Filed Pursuant to Rule 424(b)(4)
Registration No. 333-225824

Prospectus

6,000,000 shares

Common stock

This is an initial public offering of shares of common stock by Crinetics Pharmaceuticals, Inc. We are offering 6,000,000 shares of our common stock to be sold in the offering. The initial public offering price is $17.00 per share.

Prior to this offering, there has been no public market for our common stock. Our common stock has been approved for listing on the Nasdaq Global Select Market under the symbol “CRNX.”

We are an “emerging growth company” as defined under the federal securities laws and, as such, have elected to comply with certain reduced public company reporting requirements.

	Per share	Total
Initial public offering price	$ 17.00	$102,000,000
Underwriting discounts and commissions(1)	$ 1.19	$ 7,140,000
Proceeds to Crinetics Pharmaceuticals, Inc., before expenses	$ 15.81	$ 94,860,000

(1) See “Underwriting” for a description of the compensation payable to the underwriters.

We have granted the underwriters an option for a period of 30 days to purchase up to 900,000 additional shares of common stock.

Investing in our common stock involves a high degree of risk. See “Risk factors” beginning on page 11.

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

Certain of our principal stockholders, including entities affiliated with certain of our directors, have indicated an interest in purchasing an aggregate of approximately $30.0 million in shares of our common stock in this offering at the initial public offering price per share and on the same terms as the other purchasers in this offering. However, because these indications of interest are not binding agreements or commitments to purchase, the underwriters may determine to sell more, less or no shares in this offering to any or all of these stockholders, or any or all of these stockholders may determine to purchase more, less or no shares in this offering. The underwriters will receive the same underwriting discount on any shares purchased by these stockholders as they will on any other shares sold to the public in this offering.

The underwriters expect to deliver the shares to purchasers on or about July 20, 2018.

J.P. Morgan **Leerink Partners** **Piper Jaffray**

July 17, 2018

Table of contents

Neither we nor the underwriters have authorized anyone to provide you with information other than that contained in this prospectus or any free writing prospectus prepared by or on behalf of us or to which we have referred you. We and the underwriters 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 underwriters are offering to sell, and seeking offers to buy, common stock only in jurisdictions where offers and sales are permitted. The information contained in this prospectus or any free writing prospectus is accurate only as of its date, regardless of its time of delivery or of any sale of shares of our common stock. Our business, financial condition, results of operations and prospects may have changed since that date.

Through and including August 11, 2018 (the 25th day after the date of this prospectus) all dealers that effect transactions in these securities, whether or not participating in this offering, may be required to deliver a prospectus. This is in addition to the dealers' obligation to deliver a prospectus when acting as underwriters and with respect to their unsold allotments or subscriptions.

For investors outside of the United States: We have not, and the underwriters have not, done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than the United States. Persons outside of the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of the shares of common stock and the distribution of this prospectus outside of the United States.

Prospectus summary

This summary highlights information contained elsewhere in this prospectus. This summary does not contain all of the information you should consider before investing in our common stock. You should read this entire prospectus carefully, especially the section in this prospectus entitled "Risk factors" and our consolidated financial statements and the related notes thereto included at the end of this prospectus, before making an investment decision. As used in this prospectus, unless the context otherwise requires, references to "we," "us," "our," "our company" and "Crinetics" refer to Crinetics Pharmaceuticals, Inc.

Overview

We are a clinical stage pharmaceutical company focused on the discovery, development and commercialization of novel therapeutics for rare endocrine diseases and endocrine-related tumors. Endocrine pathways function to maintain homeostasis and commonly use peptide hormones acting through G protein coupled receptors, or GPCRs, to regulate many aspects of physiology including growth, energy, metabolism, gastrointestinal function and stress responses. We have assembled a seasoned team with extensive expertise in drug discovery and development in endocrine GPCRs and built a highly productive drug discovery organization. We have discovered a pipeline of oral nonpeptide (small molecule) new chemical entities that target peptide GPCRs to treat a variety of rare endocrine diseases where treatment options have significant efficacy, safety and/or tolerability limitations. Our lead product candidate, CRN00808, is currently in clinical development for the treatment of acromegaly, and we are advancing additional product candidates through preclinical 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. All of our product candidates have been discovered and developed internally and we have retained global rights to commercialize our product candidates and have no royalty or licensing obligations. The following table summarizes our product candidate pipeline and anticipated milestones.

PROGRAM	DISCOVERY	PRECLIN	PHASE 1	PHASE 2	PHASE 3	Anticipated Next Milestone
CRN00808 (Oral sst2 Agonist) Acromegaly						Initiate Ph 2 Trials: early 2019
CRN02481 (Oral sst5 Agonist) Hyperinsulinemia						Initiate Ph 1 Trial: 1H 2019 Ph 1 Results: 2019
CRN01941 (Oral sst2 Agonist) Neuroendocrine Tumors (NETs)						Initiate Ph 1 Trial: 1H 2019 Ph 1 Results: late '19/early '20

Our discovery team has significant expertise in understanding and creating product candidates to influence the dynamic behavior of GPCRs and has developed a number of proprietary methods, techniques and tools that we believe will enable us to efficiently and reliably evaluate newly synthesized molecules. We employ an iterative strategy where compounds are designed, synthesized and rapidly characterized for pharmacologic and pharmaceutical properties. There are more than 80 known peptide hormones acting at more than 120 known different receptors. Historically, it was assumed that small molecules could not replicate or compete with the complex interactions between peptides and their cognate GPCRs. As such, most drugs developed for peptide GPCRs have been and continue to be peptides themselves, which present manufacturing and formulation

difficulties and force patients to undergo frequent injections because peptides generally are not orally bioavailable. With each of our drug discovery programs, our goal is to specifically tailor a product candidate with pharmacologic and pharmaceutical properties highly optimized for its interaction with its specific GPCR target that we anticipate will translate to downstream benefits in our chosen therapeutic applications.

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 elagolix, a nonpeptide product candidate designed for the treatment of endometriosis and uterine fibroids that is currently awaiting a decision from the U.S. Food and Drug Administration, or FDA, on marketing approval. In addition, Dr. Madan held a key leadership role in the discovery and development of Ingrezza, which was approved by the FDA in 2017 for tardive dyskinesia. Our investors include 5AM Ventures, OrbiMed Advisors, Perceptive Advisors, RA Capital Management, Versant Ventures and Vivo Capital.

Our product candidates

CRN00808 for the treatment of acromegaly

Our lead product candidate, CRN00808, establishes a new class of oral selective nonpeptide somatostatin receptor type 2, or sst2, biased agonists designed for the treatment of acromegaly and is the first agent in its class with reported clinical results. 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. More than 25,000 people in the United States suffer from acromegaly, and an estimated 40% to 60% are candidates for chronic pharmacological intervention, of which somatostatin peptide analogs are the primary pharmacotherapy. In 2017, injected somatostatin peptide drugs accounted for approximately $2.7 billion in global sales for the treatment of acromegaly, neuroendocrine tumors, or NETs, and other uses. Currently marketed peptide 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.

In March 2018, we reported initial results from a Phase 1, double-blind, randomized, placebo-controlled, single- and multiple-ascending dose trial to evaluate the safety, pharmacokinetics, or PK, and pharmacodynamics, or PD, of CRN00808 in 99 healthy volunteers. CRN00808 demonstrated clinical proof-of-concept by potently suppressing stimulated GH and baseline IGF-1 in these subjects. The plasma exposure of CRN00808 indicated the drug was well absorbed with a half-life of 42 to 50 hours, supporting once daily administration in patients. The safety and tolerability of CRN00808 observed in this trial was generally consistent with that of approved peptide somatostatin analogs. The most common adverse events were mild gastrointestinal disorders and mild elevations of pancreatic enzymes. We plan to submit an investigational new drug application, or IND, to the FDA in the second half of 2018 and, if accepted, plan to initiate two Phase 2 clinical trials in acromegaly patients in early 2019. We anticipate that the first of these will be a double-blind, randomized, placebo-controlled trial conducted in patients whose IGF-1 levels are currently controlled by octreotide or lanreotide, each of which is a somatostatin analog approved for the treatment of acromegaly. We plan to conduct a second, open-label exploratory Phase 2 trial to evaluate the effects of CRN00808 on patients whose IGF-1 levels are not adequately controlled by octreotide or lanreotide alone.

CRN02481 for the treatment of hyperinsulinemias

CRN02481 represents a new class of oral selective nonpeptide somatostatin type 5 receptor, or sst5, agonists designed to treat congenital hyperinsulinism, or CHI. This is a devastating rare disease in which infants are born with mutations that cause excess secretion of the pancreatic hormone insulin resulting in profound hypoglycemia, a very low level of blood glucose. This loss of homeostatic control of blood glucose levels can lead to seizures, developmental disorders, learning disabilities, coma and even death. CHI occurs in approximately 1 in 30,000 to 50,000 new births in the United States. We believe an orally available sst5 agonist would provide an important new therapeutic option that inhibits insulin secretion while avoiding glucagon suppression, allowing these patients to maintain normal glucose levels and possibly avoid pancreatectomy, the surgical removal of all or a part of the pancreas.

To evaluate preclinical in vivo proof-of-concept, we tested CRN02481 in a rat model of CHI. When these rats were then treated with CRN02481, blood glucose levels returned to normal, and at higher doses, even to a hyperglycemic state. In addition, the drug-like characteristics of CRN02481 met our rigorous internal criteria that we use to determine if a product candidate should enter into preclinical development. We are currently optimizing the good manufacturing process, or GMP, synthesis and performing good laboratory practice, or GLP, first-in-human enabling studies for CRN02481. We expect to initiate a Phase 1 human proof-of-concept clinical trial that evaluates inhibition of insulin secretion and its effects on blood glucose in the first half of 2019. We expect results from this trial in 2019.

CRN01941 for the treatment of neuroendocrine tumors (NETs)

CRN01941 is an oral nonpeptide sst2 biased agonist designed for the treatment of NETs, which arise from cells of the enteroendocrine system in the gastrointestinal tract, lung or, more rarely, the pancreas. These tumors are usually slow growing and often initially asymptomatic. Therefore, many patients are only diagnosed at a time of extensive metastatic disease, and these patients will often progress to liver failure. In approximately 10% of cases, these tumors are associated with excess secretion of serotonin resulting in carcinoid syndrome, which is characterized by severe diarrhea and flushing. Patients with well- and moderately-differentiated tumors and distant metastases have a five-year survival probability of 35%, according to a 2012 study published in Neuroendocrinology. NETs are present in approximately 171,000 adults in the United States. Most NETs overexpress sst2 receptors and injected depots of peptide somatostatin analogs have become the first-line standard of care for many NETs patients, as detailed in recent National Comprehensive Cancer Network guidelines.

The chemical structure of CRN01941 is derived from a different chemical scaffold from that of CRN00808. In vitro pharmacology studies demonstrated that CRN01941 potently stimulated sst2 receptor activity (as measured by a decrease in cyclic adenosine monophosphate, or cAMP, accumulation in cells expressing the human sst2 receptor) and is highly biased for G_i signaling versus receptor internalization (88-fold). In addition, the drug-like characteristics of CRN01941 met our rigorous internal criteria that we use to determine if a product candidate should enter into preclinical development. We are currently optimizing GMP synthesis and performing GLP first-in-human enabling studies on CRN01941 and expect to initiate a Phase 1 human proof-of-concept clinical trial in the first half of 2019. We expect results from this trial in late 2019/early 2020.

Product candidate for the treatment of Cushing's disease

We have an ongoing discovery effort to identify and advance into development the first nonpeptide product candidate to antagonize the peptide adrenocorticotrophic hormone, or ACTH, designed for the treatment of Cushing's disease. 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. Cushing's disease is an orphan indication with a prevalence of approximately 16,000 patients in the United States.

ACTH acts through a peptide GPCR called the melanocortin type 2 receptor, or MC2, that is specifically expressed in the adrenal gland. Our discovery team has identified potent, selective nonpeptide antagonists of MC2 designed to block ACTH action and prevent its excessive stimulation of the adrenal gland in Cushing's disease patients. This program is currently in the lead optimization stage, and our goal is to select a product candidate for preclinical development in 2019.

Our strategy

Our objective is to transform the treatment of rare endocrine diseases and endocrine-related tumors by creating a diversified portfolio of novel therapeutics that will advance the standard of care. To achieve this objective, we are pursuing the following strategy:

- Focus on rare endocrine diseases and endocrine-related tumors with significant unmet medical need;
- Rapidly advance multiple product candidates in parallel to clinical proof-of-concept and late stage development by targeting diseases that require relatively small trials and employ validated biomarkers as clinical endpoints;
- Continue to expand our therapeutic pipeline for rare endocrine diseases by leveraging the capabilities of our experienced discovery team in the area of peptide hormone GPCRs;
- Retain commercialization rights to maximize the value of our product candidates; and
- Maintain an entrepreneurial, scientifically rigorous and inclusive corporate culture where employees are fully engaged and strive to bring improved therapeutic options to patients.

Risks related to our business

Our ability to execute our business strategy is subject to numerous risks, as more fully described in the section entitled "Risk factors" immediately following this prospectus summary. These risks include, among others:

- We have a limited operating history, have incurred significant operating losses since our inception and expect to incur significant losses for the foreseeable future. We may never generate any revenue or become profitable or, if we achieve profitability, we may not be able to sustain it.
- We will require substantial additional financing to achieve our goals, and a failure to obtain this necessary capital when needed on acceptable terms, or at all, could force us to delay, limit, reduce or terminate our product development programs, commercialization efforts or other operations.
- We are early in our development efforts and have only one product candidate in clinical development. All of our other research programs are still in the preclinical or discovery stage. If we are unable to successfully develop product candidates or experience significant delays in doing so, our business will be materially harmed.

- We cannot assure you that we will be able to successfully develop any product candidates.
- Preclinical and clinical drug development involves a lengthy and expensive process with an uncertain outcome, and the results of preclinical studies and early clinical trials are not necessarily predictive of future results. Our product candidates may not have favorable results in later clinical trials, if any, or receive regulatory approval.
- Any delays in the commencement or completion, or termination or suspension, of our clinical trials could result in increased costs to us, delay or limit our ability to generate revenue and adversely affect our commercial prospects.
- We face competition from entities that have developed or may develop somatostatin agonist products or other product candidates. If these companies develop technologies or product candidates more rapidly than we do or their technologies are more effective, our ability to develop and successfully commercialize products may be adversely affected.
- We rely on third parties to conduct some or all aspects of our product manufacturing, research and preclinical and clinical testing, and these third parties may not perform satisfactorily.
- Our success depends on our ability to protect our intellectual property and our proprietary technologies.

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. Our website address is www.crinetics.com. The information contained in, or accessible through, our website does not constitute part of this prospectus. We have included our website address as an inactive textual reference only.

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.

Implications of being an emerging growth company

As a company with less than $1.07 billion in revenue during our last fiscal year, we qualify as an “emerging growth company” as defined in the Jumpstart Our Business Startups Act, or the JOBS Act, enacted in April 2012. An emerging growth company may take advantage of reduced reporting requirements that are otherwise applicable to public companies. These provisions include, but are not limited to:

- being permitted to present only two years of audited financial statements and only two years of related Management’s Discussion & Analysis of Financial Condition and Results of Operations in this prospectus;
- not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, as amended, or Sarbanes-Oxley;
- reduced disclosure obligations regarding executive compensation in this prospectus and our periodic reports, proxy statements and registration statements; and

- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

We may take advantage of these provisions until the last day of our fiscal year following the fifth anniversary of the date of the first sale of our common equity securities pursuant to an effective registration statement under the Securities Act of 1933, as amended, or the Securities Act, which such fifth anniversary will occur in 2023. However, if certain events occur prior to the end of such five-year period, including if we become a “large accelerated filer” as defined in Rule 12b-2 under the Securities Exchange Act of 1934, or the Exchange Act, our annual gross revenues exceed $1.07 billion or we issue more than $1.0 billion of non-convertible debt in any three-year period, we will cease to be an emerging growth company prior to the end of such five-year period.

We have elected to take advantage of certain of the reduced disclosure obligations in the registration statement of which this prospectus is a part and may elect to take advantage of other reduced reporting requirements in future filings. As a result, the information that we provide to our stockholders may be different than you might receive from other public reporting companies in which you hold equity interests.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. We have irrevocably elected not to avail ourselves of this exemption and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

The offering

Common stock offered by us	6,000,000 shares
Common stock to be outstanding immediately after this offering	23,007,961 shares (or 23,907,961 shares if the underwriters exercise their option to purchase additional shares in full)
Option to purchase additional shares	We have granted the underwriters an option exercisable for a period of 30 days to purchase up to 900,000 additional shares of our common stock.
Use of proceeds	We intend to use the net proceeds of this offering to fund research and development of our product candidates and development programs and for working capital and general corporate purposes. See “Use of proceeds” for a more complete description of the intended use of proceeds from this offering.
Directed shares	At our request, the underwriters have reserved for sale, at the initial public offering price, up to 2% of the shares offered hereby for employees, directors and other persons associated with us who have expressed an interest in purchasing common stock in the offering. See “Underwriting” for more information.
Risk factors	You should read the “Risk factors” section of this prospectus and the other information in this prospectus for a discussion of factors to consider carefully before deciding to invest in shares of our common stock.
Nasdaq Global Select Market symbol	“CRNX”

The number of shares of our common stock to be outstanding after this offering set forth above is based on 17,007,961 shares of our common stock outstanding as of March 31, 2018, after giving effect to the automatic conversion of all outstanding shares of our convertible preferred stock into 14,712,571 shares of our common stock immediately prior to the closing of this offering, and excludes:

- 1,457,952 shares of common stock issuable upon exercise of stock options outstanding as of March 31, 2018, at a weighted-average exercise price of $1.34 per share;
- 1,027,196 shares of common stock issuable upon exercise of stock options granted after March 31, 2018, at a weighted-average exercise price of $9.81 per share;
- 1,991,637 shares of our common stock reserved for future issuance under our 2018 equity incentive plan, or the 2018 Plan, which became effective in connection with this offering (which number includes 391,637 shares remaining available for issuance under our 2015 Stock Incentive Plan as of June 30, 2018 (which shares became available for issuance under the 2018 Plan upon its effectiveness), but does not include any potential evergreen increases pursuant to the terms of the 2018 Plan); and
- 250,000 shares of common stock reserved for future issuance under our 2018 employee stock purchase plan, or ESPP, which became effective in connection with this offering (which number does not include any potential evergreen increases pursuant to the terms of the ESPP).

Unless otherwise indicated, this prospectus assumes or gives effect to the following:

- the filing and effectiveness of our amended and restated certificate of incorporation and the adoption of our amended and restated bylaws, each of which will occur immediately prior to the closing of this offering;
- the automatic conversion of all outstanding shares of our convertible preferred stock into 14,712,571 shares of our common stock immediately prior to the closing of the offering;
- a one-for-3.29 reverse stock split of our common stock which we effected on July 6, 2018;
- no exercise of the outstanding options described above; and
- no exercise by the underwriters of their option to purchase 900,000 additional shares of our common stock.

Certain of our principal stockholders, including entities affiliated with certain of our directors, have indicated an interest in purchasing an aggregate of approximately $30.0 million in shares of our common stock in this offering at the initial public offering price per share and on the same terms as the other purchasers in this offering. However, because these indications of interest are not binding agreements or commitments to purchase, the underwriters may determine to sell more, less or no shares in this offering to any or all of these stockholders, or any or all of these stockholders may determine to purchase more, less or no shares in this offering. The underwriters will receive the same underwriting discount on any shares purchased by these stockholders as they will on any other shares sold to the public in this offering.

Summary consolidated financial data

The following tables set forth a summary of our historical consolidated financial data as of, and for the periods ended on, the dates indicated. We have derived the statements of operations data for the years ended December 31, 2016 and 2017 and the balance sheet data as of December 31, 2017 from our audited consolidated financial statements included elsewhere in this prospectus. We have derived the statements of operations data for the three months ended March 31, 2017 and 2018 and the balance sheet data as of March 31, 2018 from our unaudited consolidated financial statements included elsewhere in this prospectus. The unaudited consolidated financial statements have been prepared on a basis consistent with our audited consolidated financial statements included in this prospectus and, in the opinion of management, reflect all adjustments, consisting only of normal recurring adjustments, necessary to fairly state our financial position as of March 31, 2018 and results of operations for the three months ended March 31, 2017 and 2018. You should read this data together with our consolidated financial statements and related notes included elsewhere in this prospectus and the sections in this prospectus entitled "Selected consolidated financial data" and "Management's discussion and analysis of financial condition and results of operations." Our historical results for any prior period are not necessarily indicative of our future results.

	Years Ended December 31,		Three Months Ended March 31,	
(in thousands, except share and per share data)	**2016**	**2017**	**2017**	**2018**
			(unaudited)	
Consolidated Statements of Operations Data:				
Grant revenues	$ 589	$ 2,045	$ 45	$ 442
Operating expenses:				
Research and development	5,100	9,233	2,065	4,720
General and administrative	1,533	1,939	589	1,248
Total operating expenses	6,633	11,172	2,654	5,968
Loss from operations	(6,044)	(9,127)	(2,609)	(5,526)
Other income (expense):				
Interest income	37	26	7	64
Interest expense	(11)	(8)	(2)	—
Other expense	(1)	(48)	(2)	(2)
Total other income (expense)	25	(30)	3	62
Net loss	$ (6,019)	$ (9,157)	$ (2,606)	$ (5,464)
Net loss per share, basic and diluted(1)	$ (5.96)	$ (6.68)	$ (2.18)	$ (2.92)
Weighted-average shares of common stock outstanding, basic and diluted(1)	1,010,510	1,370,578	1,197,711	1,869,576
Pro forma net loss per share, basic and diluted (unaudited)(1)		$ (1.18)		$ (0.39)
Pro forma weighted-average shares of common stock outstanding, basic and diluted (unaudited)(1)		7,746,089		13,878,156

(1) See Note 1 to our audited consolidated financial statements included elsewhere in this prospectus for an explanation of the method used to calculate the historical and pro forma net loss per share, basic and diluted, and the number of shares used in the computation of the per share amounts.

(in thousands)	As of March 31, 2018		
	Actual (unaudited)	Pro forma(1) (unaudited)	Pro forma as adjusted(1)(2) (unaudited)
Consolidated Balance Sheet Data:			
Cash and cash equivalents	$ 73,740	$ 73,740	$165,800
Working capital	71,595	71,595	163,655
Total assets	76,329	76,329	168,389
Convertible preferred stock	92,975	—	—
Accumulated deficit	(21,729)	(21,729)	(21,729)
Total stockholders' equity (deficit)	(19,976)	72,999	165,059

(1) Gives effect to the automatic conversion of all of our outstanding shares of convertible preferred stock into an aggregate of 14,712,571 shares of common stock and the related reclassification of the carrying value of the convertible preferred stock to permanent equity immediately prior to the closing of this offering.

(2) Gives effect to (i) the pro forma adjustments set forth in footnote (1) above and (ii) the issuance and sale of 6,000,000 shares of our common stock in this offering at the initial public offering price of $17.00 per share, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

Risk factors

Investing in our common stock involves a high degree of risk. You should consider carefully the risks and uncertainties described below, together with all of the other information in this prospectus, including our consolidated financial statements and related notes included elsewhere in this prospectus and "Management's discussion and analysis of financial condition and results of operations," before making an investment decision. If any of the following risks are realized, our business, financial condition, results of operations and prospects could be materially and adversely affected. In that event, the trading price of our common stock could decline and you could lose part or all of your investment.

Risks related to our limited operating history, financial position and capital requirements

We have a limited operating history, have incurred significant operating losses since our inception and expect to incur significant losses for the foreseeable future. We may never generate any revenue or become profitable or, if we achieve profitability, we may not be able to sustain it.

Pharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. We are a clinical stage pharmaceutical company with a limited operating history upon which you can evaluate our business and prospects. We commenced operations in 2010, and to date, we have focused primarily on organizing and staffing our company, business planning, raising capital, discovering potential product candidates and conducting preclinical studies and clinical trials. Our approach to the discovery and development of product candidates is unproven, and we do not know whether we will be able to develop any products of commercial value. In addition, only one of our product candidates, CRN00808, is in early clinical development, while our other development programs remain in the preclinical or discovery stages. We have not yet demonstrated an ability to successfully complete any clinical trials beyond Phase 1, obtain regulatory approvals, manufacture a commercial scale product, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. Consequently, any predictions made about our future success or viability may not be as accurate as they could be if we had a history of successfully developing and commercializing pharmaceutical products.

We have incurred significant operating losses since our inception. If our product candidates are not successfully developed and approved, we may never generate any revenue. Our net losses were $6.0 million, $9.2 million and $5.5 million for the years ended December 31, 2016 and 2017 and the three months ended March 31, 2018, respectively. As of March 31, 2018, we had an accumulated deficit of $21.7 million. Substantially all of our losses have resulted from expenses incurred in connection with our research and development programs and from general and administrative costs associated with our operations. All of our product candidates will require substantial additional development time and resources before we would be able to apply for or receive regulatory approvals and begin generating revenue from product sales. We expect to continue to incur losses for the foreseeable future, and we anticipate these losses will increase substantially as we continue our development of, seek regulatory approval for and potentially commercialize any approved products.

To become and remain profitable, we must succeed in developing and eventually commercializing products that generate significant revenue. This will require us to be successful in a range of challenging activities, including completing preclinical studies and clinical trials of our product candidates, discovering additional product candidates, obtaining regulatory approval for these product candidates and manufacturing, marketing and selling any products for which we may obtain regulatory approval. We are only in the preliminary stages of most of these activities. We may never succeed in these activities and, even if we do, may never generate revenues that are significant enough to achieve profitability. In addition, we have not yet demonstrated an ability to successfully overcome many of the risks and uncertainties frequently encountered by companies in

new and rapidly evolving fields, particularly in the biopharmaceutical industry. Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would depress the value of our company and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our product candidates or even continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment.

We will require substantial additional financing to achieve our goals, and a failure to obtain this necessary capital when needed on acceptable terms, or at all, could force us to delay, limit, reduce or terminate our product development programs, commercialization efforts or other operations.

The development of biopharmaceutical product candidates is capital-intensive. We expect our expenses to increase in connection with our ongoing activities, particularly as we conduct our ongoing and planned clinical trials of CRN00808, continue research and development and initiate clinical trials of CRN02481 and CRN01941, and seek regulatory approval for our current product candidates and any future product candidates, including product candidates that we may develop for our Cushing's disease development program. In addition, if we obtain regulatory approval for any of our product candidates, we expect to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution. Because the outcome of any preclinical study or clinical trial is highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully complete the development and commercialization of our product candidates. Furthermore, following the completion of this offering, we expect to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce or eliminate our research and development programs or any future commercialization efforts.

We believe that the net proceeds from this offering, together with our existing cash and cash equivalents, will enable us to fund our operations for at least the next 24 months. In particular, we expect that the net proceeds from this offering will allow us to complete our planned Phase 2 clinical trials for CRN00808 and our planned Phase 1 clinical trials for CRN02481 and CRN01941. We have based this estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect. Our operating plans and other demands on our cash resources may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned, through public or private equity or debt financings or other sources, such as strategic collaborations. We do not currently expect future grant revenues to be a material source of revenue. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. Attempting to secure additional financing may divert our management from our day-to-day activities, which may adversely affect our ability to develop our product candidates.

Our future capital requirements will depend on many factors, including:

- the type, number, scope, progress, expansions, results, costs and timing of, our preclinical studies and clinical trials of our product candidates which we are pursuing or may choose to pursue in the future;
- the costs and timing of manufacturing for our product candidates, including commercial manufacturing if any product candidate is approved;
- the costs, timing and outcome of regulatory review of our product candidates;

- the costs of obtaining, maintaining and enforcing our patents and other intellectual property rights;
- our efforts to enhance operational systems and hire additional personnel to satisfy our obligations as a public company, including enhanced internal controls over financial reporting;
- the costs associated with hiring additional personnel and consultants as our preclinical and clinical activities increase;
- the timing and the extent of any Australian Tax Incentive refunds and future grant revenues, if any, that we receive;
- the costs and timing of establishing or securing sales and marketing capabilities if any product candidate is approved;
- our ability to achieve sufficient market acceptance, adequate coverage and reimbursement from third-party payors and adequate market share and revenue for any approved products;
- the terms and timing of establishing and maintaining collaborations, licenses and other similar arrangements; and
- costs associated with any products or technologies that we may in-license or acquire.

Identifying potential product candidates and conducting preclinical studies and clinical trials is a time- consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain regulatory approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of products that we do not expect to be commercially available for many years, if at all.

Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans.

Raising additional capital may cause dilution to our stockholders, including purchasers of common stock in this offering, restrict our operations or require us to relinquish rights to our technologies or product candidates.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through equity offerings, debt financings or other capital sources, including potentially collaborations, licenses and other similar arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

If we raise funds through future collaborations, licenses and other similar arrangements, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us and/or that may reduce the value of our common stock.

Risks related to the discovery and development and regulatory approval of our product candidates

We are early in our development efforts and have only one product candidate in clinical development. All of our other research programs are still in the preclinical or discovery stage. If we are unable to successfully develop product candidates or experience significant delays in doing so, our business will be materially harmed.

We are in the early stages of our development efforts and have only one product candidate, CRN00808, in early clinical development. All of our other development programs, including CRN02481 and CRN01941, are still in the preclinical or drug discovery stage. We have invested substantially all of our efforts and financial resources in developing our current product candidates, potential product candidates and conducting preclinical studies and clinical trials. Our ability to generate product revenues, which we do not expect will occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of our product candidates. The success of our product candidates will depend on several factors, including the following:

- completion of preclinical studies and clinical trials with favorable results;
- acceptance of INDs by the FDA or similar regulatory filing by comparable foreign regulatory authorities for the conduct of clinical trials of our product candidates and our proposed design of future clinical trials;
- receipt of marketing approvals from applicable regulatory authorities, including new drug applications, or NDAs, from the FDA and maintaining such approvals;
- making arrangements with our third-party manufacturers for, or establishing, commercial manufacturing capabilities;
- maintaining an acceptable safety profile of our products following approval; and
- maintaining and growing an organization of scientists and business people who can develop our products and technology.

The success of our business, including our ability to finance our company and generate any revenue in the future, will primarily depend on the successful development, regulatory approval and commercialization of CRN00808, as well as our other product candidates, which may never occur. In the future, we may also become dependent on other product candidates that we may develop or acquire; however, given our early stage of development, it may be several years, if at all, before we have demonstrated the safety and efficacy of a treatment sufficient to warrant approval for commercialization. If we are unable to develop, or obtain regulatory approval for, or, if approved, successfully commercialize our product candidates, we may not be able to generate sufficient revenue to continue our business.

We cannot assure you that we will be able to successfully develop any product candidates.

The success of our business depends primarily upon our ability to discover, develop and commercialize products created with our internal capabilities, including the experience of our scientists and drug development staff. While we believe we have a highly productive drug discovery and development organization, we have not yet succeeded and may not succeed in demonstrating efficacy and safety for any product candidates in clinical trials or in obtaining marketing approval thereafter. We may be unsuccessful in moving our other product candidates from preclinical studies into clinical development, discovering additional product candidates, including for our program for Cushing's disease, and any product candidates that we are currently developing may be shown to have harmful side effects or may have other characteristics that may necessitate additional clinical testing or make the product candidates unmarketable or unlikely to receive marketing approval. If any

of these events occur, we may be forced to abandon our development efforts for a program or programs, which would have a material adverse effect on our business and could potentially cause us to cease operations.

Preclinical and clinical drug development involves a lengthy and expensive process with an uncertain outcome, and the results of preclinical studies and early clinical trials are not necessarily predictive of future results. Our product candidates may not have favorable results in later clinical trials, if any, or receive regulatory approval.

Preclinical and clinical drug development is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the preclinical study or clinical trial process. Despite promising preclinical or clinical results, any product candidate can unexpectedly fail at any stage of preclinical or clinical development. The historical failure rate for product candidates in our industry is high.

The results from preclinical studies or early clinical trials of a product candidate may not predict the results of later clinical trials of the product candidate, and interim results of a clinical trial are not necessarily indicative of final results. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy characteristics despite having progressed through preclinical studies and initial clinical trials. In particular, while we have conducted preclinical studies and have interim Phase 1 results for CRN00808, we do not know how CRN00808 will perform in future clinical trials, including as a result of any differences resulting from the use of new formulations that we may use in subsequent clinical trials of CRN00808. It is not uncommon to observe results in clinical trials that are unexpected based on preclinical studies and early clinical trials, and many product candidates fail in clinical trials despite very promising early results. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in clinical development even after achieving promising results in earlier studies. In addition, interim results from our Phase 1 clinical trial for CRN00808 showed that the current capsule formulation exhibited an approximately 85% reduction in plasma concentrations when administered with a high fat breakfast, and, as a result, our planned protocol for our Phase 2 trials will require that patients fast prior to drug therapy. This may introduce variability into our Phase 2 results due to patient compliance. We expect to conduct additional activities to improve the capsule formulation, but cannot provide any assurance we will be successful in doing so. Furthermore, although our product candidates all target endocrine diseases and/or endocrine-related tumors, we cannot assure you that our preclinical programs will be able to progress from candidate identification to Phase 1 clinical proof-of-concept in healthy volunteers at the same rate as our lead product candidate, CRN00808.

For the foregoing reasons, we cannot be certain that our ongoing and planned clinical trials and preclinical studies will be successful. Any safety concerns observed in any one of our clinical trials in our targeted indications could limit the prospects for regulatory approval of our product candidates in those and other indications, which could have a material adverse effect on our business, financial condition and results of operations.

Any delays in the commencement or completion, or termination or suspension, of our clinical trials could result in increased costs to us, delay or limit our ability to generate revenue and adversely affect our commercial prospects.

Before we can initiate clinical trials for our product candidates, we must submit the results of preclinical studies to the FDA or comparable foreign regulatory authorities along with other information, including information about product candidate chemistry, manufacturing and controls and our proposed clinical trial protocol, as part of an IND application or similar regulatory filing.

Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must conduct extensive clinical studies to demonstrate the safety and efficacy of the product candidates in

humans. Clinical testing is expensive, time consuming and uncertain as to outcome. In addition, we may rely in part on preclinical, clinical and quality data generated by clinical research organizations, or CROs, and other third parties for regulatory submissions for our product candidates. While we have or will have agreements governing these third parties' services, we have limited influence over their actual performance. If these third parties do not make data available to us, or, if applicable, make regulatory submissions in a timely manner, in each case pursuant to our agreements with them, our development programs may be significantly delayed and we may need to conduct additional studies or collect additional data independently. In either case, our development costs would increase. We conducted our Phase 1 clinical trial of CRN00808 in Australia, and we will need to submit an IND for acceptance by the FDA and comparable foreign regulatory authorities prior to initiating our planned Phase 2 clinical trials. We may conduct our future Phase 1 clinical trials for our other product candidates outside the United States. The FDA or comparable foreign regulatory authorities may require us to conduct additional preclinical studies for any product candidate before it allows us to initiate clinical trials under any IND or similar regulatory filing, which may lead to additional delays and increase the costs of our preclinical development programs. Any such delays in the commencement or completion of our ongoing and planned clinical trials for our product candidates could significantly affect our product development costs.

We do not know whether our planned trials will begin on time or be completed on schedule, if at all. The commencement and completion of clinical trials can be delayed for a number of reasons, including delays related to:

- the FDA or comparable foreign regulatory authorities disagreeing as to the design or implementation of our clinical studies;
- obtaining regulatory authorizations to commence a trial or reaching a consensus with regulatory authorities on trial design;
- any failure or delay in reaching an agreement with CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- obtaining approval from one or more institutional review boards, or IRBs;
- IRBs refusing to approve, suspending or terminating the trial at an investigational site, precluding enrollment of additional subjects, or withdrawing their approval of the trial;
- changes to clinical trial protocol;
- clinical sites deviating from trial protocol or dropping out of a trial;
- manufacturing sufficient quantities of product candidate or obtaining sufficient quantities of combination therapies for use in clinical trials;
- subjects failing to enroll or remain in our trial at the rate we expect, or failing to return for post- treatment follow-up;
- subjects choosing an alternative treatment for the indication for which we are developing our product candidates, or participating in competing clinical trials;
- lack of adequate funding to continue the clinical trial;
- subjects experiencing severe or unexpected drug-related adverse effects;
- occurrence of serious adverse events in trials of the same class of agents conducted by other companies;

- selection of clinical end points that require prolonged periods of clinical observation or analysis of the resulting data;
- a facility manufacturing our product candidates or any of their components being ordered by the FDA or comparable foreign regulatory authorities to temporarily or permanently shut down due to violations of current good manufacturing practice, or cGMP, regulations or other applicable requirements, or infections or cross-contaminations of product candidates in the manufacturing process;
- any changes to our manufacturing process that may be necessary or desired;
- third-party clinical investigators losing the licenses or permits necessary to perform our clinical trials, not performing our clinical trials on our anticipated schedule or consistent with the clinical trial protocol, good clinical practices, or GCP, or other regulatory requirements;
- third-party contractors not performing data collection or analysis in a timely or accurate manner; or
- third-party contractors becoming debarred or suspended or otherwise penalized by the FDA or other government or regulatory authorities for violations of regulatory requirements, in which case we may need to find a substitute contractor, and we may not be able to use some or all of the data produced by such contractors in support of our marketing applications.

We could also encounter delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions in which such trials are being conducted, by a Data Safety Monitoring Board for such trial or by the FDA or comparable foreign regulatory authorities. Such authorities may impose such a suspension or termination due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or comparable foreign regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. In addition, changes in regulatory requirements and policies may occur, and we may need to amend clinical trial protocols to comply with these changes. Amendments may require us to resubmit our clinical trial protocols to IRBs for reexamination, which may impact the costs, timing or successful completion of a clinical trial.

Further, conducting clinical trials in foreign countries, as we may do for our product candidates, presents additional risks that may delay completion of our clinical trials. These risks include the failure of enrolled patients in foreign countries to adhere to clinical protocol as a result of differences in healthcare services or cultural customs, managing additional administrative burdens associated with foreign regulatory schemes, as well as political and economic risks relevant to such foreign countries.

Moreover, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA or comparable foreign regulatory authorities. The FDA or comparable foreign regulatory authority may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the study. The FDA or comparable foreign regulatory authority may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA or comparable foreign regulatory authority, as the case may be, and may ultimately lead to the denial of marketing approval of one or more of our product candidates.

If we experience delays in the completion of, or termination of, any clinical trial of our product candidates, the commercial prospects of our product candidates will be harmed, and our ability to generate product revenues from any of these product candidates will be delayed. Moreover, any delays in completing our clinical trials will

increase our costs, slow down our product candidate development and approval process and jeopardize our ability to commence product sales and generate revenues.

In addition, many of the factors that cause, or lead to, termination or suspension of, or a delay in the commencement or completion of, clinical trials may also ultimately lead to the denial of regulatory approval of a product candidate. We may make formulation or manufacturing changes to our product candidates, in which case we may need to conduct additional preclinical studies to bridge our modified product candidates to earlier versions. Any delays to our clinical trials that occur as a result could shorten any period during which we may have the exclusive right to commercialize our product candidates and our competitors may be able to bring products to market before we do, and the commercial viability of our product candidates could be significantly reduced. Any of these occurrences may harm our business, financial condition and prospects significantly.

We may find it difficult to enroll patients in our clinical trials given the limited number of patients who have the diseases for which our product candidates are being developed. If we encounter difficulties enrolling subjects in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.

Subject enrollment, a significant factor in the timing of clinical trials, is affected by many factors including the size and nature of the patient population, the proximity of patients to clinical sites, the eligibility and exclusion criteria for the trial, the design of the clinical trial, the risk that enrolled patients will not complete a clinical trial, our ability to recruit clinical trial investigators with the appropriate competencies and experience, competing clinical trials and clinicians' and patients' perceptions as to the potential advantages and risks of the product candidate being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating as well as any drugs under development. We will be required to identify and enroll a sufficient number of subjects for each of our clinical trials. Potential subjects for any planned clinical trials may not be adequately diagnosed or identified with the diseases which we are targeting or may not meet the entry criteria for such trials. For example, each of our target indications is an orphan indication and, in particular, our lead product candidate, CRN00808, targets acromegaly, a condition which currently affects approximately 25,000 people in the United States. We also may encounter difficulties in identifying and enrolling subjects with a stage of disease appropriate for our planned clinical trials and monitoring such subjects adequately during and after treatment. We may not be able to initiate or continue clinical trials if we are unable to locate a sufficient number of eligible subjects to participate in the clinical trials required by the FDA or comparable foreign regulatory authorities. In addition, the process of finding and diagnosing subjects may prove costly.

We plan to submit an IND to the FDA in the second half of 2018, which must go into effect before we can proceed with clinical studies. Pending FDA authorization to proceed, we plan to initiate two Phase 2 clinical trials of CRN00808 in acromegaly patients, including those who are not adequately controlled with existing therapy, in early 2019. Additionally, we plan to initiate Phase 1 clinical trials for each of CRN02481 for CHI and CRN01941 for NETs in the first half of 2019. The timing of our clinical trials depends, in part, on the speed at which we can recruit patients to participate in our trials, as well as completion of required follow-up periods. The conditions for which we currently plan to evaluate our product candidates are orphan or rare diseases with limited patient pools from which to draw for clinical trials. The eligibility criteria of our clinical trials, once established, will further limit the pool of available trial participants. If patients are unwilling to participate in our trials for any reason, including the existence of concurrent clinical trials for similar patient populations, if they are unwilling to enroll in a clinical trial with a placebo-controlled design or the availability of approved therapies, or we otherwise have difficulty enrolling a sufficient number of patients, the timeline for recruiting subjects, conducting studies and obtaining regulatory approval of our product candidates may be delayed. Our inability to enroll a sufficient number of subjects for any of our future clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether. In addition, we expect to rely on CROs and clinical trial sites to ensure proper and timely conduct

of our future clinical trials and, while we intend to enter into agreements governing their services, we will have limited influence over their actual performance.

