefit of, any “resident” of Japan (which term as used herein means any person resident in Japan, including any corporation or other entity organized under the laws of Japan), or to others for re-offering or resale, directly or indirectly, in Japan or to or for the benefit of a resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the Financial Instruments and Exchange Act and any other applicable laws, regulations and ministerial guidelines of Japan in effect at the relevant time.

Notice to prospective investors in Hong Kong

The shares of our common stock have not been offered or sold and will not be offered or sold in Hong Kong, by means of any document, other than (a) to “professional investors” as defined in the Securities and Futures Ordinance (Cap. 571 of the Laws of Hong Kong), or the SFO, of Hong Kong and any rules made thereunder; or (b) in other circumstances which do not result in the document being a “prospectus” as defined in the Companies (Winding Up and Miscellaneous Provisions) Ordinance (Cap. 32) of Hong Kong, or the CO, or which do not constitute an offer to the public within the meaning of the CO. No advertisement, invitation or document relating to the shares of our common stock has been or will be issued or has been or will be in the possession of any person for the purposes of issue, whether in Hong Kong or elsewhere, which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to the shares of our common stock which are or are intended to be disposed of only to persons outside Hong Kong or only to “professional investors” as defined in the SFO and any rules made thereunder.

Notice to prospective investors in Singapore

Each underwriter has acknowledged that this prospectus supplement has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, each underwriter has represented and agreed that it has not offered or sold any shares of our common stock or caused the shares of our common stock to be made the subject of an invitation for subscription or purchase and will not offer or sell any shares of our common stock or cause the shares of our common stock to be made the subject of an invitation for subscription or purchase, and has not circulated or distributed, nor will it circulate or distribute, this prospectus supplement or any other document or material in connection with the offer or

sale, or invitation for subscription or purchase, of the shares of our common stock, whether directly or indirectly, to any person in Singapore other than:

- (i) to an institutional investor (as defined in Section 4A of the Securities and Futures Act (Chapter 289) of Singapore, as modified or amended from time to time, or the SFA) pursuant to Section 274 of the SFA;
- (ii) to a relevant person (as defined in Section 275(2) of the SFA) pursuant to Section 275(1) of the SFA, or any person pursuant to Section 275(1A) of the SFA, and in accordance with the conditions specified in Section 275 of the SFA; or
- (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the shares of our common stock are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

- (i) a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or
- (ii) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor,

securities or securities-based derivatives contracts (each term as defined in Section 2(1) of the SFA) of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the shares of our common stock pursuant to an offer made under Section 275 of the SFA except:

- (i) to an institutional investor or to a relevant person, or to any person arising from an offer referred to in Section 275(1A) or Section 276(4)(i)(B) of the SFA;

- (ii) where no consideration is or will be given for the transfer;
- (iii) where the transfer is by operation of law;
- (iv) as specified in Section 276(7) of the SFA; or
- (v) as specified in Regulation 37A of the Securities and Futures (Offers of Investments) (Securities and Securities-based Derivatives Contracts) Regulations 2018.

Notice to prospective investors in Bermuda

Shares may be offered or sold in Bermuda only in compliance with the provisions of the Investment Business Act of 2003 of Bermuda which regulates the sale of securities in Bermuda. Additionally, non-Bermudian persons (including companies) may not carry on or engage in any trade or business in Bermuda unless such persons are permitted to do so under applicable Bermuda legislation.

Notice to prospective investors in Saudi Arabia

This document may not be distributed in the Kingdom of Saudi Arabia except to such persons as are permitted under the Offers of Securities Regulations as issued by the board of the Saudi Arabian Capital Market Authority, or CMA, pursuant to resolution number 2-11-2004 dated 4 October 2004 as amended by resolution number 1-28-2008, as amended. The CMA does not make any representation as to the accuracy or completeness of this document and expressly disclaims any liability whatsoever for any loss arising from, or incurred in reliance upon, any part of this document. Prospective purchasers of the securities offered hereby should conduct their own due diligence on the accuracy of the information relating to the securities. If you do not understand the contents of this document, you should consult an authorized financial adviser.