We cannot assure you that our assumptions used in determining expected clinical trial timelines are correct or that we will not experience delays in enrollment, which would result in the delay of completion of such trials beyond our expected timelines.

Use of our product candidates could be associated with side effects or adverse events, which could severely harm our business, prospects, operating results and financial condition.

As is the case with pharmaceuticals generally, it is likely that there may be side effects and adverse events associated with our product candidates' use. Results of our clinical trials could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics. Undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or comparable foreign regulatory authorities. The drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly.

Moreover, if our product candidates are associated with undesirable side effects in clinical trials or have characteristics that are unexpected, we may elect to abandon their development or limit their development to more narrow uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective, which may limit the commercial expectations for the product candidate if approved. We may also be required to modify our study plans based on findings in our ongoing clinical trials. The safety and tolerability of CRN00808 observed in our Phase 1 clinical trial was generally consistent with that of approved peptide somatostatin analogs. The most common adverse events were mild gastrointestinal disorders occurring in approximately 30% of subjects (such as abdominal pain, flatulence, abdominal distension, and diarrhea) and mild elevations of pancreatic enzymes occurring in approximately 10% of subjects. One subject experienced moderate abdominal pain after a single 40 mg dose. Additional adverse events included headache, dizziness and cardiac rhythm abnormalities (including nonsustained ventricular tachycardia, or NSVT), which were not dose dependent and also observed in placebo subjects and/or prior to dosing. One serious adverse event of moderate NSVT was observed following a single 1.25 mg dose and was considered by the investigator unlikely to be related to CRN00808. Further analysis may reveal adverse events inconsistent with the safety profile observed to date. Additionally, while we have not yet initiated clinical trials for any of our other product candidates, it is likely that there may be side effects associated with their use. Many compounds that initially showed promise in early stage testing have later been found to cause side effects that prevented further development of the compound. In addition, regulatory authorities may draw different conclusions or require additional testing to confirm these determinations.

It is possible that as we test our product candidates in larger, longer and more extensive clinical trials, including with different dosing regimens, or as the use of these product candidates becomes more widespread if they receive regulatory approval, illnesses, injuries, discomforts and other adverse events that were observed in earlier trials, as well as conditions that did not occur or went undetected in previous trials, will be reported by subjects. If such side effects become known later in development or upon approval, if any, such findings may harm our business, financial condition and prospects significantly.

In addition, if one or more of our product candidates receives marketing approval, and we or others later identify undesirable side effects caused by such products, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw approvals of such product;

- we may be required to recall a product or change the way such product is administered to patients;
- regulatory authorities may require additional warnings on the label, such as a “black box” warning or a contraindication;
- we may be required to implement a Risk Evaluation and Mitigation Strategy, or REMS, or create a medication guide outlining the risks of such side effects for distribution to patients;
- we could be sued and held liable for harm caused to patients;
- the product could become less competitive; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and could significantly harm our business, results of operations and prospects.

As an organization, we are in the process of completing our first Phase 1 clinical trial, have never conducted later-stage clinical trials or submitted an NDA, and may be unable to do so for any of our product candidates.

We will need to successfully complete Phase 1 clinical trials and later-stage and pivotal clinical trials in order to obtain FDA or comparable foreign regulatory approval to market CRN00808, CRN02481, CRN01941 or any of our other product candidates. Carrying out later-stage clinical trials and the submission of a successful NDA is a complicated process. As an organization, we are in the process of completing our first Phase 1 clinical trial for CRN00808 and have not yet conducted any clinical trials for our other product candidates. We have not previously conducted any later stage or pivotal clinical trials, have limited experience in preparing, submitting and prosecuting regulatory filings and have not previously submitted an IND or an NDA or other comparable foreign regulatory submission for any product candidate. In addition, we have had limited interactions with the FDA and cannot be certain how many additional clinical trials of CRN00808 or any of our other product candidates will be required or how such trials should be designed. Consequently, we may be unable to successfully and efficiently execute and complete necessary clinical trials in a way that leads to regulatory submission and approval of CRN00808 or any of our other product candidates. We may require more time and incur greater costs than our competitors and may not succeed in obtaining regulatory approvals of product candidates that we develop. Failure to commence or complete, or delays in, our planned clinical trials, could prevent us from or delay us in commercializing CRN00808 or any other product candidate.

Our product candidates are subject to extensive regulation and compliance, which is costly and time consuming, and such regulation may cause unanticipated delays or prevent the receipt of the required approvals to commercialize our product candidates.

The clinical development, manufacturing, labeling, storage, record-keeping, advertising, promotion, import, export, marketing and distribution of our product candidates are subject to extensive regulation by the FDA in the United States and by comparable foreign regulatory authorities in foreign markets. In the United States, we are not permitted to market our product candidates until we receive regulatory approval from the FDA. The process of obtaining regulatory approval is expensive, often takes many years following the commencement of clinical trials and can vary substantially based upon the type, complexity and novelty of the product candidates involved, as well as the target indications and patient population. Approval policies or regulations may change, and the FDA has substantial discretion in the drug approval process, including the ability to delay, limit or deny approval of a product candidate for many reasons. Despite the time and expense invested in clinical development of product candidates, regulatory approval is never guaranteed. Neither we nor any future collaborator is permitted to market any of our product candidates in the United States until we receive approval of an NDA from the FDA.

Prior to obtaining approval to commercialize a product candidate in the United States or abroad, we or our potential future collaborators must demonstrate with substantial evidence from adequate and well-controlled clinical trials, and to the satisfaction of the FDA or comparable foreign regulatory authorities, that such product candidates are safe and effective for their intended uses. Results from nonclinical studies and clinical trials can be interpreted in different ways. Even if we believe the nonclinical or clinical data for our product candidates are promising, such data may not be sufficient to support approval by the FDA and comparable foreign regulatory authorities. The FDA or comparable foreign regulatory authorities, as the case may be, may also require us to conduct additional preclinical studies or clinical trials for our product candidates either prior to or post-approval, or may object to elements of our clinical development program.

The FDA or comparable foreign regulatory authorities can delay, limit or deny approval of a product candidate for many reasons, including:

- such authorities may disagree with the design or implementation of our clinical trials;
- negative or ambiguous results from our clinical trials or results may not meet the level of statistical significance required by the FDA or comparable foreign regulatory agencies for approval;
- serious and unexpected drug-related side effects may be experienced by participants in our clinical trials or by individuals using drugs similar to our product candidates;
- the population studied in the clinical trial may not be sufficiently broad or representative to assure safety in the full population for which we seek approval;
- such authorities may not accept clinical data from trials which are conducted at clinical facilities or in countries where the standard of care is potentially different from that of the United States;
- we may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- such authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- such authorities may not agree that the data collected from clinical trials of our product candidates are acceptable or sufficient to support the submission of an NDA or other submission or to obtain regulatory approval in the United States or elsewhere, and such authorities may impose requirements for additional preclinical studies or clinical trials;
- such authorities may disagree regarding the formulation, labeling and/or the specifications of our product candidates;
- approval may be granted only for indications that are significantly more limited than what we apply for and/or with other significant restrictions on distribution and use;
- such authorities may find deficiencies in the manufacturing processes or facilities of our third-party manufacturers with which we or any of our potential future collaborators contract for clinical and commercial supplies; or
- the approval policies or regulations of such authorities may significantly change in a manner rendering our or any of our potential future collaborators' clinical data insufficient for approval.

With respect to foreign markets, approval procedures vary among countries and, in addition to the foregoing risks, may involve additional product testing, administrative review periods and agreements with pricing authorities. In addition, events raising questions about the safety of certain marketed pharmaceuticals may result in increased cautiousness by the FDA and comparable foreign regulatory authorities in reviewing new drugs based on safety, efficacy or other regulatory considerations and may result in significant delays in

obtaining regulatory approvals. Any delay in obtaining, or inability to obtain, applicable regulatory approvals would prevent us or any of our potential future collaborators from commercializing our product candidates.

Of the large number of drugs in development, only a small percentage successfully complete the FDA or foreign regulatory approval processes and are commercialized. The lengthy approval process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval to market our product candidates, which would significantly harm our business, financial condition, results of operations and prospects.

Even if we eventually complete clinical trials and receive approval of an NDA or foreign marketing application for our product candidates, the FDA or comparable foreign regulatory authority may grant approval contingent on the performance of costly additional clinical trials, including Phase 4 clinical trials, and/or the implementation of a REMS, which may be required to ensure safe use of the drug after approval. The FDA or the comparable foreign regulatory authority also may approve a product candidate for a more limited indication or patient population than we originally requested, and the FDA or comparable foreign regulatory authority may not approve the labeling that we believe is necessary or desirable for the successful commercialization of a product. Any delay in obtaining, or inability to obtain, applicable regulatory approval would delay or prevent commercialization of that product candidate and would materially adversely impact our business and prospects.

We may expend our limited resources to pursue a particular product candidate and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we focus on specific product candidates, indications and discovery programs. As a result, we may forgo or delay pursuit of opportunities with other product candidates that could have had greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through future collaborations, licenses and other similar arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

We plan to seek orphan drug designation for CRN00808 and certain of our other product candidates. We may not be able to obtain or maintain orphan drug designations for any of our product candidates, and we may be unable to maintain the benefits associated with orphan drug designation, including the potential for market exclusivity.

Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act of 1983, the FDA may designate a product as an orphan product if it is intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals in the United States, or a patient population of greater than 200,000 individuals in the United States, but for which there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. In the European Union, the European Medicines Agency's, or the EMA, Committee for Orphan Medicinal Products grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than five in 10,000 persons in the European Union. We plan to seek orphan drug designation in the United States and the European Union for CRN00808 for acromegaly patients, and we intend to seek orphan drug designation for certain of our other product candidates. There can be no assurance that the FDA or the EMA's Committee for Orphan Medicinal Products will grant orphan designation for any indication for which we apply.

In the United States, orphan designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. In addition, if a product candidate that has orphan designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan drug exclusivity, which means that the FDA may not approve any other applications, including an NDA, to market the same drug for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity or where the manufacturer is unable to assure sufficient product quantity. The applicable exclusivity period is ten years in Europe, but such exclusivity period can be reduced to six years if a product no longer meets the criteria for orphan designation or if the product is sufficiently profitable so that market exclusivity is no longer justified.

Even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs can be approved for the same condition. Even after an orphan drug is approved, the FDA or comparable foreign regulatory authority can subsequently approve the same drug for the same condition if such regulatory authority concludes that the later drug is clinically superior if it is shown to be safer, more effective or makes a major contribution to patient care. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process.

We have conducted, or plan to conduct, our initial clinical trials for CRN00808 and our other product candidates outside of the United States. However, the FDA and other foreign equivalents may not accept data from such trials, in which case our development plans will be delayed, which could materially harm our business.

We have conducted our initial clinical trials for CRN00808 in Australia. We believe that clinical data generated in Australia will be accepted by the FDA and its foreign equivalents outside of Australia, and therefore will enable us to commence Phase 2 and possibly registration clinical trials in the United States or the European Union following submission of an IND or CTA, without the need for us to repeat our Phase 1 clinical trials in the United States or European Union. We have not yet received authorization from the FDA or the U.K. Medicines and Healthcare Products Regulatory Agency, or MHRA, to begin Phase 2 clinical trials for CRN00808 and there can be no assurance the FDA, MHRA or other foreign equivalents will accept data from the clinical trials we are conducting or plan to conduct in Australia for CRN00808. If the FDA, MHRA or other foreign equivalents do not accept any such data, we would likely be required to conduct additional Phase 1 clinical trials, which would be costly and time consuming, and delay aspects of our development plan, which could harm our business.

Although the FDA, MHRA and other foreign equivalents may accept data from clinical trials conducted entirely outside the United States and not under an IND, acceptance of such study data is generally subject to certain conditions. For example, the FDA requires the clinical trial to have been conducted in accordance with GCPs, and the FDA must be able to validate the data from the clinical trial through an onsite inspection if it deems such inspection necessary. In addition, when studies are conducted only at sites outside of the United States, the FDA generally does not provide advance comment on the clinical protocols for the studies, and therefore there is an additional potential risk that the FDA could determine that the study design or protocol for a non-U.S. clinical trial was inadequate, which would likely require us to conduct additional clinical trials.

Conducting clinical trials outside the United States also exposes us to additional risks, including risks associated with:

- additional foreign regulatory requirements;
- foreign exchange fluctuations;
- compliance with foreign manufacturing, customs, shipment and storage requirements;
- cultural differences in medical practice and clinical research; and
- diminished protection of intellectual property in some countries.

In addition, in June 2016, the United Kingdom held a referendum and voted in favor of leaving the European Union. This has created political and economic uncertainty, particularly in the United Kingdom and the European Union, and could cause disruptions to, and create uncertainty surrounding, our planned clinical trials and activities in the United Kingdom, including affecting our relationships with our existing and prospective customers, partners, vendors and employees, and could have a material impact on the regulatory regime applicable to our planned clinical trial in the United Kingdom.

Interim, topline and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publicly disclose preliminary or topline or data from our clinical studies, which is based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the topline results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Topline data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, topline data should be viewed with caution until the final data are available. From time to time, we may also disclose interim data from our clinical studies. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Adverse differences between preliminary or interim data and final data could significantly harm our business prospects.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular drug, drug candidate or our business. If the topline data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed, which could harm our business, operating results, prospects or financial condition.

Risks related to our reliance on third parties

We rely on third parties to conduct many of our preclinical studies and clinical trials. Any failure by a third party to conduct the clinical trials according to GCPs and in a timely manner may delay or prevent our ability to seek or obtain regulatory approval for or commercialize our product candidates.

We are dependent on third parties to conduct our preclinical studies and clinical trials, including our ongoing clinical trial for CRN00808, preclinical studies for CRN02481 and CRN01941 and any future clinical trials and preclinical studies for our product candidates. Specifically, we have used and relied on, and intend to continue to use and rely on, medical institutions, clinical investigators, CROs and consultants to conduct our clinical trials in accordance with our clinical protocols and regulatory requirements. These CROs, investigators and other third parties play a significant role in the conduct and timing of these trials and subsequent collection and

analysis of data. While we have agreements governing the activities of our third-party contractors, we have limited influence over their actual performance. Nevertheless, we are responsible for ensuring that each of our clinical trials is conducted in accordance with the applicable protocol and legal, regulatory and scientific standards, and our reliance on the CROs and other third parties does not relieve us of our regulatory responsibilities. We and our CROs are required to comply with GCP requirements, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for all of our product candidates in clinical development. Regulatory authorities enforce these GCPs through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our CROs or trial sites fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable, and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. In addition, our clinical trials must be conducted with product produced under cGMP regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process.

There is no guarantee that any such CROs, investigators or other third parties will devote adequate time and resources to such trials or perform as contractually required. If any of these third parties fail to meet expected deadlines, adhere to our clinical protocols or meet regulatory requirements, or otherwise performs in a substandard manner, our clinical trials may be extended, delayed or terminated. In addition, many of the third parties with whom we contract may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other drug development activities that could harm our competitive position. In addition, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and may receive cash or equity compensation in connection with such services. If these relationships and any related compensation result in perceived or actual conflicts of interest, or the FDA concludes that the financial relationship may have affected the interpretation of the study, the integrity of the data generated at the applicable clinical trial site may be questioned and the utility of the clinical trial itself may be jeopardized, which could result in the delay or rejection of any NDA we submit by the FDA. Any such delay or rejection could prevent us from commercializing our product candidates.

If any of our relationships with these third-parties terminate, we may not be able to enter into arrangements with alternative third parties or do so on commercially reasonable terms. Switching or adding additional CROs, investigators and other third parties involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines. Though we carefully manage our relationships with our CROs, investigators and other third parties, there can be no assurance that we will not encounter challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects.

We rely on third parties for the manufacture of our product candidates for preclinical and clinical development and expect to continue to do so for the foreseeable future. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or products or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We do not own or operate manufacturing facilities and have no plans to build our own clinical or commercial scale manufacturing capabilities. We rely, and expect to continue to rely, on third parties for the manufacture of our product candidates and related raw materials for preclinical and clinical development, as well as for commercial manufacture if any of our product candidates receive marketing approval. The facilities used by third-party manufacturers to manufacture our product candidates must be approved by the FDA pursuant to inspections that will be conducted after we submit our NDA to the FDA. We do not control the manufacturing process of, and are completely dependent on, third-party manufacturers for compliance with cGMP requirements for manufacture of drug products. If these third-party manufacturers cannot successfully

manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, including requirements related to the manufacturing of high potency compounds, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities. In addition, we have no control over the ability of third-party manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products.

In addition, we may be unable to establish any agreements with third-party manufacturers or to do so on acceptable terms. Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- failure of third-party manufacturers to comply with regulatory requirements and maintain quality assurance;
- breach of the manufacturing agreement by the third party;
- failure to manufacture our product according to our specifications;
- failure to manufacture our product according to our schedule or at all;
- misappropriation of our proprietary information, including our trade secrets and know-how; and
- termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us.

Our product candidates and any products that we may develop may compete with other product candidates and products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us.

Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval, and any related remedial measures may be costly or time-consuming to implement. We do not currently have arrangements in place for redundant supply or a second source for all required raw materials used in the manufacture of our product candidates. If our current third-party manufacturers cannot perform as agreed, we may be required to replace such manufacturers and we may be unable to replace them on a timely basis or at all.

Our current and anticipated future dependence upon others for the manufacture of our product candidates or products may adversely affect our future profit margins and our ability to commercialize any products that receive marketing approval on a timely and competitive basis.

Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.

Because we currently rely on other third parties to manufacture our product candidates and to perform quality testing, we must, at times, share our proprietary technology and confidential information, including trade secrets, with them. We seek to protect our proprietary technology, in part, by entering into confidentiality agreements, consulting agreements or other similar agreements with our advisors, employees and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information. Despite the contractual provisions employed

when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are intentionally or inadvertently incorporated into the technology of others or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets and despite our efforts to protect our trade secrets, a competitor's discovery of our proprietary technology and confidential information or other unauthorized use or disclosure would impair our competitive position and may have a material adverse effect on our business, financial condition, results of operations and prospects.

Risks related to commercialization of our product candidates

Even if we receive regulatory approval for any product candidate, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense. Additionally, our product candidates, if approved, could be subject to labeling and other restrictions on marketing or withdrawal from the market, and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our product candidates, when and if any of them are approved.

Following potential approval of any our product candidates, the FDA may impose significant restrictions on a product's indicated uses or marketing or impose ongoing requirements for potentially costly and time consuming post-approval studies, post-market surveillance or clinical trials to monitor the safety and efficacy of the product. The FDA may also require a REMS as a condition of approval of our product candidates, which could include requirements for a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. In addition, if the FDA or a comparable foreign regulatory authority approves our product candidates, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion, import, export and recordkeeping for our products will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMPs and GCP requirements for any clinical trials that we conduct post-approval. Later discovery of previously unknown problems with our products, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on the marketing or manufacturing of our products, withdrawal of the product from the market or voluntary or mandatory product recalls;
- restrictions on product distribution or use, or requirements to conduct post-marketing studies or clinical trials;
- fines, restitutions, disgorgement of profits or revenues, warning letters, untitled letters or holds on clinical trials;
- refusal by the FDA to approve pending applications or supplements to approved applications filed by us or suspension or revocation of approvals;
- product seizure or detention, or refusal to permit the import or export of our products; and
- injunctions or the imposition of civil or criminal penalties.

The occurrence of any event or penalty described above may inhibit our ability to commercialize our product candidates and generate revenue and could require us to expend significant time and resources in response and could generate negative publicity.

In addition, if any of our product candidates is approved, our product labeling, advertising and promotion will be subject to regulatory requirements and continuing regulatory review. The FDA strictly regulates the promotional claims that may be made about drug products. In particular, a product may not be promoted for uses that are not approved by the FDA as reflected in the product's approved labeling. If we receive marketing approval for a product candidate, physicians may nevertheless prescribe it to their patients in a manner that is inconsistent with the approved label. If we are found to have promoted such off-label uses, we may become subject to significant liability. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant sanctions. The federal government has levied large civil and criminal fines against companies for alleged improper promotion and has enjoined several companies from engaging in off-label promotion. The FDA has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed.

The FDA's and other regulatory authorities' policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability.

We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. For example, certain policies of the current U.S. administration may impact our business and industry. Namely, the current U.S. administration has taken several executive actions, including the issuance of a number of Executive Orders, that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine regulatory and oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. It is difficult to predict how these executive actions, including the Executive Orders, will be implemented, and the extent to which they will impact the FDA's ability to exercise its regulatory authority. If these executive actions impose constraints on FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.

The commercial success of our product candidates will depend upon the degree of market acceptance of such product candidates by physicians, patients, health care payors and others in the medical community.

Our product candidates may not be commercially successful. Even if any of our product candidates receive regulatory approval, they may not gain market acceptance among physicians, patients, healthcare payors or the medical community. The commercial success of any of our current or future product candidates will depend significantly on the broad adoption and use of the resulting product by physicians and patients for approved indications. The degree of market acceptance of our products will depend on a number of factors, including:

- demonstration of clinical efficacy and safety compared to other more-established products;
- the indications for which our product candidates are approved;
- the limitation of our targeted patient population and other limitations or warnings contained in any FDA-approved labeling;
- acceptance of a new drug for the relevant indication by healthcare providers and their patients;
- the pricing and cost-effectiveness of our products, as well as the cost of treatment with our products in relation to alternative treatments and therapies;

- our ability to obtain and maintain sufficient third-party coverage and adequate reimbursement from government healthcare programs, including Medicare and Medicaid, private health insurers and other third-party payors;
- the willingness of patients to pay all, or a portion of, out-of-pocket costs associated with our products in the absence of sufficient third-party coverage and adequate reimbursement;
- the prevalence and severity of any adverse effects;
- potential product liability claims;
- the timing of market introduction of our products as well as competitive drugs;
- the effectiveness of our or any of our potential future collaborators' sales and marketing strategies; and
- unfavorable publicity relating to the product.

If any product candidate is approved but does not achieve an adequate level of acceptance by physicians, hospitals, healthcare payors or patients, we may not generate sufficient revenue from that product and may not become or remain profitable. Our efforts to educate the medical community and third-party payors regarding the benefits of our products may require significant resources and may never be successful.

The successful commercialization of our product candidates, if approved, will depend in part on the extent to which governmental authorities and health insurers establish coverage, adequate reimbursement levels and favorable pricing policies. Failure to obtain or maintain coverage and adequate reimbursement for our products could limit our ability to market those products and decrease our ability to generate revenue.

The availability of coverage and the adequacy of reimbursement by governmental healthcare programs such as Medicare and Medicaid, private health insurers and other third-party payors are essential for most patients to be able to afford prescription medications such as our product candidates, if approved. Our ability to achieve coverage and acceptable levels of reimbursement for our products by governmental authorities, private health insurers and other organizations will have an effect on our ability to successfully commercialize those products. Even if we obtain coverage for a given product by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. We cannot be sure that coverage and reimbursement in the United States, the European Union or elsewhere will be available for any product that we may develop, and any reimbursement that may become available may be decreased or eliminated in the future.

Third-party payors increasingly are challenging prices charged for pharmaceutical products and services, and many third-party payors may refuse to provide coverage and reimbursement for particular drugs when an equivalent generic drug or a less expensive therapy is available. It is possible that a third-party payor may consider our products as substitutable and only offer to reimburse patients for the less expensive product. Even if we are successful in demonstrating improved efficacy or improved convenience of administration with our products, pricing of existing drugs may limit the amount we will be able to charge for our products. These payors may deny or revoke the reimbursement status of a given product or establish prices for new or existing marketed products at levels that are too low to enable us to realize an appropriate return on our investment in product development. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize our products and may not be able to obtain a satisfactory financial return on products that we may develop.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. In the United States, third-party payors, including private and governmental payors, such as the

Medicare and Medicaid programs, play an important role in determining the extent to which new drugs will be covered. Some third-party payors may require pre-approval of coverage for new or innovative devices or drug therapies before they will reimburse health care providers who use such therapies. It is difficult to predict at this time what third-party payors will decide with respect to the coverage and reimbursement for our products.

Obtaining and maintaining reimbursement status is time-consuming, costly and uncertain. The Medicare and Medicaid programs increasingly are used as models for how private payors and other governmental payors develop their coverage and reimbursement policies for drugs. However, no uniform policy for coverage and reimbursement for products exists among third-party payors in the United States. Therefore, coverage and reimbursement for products can differ significantly from payor to payor. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. Furthermore, rules and regulations regarding reimbursement change frequently, in some cases at short notice, and we believe that changes in these rules and regulations are likely.

Outside the United States, international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe and other countries has and will continue to put pressure on the pricing and usage of our products. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. Other countries allow companies to fix their own prices for medical products but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our products. Accordingly, in markets outside the United States, the reimbursement for our products may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenue and profits.

Moreover, increasing efforts by governmental and third-party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products and, as a result, they may not cover or provide adequate payment for our products. We expect to experience pricing pressures in connection with the sale of any of our products due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs and surgical procedures and other treatments, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products.

We face competition from entities that have developed or may develop somatostatin agonist products or other product candidates. If these companies develop technologies or product candidates more rapidly than we do or their technologies are more effective, our ability to develop and successfully commercialize products may be adversely affected.

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary and novel products and product candidates. Our competitors have developed, are developing or may develop products, product candidates and processes competitive with our product candidates. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future. We believe that a significant number of products are currently under development, and may become commercially available in the future, for the treatment of conditions for which we may attempt to develop product candidates. In particular, there is intense competition in the field of endocrine disorders. Our competitors include larger and better funded pharmaceutical, biopharmaceutical, biotechnological and therapeutics companies. Moreover, we may also compete with universities and other research institutions who may be active in endocrinology research and

could be in direct competition with us. We also compete with these organizations to recruit management, scientists and clinical development personnel, which could negatively affect our level of expertise and our ability to execute our business plan. We will also face competition in establishing clinical trial sites, enrolling subjects for clinical trials and in identifying and in-licensing new product candidates. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

With respect to CRN00808, injected peptide somatostatin agonists and GH receptor antagonists are the main medical therapies for acromegaly patients where surgery is unsuccessful. There are three injected somatostatin analogs approved for the treatment of acromegaly: octreotide (marketed by Novartis AG), lanreotide (marketed by Ipsen Biopharmaceuticals, Inc.) and pasireotide (marketed by Novartis). Pegvisomant (marketed by Pfizer Inc.) is a daily injectable growth hormone receptor antagonist and is generally used in patients not fully controlled on somatostatin analogs. Orally administered dopamine agonists, such as bromocriptine and cabergoline, are also used. In terms of other products in clinical development, all of them are new formulations of peptide somatostatin agonists or GH receptor antagonists. Chiasma, Inc. is in Phase 3 development for an oral octreotide product candidate for the maintenance therapy of adult patients with acromegaly in whom prior treatment with somatostatin analogs has been shown to be effective and tolerated. Other companies developing peptide somatostatin agonists or GH receptor antagonists include Camurus AB, Dauntless Pharmaceuticals, Inc., Enesi Pharma Limited, Ionis Pharmaceuticals, Inc./Antisense Therapeutics Ltd., Ipsen, MidaTech Pharma PLC and Novartis.

With respect to CRN02481, maintaining glucose levels through feeding or glucose infusions is the first step in managing CHI. Diazoxide (marketed by Teva Pharmaceuticals, Inc.) is the only approved therapy indicated for hyperinsulinemia. Octreotide (used off-label) is administered as subcutaneous injections in those who respond poorly to diazoxide. Patients who fail pharmacological therapy often progress to partial or nearly complete pancreatectomy, which can result in type I diabetes that must be managed for the remainder of the patient's life. Companies in or entering Phase 3 are Eli Lilly and Company and Zealand Pharma A/S with glucagon analogs, and Xeris Pharmaceuticals, Inc. with glucagon Ready-To-Use (RTU). Other companies developing products for potential use in CHI include Eiger Biopharmaceuticals, Inc. and Rezolute, Inc.

With respect to CRN01941, injected depots of peptide somatostatin analogs are used as therapy for NETs. In adults whose carcinoid syndrome symptoms are inadequately controlled by somatostatin therapy, telotristat ethyl (marketed by Lexicon Pharmaceuticals, Inc.) is an orally administered add-on therapy. Targeted therapies everolimus (marketed by Novartis) and sunitinib malate (marketed by Pfizer) are typically only used in patients with high grade tumors which constitute only a small fraction of NETs. In 2018, the FDA approved Novartis' Lutathera for the treatment of somatostatin receptor positive gastroenteropancreatic neuroendocrine tumors. Companies in Phase 3 development include Progenics Pharmaceuticals, Inc. and EUSA Pharma Inc. Other companies developing products for potential use in NETs include Apeiron Scientific, LLC, Camurus, Celgene Corporation, EpicentRx, Inc., Ipsen, Mateon Therapeutics, Inc., Merck & Co., Inc., MidaTech, Novartis, Oncoceutics, Inc. and Roche Holding AG.

As with acromegaly, first-line therapy for Cushing's disease is surgery to remove the pituitary tumor if possible. Adrenal enzyme inhibitors (metyrapone, ketoconazole) prevent the synthesis of cortisol and can improve symptoms. Mifepristone (marketed by Corcept Therapeutics, Inc.), a glucocorticoid receptor antagonist, is approved for control of hyperglycemia in Cushing's syndrome. The somatostatin agonist pasireotide is also approved for Cushing's disease. Novartis and Strongbridge Biopharma are each conducting Phase 3 clinical trials with osilodrostat and levoketoconazole, respectively. Other companies developing products for potential use in Cushing's disease include Corcept, Cyclacel Pharmaceuticals, Inc. and Millendo Therapeutics, Inc.

Many of our competitors have significantly greater financial, technical, manufacturing, marketing, sales and supply resources or experience than we do. If we successfully obtain approval for any product candidate, we will face competition based on many different factors, including the safety and effectiveness of our products, the ease with which our products can be administered and the extent to which patients accept relatively new routes of administration, the timing and scope of regulatory approvals for these products, the availability and cost of manufacturing, marketing and sales capabilities, price, reimbursement coverage and patent position. Competing products could present superior treatment alternatives, including by being more effective, safer, more convenient, less expensive or marketed and sold more effectively than any products we may develop. Competitive products may make any products we develop obsolete or noncompetitive before we recover the expense of developing and commercializing our product candidates. For example, a competitor could develop another oral formulation of a somatostatin agonist or other technology that could make administration of peptide therapies more convenient. If we are unable to compete effectively, our opportunity to generate revenue from the sale of our products we may develop, if approved, could be adversely affected.

The number of patients suffering from the rare endocrine diseases that we target, including acromegaly, CHI and NETs, is small, and have not been established with precision. If the market opportunities for our products are smaller than we believe they are, our revenue may be adversely affected, and our business may suffer.

We focus our research and product development on treatments for orphan and rare diseases. Given the small number of patients who have the diseases that we are targeting, it is critical to our ability to grow and become profitable that we continue to successfully identify patients with these diseases. Our projections of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with our products, are based on our beliefs and estimates. These estimates have been derived from a variety of sources, including the scientific literature, surveys of clinics, patient foundations or market research, and may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of these diseases. The number of patients may turn out to be lower than expected. The effort to identify patients with diseases we seek to treat is in early stages, and we cannot accurately predict the number of patients for whom treatment might be possible. Additionally, the potentially addressable patient population for each of our products may be limited or may not be amenable to treatment with our products, and new patients may become increasingly difficult to identify or gain access to, which would adversely affect our results of operations and our business. Further, even if we obtain significant market share for our products, because the potential target populations are very small, we may never achieve profitability despite obtaining such significant market share.

We may seek to enter into collaborations, licenses and other similar arrangements of our product and may not be successful in doing so, and even if we are, we may not realize the benefits of such relationships.

We may seek to enter into collaborations, licenses and other similar arrangements for the development or commercialization of our product candidates, due to capital costs required to develop or commercialize the product candidate in such markets. We may not be successful in our efforts to establish such collaborations for our product candidates because our product candidates may be deemed to be at too early of a stage of development for collaborative effort or third parties may not view our product candidates as having the requisite potential to demonstrate safety and efficacy or significant commercial opportunity. In addition, we face significant competition in seeking appropriate strategic partners, and the negotiation process can be time-consuming and complex. Further, any future collaboration agreements may restrict us from entering into additional agreements with potential collaborators. We cannot be certain that, following a strategic transaction or license, we will achieve an economic benefit that justifies such transaction.

Even if we are successful in our efforts to establish such collaborations, the terms that we agree upon may not be favorable to us, and we may not be able to maintain such collaborations if, for example, development or

approval of a product candidate is delayed, the safety of a product candidate is questioned or sales of an approved product are unsatisfactory. We also may not be able to realize the benefit of such collaborations if we are unable to successfully integrate them with our existing operations and company culture.

In addition, any potential future collaborations may be terminable by our strategic partners, and we may not be able to adequately protect our rights under these agreements. Furthermore, strategic partners may negotiate for certain rights to control decisions regarding the development and commercialization of our product candidates, if approved, and may not conduct those activities in the same manner as we do. Any termination of collaborations we enter into in the future, or any delay in entering into collaborations related to our product candidates, could delay the development and commercialization of our product candidates and reduce their competitiveness if they reach the market, which could have a material adverse effect on our business, financial condition and results of operations.

We currently have no marketing and sales organization and have no experience as a company in commercializing products, and we may have to invest significant resources to develop these capabilities. If we are unable to establish marketing and sales capabilities or enter into agreements with third parties to market and sell our products, we may not be able to generate product revenue.

We have no internal sales, marketing or distribution capabilities, nor have we commercialized a product. If any of our product candidates ultimately receives regulatory approval, we expect to establish a marketing and sales organization with technical expertise and supporting distribution capabilities to commercialize each such product in major markets, which will be expensive and time consuming. We have no prior experience as a company in the marketing, sale and distribution of pharmaceutical products and there are significant risks involved in building and managing a sales organization, including our ability to hire, retain and incentivize qualified individuals, generate sufficient sales leads, provide adequate training to sales and marketing personnel and effectively manage a geographically dispersed sales and marketing team. Any failure or delay in the development of our internal sales, marketing and distribution capabilities would adversely impact the commercialization of these products. We may also choose to collaborate with third parties that have direct sales forces and established distribution systems, either to augment our own sales force and distribution systems or in lieu of our own sales force and distribution systems. We may not be able to enter into collaborations or hire consultants or external service providers to assist us in sales, marketing and distribution functions on acceptable financial terms, or at all. In addition, our product revenues and our profitability, if any, may be lower if we rely on third parties for these functions than if we were to market, sell and distribute any products that we develop ourselves. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we are not successful in commercializing our products, either on our own or through arrangements with one or more third parties, we may not be able to generate any future product revenue and we would incur significant additional losses.

Our future growth may depend, in part, on our ability to operate in foreign markets, where we would be subject to additional regulatory burdens and other risks and uncertainties.

Our future growth may depend, in part, on our ability to develop and commercialize our product candidates in foreign markets. We are not permitted to market or promote any of our product candidates before we receive regulatory approval from applicable regulatory authorities in foreign markets, and we may never receive such regulatory approvals for any of our product candidates. To obtain separate regulatory approval in many other countries we must comply with numerous and varying regulatory requirements regarding safety and efficacy and governing, among other things, clinical trials, commercial sales, pricing and distribution of our product

candidates. If we obtain regulatory approval of our product candidates and ultimately commercialize our products in foreign markets, we would be subject to additional risks and uncertainties, including:

- different regulatory requirements for approval of drugs in foreign countries;
- reduced protection for intellectual property rights;
- the existence of additional third-party patent rights of potential relevance to our business;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;
- foreign reimbursement, pricing and insurance regimes;
- workforce uncertainty in countries where labor unrest is common;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters including earthquakes, typhoons, floods and fires.

Risks related to our business operations and industry

Our operating results may fluctuate significantly, which makes our future operating results difficult to predict and could cause our operating results to fall below expectations or any guidance we may provide.

Our quarterly and annual operating results may fluctuate significantly, which makes it difficult for us to predict our future operating results. These fluctuations may occur due to a variety of factors, many of which are outside of our control, including, but not limited to:

- the timing and cost of, and level of investment in, research, development, regulatory approval and commercialization activities relating to our product candidates, which may change from time to time;
- coverage and reimbursement policies with respect to our product candidates, if approved, and potential future drugs that compete with our products;
- the cost of manufacturing our product candidates, which may vary depending on the quantity of production and the terms of our agreements with third-party manufacturers;
- expenditures that we may incur to acquire, develop or commercialize additional product candidates and technologies;
- the level of demand for any approved products, which may vary significantly;
- future accounting pronouncements or changes in our accounting policies; and
- the timing and success or failure of preclinical studies or clinical trials for our product candidates or competing product candidates, or any other change in the competitive landscape of our industry, including consolidation among our competitors or partners.

The cumulative effects of these factors could result in large fluctuations and unpredictability in our quarterly and annual operating results. As a result, comparing our operating results on a period-to-period basis may not be meaningful. Investors should not rely on our past results as an indication of our future performance.

This variability and unpredictability could also result in our failing to meet the expectations of industry or financial analysts or investors for any period. If our revenue or operating results fall below the expectations of analysts or investors or below any forecasts we may provide to the market, or if the forecasts we provide to the market are below the expectations of analysts or investors, the price of our common stock could decline substantially. Such a stock price decline could occur even when we have met any previously publicly stated revenue or earnings guidance we may provide.

We are dependent on the services of our management and other clinical and scientific personnel, and if we are not able to retain these individuals or recruit additional management or clinical and scientific personnel, our business will suffer.

Our success depends in part on our continued ability to attract, retain and motivate highly qualified management, clinical and scientific personnel. We are highly dependent upon our senior management, particularly our Chief Executive Officer, as well as our senior scientists and other members of our senior management team. The loss of services of any of these individuals could delay or prevent the successful development of our product pipeline, initiation or completion of our planned clinical trials or the commercialization of our product candidates. Although we have executed employment agreements or offer letters with each member of our senior management team, these agreements are terminable at will with or without notice and, therefore, we may not be able to retain their services as expected. We do not currently maintain “key person” life insurance on the lives of our executives or any of our employees. This lack of insurance means that we may not have adequate compensation for the loss of the services of these individuals.

We will need to expand and effectively manage our managerial, operational, financial and other resources in order to successfully pursue our clinical development and commercialization efforts. We may not be successful in maintaining our unique company culture and continuing to attract or retain qualified management and scientific and clinical personnel in the future due to the intense competition for qualified personnel among pharmaceutical, biotechnology and other businesses, particularly in the San Diego area. Our industry has experienced a high rate of turnover of management personnel in recent years. If we are not able to attract, integrate, retain and motivate necessary personnel to accomplish our business objectives, we may experience constraints that will significantly impede the achievement of our development objectives, our ability to raise additional capital and our ability to implement our business strategy.

We may encounter difficulties in managing our growth and expanding our operations successfully.

As of June 30, 2018, we had 34 full-time employees and 2 part-time employees. As we continue development and pursue the potential commercialization of our product candidates, as well as function as a public company, we will need to expand our financial, development, regulatory, manufacturing, marketing and sales capabilities or contract with third parties to provide these capabilities for us. As our operations expand, we expect that we will need to manage additional relationships with various strategic partners, suppliers and other third parties. Our future financial performance and our ability to develop and commercialize our product candidates and to compete effectively will depend, in part, on our ability to manage any future growth effectively.

We conduct certain research and development operations through our Australian wholly-owned subsidiary. If we lose our ability to operate in Australia, or if our subsidiary is unable to receive the research and development tax credit allowed by Australian regulations, our business and results of operations could suffer.

In January 2017, we formed a wholly-owned Australian subsidiary, Crinetics Australia Pty Ltd, or CAPL, to conduct various preclinical and clinical activities for our product and development candidates in Australia. Due

to the geographical distance and lack of employees currently in Australia, as well as our lack of experience operating in Australia, we may not be able to efficiently or successfully monitor, develop and commercialize our lead products in Australia, including conducting clinical trials. Furthermore, we have no assurance that the results of any clinical trials that we conduct for our product candidates in Australia will be accepted by the FDA or foreign regulatory authorities for development and commercialization approvals.

In addition, current Australian tax regulations provide for a refundable research and development tax credit equal to 43.5% of qualified expenditures. If we lose our ability to operate CAPL in Australia, or if we are ineligible or unable to receive the research and development tax credit, or the Australian government significantly reduces or eliminates the tax credit, our business and results of operation may be adversely affected.

We are subject to various federal and state healthcare laws and regulations, and our failure to comply with these laws and regulations could harm our results of operations and financial condition.

Our business operations and current and future arrangements with investigators, healthcare professionals, consultants, third-party payors and customers expose us to broadly applicable federal and state fraud and abuse and other healthcare laws and regulations. These laws may constrain the business or financial arrangements and relationships through which we conduct our operations, including how we research, market, sell and distribute any products for which we obtain marketing approval. Such laws include:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or providing any remuneration (including any kickback, bribe or certain rebates), directly or indirectly, overtly or covertly, in cash or in kind, in return for, either the referral of an individual or the purchase, lease, or order, or arranging for or recommending the purchase, lease, or order of any good, facility, item or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the federal Anti- Kickback Statute or specific intent to violate it in order to have committed a violation. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act;
- the federal false claims and civil monetary penalties laws, including the civil False Claims Act, which, among other things, impose criminal and civil penalties against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment or approval that are false or fraudulent, knowingly making, using or causing to be made or used, a false record or statement material to a false or fraudulent claim, or from knowingly making or causing to be made a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which imposes criminal and civil liability for, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement, in connection with the delivery of, or payment for, healthcare benefits, items or services. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and its implementing regulations, also impose obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information without appropriate authorization by covered entities subject to the rule, such as certain health

plans, healthcare clearinghouses and healthcare providers as well as their business associates that perform certain services for or on their behalf involving the use or disclosure of individually identifiable health information;

- the federal Physician Payments Sunshine Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to the government information related to payments and other "transfers of value" made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, as well as ownership and investment interests held by the physicians described above and their immediate family members; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to our business practices, including but not limited to, research, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by non- governmental third-party payors, including private insurers, or by the patients themselves; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws and regulations that require drug manufacturers to file reports relating to pricing and marketing information, which requires tracking gifts and other remuneration and items of value provided to physicians, other healthcare providers and entities; state and local laws that require the registration of pharmaceutical sales representatives; and state and foreign laws governing the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Ensuring that our internal operations and business arrangements with third-parties comply with applicable healthcare laws and regulations could involve substantial costs. It is possible that governmental authorities will conclude that our business practices, including our consulting and advisory board arrangements with physicians and other healthcare providers, some of whom receive stock options as compensation for services provided, do not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of the laws described above or any other governmental laws and regulations that may apply to us, we may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, exclusion from U.S. government funded healthcare programs, such as Medicare and Medicaid, or similar programs in other countries or jurisdictions, disgorgement, individual imprisonment, contractual damages, reputational harm, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, diminished profits and the curtailment or restructuring of our operations. Further, defending against any such actions can be costly, time-consuming and may require significant financial and personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired. If any of the physicians or other providers or entities with whom we expect to do business are found to not be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusion from government funded healthcare programs and imprisonment. If any of the above occur, it could adversely affect our ability to operate our business and our results of operations.

Recently enacted legislation, future legislation and healthcare reform measures may increase the difficulty and cost for us to obtain marketing approval for and commercialize our product candidates and may affect the prices we may set.

In the United States and some foreign jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes to the healthcare system, including cost-containment measures that may reduce or limit coverage and reimbursement for newly approved drugs and affect our ability to profitably sell any product candidates for which we obtain marketing approval. In particular, there have been and continue to be a number of initiatives at the U.S. federal and state levels that seek to reduce healthcare costs and improve the quality of healthcare.

For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, collectively the Affordable Care Act, was enacted in the United States. Among the provisions of the Affordable Care Act of importance to our potential product candidates, the Affordable Care Act: establishes an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents; expands eligibility criteria for Medicaid programs; increases the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program; creates a new Medicare Part D coverage gap discount program; establishes a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in and conduct comparative clinical effectiveness research, along with funding for such research; and establishes a Center for Medicare Innovation at the Centers for Medicare and Medicaid Services to test innovative payment and service delivery models to lower Medicare and Medicaid spending. At this time, we are unsure of the full impact that Affordable Care Act will have on our business. There have been judicial and Congressional challenges to certain aspects of the Affordable Care Act, as well as recent efforts by the Trump administration to repeal or replace certain aspects of the Affordable Care Act and we expect such challenges and amendments to continue. For example, the Tax Cuts and Jobs Act of 2017 includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the Affordable Care Act on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the “individual mandate.” Additionally, on January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain Affordable Care Act-mandated fees, including the so-called “Cadillac” tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share. Further, the Bipartisan Budget Act of 2018, or the BBA, among other things, amends the Affordable Care Act, effective January 1, 2019, to close the coverage gap in most Medicare drug plans, commonly referred to as the “donut hole.” It remains unclear the extent to which any such change may impact our business or financial condition.

In addition, other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. On August 2, 2011, the Budget Control Act of 2011 was signed into law, which, among other things, created the Joint Select Committee on Deficit Reduction to recommend to Congress proposals for spending reductions. The Joint Select Committee did not achieve a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, triggering the legislation’s automatic reduction to several government programs. This includes reductions to Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, including the BBA, will remain in effect through 2027 unless additional Congressional action is taken. On January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, reduced Medicare payments to several providers, including hospitals, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Further, there has been heightened governmental scrutiny in the United States of pharmaceutical pricing practices in light of the rising cost of prescription drugs. Such scrutiny has resulted in several recent

congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products.

At the federal level, the Trump administration's budget proposal for fiscal year 2019 contains further drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid and to eliminate cost sharing for generic drugs for low-income patients. Additionally, on May 11, 2018, President Trump laid out his administration's "Blueprint" to reduce the cost of prescription drugs. The U.S. Department of Health and Human Services has already started the process of soliciting feedback on some of these measures and, at the same time, is implementing others under its existing authority. Although some of these, and other, proposals will require authorization through additional legislation to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs.

At the state level, individual states in the United States are also increasingly active in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. Legally mandated price controls on payment amounts by third-party payors or other restrictions could harm our business, results of operations, financial condition and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This could reduce the ultimate demand for our product candidates, if approved, or put pressure on our product pricing, which could negatively affect our business, results of operations, financial condition and prospects.

More recently, on May 30, 2018, the Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017, or Right to Try Act, was signed into law. The law, among other things, provides a federal framework for patients to access certain investigational new drug products that have completed a Phase I clinical trial. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA approval under the FDA expanded access program. The Right to Try Act did not establish any new entitlement or positive right to any party or individual, nor did it create any new mandates, directives, or additional regulations requiring a manufacturer or sponsor of an eligible investigational new drug product to provide expanded access.

We expect that the Affordable Care Act, these new laws and other healthcare reform measures that may be adopted in the future may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our product candidates, if approved.

We and any of our third-party manufacturers and suppliers may use potent chemical agents and hazardous materials, and any claims relating to improper handling, storage or disposal of these materials could be time consuming or costly.

We and any of our third-party manufacturers or suppliers will use biological materials, potent chemical agents and may use hazardous materials, including chemicals and biological agents and compounds that could be

dangerous to human health and safety of the environment. Our operations and the operations of our third-party manufacturers and suppliers also produce hazardous waste products. Federal, state and local laws and regulations govern the use, generation, manufacture, storage, handling and disposal of these materials and wastes. Compliance with applicable environmental laws and regulations may be expensive, and current or future environmental laws and regulations may impair our product development efforts. In addition, we cannot eliminate the risk of accidental injury or contamination from these materials or wastes. We do not carry specific biological or hazardous waste insurance coverage, and our property, casualty and general liability insurance policies specifically exclude coverage for damages and fines arising from biological or hazardous waste exposure or contamination. In the event of contamination or injury, we could be held liable for damages or be penalized with fines in an amount exceeding our resources, and our clinical trials or regulatory approvals could be suspended.

Although we maintain workers' compensation insurance for certain costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials or other work-related injuries, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for toxic tort claims that may be asserted against us in connection with our storage or disposal of biologic, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations, which have tended to become more stringent over time. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions or liabilities, which could materially adversely affect our business, financial condition, results of operations and prospects.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our products.

We face an inherent risk of product liability as a result of the clinical trials of our product candidates and will face an even greater risk if we commercialize our product candidates. For example, we may be sued if our product candidates allegedly cause injury or are found to be otherwise unsuitable during product testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product candidate, negligence, strict liability and a breach of warranties. Claims may be brought against us by clinical trial participants, patients or others using, administering or selling products that may be approved in the future. Claims could also be asserted under state consumer protection acts.

If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit or cease the commercialization of our products. Even a successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for our products;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- costs to defend the related litigation;
- a diversion of management's time and our resources;
- substantial monetary awards to trial participants or patients;

- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- significant negative financial impact;
- the inability to commercialize our product candidates; and
- a decline in our stock price.

We currently hold approximately AUD$20 million (or approximately USD$14.8 million based on the applicable exchange rate as of June 30, 2018) in product liability insurance coverage in the aggregate. We may need to increase our insurance coverage as we expand our clinical trials or if we commence commercialization of our product candidates. Insurance coverage is increasingly expensive. Our inability to obtain and retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of our product candidates. Although we maintain such insurance, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. Our insurance policies will also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We may have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts.

We and any of our potential future collaborators will be required to report to regulatory authorities if any of our approved products cause or contribute to adverse medical events, and any failure to do so would result in sanctions that would materially harm our business.

If we and any of our potential future collaborators are successful in commercializing our products, the FDA and foreign regulatory authorities would require that we and any of our potential future collaborators report certain information about adverse medical events if those products may have caused or contributed to those adverse events. The timing of our obligation to report would be triggered by the date we become aware of the adverse event as well as the nature of the event. We and any of our potential future collaborators or CROs may fail to report adverse events within the prescribed timeframe. If we or any of our potential future collaborators or CROs fail to comply with such reporting obligations, the FDA or a foreign regulatory authority could take action, including criminal prosecution, the imposition of civil monetary penalties, seizure of our products or delay in approval or clearance of future products.

Our internal computer systems, or those of any of our CROs, manufacturers, other contractors or consultants or potential future collaborators, may fail or suffer security breaches, which could result in a material disruption of our product development programs.

Despite the implementation of security measures, our internal computer systems and those of our current and any future CROs and other contractors, consultants and collaborators are vulnerable to damage from computer viruses, cybersecurity threats, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations, whether due to a loss of our trade secrets or other similar disruptions. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. We also rely on third parties to manufacture our product candidates, and similar events relating to their computer systems could also have a material adverse effect on our business. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development and commercialization of our product candidates could be delayed.

Business disruptions could seriously harm our future revenue and financial condition and increase our costs and expenses.

Our operations could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics and other natural or manmade disasters or business interruptions, for which we are predominantly self-insured. We rely on third- party manufacturers to produce our product candidates. Our ability to obtain clinical supplies of our product candidates could be disrupted if the operations of these suppliers were affected by a man-made or natural disaster or other business interruption. In addition, our corporate headquarters is located in San Diego, California near major earthquake faults and fire zones, and the ultimate impact on us of being located near major earthquake faults and fire zones and being consolidated in a certain geographical area is unknown. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses.

Our employees and independent contractors, including principal investigators, CROs, consultants and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

We are exposed to the risk that our employees and independent contractors, including principal investigators, CROs, consultants and vendors may engage in misconduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or disclosure of unauthorized activities to us that violate: (1) the laws and regulations of the FDA and other similar regulatory requirements, including those laws that require the reporting of true, complete and accurate information to such authorities, manufacturing standards, (2) federal and state data privacy, security, fraud and abuse and other healthcare laws and regulations in the United States and abroad or (3) laws that require the true, complete and accurate reporting of financial information or data. Activities subject to these laws also involve the improper use or misrepresentation of information obtained in the course of clinical trials, the creation of fraudulent data in our preclinical studies or clinical trials, or illegal misappropriation of drug product, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. In addition, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and financial results, including, without limitation, the imposition of significant civil, criminal and administrative penalties, damages, monetary fines, disgorgements, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, individual imprisonment, contractual damages, reputational harm, diminished profits and future earnings, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

We are subject to U.S. and certain foreign export and import controls, sanctions, embargoes, anti-corruption laws and anti-money laundering laws and regulations. Compliance with these legal standards could impair our ability to compete in domestic and international markets. We can face criminal liability and other serious consequences for violations, which can harm our business.

We are subject to export control and import laws and regulations, including the U.S. Export Administration Regulations, U.S. Customs regulations, and various economic and trade sanctions regulations administered by

the U.S. Treasury Department's Office of Foreign Assets Controls, and anti-corruption and anti-money laundering laws and regulations, including the U.S. Foreign Corrupt Practices Act of 1977, as amended, the U.S. domestic bribery statute contained in 18 U.S.C. § 201, the U.S. Travel Act, the USA PATRIOT Act, and other state and national anti-bribery and anti-money laundering laws in the countries in which we conduct activities. Anti-corruption laws are interpreted broadly and prohibit companies and their employees, agents, clinical research organizations, contractors and other collaborators and partners from authorizing, promising, offering, providing, soliciting or receiving, directly or indirectly, improper payments or anything else of value to recipients in the public or private sector. We may engage third parties for clinical trials outside of the United States, to sell our products abroad once we enter a commercialization phase, and/or to obtain necessary permits, licenses, patent registrations and other regulatory approvals. We have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities and other organizations. We can be held liable for the corrupt or other illegal activities of our employees, agents, clinical research organizations, contractors and other collaborators and partners, even if we do not explicitly authorize or have actual knowledge of such activities. Any violations of the laws and regulations described above may result in substantial civil and criminal fines and penalties, imprisonment, the loss of export or import privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm and other consequences.

We may engage in strategic transactions that could impact our liquidity, increase our expenses and present significant distractions to our management.

From time to time, we may consider strategic transactions, such as acquisitions of companies, asset purchases and out-licensing or in-licensing of intellectual property, products or technologies. Additional potential transactions that we may consider in the future include a variety of business arrangements, including spin-offs, strategic partnerships, joint ventures, restructurings, divestitures, business combinations and investments. Any future transactions could increase our near and long-term expenditures, result in potentially dilutive issuances of our equity securities, including our common stock, or the incurrence of debt, contingent liabilities, amortization expenses or acquired in-process research and development expenses, any of which could affect our financial condition, liquidity and results of operations. Future acquisitions may also require us to obtain additional financing, which may not be available on favorable terms or at all. These transactions may never be successful and may require significant time and attention of management. In addition, the integration of any business that we may acquire in the future may disrupt our existing business and may be a complex, risky and costly endeavor for which we may never realize the full benefits of the acquisition. Accordingly, although there can be no assurance that we will undertake or successfully complete any additional transactions of the nature described above, any additional transactions that we do complete could have a material adverse effect on our business, results of operations, financial condition and prospects.

Risks related to our intellectual property

Our success depends on our ability to protect our intellectual property and our proprietary technologies.

Our commercial success depends in part on our ability to obtain and maintain patent protection and trade secret protection for our product candidates, proprietary technologies and their uses as well as our ability to operate without infringing upon the proprietary rights of others. We generally seek to protect our proprietary position by filing patent applications in the United States and abroad related to our product candidates, proprietary technologies and their uses that are important to our business. Our patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless, and until, patents issue from such applications, and then only to the extent the issued claims cover the technology. There can be no assurance that our patent applications will result in additional patents being issued or that issued patents

will afford sufficient protection against competitors with similar technology, nor can there be any assurance that the patents issued will not be infringed, designed around or invalidated by third parties. Even issued patents may later be found invalid or unenforceable or may be modified or revoked in proceedings instituted by third parties before various patent offices or in courts. The degree of future protection for our proprietary rights is uncertain. Only limited protection may be available and may not adequately protect our rights or permit us to gain or keep any competitive advantage. This failure to properly protect the intellectual property rights relating to our product candidates could have a material adverse effect on our financial condition and results of operations.

Although we own three issued patents in the United States, we cannot be certain that the claims in our other U.S. pending patent applications, corresponding international patent applications and patent applications in certain foreign territories will be considered patentable by the United States Patent and Trademark Office, or USPTO, courts in the United States or by the patent offices and courts in foreign countries, nor can we be certain that the claims in our issued patents will not be found invalid or unenforceable if challenged.

The patent application process is subject to numerous risks and uncertainties, and there can be no assurance that we or any of our potential future collaborators will be successful in protecting our product candidates by obtaining and defending patents. These risks and uncertainties include the following:

- the USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process, the noncompliance with which can result in abandonment or lapse of a patent or patent application, and partial or complete loss of patent rights in the relevant jurisdiction;
- patent applications may not result in any patents being issued;
- patents may be challenged, invalidated, modified, revoked, circumvented, found to be unenforceable or otherwise may not provide any competitive advantage;
- our competitors, many of whom have substantially greater resources than we do and many of whom have made significant investments in competing technologies, may seek or may have already obtained patents that will limit, interfere with or eliminate our ability to make, use and sell our potential product candidates;
- there may be significant pressure on the U.S. government and international governmental bodies to limit the scope of patent protection both inside and outside the United States for disease treatments that prove successful, as a matter of public policy regarding worldwide health concerns; and
- countries other than the United States may have patent laws less favorable to patentees than those upheld by U.S. courts, allowing foreign competitors a better opportunity to create, develop and market competing product candidates.

The patent prosecution process is also expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner or in all jurisdictions where protection may be commercially advantageous. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection.

In addition, although we enter into non-disclosure and confidentiality agreements with parties who have access to patentable aspects of our research and development output, such as our employees, outside scientific collaborators, CROs, third-party manufacturers, consultants, advisors and other third parties, any of these parties may breach such agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection.

Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our intellectual property may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

If the scope of any patent protection we obtain is not sufficiently broad, or if we lose any of our patent protection, our ability to prevent our competitors from commercializing similar or identical product candidates would be adversely affected.

The patent position of biopharmaceutical companies generally is highly uncertain, involves complex legal and factual questions, and has been the subject of much litigation in recent years. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued which protect our product candidates or which effectively prevent others from commercializing competitive product candidates.

Moreover, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Even if patent applications we own currently or in the future issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors or other third parties from competing with us, or otherwise provide us with any competitive advantage. Any patents that we own may be challenged or circumvented by third parties or may be narrowed or invalidated as a result of challenges by third parties. Consequently, we do not know whether our product candidates will be protectable or remain protected by valid and enforceable patents. Our competitors or other third parties may be able to circumvent our patents by developing similar or alternative technologies or products in a non-infringing manner which could materially adversely affect our business, financial condition, results of operations and prospects.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our patents may be challenged in the courts or patent offices in the United States and abroad. We may be subject to a third party pre-issuance submission of prior art to the USPTO, or become involved in opposition, derivation, revocation, reexamination, post-grant review, or PGR, and *inter partes* review, or IPR, or other similar proceedings challenging our owned patent rights. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate or render unenforceable, our patent rights, allow third parties to commercialize our product candidates and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights. Moreover, our patents may become subject to post-grant challenge proceedings, such as oppositions in a foreign patent office, that challenge our or priority of invention or other features of patentability with respect to our patents and patent applications. Such challenges may result in loss of patent rights, loss of exclusivity or in patent claims being narrowed, invalidated or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our product candidates. Such proceedings also may result in substantial cost and require significant time from our scientists and management, even if the eventual outcome is favorable to us. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, regardless of the outcome, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

Most of our intellectual property has been discovered through government funded programs and thus may be subject to federal regulations such as "march-in" rights, certain reporting requirements and a preference for U.S.-based companies. Compliance with such regulations may limit our exclusive rights, and limit our ability to contract with non-U.S. manufacturers.

Most of our intellectual property rights, including those for our lead programs, have been generated through the use of U.S. government funding provided from our Small Business Innovation Research Grants, or SBIR Grants, awarded to us by the National Institute of Diabetes and Digestive and Kidney Diseases of the National Institutes of Health, and are therefore subject to certain federal regulations. As a result, the U.S. government may have certain rights to intellectual property embodied in our current or future product candidates pursuant to the Bayh-Dole Act of 1980, or Bayh-Dole Act. These U.S. government rights include a non-exclusive, non-transferable, irrevocable worldwide license to use inventions for any governmental purpose. In addition, the U.S. government has the right, under certain limited circumstances, to require us to grant exclusive, partially exclusive, or non-exclusive licenses to any of these inventions to a third party if it determines that: (i) adequate steps have not been taken to commercialize the invention; (ii) government action is necessary to meet public health or safety needs; or (iii) government action is necessary to meet requirements for public use under federal regulations (also referred to as "march-in rights"). The U.S. government also has the right to take title to these inventions if we fail to disclose the invention to the government or fail to file an application to register the intellectual property within specified time limits. Intellectual property generated under a government funded program is also subject to certain reporting requirements, compliance with which may require us to expend substantial resources. In addition, the U.S. government requires that any products embodying any of these inventions or produced through the use of any of these inventions be manufactured substantially in the United States. This preference for U.S. industry may be waived by the federal agency that provided the funding if the owner or assignee of the intellectual property can show that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the United States or that under the circumstances domestic manufacture is not commercially feasible. This preference for U.S. industry may limit our ability to contract with non-U.S. product manufacturers for products covered by such intellectual property. To the extent any of our future intellectual property is also generated through the use of U.S. government funding, the provisions of the Bayh-Dole Act may similarly apply.

Intellectual property rights do not necessarily address all potential threats to our competitive advantage.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business or permit us to maintain our competitive advantage. For example:

- others may be able to develop products that are similar to our product candidates but that are not covered by the claims of the patents that we own;
- we might not have been the first to make the inventions covered by the issued patents or patent application that we own;
- we might not have been the first to file patent applications covering certain of our inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- it is possible that our pending patent applications will not lead to issued patents;
- issued patents that we own may be held invalid or unenforceable, as a result of legal challenges by our competitors;

- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not develop additional proprietary technologies that are patentable; and
- the patents of others may have an adverse effect on our business.

Should any of these events occur, it could significantly harm our business, results of operations and prospects.

Our commercial success depends significantly on our ability to operate without infringing the patents and other proprietary rights of third parties. Claims by third parties that we infringe their proprietary rights may result in liability for damages or prevent or delay our developmental and commercialization efforts.

Our commercial success depends in part on avoiding infringement of the patents and proprietary rights of third parties. However, our research, development and commercialization activities may be subject to claims that we infringe or otherwise violate patents or other intellectual property rights owned or controlled by third parties. Other entities may have or obtain patents or proprietary rights that could limit our ability to make, use, sell, offer for sale or import our product candidates and products that may be approved in the future, or impair our competitive position. There is a substantial amount of litigation, both within and outside the United States, involving patent and other intellectual property rights in the biopharmaceutical industry, including patent infringement lawsuits, oppositions, reexaminations, IPR proceedings and PGR proceedings before the USPTO and/or corresponding foreign patent offices. Numerous third-party U.S. and foreign issued patents and pending patent applications exist in the fields in which we are developing product candidates. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates.

As the biopharmaceutical industry expands and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of the patent rights of third parties. Because patent applications are maintained as confidential for a certain period of time, until the relevant application is published we may be unaware of third-party patents that may be infringed by commercialization of any of our product candidates, and we cannot be certain that we were the first to file a patent application related to a product candidate or technology. Moreover, because patent applications can take many years to issue, there may be currently-pending patent applications that may later result in issued patents that our product candidates may infringe. In addition, identification of third-party patent rights that may be relevant to our technology is difficult because patent searching is imperfect due to differences in terminology among patents, incomplete databases and the difficulty in assessing the meaning of patent claims. There is also no assurance that there is not prior art of which we are aware, but which we do not believe is relevant to our business, which may, nonetheless, ultimately be found to limit our ability to make, use, sell, offer for sale or import our products that may be approved in the future, or impair our competitive position. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. Any claims of patent infringement asserted by third parties would be time consuming and could:

- result in costly litigation that may cause negative publicity;
- divert the time and attention of our technical personnel and management;
- cause development delays;
- prevent us from commercializing any of our product candidates until the asserted patent expires or is held finally invalid or not infringed in a court of law;
- require us to develop non-infringing technology, which may not be possible on a cost-effective basis;

- subject us to significant liability to third parties; or
- require us to enter into royalty or licensing agreements, which may not be available on commercially reasonable terms, or at all, or which might be non-exclusive, which could result in our competitors gaining access to the same technology.

Although no third party has asserted a claim of patent infringement against us as of the date of this prospectus, others may hold proprietary rights that could prevent our product candidates from being marketed. Any patent-related legal action against us claiming damages and seeking to enjoin commercial activities relating to our products or processes could subject us to potential liability for damages, including treble damages if we were determined to willfully infringe, and require us to obtain a license to manufacture or market our product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. We cannot predict whether we would prevail in any such actions or that any license required under any of these patents would be made available on commercially acceptable terms, if at all. Moreover, even if we or our future strategic partners were able to obtain a license, the rights may be nonexclusive, which could result in our competitors gaining access to the same intellectual property. In addition, we cannot be certain that we could redesign our product candidates or processes to avoid infringement, if necessary. Accordingly, an adverse determination in a judicial or administrative proceeding, or the failure to obtain necessary licenses, could prevent us from developing and commercializing our product candidates, which could harm our business, financial condition and operating results. In addition, intellectual property litigation, regardless of its outcome, may cause negative publicity and could prohibit us from marketing or otherwise commercializing our product candidates and technology.

Parties making claims against us may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or administrative proceedings, there is a risk that some of our confidential information could be compromised by disclosure. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have material adverse effect on our ability to raise additional funds or otherwise have a material adverse effect on our business, results of operations, financial condition and prospects.

We may be involved in lawsuits to protect or enforce our patents, which could be expensive, time consuming and unsuccessful. Further, our issued patents could be found invalid or unenforceable if challenged in court.

Competitors may infringe our intellectual property rights. To prevent infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. In addition, in a patent infringement proceeding, a court may decide that a patent we own is not valid, is unenforceable and/or is not infringed. If we or any of our potential future collaborators were to initiate legal proceedings against a third party to enforce a patent directed at one of our product candidates, the defendant could counterclaim that our patent is invalid and/or unenforceable in whole or in part. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge include an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, written description or non-enablement. Grounds for an unenforceability assertion could include an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO or made a misleading statement during prosecution.

Third parties may also raise similar invalidity claims before the USPTO or patent offices abroad, even outside the context of litigation. Such mechanisms include re-examination, PGR, IPR, derivation proceedings, and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). Such proceedings could result in the revocation of, cancellation of or amendment to our patents in such a way that they no longer cover our

technology or platform, or any product candidates that we may develop. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a third party were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our technology or platform, or any product candidates that we may develop. Such a loss of patent protection would have a material adverse impact on our business, financial condition, results of operations and prospects.

The outcome following legal assertions of invalidity and/or unenforceability is unpredictable, and prior art could render our patents invalid. There is no assurance that all potentially relevant prior art relating to our patents and patent applications has been found. There is also no assurance that there is not prior art of which we are aware, but which we do not believe affects the validity or enforceability of a claim in our patents and patent applications, which may, nonetheless, ultimately be found to affect the validity or enforceability of a claim.

If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on such product candidate. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates. Such a loss of patent protection would have a material adverse impact on our business.

Even if resolved in our favor, litigation or other legal proceedings relating to our intellectual property rights may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could compromise our ability to compete in the marketplace.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or other legal proceedings relating to our intellectual property rights, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation or other proceedings. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock.

In addition, the issuance of a patent does not give us the right to practice the patented invention. Third parties may have blocking patents that could prevent us from marketing our own patented product and practicing our own patented technology.

Intellectual property litigation may lead to unfavorable publicity that harms our reputation and causes the market price of our common shares to decline.

During the course of any intellectual property litigation, there could be public announcements of the initiation of the litigation as well as results of hearings, rulings on motions, and other interim proceedings in the litigation. If securities analysts or investors regard these announcements as negative, the perceived value of our existing products, programs or intellectual property could be diminished. Accordingly, the market price of

shares of our common stock may decline. Such announcements could also harm our reputation or the market for our future products, which could have a material adverse effect on our business.

Derivation proceedings may be necessary to determine priority of inventions, and an unfavorable outcome may require us to cease using the related technology or to attempt to license rights from the prevailing party.

Derivation proceedings provoked by third parties or brought by us or declared by the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our defense of derivation proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. In addition, the uncertainties associated with such proceedings could have a material adverse effect on our ability to raise the funds necessary to continue our clinical trials, continue our research programs, license necessary technology from third parties or enter into development or manufacturing partnerships that would help us bring our product candidates to market.

Recent patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents.

On September 16, 2011, the Leahy-Smith America Invents Act, or Leahy-Smith Act, was signed into law. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. In particular, under the Leahy-Smith Act, the United States transitioned in March 2013 to a “first inventor to file” system in which, assuming that other requirements of patentability are met, the first inventor to file a patent application will be entitled to the patent regardless of whether a third party was first to invent the claimed invention. A third party that files a patent application in the USPTO after March 2013 but before us could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by such third party. This will require us to be cognizant going forward of the time from invention to filing of a patent application. Furthermore, our ability to obtain and maintain valid and enforceable patents depends on whether the differences between our technology and the prior art allow our technology to be patentable over the prior art. Since patent applications in the United States and most other countries are confidential for a period of time after filing or until issuance, we cannot be certain that we were the first to either (1) file any patent application related to our product candidates or (2) invent any of the inventions claimed in our patents or patent applications.

The Leahy-Smith Act also includes a number of significant changes that affect the way patent applications will be prosecuted and also may affect patent litigation. These include allowing third-party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent by USPTO administered post-grant proceedings, including PGR, IPR, and derivation proceedings. An adverse determination in any such submission or proceeding could reduce the scope or enforceability of, or invalidate, our patent rights, which could adversely affect our competitive position.

Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in United States federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. Thus, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent

applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business, financial condition, results of operations and prospects.

Changes in U.S. patent law, or laws in other countries, could diminish the value of patents in general, thereby impairing our ability to protect our product candidates.

As is the case with other pharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the pharmaceutical industry involve a high degree of technological and legal complexity. Therefore, obtaining and enforcing pharmaceutical patents is costly, time consuming and inherently uncertain. Changes in either the patent laws or in the interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property and may increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. We cannot predict the breadth of claims that may be allowed or enforced in our patents or in third-party patents. In addition, Congress or other foreign legislative bodies may pass patent reform legislation that is unfavorable to us.

For example, the U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U.S. Congress, the U.S. federal courts, the USPTO, or similar authorities in foreign jurisdictions, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents we might obtain in the future.

We may be subject to claims challenging the inventorship or ownership of our patents and other intellectual property.

We may also be subject to claims that former employees or other third parties have an ownership interest in our patents or other intellectual property. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and distraction to management and other employees.

Patent terms may be inadequate to protect our competitive position on our product candidates for an adequate amount of time.

Patents have a limited lifespan. In the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest U.S. non-provisional filing date. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates are obtained, once the patent life has expired, we may be open to competition from competitive products. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

If we do not obtain patent term extension for our product candidates, our business may be materially harmed.

Depending upon the timing, duration and specifics of FDA marketing approval of our product candidates, one or more of our U.S. patents may be eligible for limited patent term restoration under the Drug Price Competition

and Patent Term Restoration Act of 1984, or the Hatch-Waxman Amendments. The Hatch- Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. A maximum of one patent may be extended per FDA approved product as compensation for the patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only those claims covering such approved drug product, a method for using it or a method for manufacturing it may be extended. Patent term extension may also be available in certain foreign countries upon regulatory approval of our product candidates. However, we may not be granted an extension because of, for example, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or restoration or the term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our revenue could be reduced, possibly materially. Further, if this occurs, our competitors may take advantage of our investment in development and trials by referencing our clinical and preclinical data and launch their product earlier than might otherwise be the case.

We may not be able to protect our intellectual property rights throughout the world.

Although we have three issued patents in the United States and pending patent applications in the United States and other countries, filing, prosecuting and defending patents in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection but enforcement is not as strong as that in the United States. These products may compete with our product candidates, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of many foreign countries do not favor the enforcement of patents and other intellectual property protection, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we are forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be adversely affected.

Obtaining and maintaining our patent protection depends on compliance with various procedural, documentary, fee payment and other requirements imposed by regulations and governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and/or applications will be due to the USPTO and various foreign patent offices at various points over the lifetime of our patents and/or applications. We have systems in place to remind us to pay these fees, and we rely on our outside patent annuity service to pay these fees when due. Additionally, the USPTO and various foreign patent offices require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. We employ reputable law firms and other professionals to help us comply, and in many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with rules applicable to the particular jurisdiction. However, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. If such an event were to occur, it could have a material adverse effect on our business.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

Even though we have filed three trademark registration applications in the USPTO, our registered or unregistered trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of interest. At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. Our efforts to enforce or protect our proprietary rights related to trademarks, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely affect our financial condition or results of operations.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition, we rely on the protection of our trade secrets, including unpatented know-how, technology and other proprietary information to maintain our competitive position. Although we have taken steps to protect our trade secrets and unpatented know-how, including entering into confidentiality agreements with third parties, and confidential information and inventions agreements with employees, consultants and advisors, we cannot provide any assurances that all such agreements have been duly executed, and any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets.

Moreover, third parties may still obtain this information or may come upon this or similar information independently, and we would have no right to prevent them from using that technology or information to compete with us. If any of these events occurs or if we otherwise lose protection for our trade secrets, the value of this information may be greatly reduced and our competitive position would be harmed. If we do not apply

for patent protection prior to such publication or if we cannot otherwise maintain the confidentiality of our proprietary technology and other confidential information, then our ability to obtain patent protection or to protect our trade secret information may be jeopardized.

We may be subject to claims that we have wrongfully hired an employee from a competitor or that we or our employees have wrongfully used or disclosed alleged confidential information or trade secrets of their former employers.

As is common in the pharmaceutical industry, in addition to our employees, we engage the services of consultants to assist us in the development of our product candidates. Many of these consultants, and many of our employees, were previously employed at, or may have previously provided or may be currently providing consulting services to, other pharmaceutical companies including our competitors or potential competitors. We may become subject to claims that we, our employees or a consultant inadvertently or otherwise used or disclosed trade secrets or other information proprietary to their former employers or their former or current clients. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, which could adversely affect our business. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to our management team and other employees.

Risks related to our common stock and this offering

An active, liquid and orderly market for our common stock may not develop, and you may not be able to resell your common stock at or above the public offering price.

Prior to this offering, there has been no public market for our common stock. Although our common stock has been approved for listing on the Nasdaq Global Select Market, or Nasdaq, an active trading market for our common stock may never develop or be sustained following this offering. We and the representatives of the underwriters determined the initial public offering price of our common stock through negotiation. This price will not necessarily reflect the price at which investors in the market will be willing to buy and sell our shares following this offering. In addition, an active trading market may not develop following the consummation of this offering or, if it is developed, may not be sustained. The lack of an active market may impair your ability to sell your shares at the time you wish to sell them or at a price that you consider reasonable. An inactive market may also impair our ability to raise capital by selling shares and may impair our ability to acquire other businesses or technologies using our shares as consideration, which, in turn, could materially adversely affect our business.

The trading price of the shares of our common stock could be highly volatile, and purchasers of our common stock could incur substantial losses.

Our stock price is likely to be volatile. The stock market in general and the market for stock of pharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, investors may not be able to sell their common stock at or above the initial public offering price. The market price for our common stock may be influenced by those factors discussed in this “Risk factors” section and many others, including:

- our ability to enroll subjects in our ongoing and planned clinical trials;
- results of our clinical trials and preclinical studies, and the results of trials of our competitors or those of other companies in our market sector;
- regulatory approval of our product candidates, or limitations to specific label indications or patient populations for its use, or changes or delays in the regulatory review process;

- regulatory developments in the United States and foreign countries;
- changes in the structure of healthcare payment systems, especially in light of current reforms to the U.S. healthcare system;
- the success or failure of our efforts to acquire, license or develop additional product candidates;
- innovations or new products developed by us or our competitors;
- announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures or capital commitments;
- manufacturing, supply or distribution delays or shortages;
- any changes to our relationship with any manufacturers, suppliers, future collaborators or other strategic partners;
- achievement of expected product sales and profitability;
- variations in our financial results or those of companies that are perceived to be similar to us;
- market conditions in the pharmaceutical sector and issuance of securities analysts' reports or recommendations;
- trading volume of our common stock;
- an inability to obtain additional funding;
- sales of our stock by insiders and stockholders;
- general economic, industry and market conditions other events or factors, many of which are beyond our control;
- additions or departures of key personnel; and
- intellectual property, product liability or other litigation against us.

In addition, in the past, stockholders have initiated class action lawsuits against pharmaceutical companies following periods of volatility in the market prices of these companies' stock. Such litigation, if instituted against us, could cause us to incur substantial costs and divert management's attention and resources, which could have a material adverse effect on our business, financial condition and results of operations.

Our failure to meet the continued listing requirements of the Nasdaq Global Select Market could result in a delisting of our common stock.

If, after listing, we fail to satisfy the continued listing requirements of the Nasdaq Global Select Market, such as the corporate governance requirements or the minimum closing bid price requirement, Nasdaq may take steps to delist our common stock. Such a delisting would likely have a negative effect on the price of our common stock and would impair your ability to sell or purchase our common stock when you wish to do so. In the event of a delisting, we can provide no assurance that any action taken by us to restore compliance with listing requirements would allow our common stock to become listed again, stabilize the market price or improve the liquidity of our common stock, prevent our common stock from dropping below the Nasdaq minimum bid price requirement or prevent future non-compliance with Nasdaq's listing requirements.

We may allocate the net proceeds from this offering in ways that you and other stockholders may not approve.

Our management will have broad discretion in the application of the net proceeds from this offering, including for any of the purposes described in the section titled “Use of proceeds.” 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, and the failure by our management to apply these funds effectively could harm our business. Pending their use, we may invest the net proceeds from this offering in short- and intermediate-term, interest-bearing obligations, investment-grade instruments, certificates of deposit or direct or guaranteed obligations of the U.S. government. 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 results, which could cause our stock price to decline.

You will suffer immediate and substantial dilution in the net tangible book value of the common stock you purchase.

The initial public offering price of our common stock is substantially higher than the pro forma as adjusted net tangible book value per share of our outstanding common stock immediately after the completion of this offering. Purchasers of common stock in this offering will experience immediate dilution of approximately $9.83 per share, based upon the initial public offering price of $17.00 per share. In the past, we issued options to acquire common stock at prices significantly below the initial public offering price. To the extent these outstanding options are ultimately exercised, investors purchasing common stock in this offering will sustain further dilution. For a further description of the dilution that you will experience immediately after this offering, see “Dilution.”

After this offering, our executive officers, directors and principal stockholders, if they choose to act together, will continue to have the ability to control or significantly influence all matters submitted to stockholders for approval.

Following the completion of this offering, our executive officers, directors and greater than 5% stockholders, in the aggregate, will own approximately 70.5% of our outstanding common stock (assuming no exercise of the underwriters’ option to purchase additional shares and no exercise of outstanding options). As a result, such persons, acting together, will have the ability to control or significantly influence all matters submitted to our stockholders for approval, including the election and removal of directors and approval of any significant transaction, as well as our management and business affairs. This concentration of ownership may have the effect of delaying, deferring or preventing a change in control, impeding a merger, consolidation, takeover or other business combination involving us, or discouraging a potential acquiror from making a tender offer or otherwise attempting to obtain control of our business, even if such a transaction would benefit other stockholders. Certain of our principal stockholders, including certain affiliates of our directors, have indicated an interest in purchasing shares of our common stock in this offering at the initial public offering price. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters may determine to sell more, less or no shares in this offering to any of these stockholders, or any of these stockholders may determine to purchase more, less or no shares in this offering. The foregoing discussion does not give effect to any potential purchases by these stockholders in this offering.

We do not currently intend to pay dividends on our common stock, and, consequently, your ability to achieve a return on your investment will depend on appreciation, if any, in the price of our common stock.

We have never declared or paid any cash dividend on our common stock. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate

declaring or paying any cash dividends for the foreseeable future. In addition, the terms of any future debt agreements may preclude us from paying dividends. Any return to stockholders will therefore be limited to the appreciation of their stock. There is no guarantee that shares of our common stock will appreciate in value or even maintain the price at which stockholders have purchased their shares.

Sales of a substantial number of shares of our common stock by our existing stockholders in the public market could cause our stock price to fall.

Sales of a substantial number of shares of our common stock in the public market or the perception that these sales might occur could significantly reduce the market price of our common stock and impair our ability to raise adequate capital through the sale of additional equity securities.

Based on shares of common stock outstanding as of March 31, 2018, upon the closing of this offering, we will have outstanding a total of 23,007,961 shares of common stock after this offering, assuming no exercise of the underwriters' option to purchase additional shares and no exercise of outstanding options. Of these shares, only the 6,000,000 shares of common stock sold in this offering by us, plus any shares sold upon exercise of the underwriters' option to purchase additional shares, will be freely tradable, without restriction, in the public market immediately following this offering, unless they are purchased by one of our affiliates.

Our directors and executive officers and holders of substantially all of our outstanding securities have entered into lock-up agreements with the underwriters pursuant to which they may not, with limited exceptions, for a period of 180 days from the date of this prospectus, offer, sell or otherwise transfer or dispose of any of our securities, without the prior written consent of J.P. Morgan Securities LLC, Leerink Partners LLC and Piper Jaffray & Co. The underwriters may permit our officers, directors and other stockholders and the holders of our outstanding options who are subject to the lock-up agreements to sell shares prior to the expiration of the lock-up agreements, subject to limitations. See "Underwriting." Sales of these shares, or perceptions that they will be sold, could cause the trading price of our common stock to decline. After the lock-up agreements expire, up to an additional 17,007,961 shares of common stock will be eligible for sale in the public market of which shares are held by directors, executive officers and other affiliates and will be subject to volume limitations under Rule 144 under the Securities Act.

In addition, as of March 31, 2018, up to 2,125,137 shares of common stock that are either subject to outstanding options or reserved for future issuance under our employee benefit plans will become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules, the lock-up agreements and Rule 144 and Rule 701 under the Securities Act. If these additional shares of common stock are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

After this offering, the holders of 14,712,571 shares of our outstanding common stock, or approximately 87% of our total outstanding common stock as of March 31, 2018, will be entitled to rights with respect to the registration of their shares under the Securities Act, subject to vesting and the 180-day lock-up agreements described above. See "Description of capital stock—Registration rights." Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares held by affiliates, as defined in Rule 144 under the Securities Act. Any sales of securities by these stockholders could have a material adverse effect on the trading price of our common stock.

We are an emerging growth company, and the reduced disclosure requirements applicable to emerging growth companies may make our common stock less attractive to investors.