Notice to prospective investors in the British Virgin Islands

The shares are not being, and may not be offered to the public or to any person in the British Virgin Islands for purchase or subscription by or on behalf of the Company. The shares may be offered to companies incorporated under the BVI Business Companies Act, 2004 (British Virgin Islands), or BVI Companies, but only where the offer will be made to, and received by, the relevant BVI Company entirely outside of the British Virgin Islands.

Notice to prospective investors in China

This prospectus supplement will not be circulated or distributed in the PRC and the shares will not be offered or sold, and will not be offered or sold to any person for re-offering or resale directly or indirectly to any residents of the PRC except pursuant to any applicable laws and regulations of the PRC. Neither this prospectus supplement nor any advertisement or other offering material may be distributed or published in the PRC, except under circumstances that will result in compliance with applicable laws and regulations.

Notice to prospective investors in Korea

The shares have not been and will not be registered under the Financial Investments Services and Capital Markets Act of Korea and the decrees and regulations thereunder, or the FSCMA, and the shares have been and will be offered in Korea as a private placement under the FSCMA. None of the shares may be offered, sold or delivered directly or indirectly, or offered or sold to any person for re-offering or resale, directly or indirectly, in Korea or to any resident of Korea except pursuant to the applicable laws and regulations of Korea, including the FSCMA and the Foreign Exchange Transaction Law of Korea and the decrees and regulations thereunder, or the

FETL. The shares have not been listed on any of the securities exchanges in the world including, without limitation, the Korea Exchange in Korea. Furthermore, the purchaser of the shares shall comply with all applicable regulatory requirements (including but not limited to requirements under the FETL) in connection with the purchase of the shares. By the purchase of the shares, the relevant holder thereof will be deemed to represent and warrant that if it is in Korea or is a resident of Korea, it purchased the shares pursuant to the applicable laws and regulations of Korea.

Notice to prospective investors in Malaysia

No prospectus or other offering material or document in connection with the offer and sale of the shares has been or will be registered with the Securities Commission of Malaysia, or Commission, for the Commission's approval pursuant to the Capital Markets and Services Act 2007. Accordingly, this prospectus supplement and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares may not be circulated or distributed, nor may the shares be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Malaysia other than (i) a closed end fund approved by the Commission; (ii) a holder of a Capital Markets Services License; (iii) a person who acquires the shares, as principal, if the offer is on terms that the shares may only be acquired at a consideration of not less than RM250,000 (or its equivalent in foreign currencies) for each transaction; (iv) an individual whose total net personal assets or total net joint assets with his or her spouse exceeds RM3 million (or its equivalent in foreign currencies), excluding the value of the primary residence of the individual; (v) an individual who has a gross annual income exceeding RM300,000 (or its equivalent in foreign currencies) per annum in the preceding twelve months; (vi) an individual who, jointly with his or her spouse, has a gross annual income of RM400,000 (or its equivalent in foreign currencies), per annum in the preceding twelve months; (vii) a corporation with total net assets exceeding RM10 million (or its equivalent in a foreign currencies) based on the last audited accounts; (viii) a partnership with total net assets exceeding RM10 million (or its equivalent in foreign currencies); (ix) a bank licensee or insurance licensee as defined in the Labuan Financial Services and Securities Act 2010; (x) an Islamic bank licensee or takaful licensee as defined in the Labuan Financial Services and Securities Act 2010; and (xi) any other person as may be specified by the Commission; provided that, in the each of the preceding categories (i) to (xi), the distribution of the shares is made by a holder of a Capital Markets Services License who carries on the business of dealing in securities. The distribution in Malaysia of this prospectus supplement is subject to Malaysian laws. This prospectus supplement does not constitute and may not be used for the purpose of public offering or an issue, offer for subscription or purchase, invitation to subscribe for or purchase any securities requiring the registration of a prospectus with the Commission under the Capital Markets and Services Act 2007.