We are an emerging growth company, as defined in the JOBS Act, and may remain an emerging growth company until the last day of the fiscal year following the fifth anniversary of the completion of this offering. However, if certain events occur prior to the end of such five-year period, including if we become a "large

accelerated filer," our annual gross revenues exceed $1.07 billion or we issue more than $1.0 billion of non-convertible debt in any three-year period, we will cease to be an emerging growth company prior to the end of such five-year period. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include:

- being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced "Management's discussion and analysis of financial condition and results of operations" disclosure;
- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- reduced disclosure obligations regarding executive compensation; and
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved.

We have taken advantage of reduced reporting burdens in this prospectus. In particular, in this prospectus, we have provided only two years of audited financial statements and have not included all of the executive compensation related information that would be required if we were not an emerging growth company. We cannot predict whether investors will find our common stock less attractive if we rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be reduced or more volatile. In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of these accounting standards until they would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this exemption and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

We will incur significant increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives.

As a public company, we will incur significant legal, accounting and other expenses that we did not incur as a private company. We will be subject to the reporting requirements of the Exchange Act, which will require, among other things, that we file with the U.S. Securities and Exchange Commission, or SEC, annual, quarterly and current reports with respect to our business and financial condition. In addition, Sarbanes-Oxley, as well as rules subsequently adopted by the SEC, and the Nasdaq Global Select Market to implement provisions of Sarbanes-Oxley, impose significant requirements on public companies, including requiring establishment and maintenance of effective disclosure and financial controls and changes in corporate governance practices. Further, pursuant to the Dodd-Frank Wall Street Reform and Consumer Protection Act of 2010, the SEC has adopted additional rules and regulations in these areas, such as mandatory "say on pay" voting requirements that will apply to us when we cease to be an emerging growth company. Stockholder activism, the current political environment and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate.

We expect the rules and regulations applicable to public companies to substantially increase our legal and financial compliance costs and to make some activities more time-consuming and costly. If these requirements divert the attention of our management and personnel from other business concerns, they could have a material adverse effect on our business, financial condition and results of operations. The increased costs will decrease our net income or increase our net loss, and may require us to reduce costs in other areas of our business or increase the prices of our products or services. For example, we expect these rules and regulations to make it more difficult and more expensive for us to obtain director and officer liability insurance, and we may be required to incur substantial costs to maintain the same or similar coverage. We cannot predict or estimate the amount or timing of additional costs we may incur to respond to these requirements. The impact of these requirements could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, our board committees or as executive officers.

If securities or industry analysts do not publish research or reports or publish unfavorable research or reports about our business, our stock price and trading volume could decline.

The trading market for our common stock will depend in part on the research and reports that securities or industry analysts publish about us, our business, our market or our competitors. We do not currently have and may never obtain research coverage by securities and industry analysts. If no securities or industry analysts commence coverage of our company, the trading price for our stock would be negatively impacted. In the event we obtain securities or industry analyst coverage, if one or more of the analysts who covers us downgrades our stock, our stock price would likely decline. If one or more of these analysts ceases to cover us or fails to regularly publish reports on us, interest in our stock could decrease, which could cause our stock price or trading volume to decline.

If we fail to maintain proper and effective internal control over financial reporting, our ability to produce accurate and timely financial statements could be impaired, investors may lose confidence in our financial reporting and the trading price of our common stock may decline.

Pursuant to Section 404 of Sarbanes-Oxley, our management will be required to report upon the effectiveness of our internal control over financial reporting beginning with the annual report for our fiscal year ending December 31, 2019. When we lose our status as an “emerging growth company” and reach an accelerated filer threshold, our independent registered public accounting firm will be required to attest to the effectiveness of our internal control over financial reporting. The rules governing the standards that must be met for management to assess our internal control over financial reporting are complex and require significant documentation, testing and possible remediation. To comply with the requirements of being a reporting company under the Exchange Act, we will need to upgrade our information technology systems; implement additional financial and management controls, reporting systems and procedures; and hire additional accounting and finance staff. If we or, if required, our auditors are unable to conclude that our internal control over financial reporting is effective, investors may lose confidence in our financial reporting and the trading price of our common stock may decline.

We cannot assure you that there will not be material weaknesses or significant deficiencies in our internal control over financial reporting in the future. Any failure to maintain internal control over financial reporting could severely inhibit our ability to accurately report our financial condition, results of operations or cash flows. If we are unable to conclude that our internal control over financial reporting is effective, or if our independent registered public accounting firm determines we have a material weakness or significant deficiency in our internal control over financial reporting once that firm begin its Section 404 reviews, investors may lose confidence in the accuracy and completeness of our financial reports, the market price of our common stock could decline, and we could be subject to sanctions or investigations by Nasdaq, the SEC or other regulatory authorities. Failure to remedy any material weakness in our internal control over financial reporting, or to

implement or maintain other effective control systems required of public companies, could also restrict our future access to the capital markets.

Provisions in our charter documents and under Delaware law could discourage a takeover that stockholders may consider favorable and may lead to entrenchment of management.

Our amended and restated certificate of incorporation and amended and restated bylaws that will be in effect immediately prior to the consummation of this offering will contain provisions that could significantly reduce the value of our shares to a potential acquiror or delay or prevent changes in control or changes in our management without the consent of our board of directors. The provisions in our charter documents will include the following:

- a classified board of directors with three-year staggered terms, which may delay the ability of stockholders to change the membership of a majority of our board of directors;
- no cumulative voting in the election of directors, which limits the ability of minority stockholders to elect director candidates;
- the exclusive right of our board of directors, unless the board of directors grants such right to the stockholders, to elect a director to fill a vacancy created by the expansion of the board of directors or the resignation, death or removal of a director, which prevents stockholders from being able to fill vacancies on our board of directors;
- the required approval of at least 66-2/3% of the shares entitled to vote to remove a director for cause, and the prohibition on removal of directors without cause;
- the ability of our board of directors to authorize the issuance of shares of preferred stock and to determine the price and other terms of those shares, including preferences and voting rights, without stockholder approval, which could be used to significantly dilute the ownership of a hostile acquiror;
- the ability of our board of directors to alter our amended and restated bylaws without obtaining stockholder approval;
- the required approval of at least 66-2/3% of the shares entitled to vote to adopt, amend or repeal our amended and restated bylaws or repeal the provisions of our amended and restated certificate of incorporation regarding the election and removal of directors;
- a prohibition on stockholder action by written consent, which forces stockholder action to be taken at an annual or special meeting of our stockholders;
- an exclusive forum provision providing that the Court of Chancery of the State of Delaware will be the exclusive forum for certain actions and proceedings;
- the requirement that a special meeting of stockholders may be called only by the board of directors, which may delay the ability of our stockholders to force consideration of a proposal or to take action, including the removal of directors; and
- advance notice procedures that stockholders must comply with in order to nominate candidates to our board of directors or to propose matters to be acted upon at a stockholders' meeting, which may discourage or deter a potential acquiror from conducting a solicitation of proxies to elect the acquiror's own slate of directors or otherwise attempting to obtain control of us.

We are also subject to the anti-takeover provisions contained in Section 203 of the Delaware General Corporation Law. Under Section 203, a corporation may not, in general, engage in a business combination with

any holder of 15% or more of its capital stock unless the holder has held the stock for three years or, among other exceptions, the board of directors has approved the transaction.

Our amended and restated certificate of incorporation and amended and restated bylaws will provide that the Court of Chancery of the State of Delaware will be the exclusive forum for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our amended and restated certificate of incorporation and amended and restated bylaws will provide that the Court of Chancery of the State of Delaware is the exclusive forum for any derivative action or proceeding brought on our behalf, any action asserting a breach of fiduciary duty, any action asserting a claim against us arising pursuant to the Delaware General Corporation Law, our amended and restated certificate of incorporation or our amended and restated bylaws, or any action asserting a claim against us that is governed by the internal affairs doctrine. This provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits against us and our directors, officers and other employees. Alternatively, if a court were to find this provision in our amended and restated certificate of incorporation and amended and restated bylaws to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could adversely affect our business and financial condition.

Our ability to use net operating loss carryforwards and other tax attributes may be limited in connection with this offering or other ownership changes.

We have incurred substantial losses during our history and do not expect to become profitable in the near future, and we may never achieve profitability. To the extent that we continue to generate taxable losses, unused losses will carry forward to offset future taxable income, if any, until such unused losses expire (if at all). At December 31, 2017, after reducing net operating losses, or NOLs, and research and development credits for amounts not expected to be utilized, we had federal, state and foreign NOL carryforwards of approximately $6.2 million, $6.4 million and $0.4 million, respectively. The federal and state NOL carryforwards will begin to expire in 2035, unless previously utilized. The foreign NOL carryforwards do not expire. The Company also has federal and California research and development credit carryforwards totaling $0.6 million and $0.4 million, respectively. The federal research and development credit carryforwards will begin to expire in 2030, unless previously utilized. The California research credits do not expire.

Under recently enacted U.S. tax legislation, federal NOL carryforwards generated in periods after December 31, 2017, may be carried forward indefinitely but may only be used to offset 80% of our taxable income annually. The California research and development tax carryforwards are available indefinitely. Our NOL carryforwards are subject to review and possible adjustment by the Internal Revenue Service and state tax authorities and may become subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant stockholders over a three-year period in excess of 50 percentage points, as defined under Section 382 of the Internal Revenue Code of 1986, as amended. Our ability to utilize our NOL carryforwards and other tax attributes to offset future taxable income or tax liabilities may be limited as a result of ownership changes, including potential changes in connection with this offering. Similar rules may apply under state tax laws. We have not yet determined the amount of the cumulative change in our ownership resulting from this offering or any resulting tax loss limitations. Such limitations could result in the expiration of our carryforwards before they can be utilized and, if we are profitable, our future cash flows could be adversely affected due to our increased tax liability. We have recorded a full valuation allowance related to our NOLs and other deferred tax assets due to the uncertainty of the ultimate realization of the future benefits of those assets.

Recent U.S. tax legislation may materially adversely affect our financial condition, results of operations and cash flows.

Recently enacted U.S. tax legislation, known as the Tax Cuts and Jobs Act of 2017, has significantly changed the U.S. federal income taxation of U.S. corporations, including by reducing the U.S. corporate income tax rate and revising the rules governing NOLs. Many of these changes are effective immediately, without any transition periods or grandfathering for existing transactions. The legislation is unclear in many respects and could be subject to potential amendments and technical corrections, as well as interpretations and implementing regulations by the Treasury and U.S. Internal Revenue Service, any of which could lessen or increase certain adverse impacts of the legislation. In addition, it is unclear how these U.S. federal income tax changes will affect state and local taxation, which often uses federal taxable income as a starting point for computing state and local tax liabilities. Based on our current evaluation of this legislation, the reduction of the U.S. corporate income tax rate required a provisional write-down of our deferred income tax assets (including the value of our NOL carryforwards and our tax credit carryforwards).

There may be other material adverse effects resulting from the legislation that we have not yet identified. While some of the changes made by the tax legislation may adversely affect us in one or more reporting periods and prospectively, other changes may be beneficial on a going forward basis. We continue to work with our tax advisors to determine the full impact that the recent tax legislation as a whole will have on us. We urge our investors to consult with their legal and tax advisors with respect to such legislation and the potential tax consequences of investing in our common stock.

We could be subject to securities class action litigation.

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because pharmaceutical companies have experienced significant stock price volatility in recent years. If we face such litigation, it could result in substantial costs and a diversion of management’s attention and resources, which could harm our business.

Special note regarding forward-looking statements

This prospectus contains forward-looking statements. All statements other than statements of historical facts contained in this prospectus, including statements regarding our future results of operations and financial position, business strategy, research and development costs, the anticipated timing, costs and conduct of our planned clinical trials for CRN00808 and our planned discovery actions and preclinical studies and clinical trials for our other development programs, the timing and likelihood of regulatory filings and approvals for CRN00808 and our other product candidates, our ability to commercialize CRN00808 and our other product candidates, if approved, the pricing and reimbursement of our product candidates, if approved, the potential benefits of strategic collaborations and our ability to enter into strategic arrangements, 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.

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 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 described under the sections in this prospectus entitled “Risk factors” and “Management’s discussion and analysis of financial condition and results of operations” and elsewhere in this prospectus. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified and some of which are beyond our control, you should not rely on these forward-looking statements as predictions of future events. 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. Except as required by applicable law, we undertake no obligation to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise. You should, however, review the factors and risks we describe in the reports we will file from time to time with the SEC after the date of this prospectus. See “Where you can find more information.”

In addition, statements that “we believe” and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this prospectus, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and you are cautioned not to rely unduly upon these statements.

Market and industry data

We obtained the industry, market and competitive position data used throughout this prospectus from our own internal estimates and research, as well as from independent market research, industry and general publications and surveys, governmental agencies and publicly available information in addition to research, surveys and studies conducted by third parties. Internal estimates are derived from publicly available information released by industry analysts and third-party sources, our internal research and our industry experience, and are based on assumptions made by us based on such data and our knowledge of our industry and market, which we believe to be reasonable. In some cases, we do not expressly refer to the sources from which this data is derived. In that regard, when we refer to one or more sources of this type of data in any paragraph, you should assume that other data of this type appearing in the same paragraph is derived from the same sources, unless otherwise expressly stated or the context otherwise requires. In addition, while we believe the industry, market and competitive position data included in this prospectus is reliable and based on reasonable assumptions, such data involve risks and uncertainties and are subject to change based on various factors, including those discussed in “Risk factors.” These and other factors could cause results to differ materially from those expressed in the estimates made by the independent parties or by us.

Use of proceeds

We estimate that the net proceeds to us from the sale of the common stock that we are offering will be approximately $92.1 million (or $106.3 million if the underwriters exercise their option to purchase additional shares in full), based upon the initial public offering price of $17.00 per share, and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

The principal purposes of this offering are to obtain additional capital to support our operations, to create a public market for our common stock and to facilitate our future access to the public equity markets.

We intend to use the net proceeds from the offering as follows:

- approximately $45.0 million to fund the clinical development of CRN00808;
- approximately $15.0 million to fund preclinical and clinical development of our other development programs; and
- the remainder for working capital and general corporate purposes.

We may also use a portion of the remaining net proceeds and our existing cash and cash equivalents to in-license, acquire, or invest in complementary businesses, technologies, products or assets. However, we have no current commitments or obligations to do so.

We believe, based on our current operating plan, that the net proceeds from this offering and our existing cash and cash equivalents, will be sufficient to fund our operations for at least the next 24 months, although there can be no assurance in that regard. In particular, we expect that the net proceeds from this offering will allow us to complete our planned Phase 2 clinical trials for CRN00808 and our planned Phase 1 clinical trials for CRN02481 and CRN01941. However, our expected use of proceeds from this offering described above represents our current intentions based on our present plans and business condition. As of the date of this prospectus, we cannot predict with certainty all of the particular uses for the proceeds to be received upon the completion of this offering or the actual amounts that we will spend on the uses set forth above. The net proceeds from this offering, together with our cash and cash equivalents, will not be sufficient for us to fund all of our product candidates through regulatory approval, and we will need to raise additional capital to complete the development and commercialization of all of our product candidates.

The amounts and timing of our actual expenditures will depend on numerous factors, including the time and cost necessary to conduct our planned preclinical and clinical trials, the results of our preclinical and clinical trials and other factors described under “Risk factors” in this prospectus, as well as the amount of cash used in our operations and any unforeseen cash needs. Therefore, our actual expenditures may differ materially from the estimates described above. 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.

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 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 the board of directors deems relevant, and subject to the restrictions contained in any future financing instruments.

Capitalization

The following table sets forth our cash and cash equivalents and capitalization as of March 31, 2018:

- on an actual basis;
- on a pro forma basis to reflect (1) the automatic conversion of all outstanding shares of our convertible preferred stock into 14,712,571 shares of common stock and the related reclassification of the carrying value of the convertible preferred stock to permanent equity immediately prior to the closing of this offering, and (2) the filing and effectiveness of our amended and restated certificate of incorporation immediately prior to the closing of this offering; and
- on a pro forma as adjusted basis to give further effect to our issuance and sale of 6,000,000 shares of our common stock in this offering based upon the initial public offering price of $17.00 per share, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

The pro forma as adjusted information below is illustrative only, and our capitalization following the closing of this offering will be adjusted based on the actual initial public offering price and other terms of this offering determined at pricing. You should read this information in conjunction with our consolidated financial statements and the related notes included in this prospectus and the "Management's discussion and analysis of financial condition and results of operations" section and other financial information contained in this prospectus.

	As of March 31, 2018		
(in thousands, except share and per share data)	**Actual**	**Pro forma**	**Pro forma as adjusted**
	(unaudited)	**(unaudited)**	**(unaudited)**
Cash and cash equivalents	$ 73,740	$ 73,740	$ 165,800
Convertible preferred stock, $0.001 par value per share; 48,868,345 shares authorized, 48,404,379 shares issued and outstanding, actual; no shares authorized, issued and outstanding, pro forma and pro forma as adjusted	92,975	—	—
Stockholders' equity (deficit):			
Preferred stock, $0.001 par value per share; no shares authorized, issued or outstanding, actual; 10,000,000 shares authorized and no shares issued and outstanding, pro forma and pro forma as adjusted	—	—	—
Common stock, $0.001 par value per share; 65,000,000 shares authorized; 2,295,390 shares issued and 2,191,035 outstanding, excluding 104,355 shares subject to repurchase, actual; 200,000,000 shares authorized, pro forma and pro forma as adjusted; 17,007,961 shares issued and 16,903,606 shares outstanding, excluding 104,355 shares subject to repurchase, pro forma; 23,007,961 shares issued and 22,903,606 shares outstanding, excluding 104,355 shares subject to repurchase, pro forma as adjusted	2	17	23
Additional paid in capital	1,751	94,711	186,765
Accumulated deficit	(21,729)	(21,729)	(21,729)
Total stockholders' equity (deficit)	(19,976)	72,999	165,059
Total capitalization	$ 72,999	$ 72,999	$ 165,059

The number of shares of common stock in the table above is based on 17,007,961 shares of our common stock outstanding as of March 31, 2018, after giving effect to the automatic conversion of all outstanding shares of

our convertible preferred stock into 14,712,571 shares of our common stock immediately prior to the closing of this offering, and excludes:

- 1,457,952 shares of common stock issuable upon exercise of stock options outstanding as of March 31, 2018, at a weighted-average exercise price of $1.34 per share;
- 1,027,196 shares of common stock issuable upon exercise of stock options granted after March 31, 2018, at a weighted-average exercise price of $9.81 per share;
- 1,991,637 shares of our common stock reserved for future issuance under our 2018 Plan, which became effective in connection with this offering (which number includes 391,637 shares remaining available for issuance under our 2015 Stock Incentive Plan as of June 30, 2018 (which shares became available for issuance under the 2018 Plan upon its effectiveness), but does not include any potential evergreen increases pursuant to the terms of the 2018 Plan); and
- 250,000 shares of common stock reserved for future issuance under our ESPP, which became effective in connection with this offering (which number does not include any potential evergreen increases pursuant to the terms of the ESPP).

Dilution

If you invest in our common stock in this offering, your ownership interest will be immediately diluted to the extent of the difference between the initial public offering price per share and the pro forma as adjusted net tangible book value per share of our common stock after this offering.

As of March 31, 2018, we had a historical net tangible book deficit of $(20.0) million, or $(8.70) per share of common stock based on 2,295,390 shares of common stock outstanding, including 104,355 shares subject to repurchase, as of such date. Our historical net tangible book value per share represents total tangible assets less total liabilities and convertible preferred stock, divided by the number of shares of common stock outstanding (including shares subject to repurchase) at March 31, 2018.

On a pro forma basis, after giving effect to the automatic conversion of all outstanding shares of our convertible preferred stock into 14,712,571 shares of our common stock and the related reclassification of the carrying value of the convertible preferred stock to permanent equity immediately prior to the closing of this offering stock, our pro forma net tangible book value as of March 31, 2018 would have been approximately $73.0 million, or approximately $4.29 per share of our common stock.

After giving further effect to the sale of 6,000,000 shares of common stock based on the initial public offering price of $17.00 per share, and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us, our pro forma as adjusted net tangible book value as of March 31, 2018 would have been approximately $165.1 million, or approximately $7.17 per share. This amount represents an immediate increase in pro forma net tangible book value of $2.88 per share to our existing stockholders and an immediate dilution in pro forma net tangible book value of approximately $9.83 per share to new investors purchasing shares of common stock in this offering.

Dilution per share to new investors is determined by subtracting pro forma as adjusted net tangible book value per share after this offering from the initial public offering price per share paid by new investors. The following table illustrates this dilution (without giving effect to any exercise by the underwriters of their option to purchase additional shares):

Initial public offering price per share		$17.00
Historical net tangible book deficit per share as of March 31, 2018	$ (8.70)	
Pro forma increase in historical net tangible book value per share as of March 31, 2018 attributable to the conversion of convertible preferred stock	12.99	
Pro forma net tangible book value per share as of March 31, 2018	4.29	
Increase in pro forma net tangible book value per share attributable to new investors participating in this offering	2.88	
Pro forma as adjusted net tangible book value per share after this offering		7.17
Dilution per share to new investors participating in this offering		$ 9.83

If the underwriters exercise their option to purchase additional shares of our common stock in full in this offering, the pro forma as adjusted net tangible book value after the offering would be $7.50 per share, the increase in pro forma net tangible book value per share to existing stockholders would be $3.21 per share and the dilution per share to new investors would be $9.50 per share.

The following table summarizes on the pro forma as adjusted basis described above, as of March 31, 2018, the differences between the number of shares purchased from us, the total consideration paid to us in cash and the average price per share paid by existing stockholders for shares issued prior to this offering and the price to be paid by new investors in this offering. The calculations below are based upon the initial public offering price of

$17.00 per share, before deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

	Shares purchased		Total consideration		Average price per share
	Number	Percent	Amount	Percent	
Existing stockholders before this offering(1)	17,007,961	74%	$ 93,818,000	48%	$ 5.52
New investors participating in this offering	6,000,000	26	102,000,000	52	$ 17.00
Total	23,007,961	100%	195,818,000	100%	

(1) Certain of our principal stockholders, including entities affiliated with certain of our directors, have indicated an interest in purchasing an aggregate of approximately $30.0 million in shares of our common stock in this offering at the initial public offering price per share and on the same terms as the other purchasers in this offering. However, because these indications of interest are not binding agreements or commitments to purchase, the underwriters may determine to sell more, less or no shares in this offering to any or all of these stockholders, or any or all of these stockholders may determine to purchase more, less or no shares in this offering. The underwriters will receive the same underwriting discount on any shares purchased by these stockholders as they will on any other shares sold to the public in this offering.

If all outstanding options had been exercised as of March 31, 2018, the pro forma as adjusted net tangible book value per share after this offering would be $6.83, and total dilution per share to new investors would be $10.17.

If the underwriters exercise their option to purchase additional shares of our common stock in full:

- the percentage of shares of common stock held by existing stockholders will decrease to approximately 71% of the total number of shares of our common stock outstanding after this offering; and
- the number of shares held by new investors will increase to 6,900,000, or approximately 29% of the total number of shares of our common stock outstanding after this offering.

The foregoing tables and calculations (other than the historical net tangible book value calculation) are based on 17,007,961 shares of our common stock outstanding as of March 31, 2018, including 104,355 shares subject to repurchase, after giving effect to the automatic conversion of all outstanding shares of our convertible preferred stock into 14,712,571 shares of our common stock prior to the closing of this offering, and exclude:

- 1,457,952 shares of common stock issuable upon exercise of stock options outstanding as of March 31, 2018, at a weighted-average exercise price of $1.34 per share;
- 1,027,196 shares of common stock issuable upon exercise of stock options granted after March 31, 2018, at a weighted – average exercise price of $9.81 per share:
- 1,991,637 shares of our common stock reserved for future issuance under our 2018 Plan, which became effective in connection with this offering (which number includes 391,637 shares remaining available for issuance under our 2015 Stock Incentive Plan as of June 30, 2018 (which shares became available for issuance under the 2018 Plan upon its effectiveness), but does not include any potential evergreen increases pursuant to the terms of the 2018 Plan); and
- 250,000 shares of common stock reserved for future issuance under our ESPP, which became effective in connection with this offering (which number does not include any potential evergreen increases pursuant to the terms of the ESPP).

To the extent any outstanding options are exercised, or we issue additional equity or convertible debt securities in the future, there will be further dilution to new investors.

Selected consolidated financial data

The following tables set forth selected historical consolidated financial data as of, and for the periods ended on, the dates indicated. We have derived the statements of operations data for the years ended December 31, 2016 and 2017 and the balance sheet data as of December 31, 2016 and 2017 from our audited consolidated financial statements included elsewhere in this prospectus. We have derived the statements of operations data for the three months ended March 31, 2017 and 2018 and the balance sheet data as of March 31, 2018 from our unaudited consolidated financial statements included elsewhere in this prospectus. The unaudited consolidated financial statements have been prepared on a basis consistent with our audited consolidated financial statements included in this prospectus and, in the opinion of management, reflect all adjustments, consisting only of normal recurring adjustments, necessary to fairly state our financial position as of March 31, 2018 and results of operations for the three months ended March 31, 2017 and 2018. You should read this data together with our consolidated financial statements and related notes included elsewhere in this prospectus and the section in this prospectus entitled "Management's discussion and analysis of financial condition and results of operations." Our historical results for any prior period are not necessarily indicative of our future results.

	Years Ended December 31,		Three Months Ended March 31,	
(in thousands, except share and per share data)	**2016**	**2017**	**2017**	**2018**
			(unaudited)	
Consolidated Statement of Operations Data:				
Grant revenues	$ 589	$ 2,045	$ 45	$ 442
Operating expenses:				
Research and development	5,100	9,233	2,065	4,720
General and administrative	1,533	1,939	589	1,248
Total operating expenses	6,633	11,172	2,654	5,968
Loss from operations	(6,044)	(9,127)	(2,609)	(5,526)
Other income (expense):				
Interest income	37	26	7	64
Interest expense	(11)	(8)	(2)	—
Other expense	(1)	(48)	(2)	(2)
Total other income (expense)	25	(30)	3	62
Net loss	$ (6,019)	$ (9,157)	$ (2,606)	$ (5,464)
Net loss per share, basic and diluted(1)	$ (5.96)	$ (6.68)	$ (2.18)	$ (2.92)
Weighted-average shares of common stock outstanding, basic and diluted(1)	1,010,510	1,370,578	1,197,711	1,869,576
Pro forma net loss per share, basic and diluted (unaudited)(1)		$ (1.18)		$ (0.39)
Pro forma weighted-average shares of common stock outstanding, basic and diluted (unaudited)(1)		7,746,089		13,878,156

(1) See Note 1 to our audited consolidated financial statements included elsewhere in this prospectus for an explanation of the method used to calculate the historical and pro forma net loss per share, basic and diluted, and the number of shares used in the computation of the per share amounts.

(in thousands)	As of December 31, 2016	As of December 31, 2017	As of March 31, 2018 (unaudited)
Consolidated Balance Sheet Data:			
Cash and cash equivalents	$12,152	$ 14,192	$ 73,740
Working capital	11,475	14,268	71,595
Total assets	12,599	15,598	76,329
Convertible preferred stock	17,740	29,700	92,975
Accumulated deficit	(7,108)	(16,265)	(21,729)
Total stockholders' equity (deficit)	(6,204)	(15,022)	(19,976)

Management's discussion and analysis of financial condition and results of operations

You should read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and related notes appearing in this prospectus. Some of the information contained in this discussion and analysis is set forth elsewhere in this prospectus, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the "Risk factors" section of this prospectus, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

We are a clinical stage pharmaceutical company focused on the discovery, development and commercialization of novel therapeutics for rare endocrine diseases and endocrine-related tumors. Endocrine pathways function to maintain homeostasis and commonly use peptide hormones acting through 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, CRN00808, is currently in clinical development for the treatment of acromegaly, and we are advancing additional product candidates through preclinical 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 three product candidates and discovery program:

- CRN00808, our lead product candidate, establishes a new class of oral selective nonpeptide sst2 biased agonists designed for the treatment of acromegaly and is the first agent in its class with reported clinical results. In March 2018, we reported initial results from a Phase 1, double-blind, randomized, placebo-controlled, single- and multiple-ascending dose trial to evaluate the safety, pharmacokinetics and pharmacodynamics of CRN00808 in 99 healthy volunteers. CRN00808 demonstrated clinical proof-of-concept by potently suppressing stimulated GH and baseline IGF-1 in these subjects. We plan to submit an IND to the FDA in the second half of 2018 and, if accepted, plan to initiate two Phase 2 clinical trials of CRN00808 in acromegaly patients in early 2019, including those who are not adequately controlled with existing therapy.
- CRN02481 represents a new class of oral selective nonpeptide sst5 agonists designed to treat congenital hyperinsulinism. CRN02481 is currently in first-in-human enabling studies, and we expect to initiate a Phase 1 human proof-of-concept clinical trial in the first half of 2019. We expect results from this trial in 2019.
- CRN01941 is an oral nonpeptide sst2 biased agonist designed for the treatment of neuroendocrine tumors, that originate from neuroendocrine cells commonly found in the gut, lung or pancreas. CRN01941 is currently in first-in-human enabling studies, and we expect to initiate a Phase 1 human proof-of-concept clinical trial in the first half of 2019. We expect results from this trial in late 2019/early 2020.

- We have an ongoing discovery effort to identify and advance into development the first nonpeptide product candidate to antagonize ACTH, designed for the treatment of Cushing's disease. Our goal is to select a product candidate for preclinical development in 2019.

To date, we have devoted substantially all of our resources to drug discovery, conducting preclinical studies and clinical trials, obtaining and maintaining patents related to our product candidates, and the provision of general and administrative support for these operations. We recognize revenues from various research and development grants, but do not have any products approved for sale and have not generated any product sales. We have funded our operations primarily through the private placement of preferred stock and grant revenues. To date, we have raised gross proceeds of approximately $93.5 million to fund our operations from the issuance of convertible preferred stock. As of March 31, 2018, we had cash and cash equivalents of $73.7 million.

We have incurred cumulative net losses since our inception. Our net losses were $6.0 million, $9.2 million and $5.5 million for the years ended December 31, 2016 and 2017 and the three months ended March 31, 2018, respectively. As of March 31, 2018, we had an accumulated deficit of $21.7 million. Our net losses may fluctuate significantly from quarter-to-quarter and year-to-year, depending on the timing of our preclinical studies and clinical trials and our expenditures on other research and development activities. We expect our expenses and operating losses will increase substantially as we conduct our ongoing and planned clinical trials, continue our research and development activities and conduct preclinical studies, hire additional personnel, protect our intellectual property and incur additional costs associated with being a public company, including audit, legal, regulatory, and tax-related services associated with maintaining compliance with exchange listing and SEC requirements, director and officer insurance premiums, and investor relations costs.

We do not expect to generate any revenues from product sales unless and until we successfully complete development and obtain regulatory approval for one or more of our product candidates, which we expect will take a number of years. If we obtain regulatory approval for any of our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. Accordingly, until such time as we can generate significant revenue from sales of our product candidates, if ever, we expect to finance our cash needs through equity offerings, debt financings or other capital sources, including potentially collaborations, licenses and other similar arrangements. However, we may be unable to raise additional funds or enter into such other arrangements when needed on favorable terms or at all. Our failure to raise capital or enter into such other arrangements when needed would have a negative impact on our financial condition and could force us to delay, scale back or discontinue the development of our existing product candidates or our efforts to expand our product pipeline.

Australian operations

In January 2017, we established Crinetics Australia Pty Ltd, or CAPL, a wholly-owned subsidiary which was formed to conduct various preclinical and clinical activities for our product and development candidates. We believe CAPL will be eligible for certain financial incentives made available by the Australian government for research and development expenses. Specifically, the Australian Taxation Office provides for a refundable tax credit in the form of a cash refund equal to 43.5% of qualified research and development expenditures under the Australian Research and Development Tax Incentive Program, or the Australian Tax Incentive, to Australian companies that operate the majority of their research and development activities associated with such projects in Australia. A wholly-owned Australian subsidiary of a non-Australian parent company is eligible to receive the refundable tax credit, provided that the Australian subsidiary retains the rights to the data and intellectual property generated in Australia, and provided that the total revenues of the parent company and its consolidated subsidiaries during the period for which the refundable tax credit is claimed are less than $20.0 million Australian dollars. If we lose our ability to operate CAPL in Australia, or if we are ineligible or unable to

receive the research and development tax credit, or the Australian government significantly reduces or eliminates the tax credit, the actual refund amounts we receive may differ from our estimates.

Financial operations overview

Grant revenues

To date, we have not generated any revenues from the commercial sale of approved products, and we do not expect to generate revenues from the commercial sale of our product candidates for at least the foreseeable future, if ever. For the years ended December 31, 2016 and 2017 and the three months ended March 31, 2017 and 2018, revenues were derived from SBIR Grants awarded to us by the National Institute of Diabetes and Digestive and Kidney Diseases of the National Institutes of Health. We do not currently expect future grant revenues to be a material source of funding.

Operating expenses

Research and development

To date, our research and development expenses have related primarily to discovery efforts and preclinical and clinical development of our product candidates. Research and development expenses are recognized as incurred and payments made prior to the receipt of goods or services to be used in research and development are capitalized until the goods or services are received.

Research and development expenses include:

- salaries, payroll taxes, employee benefits, and stock-based compensation charges for those individuals involved in research and development efforts;
- external research and development expenses incurred under agreements with contract research organizations, or CROs, investigative sites and consultants to conduct our clinical trials and preclinical and non-clinical studies;
- laboratory supplies;
- costs related to manufacturing our product candidates for clinical trials and preclinical studies, including fees paid to third-party manufacturers;
- costs related to compliance with regulatory requirements; and
- facilities, depreciation and other allocated expenses, which include direct and allocated expenses for rent, maintenance of facilities, insurance, equipment and other supplies.

We recognize the Australian Tax Incentive as a reduction of research and development expense. The amounts are determined based on eligible research and development expenditures. The Australian Tax Incentive is recognized when there is reasonable assurance that the Australian Tax Incentive will be received, the relevant expenditure has been incurred, and the amount of the Australian Tax Incentive can be reliably measured.

Our direct research and development expenses consist principally of external costs, such as fees paid to CROs, investigative sites and consultants in connection with our clinical trials, preclinical and non-clinical studies, and costs related to manufacturing clinical trial materials. For 2016 and 2017 and the three months ended March 31, 2018, the majority of our third-party expenses related to the research and development of CRN00808. We deploy our personnel and facility related resources across all of our research and development activities.

We plan to substantially increase our research and development expenses for the foreseeable future as we continue the development of our product candidates and discovery of new product candidates. We cannot determine with certainty the timing of initiation, the duration or the completion costs of current or future preclinical studies and clinical trials of our product candidates due to the inherently unpredictable nature of preclinical and clinical development. Clinical and preclinical development timelines, the probability of success and development costs can differ materially from expectations. We anticipate that we will make determinations as to which product candidates to pursue and how much funding to direct to each product candidate on an ongoing basis in response to the results of ongoing and future preclinical studies and clinical trials, regulatory developments and our ongoing assessments as to each product candidate's commercial potential. We will need to raise substantial additional capital in the future. In addition, we cannot forecast which product candidates may be subject to future collaborations, when such arrangements will be secured, if at all, and to what degree such arrangements would affect our development plans and capital requirements.

Our clinical development costs may vary significantly based on factors such as:

- per patient trial costs;
- the number of trials required for approval;
- the number of sites included in the trials;
- the countries in which the trials are conducted;
- the length of time required to enroll eligible patients;
- the number of patients that participate in the trials;
- the number of doses that patients receive;
- the drop-out or discontinuation rates of patients;
- potential additional safety monitoring requested by regulatory agencies;
- the duration of patient participation in the trials and follow-up;
- the cost and timing of manufacturing our product candidates;
- the phase of development of our product candidates; and
- the efficacy and safety profile of our product candidates.

General and administrative

General and administrative expenses consist primarily of salaries and employee-related costs, including stock-based compensation, for personnel in executive, finance and other administrative functions. Other significant costs include facility-related costs, legal fees relating to intellectual property and corporate matters, professional fees for accounting and consulting services and insurance costs. We anticipate that our general and administrative expenses will increase in the future to support our continued research and development activities and, if any of our product candidates receive marketing approval, commercialization activities. We also anticipate increased expenses related to audit, legal, regulatory, and tax-related services associated with maintaining compliance with exchange listing and SEC requirements, director and officer insurance premiums, and investor relations costs associated with operating as a public company.

Other income (expense)

Other income (expense) consists of interest income from our money market account, foreign exchange losses related to CAPL and interest expense on a bank loan that was repaid in 2017.

Results of operations

Comparison of the three months ended March 31, 2017 and 2018

The following table summarizes our results of operations for the three months ended March 31, 2017 and 2018:

	Three Months Ended March 31,		
(in thousands)	**2017**	**2018**	**Change**
Grant revenues	$ 45	$ 442	$ 397
Operating expenses:			
Research and development	2,065	4,720	2,655
General and administrative	589	1,248	659
Total operating expenses	2,654	5,968	3,314
Loss from operations	(2,609)	(5,526)	(2,917)
Other income (expense):			
Interest income	7	64	57
Interest expense	(2)	—	2
Other income (expense)	(2)	(2)	—
Total other income (expense)	3	62	59
Net loss	$(2,606)	$(5,464)	$ (2,858)

Grant revenues. Grant revenues were $45,000 and $0.4 million for the three months ended March 31, 2017 and 2018, respectively. The increase was primarily due to increased research and development activities related to our SBIR Grants.

Research and development expenses. Research and development expenses were $2.1 million and $4.7 million for the three months ended March 31, 2017 and 2018, respectively. The increase of $2.6 million was primarily due to increases in the following: $1.3 million of clinical study related expenses, $0.7 million of personnel related expenses, $0.4 million of manufacturing expenses, $0.3 million of external non-clinical expenditures, $0.1 million of stock-based compensation and $0.1 million of facility related expenses. For the three months ended March 31, 2018, the expenses above were offset in part by $0.3 million of Australian Tax Incentives. We recorded no Australian Tax Incentives for the three months ended March 31, 2017.

General and administrative expenses. General and administrative expenses were $0.6 million and $1.2 million for the three months ended March 31, 2017 and 2018, respectively. The increase of $0.6 million was primarily due to increases in the following: $0.2 million of stock-based compensation, $0.2 million of professional services primarily related to patent activities and corporate legal fees, $0.1 million of personnel related expenses and $0.1 million of facility related expenses and other general and administrative expenses.

Comparison of the years ended December 31, 2016 and 2017

The following table summarizes our results of operations for the years ended December 31, 2016 and 2017:

(in thousands)	Years ended December 31, 2016	2017	Change
Grant revenues	$ 589	$ 2,045	$ 1,456
Operating expenses:			
Research and development	5,100	9,233	4,133
General and administrative	1,533	1,939	406
Total operating expenses	6,633	11,172	4,539
Loss from operations	(6,044)	(9,127)	(3,083)
Other income (expense):			
Interest income	37	26	(11)
Interest expense	(11)	(8)	3
Other income (expense)	(1)	(48)	(47)
Total other income (expense)	25	(30)	(55)
Net loss	$ (6,019)	$ (9,157)	$ (3,138)

Grant revenues. Grant revenues were $0.6 million and $2.0 million for the years ended December 31, 2016 and 2017, respectively. The increase was primarily due to increased research and development activities related to our SBIR Grants.

Research and development expenses. Research and development expenses were $5.1 million and $9.2 million for the years ended December 31, 2016 and 2017, respectively. The increase of $4.1 million was primarily due to increases in the following: $1.2 million of clinical study related expenses, $1.2 million of manufacturing expenses, $1.2 million of external non-clinical expenditures, and $0.7 million of personnel related expenses. In 2017, the expenses above were offset in part by an Australian Tax Incentive of $0.5 million.

General and administrative expenses. General and administrative expenses were $1.5 million and $1.9 million for the years ended December 31, 2016 and 2017, respectively. The increase of $0.4 million was primarily due to increases in the following: $0.2 million of personnel related expenses, $0.1 million of professional services primarily related to patent activities and corporate legal fees, and $0.1 million of facility related expenses and other general and administrative expenses.

Liquidity and capital resources

We have incurred cumulative net losses and negative cash flows from operations since our inception and anticipate we will continue to incur net losses for the foreseeable future. As of March 31, 2018, we had an accumulated deficit of $21.7 million. As of March 31, 2018, we had cash and cash equivalents of $73.7 million.

The following table sets forth a summary of the net cash flow activity for each of the periods set forth below:

(in thousands)	Years ended December 31, 2016	Years ended December 31, 2017	Three Months ended March 31, 2017	Three Months ended March 31, 2018
Net cash provided by (used in):				
Operating activities	$ (5,468)	$ (9,479)	$(2,326)	$ (3,407)
Investing activities	(190)	(304)	(20)	(57)
Financing activities	(53)	11,823	51	63,512
Net increase (decrease) in cash, cash equivalents and restricted cash	$ (5,711)	$ 2,040	$(2,295)	$60,048

Operating activities

Net cash used in operating activities was $2.3 million and $3.4 million for the three months ended March 31, 2017 and 2018, respectively. The net cash used in operating activities for the three months ended March 31, 2017 was primarily due to our net loss of $2.6 million, adjusted for $0.1 million of noncash charges related to depreciation and stock-based compensation and a $0.2 million change in operating assets and liabilities. The net cash used in operating activities for the three months ended March 31, 2018 was primarily due to our net loss of $5.5 million, adjusted for $0.5 million of noncash charges primarily due to $0.4 million of stock-based compensation expense, and a $1.6 million change in operating assets and liabilities, primarily due to increased accounts payable and accrued expenses in support of our increased operating expenses and financing activities.

Net cash used in operating activities was $5.5 million and $9.5 million for the years ended December 31, 2016 and 2017, respectively. The net cash used in operating activities during the year ended December 31, 2016 was primarily due to our net loss of $6.0 million, adjusted for $0.4 million of noncash charges and a $0.2 million change in operating assets and liabilities. The noncash charges primarily related to $0.3 million of stock-based compensation charges and $0.1 million of depreciation expense. Net cash used in operating activities during the year ended December 31, 2017 was primarily due to our net loss of $9.2 million, adjusted for $0.4 million of noncash charges and a $0.7 million change in operating assets and liabilities. The noncash charges primarily related to $0.3 million of stock-based compensation charges and $0.1 million of depreciation expense.

Investing activities

Net cash used in investing activities was due to property and equipment purchases in each period.

Financing activities

Net cash provided by financing activities was $0.1 million and $63.5 million for the three months ended March 31, 2017 and 2018, respectively. Net cash provided by financing activities for the three months ended March 31, 2017 was primarily due to the proceeds from the exercise of stock options. Net cash provided by financing activities for the three months ended March 31, 2018 was primarily due to $63.4 million of net proceeds from the issuance of Series B convertible preferred stock and $0.3 million of proceeds from the exercise of stock options, offset by payment of $0.1 million of costs related to our proposed initial public offering.

Net cash used in financing activities was $0.1 million for the year ended December 31, 2016, primarily due to the principal payments on an outstanding bank loan. Net cash provided by financing activities for the year ended December 31, 2017 was the result of net proceeds of $12.0 million from the sale of Series A convertible preferred stock and $0.1 million from the exercise of common stock options, offset by principal payments on an outstanding bank loan, which was repaid in full in 2017.

We believe that our existing cash and cash equivalents and the estimated net proceeds from this offering, together with interest thereon, will be sufficient to meet our anticipated cash requirements through at least the next 24 months. In particular, we expect that the net proceeds from this offering will allow us to complete our planned Phase 2 clinical trials for CRN00808 and our planned Phase 1 clinical trials for CRN02481 and CRN01941. However, our forecast of the period of time through which our financial resources will be adequate to support our operations is a forward-looking statement that involves risks and uncertainties, and actual results could vary materially. We have based this estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we expect. Additionally, the process of testing product candidates in clinical trials is costly, and the timing of progress and expenses in these trials is uncertain.

Our future capital requirements will depend on many factors, including:

- the type, number, scope, progress, expansions, results, costs and timing of, our preclinical studies and clinical trials of our product candidates which we are pursuing or may choose to pursue in the future;
- the costs and timing of manufacturing for our product candidates, including commercial manufacturing if any product candidate is approved;
- the costs, timing and outcome of regulatory review of our product candidates;
- the costs of obtaining, maintaining and enforcing our patents and other intellectual property rights;
- our efforts to enhance operational systems and hire additional personnel to satisfy our obligations as a public company, including enhanced internal controls over financial reporting;
- the costs associated with hiring additional personnel and consultants as our preclinical and clinical activities increase;
- the timing and the extent of any Australian Tax Incentive refund and future grant revenues, if any, that we receive;
- the costs and timing of establishing or securing sales and marketing capabilities if any product candidate is approved;
- our ability to achieve sufficient market acceptance, adequate coverage and reimbursement from third-party payors and adequate market share and revenue for any approved products;
- the terms and timing of establishing and maintaining collaborations, licenses and other similar arrangements; and
- costs associated with any products or technologies that we may in-license or acquire.

Until such time, if ever, as we can generate substantial product revenues to support our cost structure, we expect to finance our cash needs through equity offerings, debt financings or other capital sources, including potentially collaborations, licenses and other similar arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our stockholders will be or could be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise funds through collaborations, licenses and other similar arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us and/or may reduce the value of our common stock. If we are

unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market our product candidates even if we would otherwise prefer to develop and market such product candidates ourselves.

Contractual obligations and commitments

The following table summarizes our contractual obligations at March 31, 2018 (in thousands):

		Payments due by period			
	Total	Less than 1 year	1 — 3 years	3 — 5 years	More than 5 years
Operating lease obligations(1)	$8,575	$ 405	$2,491	$2,387	$ 3,292
Total	$8,575	$ 405	$2,491	$2,387	$ 3,292

(1) Our operating lease obligations relate to our former corporate headquarters which we are currently using as laboratory space in San Diego, California.

We enter into contracts in the normal course of business with clinical trial sites and clinical supply manufacturers and with vendors for preclinical studies, research supplies and other services and products for operating purposes. These contracts generally provide for termination after a notice period, and, therefore, are cancelable contracts and not included in the table above.

Critical accounting policies and significant judgments and estimates

Our management's discussion and analysis of our financial condition and results of operations are based on our consolidated financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles, or U.S. GAAP. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, revenues and expenses and the disclosure of contingent assets and liabilities in our consolidated financial statements. On an ongoing basis, we evaluate our estimates and judgments, including those related to revenue recognition, accrued expenses and stock-based compensation. We base our estimates on historical experience, known trends and events, and various other factors that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in the notes to our consolidated financial statements appearing elsewhere in this prospectus, we believe the following accounting policies and estimates to be most critical to the preparation of our consolidated financial statements.

Grant revenues

Under the terms of the grants awarded, we are entitled to receive reimbursement of our allowable direct expenses, allocated overhead, general and administrative expenses and payment of other specified amounts. Revenues from development and support activities under the grants is recorded in the period in which the related costs are incurred for cost reimbursement grants. Revenue is recognized when earned and expenses are recognized when incurred. Any of the funding sources may request reimbursement for expenses or return of funds, or both, as a result of noncompliance by us with the terms of the grants. No reimbursement of expenses or return of funds for noncompliance has been requested or made since inception of the contract and grants.

Australian research and development tax incentive

CAPL is eligible to obtain a cash refund from the Australian Taxation Office for eligible research and development expenditures under the Australian Tax Incentive. The Australian Tax Incentive is recognized as a

reduction to research and development expense when there is reasonable assurance that the Australian Tax Incentive will be received, the relevant expenditure has been incurred, and the amount can be reliably measured. Although we do not expect our estimates to be materially different from amounts actually received, if our estimates of the amounts and timing of the receipt of the Australian Tax Incentive differ from actual amounts received, it could result in us reporting amounts that are too high or too low in any particular period.

Accrued expenses

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued expenses as of each balance sheet date. This process involves reviewing open contracts and purchase orders, communicating with our personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. We make estimates of our accrued expenses as of each balance sheet date based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. The significant estimates in our accrued research and development expenses include the costs incurred for services performed by our vendors in connection with research and development activities for which we have not yet been invoiced.

We base our expenses related to research and development activities on our estimates of the services received and efforts expended pursuant to quotes and contracts with vendors that conduct research and development on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the research and development expense. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or prepaid expense accordingly. Advance payments for goods and services that will be used in future research and development activities are expensed when the activity has been performed or when the goods have been received rather than when the payment is made.

Although we do not expect our estimates to be materially different from amounts actually incurred, if our estimates of the status and timing of services performed differ from the actual status and timing of services performed, it could result in us reporting amounts that are too high or too low in any particular period. To date, there have been no material differences between our estimates of such expenses and the amounts actually incurred.

Stock-based compensation expense

Stock-based compensation expense represents the cost of the grant date fair value of employee awards over the requisite service period of the awards (usually the vesting period) on a straight-line basis. For stock awards for which vesting is subject to performance-based milestones, the expense is recorded over the remaining service period after the point when the achievement of the milestone is probable or the performance condition has been achieved. We account for awards to nonemployees using the fair value method. Awards to nonemployees are subject to periodic revaluation over their vesting terms and was not material for all periods presented. We estimate the fair value of all stock option grants using the Black-Scholes option pricing model and recognize forfeitures as they occur.

Estimating the fair value of equity awards as of the grant date using valuation models, such as the Black-Scholes option pricing model, is affected by assumptions regarding a number of complex variables, including the risk-free interest rate, the expected stock price volatility, the expected term of stock options, the expected dividend yield and the fair value of the underlying common stock on the date of grant. Changes in the assumptions can materially affect the fair value and ultimately how much stock-based compensation expense is

recognized. These inputs are subjective and generally require significant analysis and judgment to develop. See Note 4 to our consolidated financial statements included elsewhere in this prospectus for information concerning certain of the specific assumptions we used in applying the Black-Scholes option pricing model to determine the estimated fair value of our stock options granted in the years ended December 31, 2016 and 2017 and the three months ended March 31, 2017 and 2018.

As of March 31, 2018, the unrecognized stock-based compensation expense related to employee stock options was $1.1 million and is expected to be recognized as expense over a weighted-average period of approximately 3.6 years. The intrinsic value of all outstanding stock options as of March 31, 2018 was approximately $22.8 million, based upon the initial public offering price of $17.00 per share, of which approximately $6.2 million related to vested options and approximately $16.6 million related to unvested options.

In May and June 2018, certain of our employees and consultants were granted options to purchase an aggregate of 1,027,196 shares of common stock at an exercise prices ranging from $9.28 to $12.01 per share.

Common stock valuations

We are required to estimate the fair value of the common stock underlying our stock-based awards when performing fair value calculations, which is the most subjective input into the Black-Scholes option pricing model. The fair value of the common stock underlying our stock-based awards was determined on each grant date by our board of directors, taking into account input from management and independent third-party valuation analyses. All options to purchase shares of our common stock are intended to be granted with an exercise price per share no less than the fair value per share of our common stock underlying those options on the date of grant, based on the information known to us on the date of grant. In the absence of a public trading market for our common stock, on each grant date we develop an estimate of the fair value of our common stock in order to determine an exercise price for the option grants. Our determinations of the fair value of our common stock were made using methodologies, approaches and assumptions consistent with the American Institute of Certified Public Accountants Audit and Accounting Practice Aid Series: *Valuation of Privately Held Company Equity Securities Issued as Compensation*, or the Practice Aid.

Our board of directors considered various objective and subjective factors, along with input from management, to determine the fair value of our common stock, including:

- valuations of our common stock performed by independent third-party valuation specialists;
- our stage of development and business strategy, including the status of research and development efforts of our product candidates, and the material risks related to our business and industry;
- our results of operations and financial position, including our levels of available capital resources;
- the valuation of publicly traded companies in the life sciences and biotechnology sectors, as well as recently completed mergers and acquisitions of peer companies;
- the lack of marketability of our common stock as a private company;
- the prices of our convertible preferred stock sold to investors in arm’s length transactions and the rights, preferences, and privileges of our convertible preferred stock relative to those of our common stock;
- the likelihood of achieving a liquidity event for the holders of our common stock, such as an initial public offering or a sale of our company, given prevailing market conditions;
- trends and developments in our industry; and
- external market conditions affecting the life sciences and biotechnology industry sectors.

Our valuations were prepared in accordance with the guidelines in the Practice Aid, which prescribes several valuation approaches for setting the value of an enterprise, such as the cost, income and market approaches, and various methodologies for allocating the value of an enterprise to its common stock. The cost approach establishes the value of an enterprise based on the cost of reproducing or replacing the property less depreciation and functional or economic obsolescence, if present. The income approach establishes the value of an enterprise based on the present value of future cash flows that are reasonably reflective of our company's future operations, discounting to the present value with an appropriate risk adjusted discount rate or capitalization rate. The market approach is based on the assumption that the value of an asset is equal to the value of a substitute asset with the same characteristics. Each valuation methodology was considered in our valuations. In determining a fair value for our common stock, we estimated the enterprise value of our business using either the market approach or back-solve method. The back-solve method assigns an implied enterprise value based on the most recent round of funding or investment and allows for the incorporation of the implied future benefits and risks of the investment decision assigned by an outside investor. In accordance with the Practice Aid, we considered the various methods for allocating the enterprise value across our classes and series of capital stock to determine the fair value of our common stock at each valuation date. Until March 2018, we concluded that the Option Pricing Method, or OPM, was most appropriate for each of the valuations of our common stock performed by independent third-party valuation specialists. We believed the OPM was the most appropriate given the expectation of various potential liquidity outcomes and the difficulty of selecting and supporting appropriate enterprise values given our early stage of development. Under the OPM, shares are valued by creating a series of call options with exercise prices based on the liquidation preferences and conversion terms of each equity class. The values of the preferred and common stock are inferred by analyzing these options. In May 2018, we changed to a hybrid OPM and Probability-Weighted Expected Return Method, or PWERM. The PWERM is a scenario-based analysis that estimates the value per share based on the probability-weighted present value of expected future investment returns, considering each of the possible outcomes available to us, as well as the economic and control rights of each share class. Under this hybrid method, we considered the expected IPO liquidity scenario, but also used the OPM to capture all other scenarios in the event a near-term initial public offering does not occur.

Following the completion of this offering, our board of directors will determine the fair value of our common stock based on its closing price as reported on the date of grant on the primary stock exchange on which our common stock is traded.

Other company information

Net operating loss and research and development carryforwards and other income tax information

At December 31, 2017, we had federal, state, and foreign net operating loss carryforwards of approximately $6.2 million, $6.4 million and $0.4 million, respectively. The federal and state loss carryforwards will begin expiring in 2035, unless previously utilized. The foreign loss carryforwards do not expire. We also have federal and California research and development credit carryforwards totaling $0.6 million and $0.4 million, respectively. The federal research and development credit carryforwards will begin to expire in 2030, unless previously utilized. The California research credits do not expire.

Management assesses the available positive and negative evidence to estimate if sufficient future taxable income will be generated to use the existing deferred tax assets. Based on the weight of all evidence including a history of operating losses, management has determined that it is more likely than not that the net deferred tax assets will not be realized. A valuation allowance of $4.9 million as of December 31, 2017 has been established to offset the deferred tax assets as realization of such assets is uncertain.

Future utilization of our net operating loss and research and development credit carryforwards to offset future taxable income may be subject to an annual limitation, pursuant to Internal Revenue Code, or IRC, Sections 382 and 383, as a result of ownership changes that may have occurred or that could occur in the future. An ownership change occurs when a cumulative change in ownership of more than 50% occurs within a three-year period. It is possible that we have already incurred ownership changes and may incur additional ownership changes in the future, including as a result of this offering. We have not completed an IRC Section 382/383 analysis regarding the limitation of net operating loss and research and development credit carryforwards. When this analysis is finalized, we plan to update our unrecognized tax benefits accordingly.

We have not provided for deferred taxes on the outside basis difference of CAPL. The deficit in earnings would result in a deferred tax asset, and it is not apparent that this temporary difference will reverse in the foreseeable future.

The Tax Cuts and Jobs Act of 2017 was enacted on December 22, 2017. The Tax Cuts and Jobs Act of 2017 includes a number of changes to existing U.S. tax laws that impact us, most notably a reduction of the U.S. federal corporate tax rate from a maximum of 35% to a flat 21%, effective January 1, 2018, and a one-time transition tax on unremitted foreign earnings. In conjunction with the tax law changes, the SEC staff issued Staff Accounting Bulletin 118, or SAB 118, to address the application of U.S. GAAP in situations when a registrant does not have the necessary information available, prepared, or analyzed (including computations) in reasonable detail to complete the accounting for certain income tax effects of the Tax Cuts and Jobs Act of 2017. In these instances, a company can record provisional amounts in its financial statements for the income tax effects for which a reasonable estimate can be determined. For items for which a reasonable estimate cannot be determined, a company should continue to apply Accounting Standards Codification, or ASC, 740, *Accounting for Income Taxes*, based on the provisions of the tax laws that were in effect immediately prior to the Tax Cuts and Jobs Act of 2017 being enacted.

As a result of the Tax Cuts and Jobs Act of 2017, we have remeasured our deferred tax assets based on the rates at which they are expected to reverse in the future, resulting in a reduction in the deferred tax asset balance of $1.6 million in 2017 which was offset by a reduction in the valuation allowance by a corresponding amount. The one-time transition tax is based on the total post-1986 earnings and profits, or E&P, previously deferred from U.S. income taxes. As we have a deficit in post-1986 E&P from CAPL, there was no increase in income tax expense as a result of the one-time transition tax. This impact is considered to be a provisional amount as we are still analyzing certain aspects of the Tax Cuts and Jobs Act of 2017 and refining our calculations. The ultimate impact may differ from this provisional amount, due to, among other things, additional analysis, changes in interpretations and assumptions we have made, additional regulatory guidance that may be issued, and actions we may take as a result of the Tax Cuts and Jobs Act of 2017.

Jumpstart Our Business Startups Act

We are an emerging growth company, as defined in the JOBS Act. Under the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards issued subsequent to the enactment of the JOBS Act until such time as those standards apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards and, therefore, will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies. We also intend to rely on other exemptions provided by the JOBS Act, including without limitation, not being required to comply with the auditor attestation requirements of Section 404(b) of Sarbanes-Oxley.

Recent accounting pronouncements

In May 2014, the Financial Accounting Standards Board, or FASB, issued Accounting Standards Update, or ASU. 2014-09, *Revenue from Contracts with Customers*, which converges the FASB and the International Accounting

Standards Board standard on revenue recognition. Areas of revenue recognition that will be affected include, but are not limited to, transfer of control, variable consideration, allocation of transfer pricing, licenses, time value of money, contract costs and disclosures. This guidance is effective for the fiscal years and interim reporting periods beginning after December 15, 2017. We adopted ASU 2014-09 on January 1, 2018. We do not currently have any contracts with customers and, as such, the adoption had no material impact on our financial position and results of operations.

In February 2016, the FASB issued ASU 2016-02, *Leases*, which outlines a comprehensive lease accounting model and supersedes the current lease guidance. The new accounting standard requires lessees to recognize lease liabilities and corresponding right-of-use assets for all leases with lease terms of greater than twelve months. It also changes the definition of a lease and expands the disclosure requirements of lease arrangements. The new accounting standard must be adopted using the modified retrospective approach and is effective for public entities for annual reporting periods beginning after December 15, 2018 with early adoption permitted. Although we are in the process of evaluating the impact of adoption of the ASU on our consolidated financial statements, we currently believe the most significant changes will be related to the recognition of lease liabilities on our consolidated balance sheets for real estate operating leases.

Recently Adopted Accounting Pronouncements

In November 2016, the FASB issued ASU No. 2016-18, *Restricted Cash*, which requires entities to show the changes in the total of cash, cash equivalents, restricted cash and restricted cash equivalents in the statement of cash flows. As a result, entities will no longer present transfers between cash and cash equivalents and restricted cash and restricted cash equivalents in the statement of cash flows. The adoption of this standard, in the first quarter of 2018, changed the presentation of our consolidated statement of cash flows to include its restricted cash balance with non-restricted cash balances. The new guidance did not have a material impact on our consolidated financial statements.

Off-balance sheet arrangements

During the periods presented we did not have, nor do we currently have, any off-balance sheet arrangements as defined under the rules of the SEC.

Quantitative and qualitative disclosures about market risk

Interest rate risk

Our cash and cash equivalents consist of cash and a money market account. We do not hold any short-term investments. As a result, the fair value of our portfolio is moderately insensitive to interest rate changes.

Foreign currency

In January 2017, we formed a wholly-owned subsidiary in Australia, which exposes us to foreign currency exchange rate risk. The functional currency of CAPL is the United States dollar. Assets and liabilities of our foreign subsidiary that are not denominated in the functional currency are remeasured into U.S. dollars at foreign currency exchange rates in effect at the balance sheet date except for nonmonetary assets and capital accounts, which are remeasured at historical foreign currency exchange rates in effect at the date of transaction. Expenses are generally remeasured at foreign currency exchange rates which approximate average rates in effect during each period. Net realized and unrealized gains and losses from foreign currency transactions and remeasurement are reported in other income (expense), net, in the consolidated statements of operations and totaled approximately $44,000 for the year ended December 31, 2017. As of March 31, 2018, the

impact of a theoretical 10% change in the exchange rate of the Australian dollar would not result in a material gain or loss. To date, we have not hedged exposures denominated in foreign currencies.

Effects of inflation

Inflation generally affects us by increasing our cost of labor and clinical trial costs. We do not believe that inflation has had a material effect on our results of operations during the periods presented.

Business

Overview

We are a clinical stage pharmaceutical company focused on the discovery, development and commercialization of novel therapeutics for rare endocrine diseases and endocrine-related tumors. Endocrine pathways function to maintain homeostasis and commonly use peptide hormones acting through G protein coupled receptors, or GPCRs, to regulate many aspects of physiology including growth, energy, metabolism, gastrointestinal function and stress responses. We have assembled a seasoned team with extensive expertise in drug discovery and development in endocrine GPCRs and built a highly productive drug discovery organization. We have discovered a pipeline of oral nonpeptide (small molecule) new chemical entities that target peptide GPCRs to treat a variety of rare endocrine diseases where treatment options have significant efficacy, safety and/or tolerability limitations. Our lead product candidate, CRN00808, is currently in clinical development for the treatment of acromegaly, and we are advancing additional product candidates through preclinical 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 three product candidates and discovery program:

- CRN00808, our lead product candidate, establishes a new class of oral selective nonpeptide somatostatin receptor type 2, or sst2, biased agonists designed for the treatment of acromegaly and is the first agent in its class with reported clinical results. 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. More than 25,000 people in the United States suffer from acromegaly, and an estimated 40% to 60% are candidates for chronic pharmacological intervention, of which somatostatin peptide analogs are the primary pharmacotherapy. In 2017, injected somatostatin peptide drugs accounted for approximately $2.7 billion in global sales for the treatment of acromegaly, neuroendocrine tumors, or NETs, and other uses. Currently marketed peptide 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.

  In March 2018, we reported initial results from a Phase 1, double-blind, randomized, placebo-controlled, single- and multiple-ascending dose trial to evaluate the safety, pharmacokinetics, or PK, and pharmacodynamics, or PD, of CRN00808 in 99 healthy volunteers. CRN00808 demonstrated clinical proof-of-concept by potently suppressing stimulated GH and baseline IGF-1 in these subjects. The plasma exposure of CRN00808 indicated the drug was well absorbed with a half-life of 42 to 50 hours, supporting once daily administration in patients. The safety and tolerability of CRN00808 observed in this trial was generally consistent with that of approved peptide somatostatin analogs. We plan to submit an investigational new drug application, or IND, to the FDA in the second half of 2018 and, if accepted, we plan to initiate two Phase 2 clinical trials of CRN00808 in acromegaly patients in early 2019, including those who are not adequately controlled with existing therapy.

- CRN02481 represents a new class of oral selective nonpeptide somatostatin type 5 receptor, or sst5, agonists designed to treat congenital hyperinsulinism, or CHI. This is a devastating rare disease in which infants are born with mutations that cause excess secretion of the pancreatic hormone insulin resulting in profound

hypoglycemia, a very low level of blood glucose. This loss of homeostatic control of blood glucose levels can lead to seizures, developmental disorders, learning disabilities, coma and even death. CHI occurs in approximately 1 in 30,000 to 50,000 new births in the United States. CRN02481 is currently in first-in-human enabling studies, and we expect to initiate a Phase 1 human proof-of-concept clinical trial in the first half of 2019. We expect results from this trial in 2019.

- CRN01941 is an oral nonpeptide sst2 biased agonist designed for the treatment of NETs that 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. Most NETs overexpress sst2 receptors and injected depots of peptide somatostatin analogs have become the first-line standard of care for many NETs patients as detailed in recent National Comprehensive Cancer Network guidelines. CRN01941 is currently in first-in-human enabling studies, and we expect to initiate a Phase 1 human proof-of-concept clinical trial in the first half of 2019. We expect results from this trial in late 2019/early 2020.
- We have an ongoing discovery effort to identify and advance into development the first nonpeptide product candidate to antagonize the peptide adrenocorticotrophic hormone, or ACTH, designed for the treatment of Cushing's disease. 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. Cushing's disease is an orphan indication with a prevalence of approximately 16,000 patients in the United States. Our goal is to select a product candidate for preclinical development in 2019.

Patients with many other debilitating endocrine diseases await new therapeutic options, and we are continuously evaluating where next to deploy our drug discovery efforts. All of our product candidates have been discovered, characterized and developed internally and are the subject of composition of matter patent applications, including an issued U.S. patent covering CRN00808 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 elagolix, a nonpeptide product candidate designed for the treatment of endometriosis and uterine fibroids that is currently awaiting a decision from the U.S. Food and Drug Administration, or FDA, on marketing approval. In addition, Dr. Madan held a key leadership role in the discovery and development of Ingrezza, which was approved by the FDA in 2017 for tardive dyskinesia. Our investors include 5AM Ventures, OrbiMed Advisors, Perceptive Advisors, RA Capital Management, Versant Ventures and Vivo Capital.

Our strategy

Our objective is to transform the treatment of rare endocrine diseases and endocrine-related tumors by creating a diversified portfolio of novel therapeutics that will advance the standard of care. To achieve this objective, we are pursuing the following strategy:

- ***Focus on rare endocrine diseases and endocrine-related tumors with significant unmet medical need.*** There are numerous rare endocrine diseases and endocrine-related tumors for which currently available pharmacological therapies (when they exist) have significant limitations in efficacy, safety and/or tolerability. Patients living with these diseases often experience significant morbidity, mortality and/or poor quality of life. We are focused on discovering, developing and commercializing orally available therapies for multiple rare indications across endocrinology to advance the standard of care for these patients.
- ***Rapidly advance multiple product candidates in parallel to clinical proof-of-concept and late stage development by targeting diseases that require relatively small trials and employ validated biomarkers as clinical endpoints.*** Phase 1 clinical trials for rare endocrine diseases and endocrine-related tumors can often measure predictive biomarkers in healthy volunteers and lower the technical risk by providing a predictive measure of efficacy early in clinical development. Clinical trials in these indications often enroll relatively small numbers of trial subjects and use validated biomarkers as registration endpoints, which we believe will allow us to efficiently develop multiple clinical programs in parallel. This advantage is exemplified by our lead product for acromegaly, CRN00808, which progressed from candidate identification to Phase 1 clinical proof-of-concept in healthy volunteers in just over one year. Similarly, our two preclinical programs in CHI and NETs follow this paradigm and should allow us to generate meaningful clinical data in Phase 1.
- ***Continue to expand our therapeutic pipeline for rare endocrine diseases by leveraging the capabilities of our experienced discovery team in the area of peptide hormone GPCRs.*** Our discovery team has significant expertise in understanding and creating product candidates to influence the dynamic behavior of GPCRs and has developed a number of proprietary methods, techniques and tools that we believe will enable us to efficiently and reliably evaluate newly synthesized molecules. We employ an iterative strategy where compounds are designed, synthesized and rapidly characterized for pharmacologic and pharmaceutical properties. This approach has led to our current pipeline, and we will continue to invest in creating additional product candidates acting at this important class of targets. Peptide hormone GPCRs regulate many aspects of physiology and are attractive drug targets for treating a broad range of diseases. There are more than 80 known peptide hormones acting at more than 120 known different receptors. With each of our drug discovery programs, our goal is to specifically tailor a product candidate with pharmacologic and pharmaceutical properties highly optimized for its interaction with its specific GPCR target that we anticipate will translate to downstream benefits in our chosen therapeutic applications.
- ***Retain commercialization rights to maximize the value of our product candidates.*** We plan to establish our own commercial organization in major markets and develop a network of third-party distributors in other selected markets. We believe this organization can be focused and modest in size due to the relatively small number of specialty endocrinologists who treat patients suffering from the diseases we target. Therefore, we do not expect that we will require larger pharmaceutical partners for commercialization of our product candidates, although we may consider partnering for certain territories or indications, or for other strategic purposes.
- ***Maintain an entrepreneurial, scientifically rigorous and inclusive corporate culture where employees are fully engaged and strive to bring improved therapeutic options to patients.*** The patients we seek to treat currently only have options with significant drawbacks and often limited efficacy, safety and/or tolerability. We are passionate about developing new pharmacological therapies to help these patients better control their

diseases and to reduce the impact of these diseases on their daily lives. We believe that building a successful and sustainable endocrine company requires not just specific expertise in multiple areas of biology, chemistry, drug discovery, development and commercialization, but a team-oriented culture that integrates and harnesses the creative energy, scientific insights and enthusiasm of the entire organization.

The endocrine system

Overview

The endocrine system regulates most of the body's physiological activities through the actions of hormones, which are chemical and biochemical messengers secreted from different organs that influence growth, gastrointestinal function, maturation and development, reproduction, stress, metabolism and nearly all aspects of homeostasis. Hormones are structurally variable and can be monoamines, steroids, amino acids, peptides or larger proteins. The endocrine system includes, among other glands and organs, the pituitary gland, hypothalamus, pancreas, adrenal gland, thyroid and parathyroid, ovaries and testes, as well as specialized enteroendocrine cells.

Hormonal secretion is complex and the body employs several mechanisms to exert positive and negative feedback control to maintain homeostasis. For example, the pituitary gland, which is located behind the eyes at the base of the brain, is sometimes referred to as "the master endocrine gland" because it regulates multiple endocrine systems. Positive and negative control of pituitary hormonal secretion is often dictated by the adjacent hypothalamus, which integrates feedback responses from other areas of the body, including the brain. In the case of GH, its synthesis and secretion is stimulated by growth hormone-releasing hormone, or GHRH, and inhibited by somatostatin, which are both hypothalamic peptides. Another example is the pancreas that secretes insulin and glucagon, which lower and raise blood glucose levels, respectively. Insulin and glucagon secretion are both inhibited by somatostatin, which is also locally produced in the pancreas.

Hormonal dysregulation can arise from endocrine organ defects, including injury, inflammation, genetic abnormalities or the growth of tumors derived from endocrine cells. These insults can result in the under-secretion or over-secretion of one or more hormones, disrupting homeostasis and causing disease. For example, several serious clinical disorders, including acromegaly and Cushing's disease, result from pituitary tumors secreting excess hormones. In the pancreas, genetic defects or cellular dysfunction can give rise to disorders of under-secretion or over-secretion of pancreatic hormones (e.g., hyperinsulinemia).

Peptide hormone GPCRs

Various GPCRs are expressed in every type of cell in the body and their function is to transmit signals from outside the cell across the membrane to signaling pathways within the cell, between cells and between organ systems. Because of these critical actions, the GPCR superfamily is the largest and single most important family of drug targets as highlighted by the large number of approved therapeutics targeting this class. However, most currently available GPCR-targeting drugs act at receptors for which the native ligands are small molecules, such as histamine, adrenaline and neurotransmitters.

Most peptide hormones bind selectively to specific receptors located on the surface of cells in the target tissue. Receptors for peptide hormones are often GPCRs, which play a central role in many biological processes and are linked to a wide range of disease areas. There are more than 80 known peptide hormones acting at more than 120 known different receptors. Historically, it was assumed that small molecules could not replicate or compete with the complex interactions between peptides and their cognate GPCRs. As such, most drugs developed for peptide GPCRs have been and continue to be peptides themselves, which present manufacturing and formulation difficulties and force patients to undergo frequent injections because peptides generally are not orally bioavailable. We believe our approach to developing novel small molecule product candidates that

uniquely engage peptide hormone GPCRs will enable us to generate orally bioavailable, and potentially more selective, effective and better tolerated therapeutics for patients.

The somatostatin receptor family of peptide GPCRs is an illustrative example of the complex and subtle control inherent in endocrine biology and peptide hormone physiology. The peptide hormone somatostatin, which was first isolated over 40 years ago, is produced by a variety of cell types and has pleiotropic effects throughout the body, many of which are related to the inhibition of secretion of other hormones or neurotransmitters, and selective activation of this activity has made somatostatin agonism a well-established, commercially-validated mechanism. These effects are mediated by five different somatostatin receptor proteins (sst1-sst5), which lower levels of cyclic adenosine monophosphate, or cAMP, a key intracellular signaling molecule regulated by GPCR activation. Each of these receptors is expressed in different subsets of tissues. For example, sst2 is the most widely expressed subtype in NETs and is the dominant receptor by which GH secretion is suppressed in the pituitary. The sst5 receptor is expressed by pancreatic islet cells where its activation potently inhibits insulin secretion.

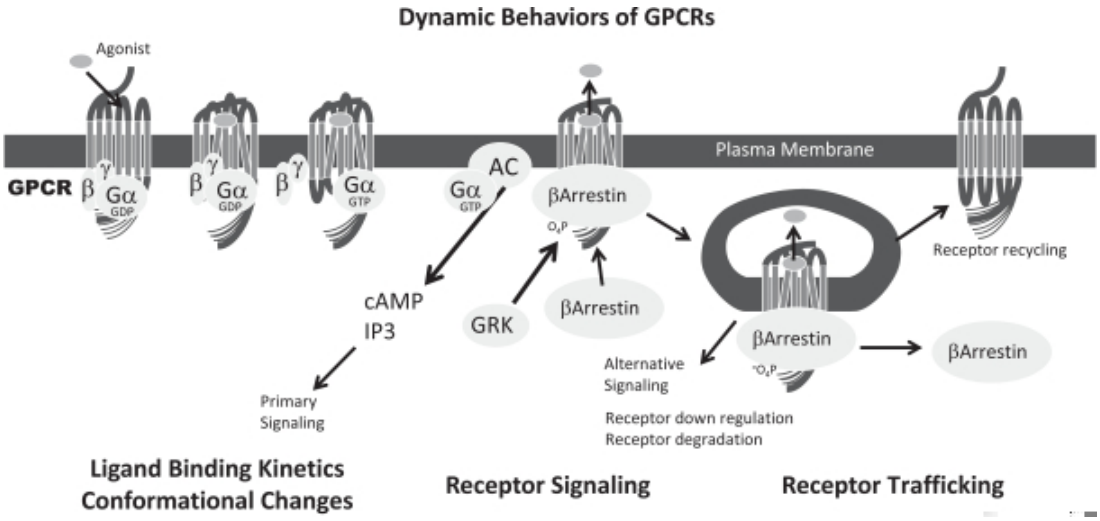


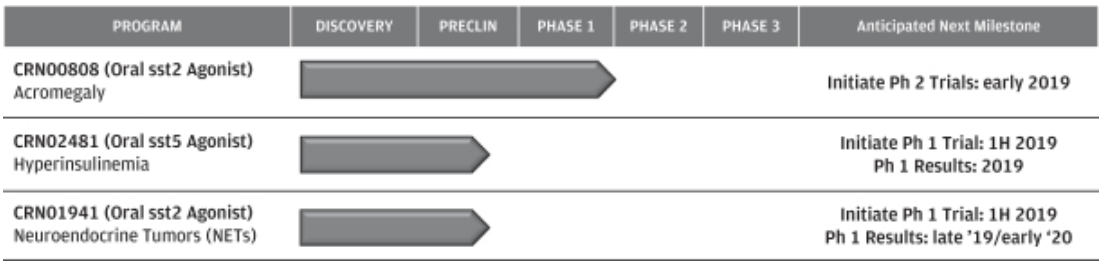
Figure 1. GPCR signaling is determined by many factors, including the binding characteristics of ligands, which dictate the responses of different signaling and regulatory pathways. Selectively favoring one pathway over others is termed biased signaling. Upon activation, GPCRs can also be trafficked into the cell, where they are either targeted for degradation or recycled back to the cell surface.

GPCRs were originally thought to function as simple on-off switches responding to hormones and neurotransmitters, but have since been shown to exhibit complex and diverse molecular and cellular behaviors. Many lines of structural and mechanistic research demonstrate that distinct signaling cascades and feedback mechanisms create multi-dimensional pathways with distinct physiological responses. These different responses are based on ligand binding kinetics, receptor regulation and trafficking (Figure 1). Some transduce signals into the cell interior to regulate various cellular functions. Other responses attenuate hormonal signals to prevent overstimulation and include receptor internalization (a removal of the GPCR from the cell surface, which makes it unavailable for external ligands), desensitization and downregulation. The capacity of a GPCR ligand to preferentially affect one of these pathways, such as G-protein signaling, over others, such as receptor downregulation, is termed biased agonism. We believe our understanding of these different signaling pathways enables us to develop oral, small molecule product candidates that not only are highly selective for specific

receptor subtypes but also are further custom-tailored to activate specific GPCR properties and ultimately improve patient outcomes.

Our product candidates

All of our product candidates have been discovered and developed internally and we have retained global rights to commercialize our product candidates and have no royalty or licensing obligations. The following table summarizes our product candidate pipeline and anticipated milestones.



CRN00808 for the treatment of acromegaly

Our lead product, CRN00808, is an oral selective nonpeptide sst2 biased agonist in clinical development for the treatment of acromegaly. CRN00808 is the first nonpeptide sst2 agonist with reported results from a clinical trial. Initial results from our Phase 1 trial of CRN00808 demonstrated clinical proof-of-concept based on observed suppression of GH and IGF-1 secretion in healthy volunteers. We plan to submit an IND to the FDA in the second half of 2018, which must go into effect before we can proceed with clinical studies. Pending FDA authorization to proceed, we plan to initiate two Phase 2 clinical trials of CRN00808 in acromegaly patients in early 2019.

Disease background

Acromegaly is typically caused by a pituitary tumor that secretes excess GH. Pituitary tumors are generally benign adenomas that, in addition to GH secretion, also express membrane receptors for somatostatin. Increased GH secretion results in excess downstream secretion of IGF-1 from the liver. GH and IGF-1 promote tissue growth and have other metabolic effects throughout the body.

The symptoms of acromegaly include abnormal growth of hands and feet and changes in shape of the bones that result in alteration of facial features. Overgrowth of bone and cartilage and thickening of tissue can lead to arthritis, carpal tunnel syndrome, joint aches, enlarged lips, nose and tongue, deepening of voice due to enlarged vocal cords, sleep apnea due to obstruction of airways and enlargement of the heart, liver and other organs. Additional symptoms can include thick, coarse, oily skin, skin tags, excessive sweating and skin odor, fatigue and weakness, headaches, goiter, decreased libido, menstrual abnormalities in women and erectile dysfunction in men. As the tumor grows, it can impinge on the nerves in the optic chiasm leading to visual problems and potentially vision loss. Compression of the surrounding normal pituitary tissues can decrease production of other pituitary hormones, resulting in hypopituitarism. Acromegaly patients experience increased mortality rates, principally due to cardiovascular diseases (diabetes, hypertension), respiratory disease and cerebrovascular diseases.

Acromegaly is often suspected when the patient exhibits enlargement of extremities and an alteration of facial features. Pituitary tumors are also often found during clinical workup for severe headaches, vision changes or incidentally on cranial imaging initiated for other reasons. Elevation of serum IGF-1 levels confirms the

suspicion of acromegaly, but a formal diagnosis requires lack of suppression of serum GH levels in response to an oral glucose tolerance test. A magnetic resonance imaging (MRI) or computerized tomography (CT) scan of the pituitary is then used to locate the tumor, determine its size and assess the potential for surgical intervention. There are an estimated 25,000 patients in the United States with acromegaly.

Current treatments and limitations

The major goals of treatment are to reduce serum GH and normalize IGF-1 levels, ameliorate symptoms and relieve any pressure resulting from the tumor. Surgical removal of the pituitary tumor is the first treatment option and often results in rapid improvement of symptoms. Surgery can be curative if the tumor is small and accessible enough to be fully resected. However, an estimated 40% to 60% of acromegaly patients turn to pharmacological treatments if they are not candidates for surgery or surgery was unsuccessful. Somatostatin analogs octreotide (marketed as Sandostatin) and lanreotide (marketed as Somatuline) are selective for sst2 receptors and are the preferred first-line pharmacologic treatments. However, these peptides leave many patients inadequately controlled. For example, a meta-analysis published in 2014 by the Journal of Clinical Endocrinology and Metabolism showed that approximately 50% of over 4,000 acromegaly patients treated with octreotide or lanreotide failed to achieve biochemical control. Pegvisomant (marketed as Somavert) is a daily injectable GH receptor antagonist and is generally used in patients resistant to or intolerant of somatostatin analogs. Pasireotide (marketed as Signifor) is a less-selective sst receptor agonist that is also used and has activity toward sst5, sst3 and sst2 receptors. However, pasireotide treatment leads to an increase in fasting plasma glucose levels in patients within the first two or three weeks of treatment and a pronounced shift to pre-diabetes and diabetes (as judged by HbA1c levels) within six months due to its insulin-suppressing sst5 activity. Orally administered dopamine agonists, such as bromocriptine and cabergoline, are also used, but do not achieve hormone normalization in most patients. For this reason, dopamine agonists are usually used as adjunct to somatostatin analogs. While these currently approved drugs reduce the disease burden, many patients still report acromegaly symptoms despite treatment, particularly at the end of the monthly dosing cycle.

Currently available therapies for acromegaly are peptide drugs that require injection, making them both painful and inconvenient. Octreotide and pasireotide are typically a monthly intramuscular injection, lanreotide a monthly deep subcutaneous injection and pegvisomant a daily subcutaneous injection. Patients report pain, swelling and bruising both at the time of injection and for days following injections. In addition, octreotide, lanreotide and pasireotide labels require injections by a trained healthcare provider and are therefore inconvenient for patients. Finally, the reconstitution of ocreotide and pasireotide can be complex and prone to error for healthcare providers.

We believe that a once-daily oral nonpeptide somatostatin agonist that reduces excess GH secretion and normalizes IGF-1 levels in acromegaly patients would represent a major clinical advance by eliminating painful injections and reducing the frequency of physician office visits. Additionally, we believe it should allow physicians to more quickly determine optimal dosing regimens compared to existing depot therapies.

CRN00808 overview and clinical development

CRN00808, our lead product candidate, pioneers a new class of oral selective nonpeptide sst2 biased agonists designed for the treatment of acromegaly and is the first agent in its class with reported clinical results. It is designed to reduce excess GH secretion from benign pituitary tumors and normalize IGF-1 levels in patients with acromegaly. In vitro pharmacology studies demonstrated that CRN00808 potently stimulated sst2 receptor activity as measured by a decrease in cAMP accumulation in cells expressing the human sst2 receptor (EC_{50}=0.25 nM, the concentration that achieves 50% cAMP inhibition). Analogous experiments using the other sst receptor subtypes showed CRN00808’s selectivity for sst2 was 4,000 times greater than the other sst receptor subtypes.