Notice to prospective investors in Taiwan

The shares have not been and will not be registered with the Financial Supervisory Commission of Taiwan pursuant to relevant securities laws and regulations and may not be sold, issued or offered within Taiwan through a public offering or in circumstances which constitutes an offer within the meaning of the Securities and Exchange Act of Taiwan that requires a registration or approval of the Financial Supervisory Commission of Taiwan. No person or entity in Taiwan has been authorized to offer, sell, give advice regarding or otherwise intermediate the offering and sale of the shares in Taiwan.

Notice to prospective investors in South Africa

Due to restrictions under the securities laws of South Africa, no "*offer to the public*" (as such term is defined in the South African Companies Act, No. 71 of 2008 (as amended or re-enacted), or the South African Companies

Act) is being made in connection with the issue of the shares in South Africa. Accordingly, this document does not, nor is it intended to, constitute a “*registered prospectus*” (as that term is defined in the South African Companies Act) prepared and registered under the South African Companies Act and has not been approved by, and/or filed with, the South African Companies and Intellectual Property Commission or any other regulatory authority in South Africa. The shares are not offered, and the offer shall not be transferred, sold, renounced or delivered, in South Africa or to a person with an address in South Africa, unless one or other of the following exemptions stipulated in section 96 (1) applies:

- Section 96 (1) (a) the offer, transfer, sale, renunciation or delivery is to:
- (i) persons whose ordinary business, or part of whose ordinary business, is to deal in securities, as principal or agent;
 - (ii) the South African Public Investment Corporation;
 - (iii) persons or entities regulated by the Reserve Bank of South Africa;
 - (iv) authorised financial service providers under South African law;
 - (v) financial institutions recognised as such under South African law;
 - (vi) a wholly-owned subsidiary of any person or entity contemplated in ©, (d) or ©, acting as agent in the capacity of an authorized portfolio manager for a pension fund, or as manager for a collective investment scheme (in each case duly registered as such under South African law); or
 - (vii) any combination of the person in (i) to (vi); or
- Section 96 (1) (b) the total contemplated acquisition cost of the securities, for any single addressee acting as principal is equal to or greater than ZAR1,000,000 or such higher amount as may be promulgated by notice in the Government Gazette of South Africa pursuant to section 96(2)(a) of the South African Companies Act.

Information made available in this prospectus supplement should not be considered as “advice” as defined in the South African Financial Advisory and Intermediary Services Act, 2002.

Notice to prospective investors in Israel

In the State of Israel this prospectus supplement shall not be regarded as an offer to the public to purchase shares of common stock under the Israeli Securities Law, 5728—1968, which requires a prospectus to be published and authorized by the Israel Securities Authority, if it complies with certain provisions of Section 15 of the Israeli Securities Law, 5728—1968, including, inter alia, if: (i) the offer is made, distributed or directed to not more than 35 investors, subject to certain conditions (the “Addressed Investors”); or (ii) the offer is made, distributed or directed to certain qualified investors defined in the First Addendum of the Israeli Securities Law, 5728—1968, subject to certain conditions (the “Qualified Investors”). The Qualified Investors shall not be taken into account in the count of the Addressed Investors and may be offered to purchase securities in addition to the 35 Addressed Investors. We have not and will not take any action that would require us to publish a prospectus in accordance with and subject to the Israeli Securities Law, 5728—1968. We have not and will not distribute this prospectus supplement or make, distribute or direct an offer to subscribe for our shares of common stock to any person within the State of Israel, other than to Qualified Investors and up to 35 Addressed Investors. Qualified Investors may have to submit written evidence that they meet the definitions set out in of the First Addendum to the Israeli Securities Law, 5728—1968. In particular, we may request, as a condition to be