Internalization and desensitization of sst2 is thought to contribute to the inability of some patients to fully respond to octreotide. Therefore, in creating CRN00808, we focused our discovery efforts on identifying biased agonists that were selective for inhibition of cAMP accumulation while minimizing receptor internalization. In vitro studies have shown that CRN00808 was 75 times more potent for cAMP inhibition than receptor internalization. Figure 2 illustrates the difference in bias between octreotide and CRN00808. Concentrations of octreotide where cAMP is maximally suppressed also induced extensive internalization of sst2 receptors whereas in the same experiment, nearly all receptors remained on the cell surface at concentrations where CRN00808 maximally suppressed cAMP. We believe that this increased bias suggests a reduced likelihood of desensitization of the sst2 receptor by CRN00808 at pharmacologically relevant concentrations.

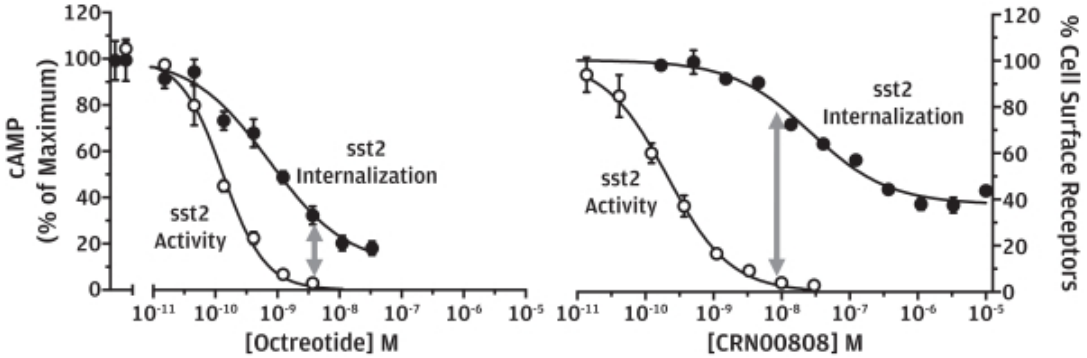


Figure 2. Dose response curves are shown from individual representative experiments. All points are the mean ± standard error of either triplicate or quadruplicate readings. White circles are from a cAMP assay measuring sst2 activation. Black circles are from an internalization assay measuring the amount of cell surface receptors. M = molar concentration.

In addition to somatostatin receptor-directed pharmacology, CRN00808 showed little off-target activity in a variety of assays for other GPCRs, enzymes, ion channels and transporters. Based on further in vivo studies in rats and dogs, CRN00808 suppressed GH and IGF-1 consistent with its mechanism of action. We conducted 28-day good laboratory practice, or GLP, toxicity studies in rats and dogs and identified no dose-limiting toxicities, which supported moving CRN00808 into human clinical trials.

We began a Phase 1, double-blind, placebo-controlled trial in late 2017 to assess the safety, tolerability, PK and PD of CRN00808 in 99 healthy human volunteers. This trial was performed at a single center in Melbourne, Australia, and the overall trial design is shown in Figure 3. Safety, tolerability and PK were monitored in all subjects. Subjects in the single ascending dose, or SAD, arm (up to 20 mg) were also evaluated for the ability of CRN00808 to suppress GH secretion. Because GH secretion is pulsatile during the day, subjects in the first five SAD cohorts were given an intravenous bolus of GHRH (50 µg) to ensure a reliable window of high GH secretion. These GH responses were evaluated on day -1 (the day prior to dosing) and again on day 1 (the day of dosing either CRN00808 or placebo). The ability of CRN00808 to suppress serum IGF-1 was evaluated in the multiple ascending dose, or MAD, cohorts. A summary of the trial cohorts and a preliminary analysis of the data from this trial is presented below.

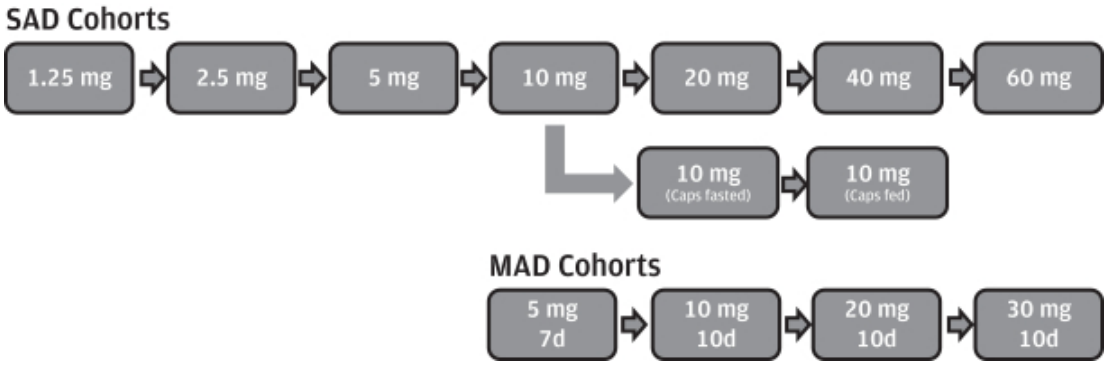


Figure 3. Design of CRN00808 Phase 1 trial. The SAD phase (N=8* per cohort (6 active, 2 placebo)) initially used an oral solution (1.25-20 mg) and switched to capsules for later cohorts (40-60 mg). The 10 mg SAD cohort also compared the plasma exposure of CRN00808 when it was administered as an oral solution, first generation capsules when fasted and as first generation capsules when taken with a high-fat breakfast. The MAD phase (N=9 per cohort (6 active, 3 placebo)) only used capsules (5-30 mg). There was an additional cohort (N=8) to assess the potential for drug-drug-interactions (midazolam +/- 20 mg CRN00808). *The 20 mg SAD Cohort only enrolled 7 subjects due to a subject's last-minute cancellation.

Figure 4 shows a summary of PK/PD data from the SAD arm of the trial. As illustrated for the 10 mg cohort in Figure 4a, administration of GHRH on day -1 resulted in a rapid surge of serum GH that lasted approximately 2 hours. In contrast to day -1, the presence of CRN00808 in plasma strongly suppressed (approximately 92%) stimulated GH secretion, consistent with the compound's activity as an sst2 agonist. This response was dose dependent as shown in Figure 4b. The first-generation capsule achieved approximately 75% of the total plasma exposure (area under the curve, or AUC) of the same dose administered as an oral solution to fasted subjects (Figure 4c). However, when the capsule was administered with a standardized high fat meal, plasma AUC was reduced by approximately 83%, suggesting that the current formulation should be taken under fasted conditions. In the drug-drug interaction cohort, repeated dosing of CRN00808 resulted in no change in the exposure of the sensitive CYP3A4 reporter midazolam, suggesting that CRN00808 is not likely to cause drug interactions by inhibiting the metabolism of other drugs that are primarily metabolized by the major CYP enzymes in the liver.

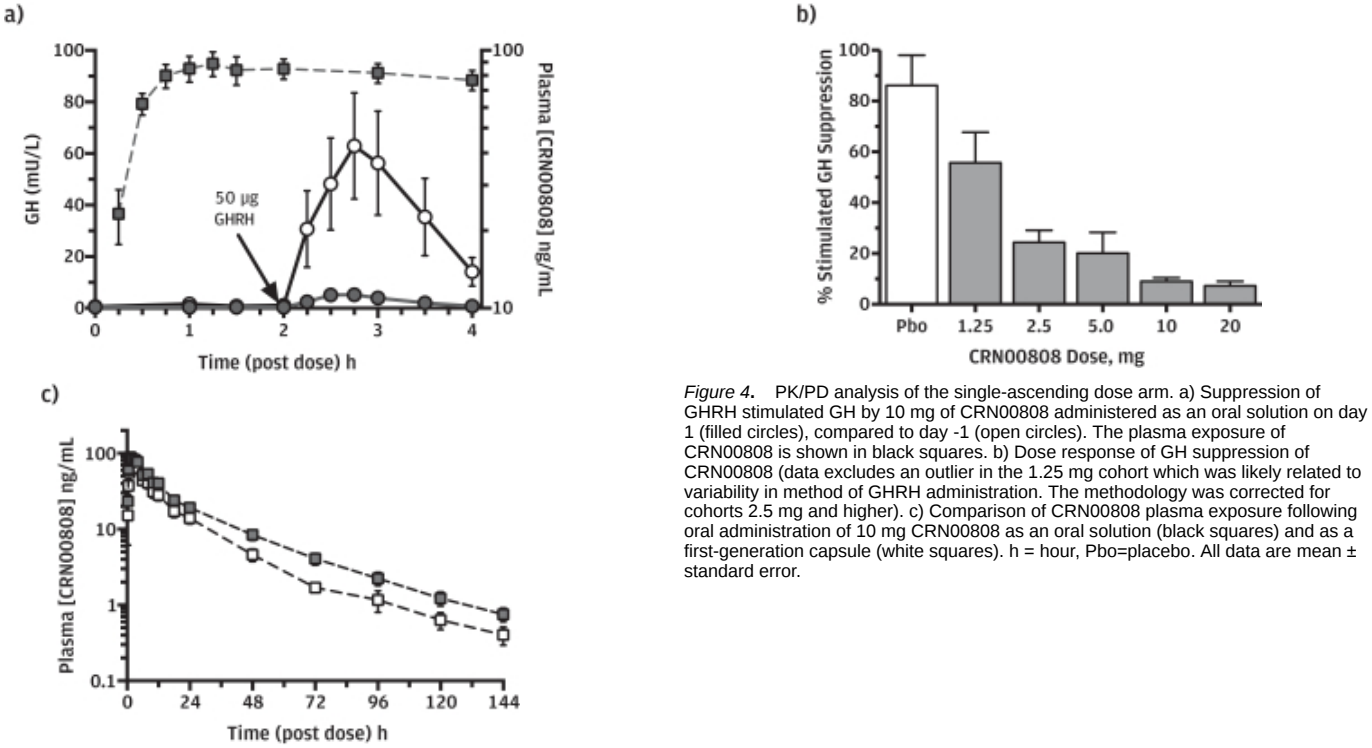


Figure 4. PK/PD analysis of the single-ascending dose arm. a) Suppression of GHRH stimulated GH by 10 mg of CRN00808 administered as an oral solution on day 1 (filled circles), compared to day -1 (open circles). The plasma exposure of CRN00808 is shown in black squares. b) Dose response of GH suppression of CRN00808 (data excludes an outlier in the 1.25 mg cohort which was likely related to variability in method of GHRH administration. The methodology was corrected for cohorts 2.5 mg and higher). c) Comparison of CRN00808 plasma exposure following oral administration of 10 mg CRN00808 as an oral solution (black squares) and as a first-generation capsule (white squares). h = hour, Pbo=placebo. All data are mean ± standard error.

In the MAD arm, subjects were dosed with CRN00808 for seven days (5 mg cohort) or ten days (10-30 mg cohorts) and serum IGF-1 levels were measured each day. In both acromegaly patients and healthy volunteers, sustained suppression of GH release results in lowering of serum IGF-1 levels. However, in contrast to the rapid effects of the GH response, IGF-1 levels are known to decrease more gradually and require several days of exposure to somatostatin agonists to produce an observable effect. Figure 5a illustrates the PK/PD relationship between trough plasma CRN00808 concentrations and IGF-1 levels. As CRN00808 concentrations reached steady state, serum IGF-1 concentrations began to decline. This decline reached steady state in approximately seven days. Of note, IGF-1 remained suppressed for several days after the final dose, but began to recover as CRN00808 plasma concentrations fell.

As shown in Figure 5b, CRN00808 exhibited dose-proportional increase in exposure and a half-life of 42 to 50 hours, consistent with potential for once daily administration. Suppression of IGF-1 levels for the 10 mg, 20 mg and 30 mg cohorts was similar (Figure 5c) indicating that the 10 mg dose achieved a maximal response. This degree of IGF-1 suppression by CRN00808 was similar to that observed for peptide somatostatin analogs (octreotide, lanreotide) in previously reported healthy volunteer studies. Concentrations of somatostatin analogs in healthy volunteers that result in this level of suppression in healthy volunteers are comparable to the trough concentrations in patients on the highest approved dose. This suggests that drug concentrations that result in maximal suppression of IGF-1 in healthy volunteers translates to meaningful suppression of IGF-1 in acromegaly patients.

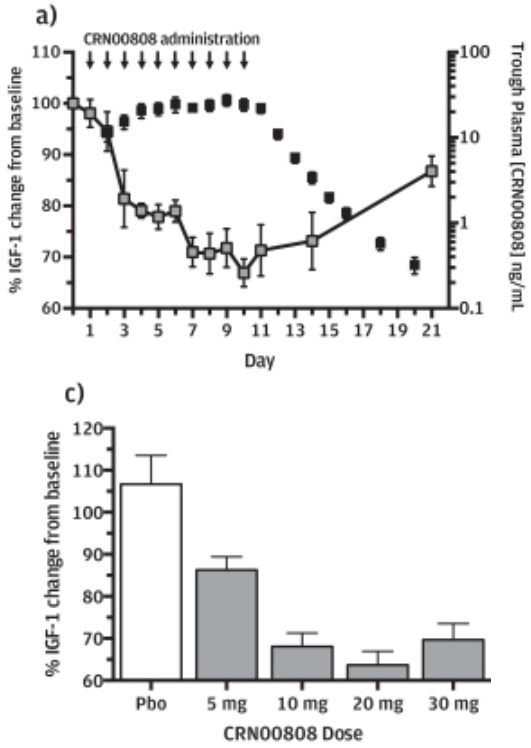


Figure 5. PK/PD analysis of the multiple-ascending dose arm. a) Time-course of plasma CRN00808 trough concentrations (black squares) and IGF-1 concentrations (grey squares) in the 10 mg MAD cohort. b) Plasma concentration of CRN00808 on last day of dosing. 30 mg (black circles), 20 mg (white circles), 10 mg (black squares), 5 mg (white squares). c) Dose response of IGF-1 suppression on last day of dosing for MAD cohorts compared to placebo (Pbo). All data are mean ± standard error.

The safety and tolerability of CRN00808 in the trial was generally consistent with that of approved peptide somatostatin analogs. In the trial, CRN00808 resulted in mild gastrointestinal disorders (such as abdominal pain, flatulence, abdominal distension, and diarrhea) in approximately 30% of subjects and mild elevations of pancreatic enzymes in approximately 10% of subjects. One subject experienced moderate abdominal pain after a single 40 mg dose. Additional adverse events included headache, dizziness and cardiac rhythm abnormalities (including nonsustained ventricular tachycardia, or NSVT) which were not dose dependent and also observed in placebo subjects and/or prior to dosing. One serious adverse event of moderate NSVT was observed following a single 1.25 mg dose and was considered unlikely to be related to CRN00808. Based on the conclusions from this Phase 1 clinical study, we selected 10 mg as the initial dose in our Phase 2 trials.

Based on the initial results of our Phase 1 clinical trial, we believe we have demonstrated proof-of-concept for the ability of CRN00808 to suppress the GH axis in humans. We plan to initiate two Phase 2 clinical trials in acromegaly patients in early 2019. We anticipate that the first of these will be a double-blind, randomized, placebo-controlled trial conducted in approximately 36 patients whose IGF-1 levels are currently controlled by octreotide or lanreotide. We plan to conduct a second, open-label exploratory trial to evaluate the effects of CRN00808 on approximately 45 patients whose IGF-1 levels are not adequately controlled by octreotide or lanreotide alone. In parallel, we are developing a second-generation capsule formulation that may mitigate the food effect observed with the first-generation capsule.

CRN02481 for the treatment of hyperinsulinemias

CRN02481 is an oral selective nonpeptide sst5 receptor agonist designed to inhibit the excess insulin secretion associated with congenital and acquired disorders of hyperinsulinism, with our initial focus on CHI. We are

currently conducting first-in-human enabling studies for CRN02481 and expect results from a planned Phase 1 human proof-of-concept clinical trial in 2019.

Disease background

Hyperinsulinemia is a heterogeneous condition in which dangerously low blood sugar levels are caused by increased insulin secretion from pancreatic ß-cells. The most severe form of hyperinsulinemia arises from CHI, a disorder whose underlying pathology is driven by genetic mutations in key genes involved in regulating insulin secretion from ß-cells. The incidence of CHI is approximately 1 in 30,000 to 50,000 new births in the United States. Hyperinsulinemia is one of the most frequent causes of persistent hypoglycemia in neonates and infants. Early diagnosis is vital to prevent neurological complications due to chronic low blood sugar, which can result in apneas, seizures, developmental delays, learning disabilities, epilepsy and even death.

Hyperinsulinemia can also be a severe complication for patients with insulin secreting tumors (insulinomas). Insulinomas are a specific type of NET derived from pancreatic ß-cells that secrete insulin and cause hypoglycemia. The incidence of insulinomas is 1 to 4 in 1,000,000 persons. In addition, hyperinsulinemic hyperglycemia following meals in patients who have undergone gastric bypass surgery (commonly referred to as Dumping Syndrome) occurs in approximately 10 to 15% of these patients. The number of gastric bypass surgeries continues to increase, from an estimated 158,000 surgeries in 2011 to 216,000 in 2016.

Current treatments and limitations

Maintaining glucose levels through feeding or glucose infusions is the first step in managing CHI. Diazoxide is the only approved therapy indicated for hyperinsulinemia. It acts at the ATP-sensitive potassium channels, or K_{ATP}, that are involved in insulin secretion and inhibits insulin secretion. However, mutations in these channels are present in approximately 55% to 60% of CHI patients, which limits the efficacy of the drug in this population. There are also serious side effects of diazoxide, which include hypertrichosis (abnormal and excessive hair growth over much of the body) and pulmonary hypertension, for which the FDA issued a warning regarding its use in infants and children. Octreotide (used off-label) is administered as subcutaneous injections up to six times/day in those who respond poorly to diazoxide. Octreotide is an sst2 agonist, which can suppress both insulin and glucagon secretion (Figure 6). As glucagon is a primary physiologic defense mechanism against hypoglycemia, targeting sst2 is not optimal for CHI patients, and octreotide therapy fails for approximately 70% to 75% of patients. Patients who fail pharmacological therapy often progress to partial or nearly complete pancreatectomy, which can result in type I diabetes that must be managed for the remainder of the patient's life. We believe an orally available sst5 agonist would provide an important new therapeutic option that inhibits insulin secretion while avoiding glucagon suppression, allowing these patients to maintain normal glucose levels and possibly avoid pancreatectomy, the surgical removal of all or a part of the pancreas.

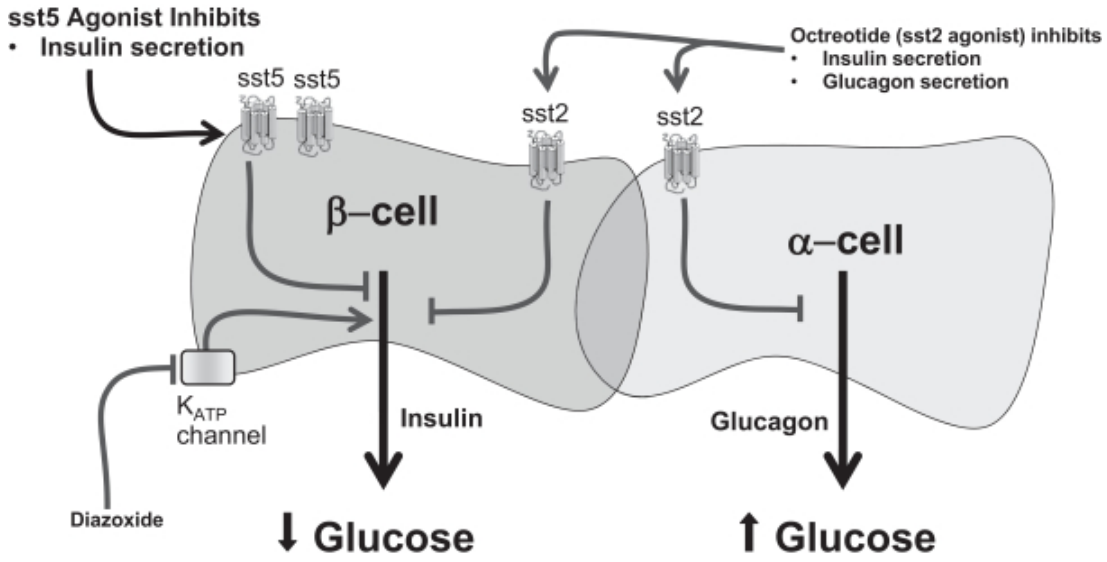


Figure 6. Hyperinsulinemia arising in CHI and the potential utility of sst5 agonists.

CRN02481 overview and preclinical development

CRN02481 is an optimized, orally available, nonpeptide sst5 agonist that is designed to reduce the excess secretion of insulin in patients with CHI, insulinomas and post-meal hypoglycemia that occurs in some patients who have undergone bariatric surgery.

In the process of discovering CRN00808, we synthesized many other drug-like nonpeptides, some of which also showed activity at other somatostatin receptor subtypes including sst5. Because activation of sst5 is known to strongly inhibit insulin secretion, we focused on optimizing selective sst5 agonists to identify potential product candidates, eventually selecting CRN02481. This molecule is a highly potent agonist of the sst5 receptor (EC_{50} = 0.4 nM) with selectivity against other somatostatin receptors (>15-10,000-fold).

CRN02481 was examined in a rat model of CHI (Figure 7). In this model, rats were treated with sulfonylurea glyburide, which promotes insulin release by acting at K_{ATP} channels. This activity mimics the K_{ATP} channel mutations found in about half of CHI patients. This high level of insulin produced a decrease of blood glucose in rats. When these rats were then treated with CRN02481, blood glucose levels returned to normal, and at higher doses, even to a hyperglycemic state. Repeat dose experiments demonstrated that insulin continued to be suppressed after seven days. Further, glucagon secretion was not suppressed in these experiments.

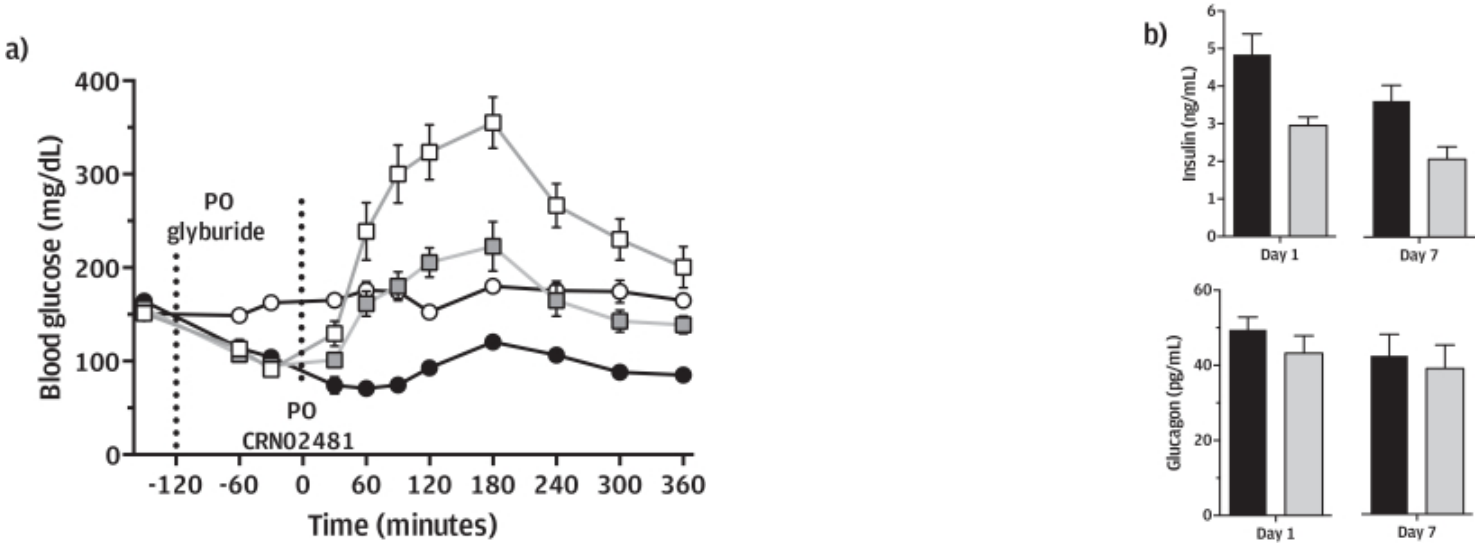


Figure 7. a) Rescue of glyburide-induced hypoglycemia by CRN02481 in rats. To mimic a high insulin state similar to CHI, rats were treated with the sulfonylurea glyburide (30 mg/kg, black circles) or vehicle (white circles). CRN02481 was administered orally two hours after glyburide administration at either 3 mg/Kg (grey squares) or 10 mg/Kg (white squares). b) Effects on insulin and glucagon secretion by CRN02481 in rats. Animals were orally administered 30 mg/Kg glyburide (black bars) or glyburide + 10 mg/Kg CRN02481 (grey bars) daily for 7 days. Insulin and glucagon were measured three hours after CRN02481 administration on the first and last day of dosing. All data are mean ± standard error.

In addition, the drug-like characteristics of CRN02481 met our rigorous internal criteria that we use to determine if a product candidate should enter into preclinical development. This includes extensive evaluation of pharmacology, selectivity, drug interaction potential, oral bioavailability and PK in multiple species, synthetic accessibility and preliminary non-GLP safety assessments including 14-day screening toxicology in rats and cardiovascular safety studies in dogs.

We are currently optimizing the good manufacturing process, or GMP, synthesis and performing GLP first-in-human enabling studies for CRN02481. We expect to initiate a Phase 1 human proof-of-concept clinical trial that evaluates inhibition of insulin secretion and its effects on blood glucose in the first half of 2019. We expect results from this trial in 2019.

CRN01941 for the treatment of neuroendocrine tumors (NETs)

CRN01941 is an oral, selective nonpeptide sst2 biased agonist designed for the treatment of NETs that originate from neuroendocrine cells commonly found in the gut, lung or pancreas. We are currently conducting first-in-human enabling studies for CRN01941 and expect results from a planned Phase 1 human proof-of-concept clinical trial in late 2019/early 2020.

Disease background

NETs arise from cells of the enteroendocrine system in the gastrointestinal tract (approximately 70% of cases), but can also arise from neuroendocrine cells in the lung (approximately 25% of cases) or, more rarely, the pancreas. These tumors are usually slow growing and often initially asymptomatic. Therefore, many patients are only diagnosed at a time of extensive metastatic disease, and these patients will often progress to liver

failure. In approximately 10% of cases, these tumors are associated with excess secretion of serotonin resulting in carcinoid syndrome, which is characterized by severe diarrhea and flushing. Patients with well- and moderately-differentiated tumors and distant metastases have a five-year survival probability of 35%, according to a study published in the Journal of Clinical Oncology. NETs are present in approximately 171,000 adults in the United States and while still an orphan disease, it is the second most common gastrointestinal malignancy after colon cancer.

Current treatments and limitations

Most NETs overexpress sst2 receptors and injected depots of peptide somatostatin analogs have become a standard of care for patients with carcinoid syndrome. While somatostatin analogs have been historically indicated primarily for patients with carcinoid syndrome, there is an evolving understanding of the positive impact of somatostatin analog treatment on the broader NETs patient population. For example, lanreotide was approved for the treatment of gastroenteropancreatic NETs based on a long-term study that showed significant improvement in progression free survival. However, many patients eventually become increasingly resistant to somatostatin analogs requiring increased dosage of depot preparations or use of short-acting analogs as an add-on therapy. In 2017, the serotonin synthesis inhibitor, telotristat, was approved as an add-on therapy to somatostatin analogs to help prevent breakthrough symptoms of carcinoid syndrome. Second-line targeted therapies Afinitor and Sutent are typically only used in patients with high grade tumors which constitute only a small fraction of NETs.

The overexpression of sst2 in NETs is also the basis for somatostatin targeted radioimaging of the tumors for diagnosis and staging. Peptide somatostatin analogs modified to incorporate a chelating agent can use their sst2 binding activity to concentrate radioisotopes in tumor tissue that can then be imaged using positron-emission tomography (PET). More recently, this approach has been adapted to deliver the alpha particle emitter ^{177}Lu for anti-tumor activity. A drug using this mechanism, Lutathera, significantly improved progression free survival and led to a substantial reduction in the risk of disease progression or death when added onto octreotide LAR therapy compared to a double dose of octreotide LAR, in a Phase 3 trial in NET patients who had failed on somatostatin analog therapy.

CRN01941 overview and preclinical development

CRN01941 is an optimized, selective, orally available, nonpeptide biased agonist of sst2 receptor designed for the treatment of patients with NETs. The chemical structure of CRN01941 is derived from a different chemical scaffold from that of CRN00808. In vitro pharmacology studies demonstrated that CRN01941 potently (EC_{50}=0.1 nM) stimulated sst2 receptor activity (as measured by a decrease in cAMP accumulation in cells expressing the human sst2 receptor) and is highly biased for G_i signaling versus receptor internalization (88-fold). Analogous experiments using the other sst receptor subtypes showed selectivity for sst2 was greater than 100-fold over the other sst receptor subtypes.

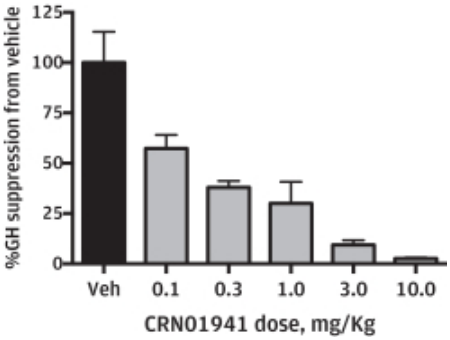


Figure 8. Suppression of GHRH-stimulated GH secretion in normal rats by CRN01941 administered as an oral solution (grey bars) compared to vehicle (black bar).

In a preclinical rodent model of efficacy, CRN01941 potently inhibited GHRH-induced GH production (Figure 8). This model is analogous to the PK-PD component in the Phase 1 clinical trial that we performed for CRN00808. In addition, the drug-like characteristics of CRN01941 met our rigorous internal criteria that we use to determine if a product candidate should enter into preclinical development. This includes extensive evaluation of pharmacology, selectivity, drug interaction potential, oral bioavailability and PK in multiple species, synthetic accessibility and preliminary non-GLP safety assessments including 14-day screening toxicology in rats and cardiovascular safety studies in dogs.

We are currently optimizing GMP synthesis and performing GLP first-in-human enabling studies on CRN01941 and expect to initiate a Phase 1 human proof-of-concept clinical trial in the first half of 2019. We expect results from this trial in late 2019/early 2020.

Product candidate for the treatment of Cushing's disease

We have identified selective, orally available nonpeptide ACTH antagonist leads intended for the treatment of Cushing's disease that are designed to prevent excessive stimulation of the adrenal glands by the high circulating levels of ACTH found in Cushing's disease patients. This program is currently in the lead optimization stage, and our goal is to select a product candidate for preclinical development in 2019.

Disease background

Cushing's syndrome was first described by Harvey Cushing over a century ago and results from a prolonged exposure to elevated levels of glucocorticoids, particularly cortisol. Common signs include growth of fat pads (collarbone, back of neck, face, trunk), excessive sweating, dilation of capillaries, thinning of the skin, muscle weakness, hirsutism, depression/anxiety, hypertension, osteoporosis, insulin resistance and hyperglycemia, heart disease and a range of other metabolic disturbances resulting in high morbidity. While excessive synthetic steroid administration or adrenal tumors can cause ACTH-independent forms of the disease, ACTH dependent Cushing's syndrome (known as Cushing's disease) is the most common form accounting for 60-80% of all cases and is most often due to tumors of pituitary corticotrophic cells that secrete excess ACTH.

Cushing's disease is an orphan indication with a prevalence of approximately 16,000 patients in the United States. It presents much more commonly in women, and usually between 30 and 50 years of age. Cushing's disease often takes many years to diagnose and may well be under-diagnosed in the general population as many of its symptoms such as lethargy, depression, obesity, hypertension, hirsuitism and menstrual irregularity can be incorrectly attributed to other more common disorders.

Current treatments and limitations

As with acromegaly, first-line therapy for Cushing's disease is surgery to remove the pituitary tumor if possible. Pharmacological therapy is required when surgery is delayed, contraindicated or unsuccessful. Adrenal enzyme inhibitors (e.g., metyrapone and ketoconazole) prevent the synthesis of cortisol and can improve symptoms, but suffer from mechanistic side effects as a result of accumulation of precursor steroids and the resulting lack of negative feedback. For example, metyrapone is associated with hirsuitism in women and patients must be monitored carefully to avoid hypoadrenalism. Ketoconazole often requires progressively increasing dosage to maintain disease control but this is ultimately limited by the hepatotoxicity of the drug. In addition, it is a potent inhibitor of one of the most important drug metabolizing enzymes in the liver, CYP3A4, resulting in the potential for negative drug-interactions as a side effect. Mifepristone, a potent glucocorticoid receptor antagonist, is approved for control of hyperglycemia in Cushing's syndrome, but is difficult to titrate and has significant liabilities due to its potent anti-progesterone activity. The recently approved somatostatin analog, pasireotide, inhibits ACTH secretion, but in a recently published study, only 15-26% of patients in a Phase 3 trial

achieved normalization of urinary free cortisol while 73% of patients experienced a hyperglycemia-related adverse event due to the compound's potent inhibition of insulin secretion. Therefore, we believe a significant unmet medical need exists for improved agents to treat Cushing's disease.

Product candidate discovery program

ACTH acts through a peptide GPCR called the melanocortin type 2 receptor, or MC2, that is specifically expressed in the adrenal gland. Activation of MC2 by ACTH results in increased synthesis of cAMP, enhanced synthesis and secretion of cortisol and hypertrophy of adrenal cells. Our discovery team has identified potent, selective nonpeptide antagonists of MC2 designed to block ACTH action and prevent its excessive stimulation of the adrenal gland in Cushing's disease patients. In vitro and in vivo pharmacology data from one of our initial antagonists are shown in Figure 9 below. Pharmacological mechanism is confirmed both by blocking of radiolabeled ACTH in a binding assay, as well as inhibiting the agonistic ability of ACTH to stimulate cAMP in cells expressing MC2. In vivo proof-of-concept is demonstrated by the antagonist's capacity to block corticosterone (CORT, the rat analog of cortisol) secretion in a rodent ACTH-challenge model, which mimics aspects of Cushing's disease. This program is currently in the lead optimization stage, and our goal is to select a product candidate for preclinical development in 2019.

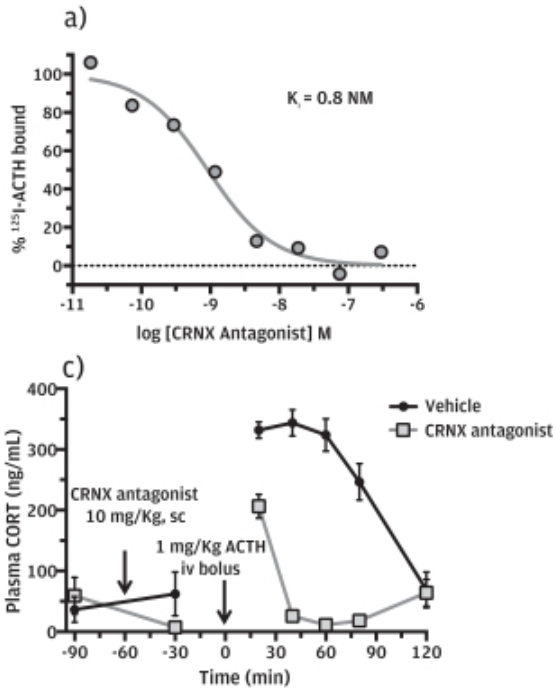


Figure 9. In vitro and in vivo characterization of an initial nonpeptide ACTH antagonist. a) Competition binding assay showing displacement of radiolabeled ACTH by CRNX antagonist. b) Functional assay showing that increasing concentrations of CRNX antagonist shifted the dose-response curve of ACTH stimulated cAMP accumulation in MC2 cells. c) Suppression of ACTH stimulated corticosterone release (CORT) in rats by 10 mg/Kg of CRNX antagonist administered subcutaneously (grey squares), compared to vehicle treated animals (black circles).

Competition

The commercialization of new drugs is competitive and we could face competition from a number of pharmaceutical or biotechnology companies around the world. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects or more convenient than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we do. The key competitive factors affecting the success of all of our programs are likely to be their efficacy, safety and convenience.

With respect to CRN00808, injected peptide somatostatin agonists and GH receptor antagonists are the main medical therapies for acromegaly patients where surgery is unsuccessful. There are three injected somatostatin analogs approved for the treatment of acromegaly: octreotide (marketed by Novartis AG), lanreotide (marketed by Ipsen Biopharmaceuticals, Inc.) and pasireotide (marketed by Novartis). Pegvisomant (marketed by Pfizer Inc.) is a daily injectable growth hormone receptor antagonist and is generally used in patients not fully controlled on somatostatin analogs. Orally administered dopamine agonists, such as bromocriptine and cabergoline, are also used. In terms of other products in clinical development, all of them are new formulations of peptide somatostatin agonists or GH receptor antagonists. Chiasma, Inc. is in Phase 3 development for an oral octreotide product candidate for the maintenance therapy of adult patients with acromegaly in whom prior treatment with somatostatin analogs has been shown to be effective and tolerated. Other companies developing peptide somatostatin agonists or GH receptor antagonists include Camurus AB, Dauntless Pharmaceuticals, Inc., Enesi Pharma Limited, Ionis Pharmaceuticals, Inc./Antisense Therapeutics Ltd., Ipsen, MidaTech Pharma PLC and Novartis.

With respect to CRN02481, maintaining glucose levels through feeding or glucose infusions is the first step in managing CHI. Diazoxide (marketed by Teva Pharmaceuticals, Inc.) is the only approved therapy indicated for hyperinsulinemia. Octreotide (used off-label) is administered as subcutaneous injections in those who respond poorly to diazoxide. Patients who fail pharmacological therapy often progress to partial or nearly complete pancreatectomy, which can result in type I diabetes that must be managed for the remainder of the patient's life. Companies in or entering Phase 3 are Eli Lilly and Company and Zealand Pharma A/S with glucagon analogs, and Xeris Pharmaceuticals, Inc. with glucagon Ready-To-Use (RTU). Other companies developing products for potential use in CHI include Eiger Biopharmaceuticals, Inc. and Rezolute, Inc.

With respect to CRN01941, injected depots of peptide somatostatin analogs are used as therapy for NETs. In adults whose carcinoid syndrome symptoms are inadequately controlled by somatostatin therapy, telotristat ethyl (marketed by Lexicon Pharmaceuticals, Inc.) is an orally administered add-on therapy. Targeted therapies everolimus (marketed by Novartis) and sunitinib malate (marketed by Pfizer) are typically only used in patients with high grade tumors which constitute only a small fraction of NETs. In 2018, the FDA approved Novartis' Lutathera for the treatment of somatostatin receptor positive gastroenteropancreatic neuroendocrine tumors. Companies in Phase 3 development include Progenics Pharmaceuticals, Inc. and EUSA Pharma Inc. Other companies developing products for potential use in NETs include Apeiron Scientific, LLC, Camurus, Celgene Corporation, EpicentRx, Inc., Ipsen, Mateon Therapeutics, Inc., Merck & Co., Inc., MidaTech, Novartis, Oncoceutics, Inc. and Roche Holding AG.

As with acromegaly, first-line therapy for Cushing's disease is surgery to remove the pituitary tumor if possible. Adrenal enzyme inhibitors (metyrapone, ketoconazole) prevent the synthesis of cortisol and can improve symptoms. Mifepristone (marketed by Corcept Therapeutics, Inc.), a glucocorticoid receptor antagonist, is approved for control of hyperglycemia in Cushing's syndrome. The somatostatin agonist pasireotide is also approved for Cushing's disease. Novartis and Strongbridge Biopharma are each conducting Phase 3 clinical trials with osilodrostat and levoketoconazole, respectively. Other companies developing products for potential use in Cushing's disease include Corcept, Cyclacel Pharmaceuticals, Inc. and Millendo Therapeutics, Inc.

There may be other earlier stage clinical programs that, if approved, would compete with our products. Many of our competitors have substantially greater financial, technical and human resources than we have. Additional mergers and acquisitions in the pharmaceutical industry may result in even more resources being concentrated in our competitors. Competition may increase further as a result of advances made in the commercial applicability of technologies and greater availability of capital for investment in these fields. Our success will be based in part on our ability to build and actively manage a portfolio of drugs that addresses unmet medical needs and creates value in patient therapy.

Intellectual property

We strive to protect and enhance the proprietary technology, inventions and improvements that are commercially important to our business, including seeking, maintaining and defending our patent rights. We own the issued patents and patent applications relating to our lead product candidate CRN00808, as well as our other product candidates, including CRN02481 and CRN01941. Our policy is to seek to protect our proprietary position by, among other methods, filing patent applications in the United States and in jurisdictions outside of the United States directed to our proprietary technology, inventions, improvements and product candidates that are important to the development and implementation of our business. We also rely on trade secrets and know-how relating to our proprietary technology and product candidates and continuing innovation to develop, strengthen and maintain our proprietary position in the field of endocrinology. We also plan to rely on data exclusivity, market exclusivity and patent term extensions when available. Our commercial success will depend in part on our ability to obtain and maintain patent and other proprietary protection for our technology, inventions and improvements; to preserve the confidentiality of our trade secrets; to defend and enforce our proprietary rights, including any patents that we may own in the future; and to operate without infringing on the valid and enforceable patents and other proprietary rights of third parties.

As of June 8, 2018, we own three U.S. patents, one pending U.S. patent application, five pending U.S. provisional patent applications and seven pending foreign patent applications, two of which are international patent applications filed under the Paris Cooperation Treaty (PCT) and two of which are European regional patent applications. More specifically, we own one U.S. patent with claims directed to our lead product candidate CRN00808 and other related compounds, as a composition of matter, as well as claims directed to pharmaceutical compositions and uses of such compounds, including the use of CRN00808, to treat acromegaly, neuroendocrine tumors, and/or pain. This U.S. patent is expected to expire in July 2037, absent any patent term extensions for regulatory delay. The other patents and patent applications are directed to various compounds as compositions of matter, pharmaceutical compositions comprising such compounds, and related methods of using such compounds. These issued patents, and any patents that may issue from our pending patent applications are expected to expire between 2036 and 2039, absent any patent term adjustments or extensions. We also possess substantial know-how and trade secrets relating to the development and commercialization of our product candidates, including related manufacturing processes and technology. We also own three trademark registration applications.

With respect to our product candidates and processes we intend to develop and commercialize in the normal course of business, we intend to pursue patent protection covering, when possible, compositions, methods of use, dosing and formulations. We may also pursue patent protection with respect to manufacturing and drug development processes and technologies.

Issued patents can provide protection for varying periods of time, depending upon the date of filing of the patent application, the date of patent issuance and the legal term of patents in the countries in which they are obtained. In general, patents issued for applications filed in the United States can provide exclusionary rights for 20 years from the earliest effective filing date. In addition, in certain instances, the term of an issued U.S. patent that covers or claims an FDA approved product can be extended to recapture a portion of the term effectively lost as a result of the FDA regulatory review period, which is called patent term extension. The restoration period cannot be longer than five years and the total patent term, including the restoration period, must not exceed 14 years following FDA approval. The term of patents outside of the United States varies in accordance with the laws of the foreign jurisdiction, but typically is also 20 years from the earliest effective filing date. However, the actual protection afforded by a patent varies on a product-by-product basis, from country-to-country, and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country and the validity and enforceability of the patent.

The patent positions of companies like ours are generally uncertain and involve complex legal and factual questions. No consistent policy regarding the scope of claims allowable in patents in the field of endocrinology has emerged in the United States. The relevant patent laws and their interpretation outside of the United States is also uncertain. Changes in either the patent laws or their interpretation in the United States and other countries may diminish our ability to protect our technology or product candidates and could affect the value of such intellectual property. In particular, our ability to stop third parties from making, using, selling, offering to sell or importing products that infringe our intellectual property will depend in part on our success in obtaining and enforcing patent claims that cover our technology, inventions and improvements. We cannot guarantee that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications we may file in the future, nor can we be sure that any patents that may be granted to us in the future will be commercially useful in protecting our products, the methods of use or manufacture of those products. Moreover, even our issued patents do not guarantee us the right to practice our technology in relation to the commercialization of our products. Patent and other intellectual property rights in the pharmaceutical and biotechnology space are evolving and involve many risks and uncertainties. For example, third parties may have blocking patents that could be used to prevent us from commercializing our product candidates and practicing our proprietary technology, and our issued patents may be challenged, invalidated or circumvented, which could limit our ability to stop competitors from marketing related products or could limit the term of patent protection that otherwise may exist for our product candidates. In addition, the scope of the rights granted under any issued patents may not provide us with protection or competitive advantages against competitors with similar technology. Furthermore, our competitors may independently develop similar technologies that are outside the scope of the rights granted under any issued patents. For these reasons, we may face competition with respect to our product candidates. Moreover, because of the extensive time required for development, testing and regulatory review of a potential product, it is possible that, before any particular product candidate can be commercialized, any patent protection for such product may expire or remain in force for only a short period following commercialization, thereby reducing the commercial advantage the patent provides.

In addition, most of our intellectual property rights, including those for our lead programs, have been generated through the use of U.S. government funding provided from our Small Business Innovation Research Grants, or SBIR Grants, awarded to us by the National Institute of Diabetes and Digestive and Kidney Diseases of the National Institutes of Health, and are therefore subject to certain federal regulations. As a result, the U.S. government may have certain rights to intellectual property embodied in our current or future product candidates pursuant to the Bayh-Dole Act of 1980. These U.S. government rights include a non-exclusive, non-transferable, irrevocable worldwide license to use inventions for any governmental purpose. In addition, the U.S. government has the right, under certain limited circumstances, to require us to grant exclusive, partially exclusive, or non-exclusive licenses to any of these inventions to a third party in certain circumstances. The U.S. government also has the right to take title to these inventions if we fail to disclose the invention to the government or fail to file an application to register the intellectual property within specified time limits.

Manufacturing

Manufacturing, testing and storage of our product candidates for nonclinical and clinical studies is conducted at third-party contract manufacturers and distributors. We do not plan to build plants or facilities for development or commercial scale manufacture or storage of our product candidates. To date, the contract manufacturers have met our manufacturing requirements, and we expect them to be capable of providing sufficient quantities of our product candidates to meet estimated full-scale commercial needs. However, the contract manufacturers may be required to increase production scale, or we may need to secure alternate suppliers.

Sales and marketing

We intend to build the commercial infrastructure in major markets to effectively support the commercialization of all of our product candidates, if and when we believe a regulatory approval of the first of such product candidates in a particular geographic market appears imminent. The commercial infrastructure for orphan products typically consists of a targeted, specialty sales force that calls on a focused group of physicians supported by sales management, medical liaisons, internal sales support, an internal marketing group and distribution support. One challenge unique to commercializing therapies for rare diseases is the difficulty in identifying eligible patients due to the very small and sometimes heterogeneous disease populations.

Additional capabilities important to the orphan marketplace include the management of key accounts, such as managed care organizations, group purchasing organizations, specialty pharmacies and government accounts. To develop the appropriate commercial infrastructure, we will have to invest significant amounts of financial and management resources, some of which will be committed prior to any confirmation that any of our product candidates will be approved.

Where appropriate, we may elect in the future to utilize strategic partners, distributors or contract sales forces to assist in the commercialization of our product candidates. In certain instances, we may consider building our own commercial infrastructure.

Government regulation

Government authorities in the United States, at the federal, state and local level, and other countries extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, marketing and export and import of products such as those we are developing. A new drug must be approved by the FDA through the new drug application, or NDA, process before it may be legally marketed in the United States.

U.S. drug development process

In the United States, the FDA regulates drugs under the federal Food, Drug, and Cosmetic Act, or the FDCA, and its implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval may subject an applicant to administrative or judicial sanctions. These sanctions could include the FDA's refusal to approve pending applications, withdrawal of an approval, a clinical hold, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us.

The process required by the FDA before a drug may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in accordance with GLP regulations and other applicable regulations;
- submission to the FDA of an IND, which must become effective before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, at each clinical site before each trial may be initiated;

- performance of adequate and well-controlled human clinical trials in accordance with good clinical practice, or GCP, regulations to establish the safety and efficacy of the proposed drug for its intended use;
- submission to the FDA of an NDA;
- satisfactory completion of an FDA advisory committee review, if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the drug is produced to assess compliance with current GMP, or cGMP, requirements to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity; and
- FDA review and approval of the NDA.

Once a pharmaceutical candidate is identified for development, it enters the preclinical testing stage. Preclinical tests include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information and analytical data, to the FDA as part of the IND. The sponsor will also include a protocol detailing, among other things, the objectives of the first phase of the clinical trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated, if the first phase lends itself to an efficacy evaluation. Some preclinical testing may continue even after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, places the clinical trial on a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. Clinical holds also may be imposed by the FDA at any time before or during clinical trials due to safety concerns about on-going or proposed clinical trials or non-compliance with specific FDA requirements, and the trials may not begin or continue until the FDA notifies the sponsor that the hold has been lifted.

All clinical trials must be conducted under the supervision of one or more qualified investigators in accordance with GCP regulations, which include the requirement that all research subjects provide their informed consent in writing for their participation in any clinical trial. They must be conducted under protocols detailing the objectives of the trial, dosing procedures, subject selection and exclusion criteria and the safety and effectiveness criteria to be evaluated. Each protocol must be submitted to the FDA as part of the IND, and timely safety reports must be submitted to the FDA and the investigators for serious and unexpected adverse events. An IRB at each institution participating in the clinical trial must review and approve each protocol before a clinical trial commences at that institution and must also approve the information regarding the trial and the consent form that must be provided to each trial subject or his or her legal representative, monitor the study until completed and otherwise comply with IRB regulations.

Human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

- *Phase 1:* The product candidate is initially introduced into healthy human subjects and tested for safety, dosage tolerance, absorption, metabolism, distribution and excretion and, if possible, to gain an early indication of its effectiveness. In the case of some products for severe or life-threatening diseases, such as cancer, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients. Sponsors sometimes designate their Phase 1 clinical trials as Phase 1a or Phase 1b. Phase 1b clinical trials are typically aimed at confirming dosing, pharmacokinetics and safety in larger number of patients. Some Phase 1b studies evaluate biomarkers or surrogate markers that may be associated with efficacy in patients with specific types of diseases.
- *Phase 2:* This phase involves clinical trials in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and appropriate dosage.

- *Phase 3:* Clinical trials are undertaken to further evaluate dosage, clinical efficacy and safety in an expanded patient population, generally at geographically dispersed clinical study sites. These clinical trials are intended to establish the overall risk-benefit ratio of the product candidate and provide, if appropriate, an adequate basis for product labeling.

Post-approval trials, sometimes referred to as Phase 4 studies, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition of approval of an NDA.

The FDA or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. In addition, some clinical trials are overseen by an independent group of qualified experts organized by the sponsor, known as a data safety monitoring board or committee. Depending on its charter, this group may determine whether a trial may move forward at designated check points based on access to certain data from the trial.

During the development of a new drug, sponsors are given opportunities to meet with the FDA at certain points. These points may be prior to submission of an IND, at the end of Phase 2, and before an NDA is submitted. Meetings at other times may be requested. These meetings can provide an opportunity for the sponsor to share information about the data gathered to date, for the FDA to provide advice, and for the sponsor and the FDA to reach agreement on the next phase of development. Sponsors typically use the meetings at the end of the Phase 2 trial to discuss Phase 2 clinical results and present plans for the pivotal Phase 3 clinical trials that they believe will support approval of the new drug.

Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug and finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, the manufacturer must develop methods for testing the identity, strength, quality and purity of the final drug. In addition, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

While the IND is active and before approval, progress reports summarizing the results of the clinical trials and nonclinical studies performed since the last progress report must be submitted at least annually to the FDA, and written IND safety reports must be submitted to the FDA and investigators for serious and unexpected suspected adverse events, findings from other studies suggesting a significant risk to humans exposed to the same or similar drugs, findings from animal or *in vitro* testing suggesting a significant risk to humans, and any clinically important increased incidence of a serious suspected adverse reaction compared to that listed in the protocol or investigator brochure.

There are also requirements governing the reporting of ongoing clinical trials and completed trial results to public registries. Sponsors of certain clinical trials of FDA-regulated products are required to register and disclose specified clinical trial information, which is publicly available at www.clinicaltrials.gov. Information related to the product, patient population, phase of investigation, trial sites and investigators and other aspects of the clinical trial is then made public as part of the registration. Sponsors are also obligated to discuss the results of their clinical trials after completion. Disclosure of the results of these trials can be delayed until the new product or new indication being studied has been approved.

U.S. review and approval process

The results of product development, preclinical and other non-clinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on the chemistry of the drug, proposed labeling and other relevant information are submitted to the FDA as part of an NDA requesting approval to market the product. The submission of an NDA is subject to the payment of substantial user fees; a waiver of such fees may be obtained under certain limited circumstances. The FDA reviews an NDA to determine, among other things, whether a product is safe and effective for its intended use and whether its manufacturing is cGMP-compliant to assure and preserve the product's identity, strength, quality and purity. Under the Prescription Drug User Fee Act, or PDUFA, guidelines that are currently in effect, the FDA has a goal of ten months from the date of "filing" of a standard NDA for a new molecular entity to review and act on the submission. This review typically takes twelve months from the date the NDA is submitted to FDA because the FDA has approximately two months to make a "filing" decision after it the application is submitted. The FDA conducts a preliminary review of all NDAs within the first 60 days after submission, before accepting them for filing, to determine whether they are sufficiently complete to permit substantive review The FDA may request additional information rather than accept an NDA for filing. In this event, the NDA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing.

The FDA may refer an application for a novel drug to an advisory committee. An advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. Before approving an NDA, the FDA will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA may inspect one or more clinical trial sites to assure compliance with GCP requirements.

After the FDA evaluates an NDA, it will issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the drug with prescribing information for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete and the application will not be approved in its present form. A Complete Response Letter usually describes the specific deficiencies in the NDA identified by the FDA and may require additional clinical data, such as an additional pivotal Phase 3 trial or other significant and time-consuming requirements related to clinical trials, nonclinical studies or manufacturing. If a Complete Response Letter is issued, the sponsor must resubmit the NDA or, addressing all of the deficiencies identified in the letter, or withdraw the application. Even if such data and information are submitted, the FDA may decide that the NDA does not satisfy the criteria for approval.

If a product receives regulatory approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. In addition, the FDA may require a sponsor to conduct Phase 4 testing, which involves clinical trials designed to further assess a drug's safety and effectiveness after NDA approval, and may require testing and surveillance programs to monitor the safety of approved products which have been commercialized. The FDA may also place other conditions on approval including the requirement for a risk evaluation and mitigation strategy, or REMS, to assure the safe use of the drug. If the FDA concludes a REMS is needed, the sponsor of the NDA must submit a proposed REMS. The FDA will not approve the NDA without an approved REMS, if required. A REMS could include medication guides, physician communication plans or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. Any of these limitations on approval or marketing could restrict the commercial promotion, distribution, prescription or dispensing of

products. Marketing approval may be withdrawn for non-compliance with regulatory requirements or if problems occur following initial marketing.

The Pediatric Research Equity Act, or PREA, requires a sponsor to conduct pediatric clinical trials for most drugs, for a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration. Under PREA, original NDAs and supplements must contain a pediatric assessment unless the sponsor has received a deferral or waiver. The required assessment must evaluate the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The sponsor or FDA may request a deferral of pediatric clinical trials for some or all of the pediatric subpopulations. A deferral may be granted for several reasons, including a finding that the drug is ready for approval for use in adults before pediatric clinical trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric clinical trials begin. The FDA must send a non-compliance letter to any sponsor that fails to submit the required assessment, keep a deferral current or fails to submit a request for approval of a pediatric formulation.

Orphan drug designation

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug intended to treat a rare disease or condition, which is a disease or condition that affects fewer than 200,000 individuals in the United States or, if it affects more than 200,000 individuals in the United States, there is no reasonable expectation that the cost of developing and making a drug product available in the United States for this type of disease or condition will be recovered from sales of the product. Orphan designation must be requested before submitting an NDA. After the FDA grants orphan designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same drug for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity or inability to manufacture the product in sufficient quantities. The designation of such drug also entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. However, competitors, may receive approval of different products for the indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan product has exclusivity. Orphan exclusivity also could block the approval of one of our product candidates for seven years if a competitor obtains approval of the same drug as defined by the FDA or if our product candidate is determined to be contained within the competitor’s product for the same indication or disease. In addition, if an orphan designated product receives marketing approval for an indication broader than what is designated, it may not be entitled to orphan exclusivity.

Expedited development and review programs

The FDA has a fast track designation program that is intended to expedite or facilitate the process for reviewing new drug products that meet certain criteria. Specifically, new drugs are eligible for Fast Track designation if they are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. Unique to a fast track product, the FDA may consider for review sections of the NDA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA.

Any product submitted to the FDA for approval, including a product with a fast track designation, may also be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval. A product is eligible for priority review if it has the potential to provide safe and effective therapy where no satisfactory alternative therapy exists or a significant improvement in the treatment, diagnosis or prevention of a disease compared to marketed products. The FDA will attempt to direct additional resources to the evaluation of an application for a new drug designated for priority review in an effort to facilitate the review. The FDA endeavors to review applications with priority review designations within six months of the filing date as compared to ten months for review of new molecular entity NDAs under its current PDUFA review goals.

In addition, a product may be eligible for accelerated approval. Drug products intended to treat serious or life-threatening diseases or conditions may be eligible for accelerated approval upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require that a sponsor of a drug receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product. Fast track designation, priority review and accelerated approval do not change the standards for approval but may expedite the development or approval process.

FDASIA established a category of drugs referred to as “breakthrough therapies” that may be eligible to receive breakthrough therapy designation. A sponsor may seek FDA designation of a product candidate as a “breakthrough therapy” if the product is intended, alone or in combination with one or more other products, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The designation includes all of the fast track program features, as well as more intensive FDA interaction and guidance. The breakthrough therapy designation is a distinct status from both accelerated approval and priority review, which can also be granted to the same drug if relevant criteria are met. If a product is designated as breakthrough therapy, the FDA will work to expedite the development and review of such drug.

Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. We may explore some of these opportunities for our product candidates as appropriate.

Post-approval requirements

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product may result in restrictions on the product or even complete withdrawal of the product from the market. After approval, some types of changes to the approved product, such as adding new indications, certain manufacturing changes and additional labeling claims, are subject to further FDA review and approval. Drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP regulations and other laws and regulations. In addition, the FDA may impose a number of post-approval requirements as a condition of approval of an NDA. For example, the FDA may require post-marketing testing, including Phase 4 clinical trials, and surveillance to further assess and monitor the product’s safety and effectiveness after commercialization.

Any drug products manufactured or distributed by us or our partners pursuant to FDA approvals will be subject to continuing regulation by the FDA, including, among other things, record-keeping requirements, reporting of adverse experiences with the drug, providing the FDA with updated safety and efficacy information, drug sampling and distribution requirements, complying with certain electronic records and signature requirements, and complying with FDA promotion and advertising requirements. The FDA strictly regulates labeling, advertising, promotion and other types of information on products that are placed on the market and imposes requirements and restrictions on drug manufacturers, such as those related to direct-to-consumer advertising, the prohibition on promoting products for uses or in patient populations that are not described in the product's approved labeling (known as "off-label use"), industry-sponsored scientific and educational activities, and promotional activities involving the internet. Discovery of previously unknown problems or the failure to comply with the applicable regulatory requirements may result in restrictions on the marketing of a product or withdrawal of the product from the market as well as possible civil or criminal sanctions. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant or manufacturer to administrative or judicial civil or criminal sanctions and adverse publicity. FDA sanctions could include refusal to approve pending applications, withdrawal of an approval, clinical holds on post-approval clinical trials, warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, mandated corrective advertising or communications with doctors, debarment, restitution, disgorgement of profits, or civil or criminal penalties.

Marketing exclusivity

Market exclusivity provisions under the FDCA can delay the submission or the approval of certain marketing applications. The FDCA provides a five-year period of non-patent marketing exclusivity within the United States to the first applicant to obtain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not approve or even accept for review an abbreviated new drug application, or ANDA, or an NDA submitted under Section 505(b)(2), or 505(b)(2) NDA, submitted by another company for another drug based on the same active moiety, regardless of whether the drug is intended for the same indication as the original innovative drug or for another indication, where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement to one of the patents listed with the FDA by the innovator NDA holder.

The FDCA alternatively provides three years of marketing exclusivity for an NDA, or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the modification for which the drug received approval on the basis of the new clinical investigations and does not prohibit the FDA from approving ANDAs or 505(b)(2) NDAs for drugs containing the active agent for the original indication or condition of use. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Pediatric exclusivity is another type of marketing exclusivity available in the United States. Pediatric exclusivity provides for an additional six months of marketing exclusivity attached to another period of exclusivity if a sponsor conducts clinical trials in children in response to a written request from the FDA. The issuance of a written request does not require the sponsor to undertake the described clinical trials. In addition, orphan drug

exclusivity, as described above, may offer a seven-year period of marketing exclusivity, except in certain circumstances.

U.S. coverage and reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any therapeutic product candidate for which we may seek regulatory approval. Sales in the United States will depend in part on the availability of sufficient coverage and adequate reimbursement from third-party payors, which include government health programs such as Medicare, Medicaid, TRICARE and the Veterans Administration, as well as managed care organizations and private health insurers. Prices at which we or our customers seek reimbursement for our therapeutic product candidates can be subject to challenge, reduction or denial by payors.

The process for determining whether a payor will provide coverage for a product is typically separate from the process for setting the reimbursement rate that the payor will pay for the product. A payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be available. Additionally, in the United States there is no uniform policy among payors for coverage or reimbursement. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own coverage and reimbursement policies, but also have their own methods and approval processes. Therefore, coverage and reimbursement for products can differ significantly from payor to payor. If coverage and adequate reimbursement are not available, or are available only at limited levels, successful commercialization of, and obtaining a satisfactory financial return on, any product we develop may not be possible.

Third-party payors are increasingly challenging the price and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. In order to obtain coverage and reimbursement for any product that might be approved for marketing, we may need to conduct expensive studies in order to demonstrate the medical necessity and cost-effectiveness of any products, which would be in addition to the costs expended to obtain regulatory approvals. Third-party payors may not consider our product candidates to be medically necessary or cost-effective compared to other available therapies, or the rebate percentages required to secure favorable coverage may not yield an adequate margin over cost or may not enable us to maintain price levels sufficient to realize an appropriate return on our investment in drug development.

Healthcare reform

In the United States and some foreign jurisdictions, there have been, and continue to be, several legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of drug product candidates, restrict or regulate post-approval activities, and affect the profitable sale of drug product candidates.

Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. In March 2010, the Patient Protection and Affordable Care Act, or ACA, was passed, which substantially changed the way healthcare is financed by both the government and private insurers, and significantly impacts the U.S. pharmaceutical industry. The ACA, among other things: (1) increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extends the rebate program to individuals enrolled in Medicaid managed care organizations; (2) established an annual, nondeductible fee on any entity that manufactures or imports certain specified branded prescription drugs and biologic agents apportioned among these entities according to their market share in some government healthcare programs; (3) expanded the availability of lower pricing under the 340B drug pricing program by adding new entities to the program; (4) increased the statutory minimum

rebates a manufacturer must pay under the Medicaid Drug Rebate Program; (5) expanded the eligibility criteria for Medicaid programs; (6) created a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; (7) created a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% (and 70% commencing January 1, 2019) point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D; (8) established a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and (9) established a Center for Medicare Innovation at the Centers for Medicare & Medicaid Services, or CMS, to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drugs.

Some of the provisions of the ACA have yet to be implemented, and there have been judicial and Congressional challenges to certain aspects of the ACA, as well as recent efforts by the Trump administration to repeal or replace certain aspects of the ACA. For example, President Trump has signed Executive Orders and other directives designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. Concurrently, Congress has considered legislation that would repeal or repeal and replace all or part of the ACA. While Congress has not passed comprehensive repeal legislation, bills affecting the implementation of certain taxes under the ACA have been signed into law. The Tax Cuts and Jobs Act of 2017 includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." Additionally, on January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain ACA-mandated fees, including the so-called "Cadillac" tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. Further, the Bipartisan Budget Act of 2018, among other things, amends the ACA, effective January 1, 2019, to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole."

Other legislative changes have been proposed and adopted since the ACA was enacted, including aggregate reductions of Medicare payments to providers of 2% per fiscal year and reduced payments to several types of Medicare providers. Moreover, there has recently been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. At the federal level, the Trump administration's budget proposal for fiscal year 2019 contains further drug price control measures. While any proposed measures will require authorization through additional legislation to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

More recently, on May 30, 2018, the Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017, or Right to Try Act, was signed into law. The law, among other things, provides a federal framework for patients to access certain investigational new drug products that have completed a Phase I clinical trial. Under certain circumstances, eligible patients can seek treatment without enrolling in

clinical trials and without obtaining FDA approval under the FDA expanded access program. The Right to Try Act did not establish any new entitlement or positive right to any party or individual, nor did it create any new mandates, directives, or additional regulations requiring a manufacturer or sponsor of an eligible investigational new drug product to provide expanded access.

U.S. healthcare fraud and abuse laws and compliance requirements

Federal and state healthcare laws and regulations restrict business practices in the biopharmaceutical industry. These laws include anti-kickback and false claims laws and regulations, data privacy and security, and transparency laws and regulations.

The federal Anti-Kickback Statute prohibits, among other things, individuals or entities from knowingly and willfully offering, paying, soliciting or receiving remuneration, directly or indirectly, overtly or covertly, in cash or in kind to induce or in return for purchasing, leasing, ordering or arranging for or recommending the purchase, lease or order of any item or service reimbursable under Medicare, Medicaid or other federal healthcare programs. A person or entity does not need to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act and the civil monetary penalties statute.

The federal civil and criminal false claims laws, including the civil False Claims Act, prohibit, among other things, any individual or entity from knowingly presenting, or causing to be presented, a false claim for payment to the federal government or knowingly making, using or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government.

The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, created additional federal civil and criminal statutes that prohibit, among other things, knowingly and willfully executing a scheme to defraud any healthcare benefit program. In addition, HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, imposes certain requirements relating to the privacy, security and transmission of protected health information on HIPAA covered entities, which include certain healthcare provider, health plans and healthcare clearinghouses, and their business associates who conduct certain activities involving protected health information on their behalf.

The federal Physician Payments Sunshine Act requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children’s Health Insurance Program, with specific exceptions, to report annually to CMS information related to payments or other transfers of value made to physicians and teaching hospitals, and applicable manufacturers and applicable group purchasing organizations to report annually to CMS ownership and investment interests held by physicians and their immediate family members.

Similar state and foreign laws and regulations may also restrict business practices in the biopharmaceutical industry, such as state anti-kickback and false claims laws, which may apply to business practices, including but not limited to, research, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by non- governmental third-party payors, including private insurers, or by patients themselves; state laws that require pharmaceutical companies to comply with the pharmaceutical industry’s voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws and regulations that require drug manufacturers to file reports relating to pricing and marketing information, which requires tracking gifts and other remuneration and items of value provided to physicians, other healthcare providers and entities; state and local laws that require the registration of pharmaceutical sales representatives; and state and foreign laws governing the privacy and security of health

information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Efforts to ensure compliance with applicable healthcare laws and regulations can involve substantial costs. Violations of healthcare laws can result in significant penalties, including the imposition of significant civil, criminal and administrative penalties, damages, monetary fines, disgorgement, individual imprisonment, possible exclusion from participation in Medicare, Medicaid and other U.S. healthcare programs, integrity oversight and reporting obligations, contractual damages, reputational harm, diminished profits and future earnings, and curtailment or restructuring of operations.

Employees

As of June 30, 2018, we had 34 full-time employees, 14 of whom have a Ph.D. or M.D., and 2 part-time employees. None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good.

Research and development

We have invested $5.1 million, $9.2 million, $2.1 million and $4.7 million in research and development for the years ended December 31, 2016 and 2017 and the three months ended March 31, 2017 and 2018, respectively.

Facilities

As of May 2018, we have transitioned into a new corporate headquarters, consisting of a 29,499 square foot facility in San Diego, California. We use our corporate headquarters primarily for corporate, research, development, clinical, regulatory, manufacturing and quality functions. Our lease for this facility expires in February 2025, with the option to extend the term of the lease for an additional five years, subject to certain conditions.

We also continue to lease an 8,624 square foot facility in San Diego, California, which served as our prior corporate headquarters. We intend to continue using this facility as laboratory space until the third quarter of 2018.

We believe that our facilities are adequate to meet our current needs, and that suitable additional alternative spaces will be available in the future on commercially reasonable terms, if required.

Legal proceedings

We are not currently subject to any material legal proceedings. From time to time, we may be involved in legal proceedings or subject to claims incident to the ordinary course of business. Regardless of the outcome, such proceedings or claims can have an adverse impact on us because of defense and settlement costs, diversion of resources and other factors, and there can be no assurances that favorable outcomes will be obtained.

Management

Executive officers, key employees and directors

The following table sets forth the name, age and position of each of our executive officers, key employees and directors as of June 30, 2018.

Name	Age	Position
Executive Officers		
R. Scott Struthers, Ph.D.	56	President, Chief Executive Officer and Director
Marc Wilson	39	Chief Financial Officer
Alan Krasner, M.D.	54	Chief Medical Officer
Key Employees		
Stephen F. Betz, Ph.D.	52	Vice President, Biology
Ajay Madan, Ph.D., D.A.B.T.	50	Vice President, Development
Yun-Fei (Frank) Zhu, Ph.D.	55	Vice President, Chemistry
Non-Employee Directors		
Wendell Wierenga, Ph.D.(1)(3)	70	Chairman of the Board of Directors
Mason Freeman, M.D.(3)	67	Director
Matthew K. Fust(1)(2)	53	Director
Stephen Kaldor, Ph.D.(1)	56	Director
Weston Nichols, Ph.D.(2)	33	Director
Jack B. Nielsen, M.Sc.(2)(3)	54	Director

(1) Member of the compensation committee

(2) Member of the audit committee

(3) Member of the nominating and corporate governance committee

Executive officers

R. Scott Struthers, Ph.D., is our co-founder and has served on our board of directors since November 2008 and as our President and Chief Executive Officer since December 2008. Prior to Crinetics, he was senior director and head of endocrinology and metabolism at Neurocrine Biosciences, Inc., from 1998 to 2008. At Neurocrine, he initiated and led the company's efforts to discover and develop orally active, nonpeptide GnRH antagonists, including elagolix. Prior to Neurocrine, from 1995 to 1998, he co-founded ScienceMedia Inc. to develop eLearning solutions for the life sciences and higher education markets and led contract research efforts at Biosym Technologies, from 1992 to 1995, to develop and apply computational tools for drug discovery. Dr. Struthers is also a co-founder of the San Diego Entrepreneurs Exchange, a nonprofit organization which he has served on the board of directors of since January 2009. He holds a Ph.D. in physiology and pharmacology from the University of California, San Diego based on the work he performed at the Salk Institute for Biological Studies. Dr. Struthers' knowledge of our business, as well as his extensive development and clinical experience, contributed to our board of directors' conclusion that he should serve as a director of our company.

Marc Wilson has served as our Chief Financial Officer since January 2018. Prior to Crinetics, Mr. Wilson was Vice President of Finance and Accounting and Chief Accounting Officer at Cidara Therapeutics, Inc., a publicly-traded

biotechnology company, from September 2014 to January 2018. Prior to Cidara, from October 2010 to August 2014, Mr. Wilson was Director of Accounting and Controller at Trius Therapeutics, a biopharmaceutical company, until its acquisition by Cubist Pharmaceuticals. Prior to Trius, Mr. Wilson worked at Neurocrine Biosciences, Inc. from 2007 to 2010. Mr. Wilson began his career in 2001 with PricewaterhouseCoopers LLP and is a certified public accountant. Mr. Wilson earned a bachelor's degree in Economics and Accounting from the College of the Holy Cross.

Alan Krasner, M.D. has served as our Chief Medical Officer since June 2018. From December 2015 to June 2018, Dr. Krasner served as Global Clinical Development Lead at Shire plc, a global biotechnology company focused on the treatment of rare diseases. Before joining Shire, Dr. Krasner served from May 2008 to November 2015 as Chief Medical Officer for Biodel Inc., a specialty biopharmaceutical company focused on the treatment of diabetes. Prior to Biodel, from 2002 to 2008, Dr. Krasner served as Director in the Department of Clinical Research Metabolic Diseases at Pfizer Global Research and Development, where he was responsible for the design, execution, clinical analysis, and reporting of multiple, global clinical trials supporting registration of late stage drug candidates. Dr. Krasner served as a consulting physician at the Joslin Diabetes and Endocrinology Center of the Lawrence and Memorial Hospital in New London, Connecticut until July 2017. Dr. Krasner holds a B.S. from the Medical Education Honors Program at Northwestern University and a M.D. from Northwestern University Medical School. He completed his residency at Johns Hopkins Hospital in internal medicine and subsequently completed his fellowship at Johns Hopkins Hospital in endocrinology and metabolism.

Key employees

Stephen F. Betz, Ph.D., is our co-founder and has served as our Vice President, Biology since December 2009. Previously, from June 2003 to May 2009, he was Director of Endocrinology and Metabolism at Neurocrine Biosciences, Inc., where he worked on the discovery and development of GnRH receptor antagonists and nonpeptide modulators of other endocrine targets. Prior to Neurocrine, from 2001 to 2003, he led laboratory efforts at GeneFormatics, Inc., and from 1996 to 2000, he worked in pharmaceutical discovery at Abbott Laboratories, including structure-guided drug design, assay development, and compound screening in the Research Nuclear Magnetic Resonance Group. From 1993 to 1996, he worked at the Dupont Merck Pharmaceutical Company focusing on protein engineering and design. He holds a B.S. in chemistry from the University of Delaware and a Ph.D. in chemistry from the University of North Carolina at Chapel Hill.

Ajay Madan, Ph.D., D.A.B.T., has served as our Vice President, Development since May 2016. Previously, from May 2002 to July 2016, Dr. Madan worked at Neurocrine Biosciences, Inc., including as Vice President of Preclinical Development from February 2013 to July 2016, where he was responsible for drug metabolism, pharmacokinetics, toxicology, and clinical pharmacology in support of a number of drug discovery and development programs. Since 2004, Dr. Madan has also taught, and continues to teach, courses at the University of California San Diego (UCSD) on selecting promising drug candidates and preclinical drug discovery and development. Prior to Neurocrine, from 1994 to 2002, Dr. Madan worked at XenoTech LLC, an in vitro drug research company, including as the Chief Scientific Officer, from 2001 to 2002. Dr. Madan is an author of more than 50 scientific publications, and he has been a diplomat of the American Board of Toxicology since 2005. He holds a B.Pharm. degree from Birla Institute of Technology and a Ph.D. in pharmacology and toxicology from the University of Kansas.

Yun-Fei (Frank) Zhu, Ph.D., is our co-founder and has served as our Vice President, Chemistry since December 2009. Previously, from 1997 until May 2009, he worked at Neurocrine Biosciences, Inc., including as the Director of Medicinal Chemistry in the endocrinology and metabolism group from January 2005 to May 2009. At Neurocrine, he led discovery for the backup nonpeptide GnRH antagonist program. Prior to Neurocrine, from 1991 to 1997, he worked at CombiChem, Inc., a combinatorial chemistry-based drug discovery company, and BioResearch, Inc., a chemical technology company. He was a postdoctoral fellow at the University of California,

San Diego from 1990 to 1991. He holds a B.S. in chemistry from Hangzhou University and a Ph.D. in organic chemistry from Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences.

Non-employee directors

Wendell Wierenga, Ph.D. joined our board of directors as Chairman in October 2015. Dr. Wierenga brings to our board over four decades of experience in research, drug discovery and drug development, including clinical research, regulatory affairs, manufacturing, safety, and medical affairs. He has an extensive background serving as a public company executive and board member in the pharmaceutical and biotechnology industries. He most recently served as Executive Vice President, Research and Development, at Santarus, Inc., a specialty biopharmaceutical company, from June 2011 until its acquisition by Salix Pharmaceuticals, Inc. in 2014. Prior to Santarus, he was Executive Vice President of Research and Development at Ambit Biosciences Corporation from 2007 until 2011 and Neurocrine Biosciences, Inc. from 2003 until 2006. Additionally, Dr. Wierenga served as Chief Executive Officer of Syrrx, Inc. (now part of Takeda Pharmaceutical Company), Senior Vice President of Worldwide Pharmaceutical Sciences, Technologies and Development at Parke-Davis/Warner Lambert Company LLC (now Pfizer, Inc.), and he spent 16 years at Upjohn Pharmaceuticals in research and drug discovery roles. Dr. Wierenga serves as a member of the board of directors of Patara Pharma LLC and Dermata Therapeutics, LLC, both private companies. He also serves on the board of the following publicly-traded companies: Apricus Biosciences, Inc., a urology and rheumatology company, Concert Pharmaceuticals, Inc., a biopharmaceutical company focused on deuterium chemistry, and Cytokinetics Inc., a biopharmaceutical company. He was previously on the board of directors of Onyx Pharmaceuticals, Inc. (acquired by Amgen), Anacor Pharmaceuticals Inc. (acquired by Pfizer) XenoPort, Inc. (acquired by Arbor Pharmaceuticals) and Ocera Therapeutics Inc. (acquired by Mallinckrodt). Additionally, Dr. Wierenga serves on multiple scientific advisory boards, including Concert Pharmaceuticals, Ferring Pharmaceuticals, and aTyr Pharma, Inc. He holds a Ph.D. in Chemistry from Stanford University and a B.A. in Chemistry from Hope College. Dr. Wierenga's scientific background and ability to contribute to the Board's understanding of technical matters relating to our business, as well as Dr. Wierenga's broader business development and corporate experience on the boards of directors of several biopharmaceutical companies, contributed to our board's conclusion that he should serve as a director of our company.

Mason Freeman, M.D. has served on our board of directors since October 2015. Dr. Freeman joined 5AM Ventures, a life science focused investment firm, as a scientific advisor in 2007 and became a venture partner in 2008. He serves as Chief of the Lipid Metabolism Unit and director of translational medicine at Massachusetts General Hospital (MGH) and is a professor at Harvard Medical School. Dr. Freeman currently serves on the Scientific Advisory Board of Homology Medicines, Inc., a public genetic medicines company, and Mitobridge, Inc., a biotechnology company that was acquired by Astrellas Pharma Inc. in January 2018, and serves as a Clinical Advisor to ScPharmaceuticals, Inc., a public pharmaceutical company. Dr. Freeman previously served as Clinical Advisor to Relypsa, Inc., a biopharmaceutical company focused on protein therapeutics, and previously served as a director of Envoy Therapeutics, Inc., a biopharmaceutical company, until its acquisition by Takeda. Trained in internal medicine and endocrinology, Dr. Freeman has spent twenty-five years studying the trafficking of cholesterol into and out of cells. Following post-doctoral research fellowships in the Biology Department at MIT and the Endocrine Division at MGH, he became Chief of the MGH's Lipid Metabolism Unit, in 1992, which he continues to direct as well as the translational medicine programs at the MGH center for computational and integrative biology and the MGH clinical research program. In these roles, he oversees a basic science research laboratory devoted to studying lipid trafficking as well as a clinical investigative team developing a novel oral anti-diabetic drug. From 2005 to 2007, he served as a head of the Novartis translational medicine program for cardiovascular & metabolic diseases as well as global head of biomarker development. Dr. Freeman is an editor of the adult primary care lipid section of a leading medical textbook, UpToDate. Dr. Freeman holds a B.A. from Harvard College and M.D. from the University of California, San Francisco.

Dr. Freeman's significant academic and clinical experience, and his experience as a venture capitalist, contributed to our board of directors' conclusion that he should serve as a director of our company.

Matthew K. Fust has served on our board of directors since February 2018. He is currently a board member and advisor to life sciences companies. Mr. Fust retired as Executive Vice President and Chief Financial Officer of Onyx Pharmaceuticals, Inc., a biopharmaceutical company, where he served from January 2009 through its acquisition by Amgen Inc. in October 2013. From May 2003 to December 2008, Mr. Fust served as Chief Financial Officer at Jazz Pharmaceuticals, Inc., a specialty pharmaceutical company. From 2002 to 2003, Mr. Fust served as Chief Financial Officer at Perlegen Sciences, a biopharmaceutical company. Previously, he was Senior Vice President and Chief Financial Officer at ALZA Corporation, a pharmaceutical company, where he was an executive from 1996 until 2002. Prior to these roles, he was a member of the healthcare strategy consulting practice at Andersen Consulting (now Accenture). Mr. Fust serves on the board of directors of the following publicly traded companies: Dermira, Inc., a medical dermatology company, Atara Biotherapeutics, Inc., an immunotherapy company, MacroGenics, Inc., a clinical-stage biopharmaceutical company, and Ultragenyx Pharmaceutical, Inc., a rare disease company. Mr. Fust previously served on the board of directors Sunesis Pharmaceuticals, Inc. from May 2005 until May 2017. Mr. Fust received a B.A. from the University of Minnesota and an M.B.A. from the Stanford University Graduate School of Business. Mr. Fust's experience as a chief financial officer in the life sciences industry, his leadership and management experience, and his service as a director of other biopharmaceutical companies, contributed to our board of directors' conclusion that he should serve as a director of our company.

Stephen Kaldor, Ph.D. has served on our board of directors since October 2015. Dr. Kaldor has over 25 years of experience in the biotech and pharmaceutical industries. He currently serves as a director and Chief Executive Officer of Fount Therapeutics, LLC, a biotechnology company. Dr. Kaldor previously served as President and Chief Executive Officer at Quanticel Pharmaceuticals Inc., a privately-held cancer drug discovery company, from February 2011 until its acquisition by Celgene Corporation in October 2015. Dr. Kaldor was also a venture partner at Versant Ventures from January 2011 until October 2015. Prior to that, Dr. Kaldor served as President and Chief Executive Officer of Ambrx Inc., a biotechnology company. from July 2007 to June 2010. He was the President and Chief Scientific Officer at Syrrx Inc., a privately-held biotechnology company, from March 2003 until its acquisition by Takeda San Diego, Inc., the U.S. Discovery Research Center for Takeda Pharmaceuticals, in March 2005, and he continued on as President and Chief Scientific Officer at Takeda until July 2007. Dr. Kaldor has served on the board of directors of Resolute Therapeutics, Inc., a biotechnology company, since October 2016, as a strategic advisor to FronThera US Pharmaceuticals LLC, a small molecule drug company, since March 2016 and as a scientific advisory board member of Crown Bioscience, Inc., a translational technology company, since January 2009. Previously, Dr. Kaldor served as a director of Furiex Pharmaceuticals, Inc., a publicly-traded biotechnology company, from November 2010 until its acquisition by Forest Laboratories, Inc. in 2014 and as a director of Amira Pharmaceuticals, Inc., a privately-held pharmaceutical company, from March 2008 until its acquisition by Bristol-Myers Squibb Company in 2011. He started his career at Eli Lilly and Company in 1990 and is a chemist by training. He holds a B.A. in chemistry from Columbia University and a Ph.D. in organic chemistry from Harvard University. Dr. Kaldor's extensive experience as an executive in the biopharmaceutical industry and his experience serving on numerous boards contributed to our board of directors' conclusion that he should serve as a director of our company.