offered shares of common stock, that Qualified Investors will each represent, warrant and certify to us and/or to anyone acting on our behalf: (i) that it is an investor falling within one of the categories listed in the First Addendum to the Israeli Securities Law, 5728—1968; (ii) which of the categories listed in the First Addendum to the Israeli Securities Law, 5728—1968 regarding Qualified Investors is applicable to it; (iii) that it will abide by all provisions set forth in the Israeli Securities Law, 5728—1968 and the regulations promulgated thereunder in connection with the offer to be issued shares of common stock; (iv) that the shares of common stock that it will be issued are, subject to exemptions available under the Israeli Securities Law, 5728—1968: (a) for its own account; (b) for investment purposes only; and (c) not issued with a view to resale within the State of Israel, other than in accordance with the provisions of the Israeli Securities Law, 5728—1968; and (v) that it is willing to provide further evidence of its Qualified Investor status. Addressed Investors may have to submit written evidence in respect of their identity and may have to sign and submit a declaration containing, inter alia, the Addressed Investor's name, address and passport number or Israeli identification number.

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, New York, New York.

Experts

The consolidated financial statements as of December 31, 2022 and 2021 and for each of the three years in the period ended December 31, 2022 and management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2022 incorporated by reference in this Prospectus Supplement and in the Registration Statement have been so incorporated in reliance on the reports of BDO USA, LLP (n/k/a BDO USA, P.C.), 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 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, 2022, filed with the SEC on February 28, 2023;
- our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2023 and June 30, 2023, filed with the SEC on [May 9, 2023](#) and [August 8, 2023](#), respectively;
- our Current Reports on Form 8-K filed with the SEC on [March 13, 2023](#), [June 21, 2023](#) and [September 11, 2023](#);

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- our Definitive Proxy Statement on [Schedule 14A](#) (other than information furnished rather than filed), filed with the SEC on April 27, 2023; 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 $\text{IGF-1} \leq 1.0 \times \text{ULN}$ 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

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 ORILISSA (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

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;

- 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

- 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

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.

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.

11,441,648 shares



Common stock

Prospectus supplement

Joint book-running managers

J.P. Morgan

Morgan Stanley

Leerink Partners

Piper Sandler

Lead manager

LifeSci Capital

September 12, 2023

Calculation of Filing Fee Tables

424(b)(5)

(Form Type)

Crinetics Pharmaceuticals, Inc.

(Exact Name of Registrant as Specified in its Charter)

Table 1: Newly Registered and Carry Forward Securities

	Security Type	Security Class Title	Fee Calculation or Carry Forward Rule	Amount Registered	Proposed Maximum Offering Price Per Unit	Maximum Aggregate Offering Price	Fee Rate	Amount of Registration Fee	Carry Forward Form Type	Carry Forward File Number	Carry Forward Initial effective date	Filing Fee Previously Paid In Connection with Unsold Securities to be Carried Forward
Fees to Be Paid	Equity	Common Stock, \$0.001 par value per share	Rule 457(r)	13,157,895(1)	\$30.59	\$402,500,008.05	0.00011020	\$44,355.51(2)	—	—	—	—
Fees Previously Paid												
Carry Forward Securities												
Carry Forward Securities	—		—	—	—	—	—	—	—	—	—	—
	Total Offering Amounts					\$402,500,008.05		\$44,355.51				
	Total Fees Previously Paid							—				
	Total Fee Offsets							—				
	Net Fee Due							\$44,355.51				

- (1) The amount registered includes 1,716,247 shares of Common Stock that may be purchased by the underwriters pursuant to their option to purchase additional shares of Common Stock.
- (2) Calculated in accordance with Rule 457(r) under the Securities Act of 1933, as amended (the “Securities Act”). Payment of the registration fee at the time of filing of the registrant’s Registration Statement on Form S-3ASR (File No. 333-258694) filed by the Registrant on August 10, 2021 was deferred pursuant to Rules 456(b) and 457(r) under the Securities Act and is paid herewith.