Weston Nichols, Ph.D. has served on our board of directors since February 2018. Since April 2016, Dr. Nichols has served as an analyst for Perceptive Advisors, a life sciences focused investment firm. From January 2015 to April 2016, Dr. Weston was an analyst at Balyasny Asset Management, an investment management firm, and from May 2014 to December 2014, he was a biotechnology equity research associate at SunTrust Robinson Humphrey. Dr. Weston holds a B.S. in biological engineering from Cornell University, and a Ph.D. in neuroscience from Caltech. Dr. Weston's experience as venture capitalist in the life science industry contributed to our board of directors' conclusion that he should serve as a director of our company.

Jack B. Nielsen, M.Sc. has served on our board of directors since February 2018. Mr. Nielsen has served as a Managing Director at Vivo Capital LLC, a healthcare focused investment firm, since August 2017, and served as a consultant there from March 2017 to July 2017. From 2001 to February 2017, Mr. Nielsen worked within the Novo A/S (Novozymes) organization and its venture activities in several roles, most recently being employed as a Senior Partner based in Copenhagen, Denmark. From 2006 to 2012, Mr. Nielsen was employed as a Partner at Novo Ventures (US) Inc. in San Francisco, where he established the office which provides certain consultancy services to Novo A/S. Mr. Nielsen currently serves on the Board of Directors of Reata Pharmaceuticals, Inc. which is a publicly listed pharmaceutical company. He previously served on the board of directors of other public biotech companies: Merus, N.V., an immuno-oncology company, Apollo Endosurgery, a medical device company developing and marketing products for treatment of obesity, and Akebia Therapeutics, which develops treatments for certain anemias. He previously served as a member of the board of directors of a number of other private biopharmaceutical companies. Mr. Nielsen received a M.Sc. in Chemical Engineering from the Technical University of Denmark, and a Masters in Management of Technology from Center for Technology, Economics and Management, Technical University of Denmark. Mr. Nielsen's experience as a venture capitalist and serving on various biotechnology company boards contributed to our board of directors' conclusion that he should serve as a director of our company.

Board composition and election of directors

Director independence

Our board of directors currently consists of seven members. Our board of directors has determined that all of our directors, other than Dr. Struthers, are independent directors in accordance with the listing requirements of the Nasdaq Global Select Market. The Nasdaq independence definition includes a series of objective tests, including that the director is not, and has not been for at least three years, one of our employees and that neither the director nor any of his family members has engaged in various types of business dealings with us. In addition, as required by Nasdaq rules, our board of directors has made a subjective determination as to each independent director that no relationships exist, which, in the opinion of our board of directors, would interfere with the exercise of independent judgment in carrying out the responsibilities of a director. In making these determinations, our board of directors reviewed and discussed information provided by the directors and us with regard to each director's business and personal activities and relationships as they may relate to us and our management. There are no family relationships among any of our directors or executive officers.

Classified board of directors

In accordance with the terms of our amended and restated certificate of incorporation that will go into effect immediately prior to the closing of this offering, our board of directors will be divided into three classes with staggered, three-year terms. At each annual meeting of stockholders, the successors to directors whose terms then expire will be elected to serve from the time of election and qualification until the third annual meeting following election. Effective upon the closing of this offering, our directors will be divided among the three classes as follows:

- the Class I directors will be Mason Freeman, M.D. and R. Scott Struthers, and their terms will expire at our first annual meeting of stockholders following this offering;
- the Class II directors will be Weston Nichols, Ph.D. and Jack B. Nielsen, M.Sc., and their terms will expire at our second annual meeting of stockholders following this offering; and
- the Class III directors will be Matthew K. Fust, Stephen Kaldor, Ph.D. and Wendell Wierenga, Ph.D., and their terms will expire at our third annual meeting of stockholders following this offering.

Our amended and restated certificate of incorporation that will go into effect immediately prior to the closing of this offering will provide that the authorized number of directors may be changed only by resolution of the board of directors. Any additional directorships resulting from an increase in the number of directors will be distributed among the three classes so that, as nearly as possible, each class will consist of one-third of the directors. The division of our board of directors into three classes with staggered three-year terms may delay or prevent a change of our management or a change in control of our company. Our directors may be removed only for cause by the affirmative vote of the holders of at least two thirds of our outstanding voting stock then entitled to vote in the election of directors.

Board leadership structure

Our board of directors is currently led by its chairman, Dr. Wierenga. Our board of directors recognizes that it is important to determine an optimal board leadership structure to ensure the independent oversight of management as the company continues to grow. We separate the roles of chief executive officer and chairman of the board in recognition of the differences between the two roles. The chief executive officer is responsible for setting the strategic direction for the company and the day-to-day leadership and performance of the company, while the chairman of the board of directors provides guidance to the chief executive officer and presides over meetings of the full board of directors. We believe that this separation of responsibilities provides a balanced approach to managing the board of directors and overseeing the company.

Our board of directors has concluded that our current leadership structure is appropriate at this time. However, our board of directors will continue to periodically review our leadership structure and may make such changes in the future as it deems appropriate.

Role of board in risk oversight process

Our board of directors has responsibility for the oversight of the company's risk management processes and, either as a whole or through its committees, regularly discusses with management our major risk exposures, their potential impact on our business and the steps we take to manage them. The risk oversight process includes receiving regular reports from board committees and members of senior management to enable our board to understand the company's risk identification, risk management and risk mitigation strategies with respect to areas of potential material risk, including operations, finance, legal, regulatory, strategic and reputational risk.

The audit committee reviews information regarding liquidity and operations, and oversees our management of financial risks. Periodically, the audit committee reviews our policies with respect to risk assessment, risk management, loss prevention and regulatory compliance. Oversight by the audit committee includes direct communication with our external auditors, and discussions with management regarding significant risk exposures and the actions management has taken to limit, monitor or control such exposures. The compensation committee is responsible for assessing whether any of our compensation policies or programs has the potential to encourage excessive risk-taking. The nominating and corporate governance committee manages risks associated with the independence of the board, corporate disclosure practices, and potential conflicts of interest. While each committee is responsible for evaluating certain risks and overseeing the management of such risks, the entire board is regularly informed through committee reports about such risks. Matters of significant strategic risk are considered by our board as a whole.

Board committees and independence

Our board of directors has established three standing committees – audit, compensation and nominating and corporate governance – each of which operates under a charter that has been approved by our board.

Audit committee

The audit committee's main function is to oversee our accounting and financial reporting processes and the audits of our consolidated financial statements. This committee's responsibilities include, among other things:

- appointing our independent registered public accounting firm;
- evaluating the qualifications, independence and performance of our independent registered public accounting firm;
- approving the audit and non-audit services to be performed by our independent registered public accounting firm;
- reviewing the design, implementation, adequacy and effectiveness of our internal accounting controls and our critical accounting policies;
- discussing with management and the independent registered public accounting firm the results of our annual audit and the review of our quarterly unaudited financial statements;
- reviewing, overseeing and monitoring the integrity of our consolidated financial statements and our compliance with legal and regulatory requirements as they relate to financial statements or accounting matters;
- reviewing on a periodic basis, or as appropriate, any investment policy and recommending to our board any changes to such investment policy;
- reviewing with management and our auditors any earnings announcements and other public announcements regarding our results of operations;
- preparing the report that the SEC requires in our annual proxy statement;
- reviewing and approving any related party transactions and reviewing and monitoring compliance with our code of conduct and ethics; and
- reviewing and evaluating, at least annually, the performance of the audit committee and its members including compliance of the audit committee with its charter.

The members of our audit committee are Matthew K. Fust, Weston Nichols, Ph.D. and Jack B. Nielsen, M.Sc. Mr. Fust serves as the chairperson of the committee. All members of our audit committee meet the requirements for financial literacy under the applicable rules and regulations of the SEC and the Nasdaq Global Select Market. Our board of directors has determined that Mr. Fust is an "audit committee financial expert" as defined by applicable SEC rules and has the requisite financial sophistication as defined under the applicable Nasdaq rules and regulations. Our board of directors has determined each of Mr. Fust, Dr. Nichols and Mr. Nielsen is independent under the applicable rules of the SEC and the Nasdaq Global Select Market. Upon the listing of our common stock on the Nasdaq Global Select Market, the audit committee will operate under a written charter that satisfies the applicable standards of the SEC and the Nasdaq Global Select Market.

Compensation committee

Our compensation committee approves policies relating to compensation and benefits of our officers and employees. The compensation committee approves corporate goals and objectives relevant to the compensation of our Chief Executive Officer and other executive officers, evaluates the performance of these officers in light of those goals and objectives and approves the compensation of these officers based on such evaluations. The compensation committee also approves the issuance of stock options and other awards under

our equity plan. The compensation committee will review and evaluate, at least annually, the performance of the compensation committee and its members, including compliance by the compensation committee with its charter.

The members of our compensation committee are Stephen Kaldor, Ph.D., Matthew K. Fust and Wendell Wierenga, Ph.D. Dr. Kaldor serves as the chairperson of the committee. Our board of directors has determined that each of Dr. Kaldor, Mr. Fust and Dr. Wierenga is independent under the applicable rules and regulations of the Nasdaq Global Select Market, is a “non-employee director” as defined in Rule 16b-3 promulgated under the Exchange Act. Upon the listing of our common stock on the Nasdaq Global Select Market, the compensation committee will operate under a written charter, which the compensation committee will review and evaluate at least annually.

Nominating and corporate governance committee

The nominating and corporate governance committee is responsible for assisting our board of directors in discharging the board’s responsibilities regarding the identification of qualified candidates to become board members, the selection of nominees for election as directors at our annual meetings of stockholders (or special meetings of stockholders at which directors are to be elected), and the selection of candidates to fill any vacancies on our board of directors and any committees thereof. In addition, the nominating and corporate governance committee is responsible for overseeing our corporate governance policies, reporting and making recommendations to our board of directors concerning governance matters and oversight of the evaluation of our board of directors. The members of our nominating and corporate governance committee are Wendell Wierenga, Ph.D., Mason Freeman, M.D. and Jack B. Nielsen, M.Sc. Dr. Wierenga serves as the chairperson of the committee. Our board has determined that each of Dr. Wierenga, Dr. Mason and Mr. Nielsen is independent under the applicable rules and regulations of the Nasdaq Global Select Market relating to nominating and corporate governance committee independence. Upon the listing of our common stock on the Nasdaq Global Select Market, the nominating and corporate governance committee will operate under a written charter, which the nominating and corporate governance committee will review and evaluate at least annually.

Compensation committee interlocks and insider participation

None of the members of our compensation committee has ever been one of our officers or employees. None of our executive officers currently serves, or has served, as a member of the board of directors or compensation committee of any entity that has one or more executive officers serving as a member of our board of directors or compensation committee.

Board diversity

Upon the closing of this offering, our nominating and corporate governance committee will be responsible for reviewing with the board of directors, on an annual basis, the appropriate characteristics, skills and experience required for the board of directors as a whole and its individual members. In evaluating the suitability of individual candidates (both new candidates and current members), the nominating and corporate governance committee, in recommending candidates for election, and the board of directors, in approving (and, in the case of vacancies, appointing) such candidates, will take into account many factors, including the following:

- personal and professional integrity, ethics and values;
- experience in corporate management, such as serving as an officer or former officer of a publicly-held company;
- experience as a board member or executive officer of another publicly-held company;

- strong finance experience;
- diversity of expertise and experience in substantive matters pertaining to our business relative to other board members;
- diversity of background and perspective, including, but not limited to, with respect to age, gender, race, place of residence and specialized experience;
- experience relevant to our business industry and with relevant social policy concerns; and
- relevant academic expertise or other proficiency in an area of our business operations.

Currently, our board of directors evaluates, and following the closing of this offering will evaluate, each individual in the context of the board of directors as a whole, with the objective of assembling a group that can best maximize the success of the business and represent stockholder interests through the exercise of sound judgment using its diversity of experience in these various areas.

Code of business conduct and ethics

We have adopted a written code of business conduct and ethics that applies to our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. Upon the closing of this offering, our code of business conduct and ethics will be available under the Corporate Governance section of our website at www.crinetics.com. In addition, we intend to post on our website all disclosures that are required by law or the listing standards of the Nasdaq Global Select Market concerning any amendments to, or waivers from, any provision of the code. The reference to our website address does not constitute incorporation by reference of the information contained at or available through our website, and you should not consider it to be a part of this prospectus.

Executive and director compensation

This section discusses the material components of the executive compensation program for our executive officers who are named in the "Summary compensation table" below. In 2017, our only "named executive officer" was R. Scott Struthers, our President and Chief Executive Officer.

Marc Wilson, our Chief Financial Officer, and Alan Krasner, M.D., our Chief Medical Officer, commenced employment in January 2018 and June 2018, respectively, so are not named executive officers for 2017.

This discussion may contain forward-looking statements that are based on our current plans, considerations, expectations and determinations regarding future compensation programs. Actual compensation programs that we adopt following the closing of this offering may differ materially from the currently planned programs summarized in this discussion.

Summary compensation table

The following table presents summary information regarding the total compensation that was awarded to, earned by or paid to our named executive officer for services rendered during the year ended December 31, 2017.

Name and principal position	Year	Salary ($)	Bonus ($)(1)	Stock awards ($)	Option awards ($)	Non-equity incentive plan compensation ($)	All other compensation ($)(2)	Total ($)
R. Scott Struthers *President and Chief Executive Officer*	2017	350,000	29,200	—	—	—	6,322	385,522

(1) This column reflects the discretionary cash bonus paid to Dr. Struthers in September 2017.

(2) Includes the value of health insurance premiums and life insurance premiums paid by us on Dr. Struthers' behalf during 2017.

Narrative disclosure to compensation tables

Annual base salary

The compensation of our executive officers is generally determined and approved at the beginning of each year or, if later, in connection with the commencement of employment of the executive, by our board of directors or the compensation committee. As noted in the Summary Compensation Table above, Dr. Struthers' base salary for 2017 was $350,000.

Bonus compensation

From time to time our board of directors or compensation committee may approve bonuses for our named executive officers based on individual performance, company performance or as otherwise determined appropriate. No formal bonus plan was in effect for Dr. Struthers during 2017. In 2017, our board of directors determined to pay a one-time discretionary cash bonus of $29,200 to Dr. Struthers in recognition of his contributions to the company.

Equity-based incentive awards

Our equity-based incentive awards are designed to align our interests and the interests of our stockholders with those of our employees and consultants, including our named executive officers. The board of directors is responsible for approving equity grants.

Prior to this offering, since the adoption of our 2015 Stock Incentive Plan, or the 2015 Plan, we have granted equity awards pursuant to the 2015 Plan. Prior to the adoption of the 2015 Plan, we granted some equity awards on a stand-alone basis and not pursuant to any formal plan. Following this offering, we will grant equity incentive awards under the terms of our 2018 equity incentive plan, or the 2018 Plan. The terms of our equity plans are described below under "—Incentive award plans."

No equity awards were granted to Dr. Struthers during 2017 and, as of December 31, 2017, Dr. Struthers did not hold any outstanding equity awards of the company other than restricted stock as described below under "—Narrative disclosure to outstanding equity awards at fiscal year-end table." Dr. Struthers' restricted stock vested in full in February 2018 in connection with our Series B preferred stock financing.

On May 25, 2018, we granted stock options to purchase an aggregate of 729,481 shares of our common stock under the 2015 Plan to Dr. Struthers, Mr. Wilson and our key employees listed above as follows: Dr. Struthers, 364,741 stock options, and 91,185 stock options for each of Mr. Wilson, Dr. Betz, Dr. Madan and Dr. Zhu. The options were granted with an exercise price equal to $9.28 per share, which represented the fair market value per share on the date of grant, as determined by our board of directors and an independent third party valuation. The stock options vest over a period of four years from the date of grant in equal monthly installments; provided that, one-half of the stock options are subject to the further condition that they may not be exercised until the occurrence of our initial public offering and, in the event our initial public offering does not occur prior to the first anniversary of the date of grant, such portion of the stock options shall be automatically forfeited. The stock options have a term of ten years from the date of grant. The stock options will be subject to accelerated vesting pursuant to the employment agreements with each individual and our 2015 Plan.

On June 16, 2018, we granted stock options to purchase 167,173 shares of our common stock under the 2015 Plan to Dr. Krasner in connection with his commencement of employment. The options were granted with an exercise price equal to $12.01 per share, which represented the fair market value per share on the date of grant, as determined by our board of directors and an independent third party valuation. The stock options vest over a period of four years, with 25% of the options vesting on the first anniversary of Dr. Krasner's commencement of employment, and the remainder vesting in equal monthly installments over the three years thereafter, subject to Dr. Krasner's continuous service through each vesting date. The stock options have a term of ten years from the date of grant. The stock options will be subject to accelerated vesting pursuant to the employment agreement with Dr. Krasner and our 2015 Plan.

For a description of the accelerated vesting applicable to the stock options granted to our executive officers, see "Employment agreements with our executive officers" below.

Employment agreements with our executive officers

Below are written descriptions of our employment agreements with each of our executive officers. Each of our executive officers' employment is "at will" and may be terminated at any time.

Employment agreement with Dr. Struthers

We entered into an employment agreement with Dr. Struthers in October 2015, setting forth the terms of his employment as our President and Chief Executive Officer. We amended and restated the employment agreement with Dr. Struthers on May 25, 2018. Pursuant to the agreement, Dr. Struthers is entitled to an annual base salary of $350,000, which amount is subject to annual review by and at the sole discretion of our compensation committee of the board of directors or its designee. Effective upon the consummation of our initial public offering, Dr. Struthers' annual base salary will automatically be increased to $495,000. Dr. Struthers is also eligible to participate in any bonus plan maintained by the company for our senior executives and his target bonus is 50% of his annual base salary.

Pursuant to his employment agreement, if we terminate Dr. Struthers' employment other than for cause (as defined below) or Dr. Struthers terminates his employment for good reason (as defined below), he is entitled to the following payments and benefits, subject to his timely execution and non-revocation of a general release of claims in favor of the company and his continued compliance with the restrictive covenants set forth in his employment agreement: (1) his fully earned but unpaid base salary and accrued and unused paid time off, or PTO, through the date of termination at the rate then in effect, plus all other amounts under any compensation plan or practice to which he is entitled; (2) a payment equal to 12 months of his then-current base salary, payable in a lump sum payment 60 days following the termination date; (3) payment for continued health plan coverage for up to 12 months following the date of termination or, if earlier, up to the date Dr. Struthers' becomes eligible to receive equivalent or increased health plan coverage by means of subsequent employment or self-employment; and (4) if such termination occurs prior to a change in control (as defined below), automatic acceleration of the vesting and exercisability of his unvested stock awards as to the number of stock awards that would vest over the 12-month period following the date of termination.

If Dr. Struthers' employment is terminated by us other than for cause or by Dr. Struthers for good reason within 12 months after a change in control, in lieu of the severance benefits described above, he is entitled to the following payments and benefits, subject to his timely execution and non-revocation of a general release of claims in favor of the company and his continued compliance with the restrictive covenants set forth in his employment agreement: (1) his fully earned but unpaid base salary and accrued and unused PTO through the date of termination at the rate then in effect, plus all other amounts under any compensation plan or practice to which he is entitled; (2) a payment equal to 18 months of his then-current base salary, payable in a lump sum payment 60 days following the termination date; (3) payment for continued health plan coverage for up to 18 months following the date of termination or, if earlier, up to the date Dr. Struthers' becomes eligible to receive equivalent or increased health plan coverage by means of subsequent employment or self-employment; and (4) a payment equal to Dr. Struthers' then-current target annual bonus opportunity, payable in a lump sum payment 60 days following the date of termination.

In addition, in the event of a change in control and subject to Dr. Struthers' timely execution and non-revocation of a general release of claims in favor of the company, 100% of Dr. Struthers' outstanding unvested stock awards shall be automatically accelerated on the first to occur of (1) Dr. Struthers' termination by us without cause or by Dr. Struthers for good reason after a change in control or (2) the first anniversary of the closing of such change in control.

In addition, in the event of Dr. Struthers' termination of employment by reason of his death or permanent disability, and subject to Dr. Struthers' (or his estate's) timely execution and non-revocation of a general release of claims in favor of the company, 100% of Dr. Struthers' outstanding unvested stock awards shall be automatically accelerated on the date of termination.

In the event we terminate Dr. Struthers' employment for cause, he terminates his employment without good reason, or upon his death or permanent disability, he is entitled to receive only his fully earned but unpaid base salary and accrued and unused PTO through the date of termination at the rate then in effect, plus all other amounts under any compensation plan or practice to which he is entitled.

Employment agreement with Marc Wilson

We entered into an employment agreement with Mr. Wilson in January 2018, setting forth the terms of his employment as our Chief Financial Officer. We amended and restated the employment agreement with Mr. Wilson on May 22, 2018. Pursuant to the agreement, Mr. Wilson is entitled to an annual base salary of $255,000, which amount is subject to annual review by and at the sole discretion of our compensation committee of the board of directors or its designee. Effective upon the consummation of our initial public

offering, Mr. Wilson's annual base salary will automatically be increased to $330,000. Mr. Wilson is also eligible to participate in any bonus plan maintained by us for our senior executives and his target bonus is 35% of his annual base salary, pro-rated for his partial year of service for 2018.

Pursuant to his employment agreement, if Mr. Wilson's employment is terminated by us other than for cause (as defined below) or by Mr. Wilson for good reason (as defined below), he is entitled to the following payments and benefits, subject to his timely execution and non-revocation of a general release of claims in favor of the company and his continued compliance with the restrictive covenants set forth in his employment agreement: (1) his fully earned but unpaid base salary and accrued and unused PTO through the date of termination at the rate then in effect, plus all other amounts under any compensation plan or practice to which he is entitled; (2) a payment equal to 9 months of his then-current base salary, payable in a lump sum payment 60 days following the termination date; (3) payment for continued health plan coverage for up to 9 months following the date of termination or, if earlier, up to the date Mr. Wilson becomes eligible to receive equivalent or increased health plan coverage by means of subsequent employment or self-employment; and (4) if such termination occurs prior to a change in control (as defined below), automatic acceleration of the vesting and exercisability of his unvested stock awards as to the number of stock awards that would vest over the 9-month period following the date of termination.

If Mr. Wilson's employment is terminated by us other than for cause or by Mr. Wilson for good reason within 12 months after a change in control, in lieu of the severance benefits described above, he is entitled to the following payments and benefits, subject to his timely execution and non-revocation of a general release of claims in favor of the company and his continued compliance with the restrictive covenants set forth in his employment agreement: (1) his fully earned but unpaid base salary and accrued and unused PTO through the date of termination at the rate then in effect, plus all other amounts under any compensation plan or practice to which he is entitled; (2) a payment equal to 12 months of his then-current base salary, payable in a lump sum payment 60 days following the termination date; (3) payment for continued health plan coverage for up to 12 months following the date of termination or, if earlier, up to the date Mr. Wilson becomes eligible to receive equivalent or increased health plan coverage by means of subsequent employment or self-employment; and (4) a payment equal to Mr. Wilson's then-current target annual bonus opportunity, payable in a lump sum payment 60 days following the date of termination.

In addition, in the event of a change in control and subject to Mr. Wilson's timely execution and non-revocation of a general release of claims in favor of the company, 100% of Mr. Wilson's outstanding unvested stock awards shall be automatically accelerated on the first to occur of (1) Mr. Wilson's termination by us without cause or by Mr. Wilson for good reason after a change in control or (2) the first anniversary of the closing of such change in control.

In addition, in the event of Mr. Wilson's termination of employment by reason of his death or permanent disability, and subject to Mr. Wilson's (or his estate's) timely execution and non-revocation of a general release of claims in favor of the company and, in the case of his permanent disability, his continued compliance with the restrictive covenants set forth in his employment agreement, 100% of Mr. Wilson's outstanding unvested stock awards shall be automatically accelerated on the date of termination.

In the event we terminate Mr. Wilson's employment for cause, he terminates his employment without good reason, or upon his death or permanent disability, he is entitled to receive only his fully earned but unpaid base salary and accrued and unused PTO through the date of termination at the rate then in effect, plus all other amounts under any compensation plan or practice to which he is entitled.

Employment agreement with Alan Krasner, M.D.

We entered into an employment agreement with Dr. Krasner in June 2018, setting forth the terms of his employment as our Chief Medical Officer. Pursuant to the agreement, Dr. Krasner is entitled to an annual base

salary of $375,000, which amount is subject to annual review by and at the sole discretion of our compensation committee of the board of directors or its designee. Dr. Krasner is also eligible to participate in any bonus plan maintained by us for our senior executives and his target bonus is 35% of his annual base salary, pro-rated for his partial year of service for 2018.

Pursuant to his employment agreement, if Dr. Krasner's employment is terminated by us other than for cause (as defined below) or by Dr. Krasner for good reason (as defined below), he is entitled to the following payments and benefits, subject to his timely execution and non-revocation of a general release of claims in favor of the company and his continued compliance with the restrictive covenants set forth in his employment agreement: (1) his fully earned but unpaid base salary and accrued and unused PTO through the date of termination at the rate then in effect, plus all other amounts under any compensation plan or practice to which he is entitled; (2) a payment equal to 9 months of his then-current base salary, payable in a lump sum payment 60 days following the termination date; (3) payment for continued health plan coverage for up to 9 months following the date of termination or, if earlier, up to the date Dr. Krasner becomes eligible to receive equivalent or increased health plan coverage by means of subsequent employment or self-employment; and (4) if such termination occurs prior to a change in control (as defined below), automatic acceleration of the vesting and exercisability of his unvested stock awards as to the number of stock awards that would vest over the 9-month period following the date of termination.

If Dr. Krasner's employment is terminated by us other than for cause or by Dr. Krasner for good reason within 12 months after a change in control, in lieu of the severance benefits described above, he is entitled to the following payments and benefits, subject to his timely execution and non-revocation of a general release of claims in favor of the company and his continued compliance with the restrictive covenants set forth in his employment agreement: (1) his fully earned but unpaid base salary and accrued and unused PTO through the date of termination at the rate then in effect, plus all other amounts under any compensation plan or practice to which he is entitled; (2) a payment equal to 12 months of his then-current base salary, payable in a lump sum payment 60 days following the termination date; (3) payment for continued health plan coverage for up to 12 months following the date of termination or, if earlier, up to the date Dr. Krasner becomes eligible to receive equivalent or increased health plan coverage by means of subsequent employment or self-employment; and (4) a payment equal to Dr. Krasner's then-current target annual bonus opportunity, payable in a lump sum payment 60 days following the date of termination.

In addition, in the event of a change in control and subject to Dr. Krasner's timely execution and non-revocation of a general release of claims in favor of the company, 100% of Dr. Krasner's outstanding unvested stock awards shall be automatically accelerated on the first to occur of (1) Dr. Krasner's termination by us without cause or by Dr. Krasner for good reason after a change in control or (2) the first anniversary of the closing of such change in control.

In addition, in the event of Dr. Krasner's termination of employment by reason of his death or permanent disability, and subject to Dr. Krasner's (or his estate's) timely execution and non-revocation of a general release of claims in favor of the company and, in the case of his permanent disability, his continued compliance with the restrictive covenants set forth in his employment agreement, 100% of Dr. Krasner's outstanding unvested stock awards shall be automatically accelerated on the date of termination.

In the event we terminate Dr. Krasner's employment for cause, he terminates his employment without good reason, or upon his death or permanent disability, he is entitled to receive only his fully earned but unpaid base salary and accrued and unused PTO through the date of termination at the rate then in effect, plus all other amounts under any compensation plan or practice to which he is entitled.

Defined terms applicable to executive employment arrangements

For purposes of the executive employment agreements, "cause" means any of the following: (1) the commission of an act of fraud, embezzlement or dishonesty, or the commission of some other illegal act, that causes material harm to us or any successor or affiliate; (2) conviction of, or plea of "guilty" or "no contest" to, a felony or any crime involving fraud, dishonesty or moral turpitude under the laws of the United States or any state thereof; (3) any intentional unauthorized use or disclosure of our confidential information or trade secrets; (4) gross negligence, insubordination or material violation of any duty of loyalty to us or any successor or affiliate, or any other material misconduct; (5) ongoing and repeated failure or refusal to perform or neglect of duties, which failure, refusal or neglect continues for 15 days following receipt of written notice from the board of directors (or in the case of Mr. Wilson, our CEO) stating with specificity the nature of such failure, refusal or neglect; or (6) intentional, material breach of any company policy or any contract or agreement between the executive and us.

For purposes of the executive employment agreements, "change in control" means an "acquisition" or "asset transfer," as such terms are defined in our amended and restated certificate of incorporation as may be amended from time to time. However, after the consummation of our initial public offering, for purposes of the executive employment agreements, "change in control" will have the same meaning given to such term in our 2018 Plan, as described below.

For purposes of the executive employment agreements, "good reason" means the occurrence of any of the following events or conditions without the executive's written consent: (1) a material diminution in authority, duties or responsibilities; (2) a material diminution in base compensation, unless such a reduction is imposed across-the-board to our senior management; (3) a material change in the geographic location at which the executive must perform his or her duties; or (4) any other action or inaction that constitutes a material breach by us or any successor or affiliate of our obligations under the employment agreement. The executive must provide written notice to us of the occurrence of any of the foregoing events or conditions within 60 days of the occurrence of such event and we will have a period of 30 days to cure such event or condition after receipt of such notice. An executive's separation from service by reason of resignation for good reason must occur within 30 days following the expiration of the foregoing 30 day cure period.

Outstanding equity awards at fiscal year-end

The following table sets forth certain information regarding equity awards granted to Dr. Struthers that remained outstanding as of December 31, 2017.

		Option awards				Stock awards	
	Grant Date	Number of securities underlying unexercised options exercisable (#)	Number of securities underlying unexercised options unexercisable (#)	Option exercise price ($)	Option expiration date	Number of shares or units of stock that have not vested (#)	Market value of shares or units of stock that have not vested ($)(1)
R. Scott Struthers	10/30/2015	—	—	—	—	334,346(2)	5,683,882

(1) The market value was computed using $17.00 per share, which is the initial public offering price.

(2) Pursuant to a stock restriction agreement entered into between us and Dr. Struthers dated October 30, 2015, Dr. Struthers' previously-owned 1,215,805 shares of our common stock were subjected to new vesting conditions, such that 486,322 shares were deemed vested as of October 30, 2015 and the remaining 729,483 shares were converted into unvested shares of restricted stock that vest in equal monthly installments over the 48 months thereafter ending on October 30, 2019. For a description of the accelerated vesting provisions applicable to the restricted stock, see "Narrative disclosure to outstanding equity awards at fiscal year-end table" below.

Narrative disclosure to outstanding equity awards at fiscal year-end table

On October 30, 2015, we entered into a stock restriction agreement with Dr. Struthers pursuant to which Dr. Struthers' previously-owned 1,215,805 shares our common stock were subjected to new vesting conditions, such that 486,322 shares were deemed vested as of October 30, 2015 and the remaining 729,483 shares were converted into unvested shares of restricted stock that vest in equal monthly installments over the 48 months thereafter ending on October 30, 2019.

Under the stock restriction agreement, 100% of any unvested shares will automatically accelerate upon (1) Dr. Struthers' termination of employment by us without cause or by Dr. Struthers for good reason in connection with a change in control or, if earlier, upon the first anniversary of a change in control; (2) our initial public offering; (3) upon Dr. Struthers' termination of employment by us other than for cause or by Dr. Struthers for good reason; (4) the date on which the Series A investors have sold 50% or more of the capital stock purchased by the Series A investors ; (5) the date of the closing of a Series B preferred stock financing; or (6) upon a termination due to death or permanent disability. The definitions of "cause", "change in control" and "good reason" have the same definitions as those set forth under Dr. Struthers employment agreement, as described above. All of Dr. Struthers' restricted stock vested in February 2018 in connection with our Series B preferred stock financing.

Other elements of compensation

Perquisites, health, welfare and retirement benefits

Our named executive officers are eligible to participate in our employee benefit plans, including our medical, dental, vision, group life, disability and accidental death and dismemberment insurance plans, in each case on the generally on same basis as all of our other employees. We do, however, pay all of the health insurance premiums for Dr. Struthers. We provide a 401(k) plan to our employees, including our current named executive officers, as discussed in the section below entitled "—401(k) plan."

We generally do not provide perquisites or personal benefits to our named executive officers, except in limited circumstances. We do, however, pay the premiums for term life insurance and disability insurance for all of our employees, including our executive officers. Our board of directors may elect to adopt qualified or non-qualified benefit plans in the future if it determines that doing so is in our best interests.

401(k) plan

We maintain a defined contribution employee retirement plan, or 401(k) plan, for our employees. Our named executive officers are eligible to participate in the 401(k) plan on the same basis as our other employees. The 401(k) plan is intended to qualify as a tax-qualified plan under Section 401(k) of the Internal Revenue Code. The 401(k) plan provides that each participant may make pre-tax deferrals from his or her compensation up to the statutory limit, which is $18,500 for calendar year 2018, and other testing limits. Participants that are 50 years or older can also make "catch-up" contributions, which in calendar year 2018 may be up to an additional $6,000 above the statutory limit. Although the 401(k) plan provides for discretionary matching and profit sharing contributions, we currently do not make either type of contribution to the 401(k) plan. Participant contributions are held and invested, pursuant to the participant's instructions, by the plan's trustee.

Nonqualified deferred compensation

We do not maintain nonqualified defined contribution plans or other nonqualified deferred compensation plans. Our board of directors may elect to provide our officers and other employees with non-qualified defined contribution or other nonqualified deferred compensation benefits in the future if it determines that doing so is in our best interests.

Change in control benefits

Our executive officers may become entitled to certain benefits or enhanced benefits in connection with a change in control of our company. Each of our executive officers' employment agreements entitles them to accelerated vesting of all outstanding equity awards, as well as certain other benefits, upon a qualifying termination and in connection with a change in control of our company. For additional discussion, please see "—Employment agreements with our executive officers" above.

Incentive award plans

2018 Incentive Award Plan

Our board of directors and stockholders have approved the 2018 Plan, which became effective in connection with this offering. Under the 2018 Plan, we may grant cash and equity incentive awards to eligible service providers in order to attract, motivate and retain the talent for which we compete. The material terms of the 2018 Plan are summarized below.

Eligibility and administration

Our employees, consultants and directors, and employees and consultants of our subsidiaries, will be eligible to receive awards under the 2018 Plan. Following our initial public offering, the 2018 Plan will generally be administered by our board of directors with respect to awards to non-employee directors and by our compensation committee with respect to other participants, each of which may delegate its duties and responsibilities to committees of our directors and/or officers (referred to collectively as the plan administrator below), subject to certain limitations that may be imposed under the 2018 Plan, Section 16 of the Exchange Act and/or stock exchange rules, as applicable. The plan administrator will have the authority to make all determinations and interpretations under, prescribe all forms for use with, and adopt rules for the administration of, the 2018 Plan, subject to its express terms and conditions. The plan administrator will also set the terms and conditions of all awards under the 2018 Plan, including any vesting and vesting acceleration conditions.

Limitation on awards and shares available

An aggregate of 1,600,000 shares of our common stock will initially be available for issuance under awards granted pursuant to the 2018 Plan. The number of shares initially available for issuance will be increased by (1) the number of shares of common stock available for issuance and not subject to options granted under our 2015 Plan as of the effective date of the 2018 Plan, (2) the number of shares subject to stock options or similar awards granted under our 2015 Plan that expire or otherwise terminate without having been exercised in full after the effective date of the 2018 Plan and unvested shares issued pursuant to awards granted under the 2015 Plan that are forfeited to or repurchased by us after the effective date of the 2018 Plan, with the maximum number of shares to be added to the 2018 Plan pursuant to clauses (1) and (2) above equal to 3,142,857 shares, and (3) an annual increase on January 1 of each calendar year beginning in 2019 and ending in 2028, equal to the lesser of (a) 5% of the shares of common stock outstanding on the final day of the immediately preceding calendar year and (b) such smaller number of shares as determined by our board of directors. No more than 15,000,000 shares of common stock may be issued upon the exercise of incentive stock options under the 2018 Plan. Shares issued under the 2018 Plan may be authorized but unissued shares, shares purchased in the open market or treasury shares.

If an award under the 2018 Plan or the 2015 Plan expires, lapses or is terminated, exchanged for cash, surrendered, repurchased, canceled without having been fully exercised or forfeited, any shares subject to such award will, as applicable, become or again be available for new grants under the 2018 Plan. Further, shares

delivered to us to satisfy the applicable exercise or purchase price of an award under the 2018 Plan or the 2015 Plan and/or to satisfy any applicable tax withholding obligations (including shares retained by us from the award under the 2018 Plan or the 2015 Plan being exercised or purchased and/or creating the tax obligation) will become or again be available for award grants under the 2018 Plan. Awards granted under the 2018 Plan upon the assumption of, or in substitution for, awards authorized or outstanding under a qualifying equity plan maintained by an entity with which we enter into a merger or similar corporate transaction will not reduce the shares available for grant under the 2018 Plan.

Awards

The 2018 Plan provides for the grant of stock options, including incentive stock options, or ISOs, and nonqualified stock options, or NSOs, restricted stock, dividend equivalents, restricted stock units, or RSUs, stock appreciation rights, or SARs, and other stock or cash-based awards. Certain awards under the 2018 Plan may constitute or provide for a deferral of compensation, subject to Section 409A of the Internal Revenue Code, which may impose additional requirements on the terms and conditions of such awards. All awards under the 2018 Plan will be set forth in award agreements, which will detail the terms and conditions of the awards, including any applicable vesting and payment terms and post-termination exercise limitations. A brief description of each award type follows.

Stock options. Stock options provide for the purchase of shares of our common stock in the future at an exercise price set on the grant date. ISOs, by contrast to NSOs, may provide tax deferral beyond exercise and favorable capital gains tax treatment to their holders if certain holding period and other requirements of the Internal Revenue Code are satisfied. The exercise price of a stock option will not be less than 100% of the fair market value of the underlying share on the date of grant (or 110% in the case of ISOs granted to certain significant stockholders), except with respect to certain substitute options granted in connection with a corporate transaction. The term of a stock option may not be longer than ten years (or five years in the case of ISOs granted to certain significant stockholders). Vesting conditions determined by the plan administrator may apply to stock options and may include continued service, performance and/or other conditions. ISOs generally may be granted only to our employees and employees of our parent or subsidiary corporations, if any.

SARs. SARs entitle their holder, upon exercise, to receive from us an amount equal to the appreciation of the shares subject to the award between the grant date and the exercise date. The exercise price of a SAR will not be less than 100% of the fair market value of the underlying share on the date of grant (except with respect to certain substitute SARs granted in connection with a corporate transaction), and the term of a SAR may not be longer than ten years. Vesting conditions determined by the plan administrator may apply to SARs and may include continued service, performance and/or other conditions.

Restricted stock and RSUs. Restricted stock is an award of nontransferable shares of our common stock that remain forfeitable unless and until specified conditions are met, and which may be subject to a purchase price. RSUs are contractual promises to deliver shares of our common stock in the future, which may also remain forfeitable unless and until specified conditions are met and may be accompanied by the right to receive the equivalent value of dividends paid on shares of our common stock prior to the delivery of the underlying shares. Delivery of the shares underlying RSUs may be deferred under the terms of the award or at the election of the participant, if the plan administrator permits such a deferral. Conditions applicable to restricted stock and RSUs may be based on continuing service, the attainment of performance goals and/or such other conditions as the plan administrator may determine.

Other stock or cash-based awards. Other stock or cash-based awards are awards of cash, fully vested shares of our common stock and other awards valued wholly or partially by referring to, or otherwise based on, shares of our common stock. Other stock or cash-based awards may be granted to participants and may also be available

as a payment form in the settlement of other awards, as standalone payments and as payment in lieu of base salary, bonus, fees or other cash compensation otherwise payable to any individual who is eligible to receive awards. The plan administrator will determine the terms and conditions of other stock or cash-based awards, which may include vesting conditions based on continued service, performance and/or other conditions.

Performance awards

Performance awards include any of the foregoing awards that are granted subject to vesting and/or payment based on the attainment of specified performance goals or other criteria the plan administrator may determine, which may or may not be objectively determinable. Performance criteria upon which performance goals are established by the plan administrator may include: net earnings or losses (either before or after one or more of interest, taxes, depreciation, amortization and non-cash equity-based compensation expense); gross or net sales or revenue or sales or revenue growth; net income (either before or after taxes) or adjusted net income; profits (including, but not limited to, gross profits, net profits, profit growth, net operation profit or economic profit), profit return ratios or operating margin; budget or operating earnings (either before or after taxes or before or after allocation of corporate overhead and bonus); cash flow (including operating cash flow and free cash flow or cash flow return on capital); return on assets; return on capital or invested capital; cost of capital; return on stockholders' equity; total stockholder return; return on sales; costs, reductions in costs and cost control measures; expenses; working capital; earnings or loss per share; adjusted earnings or loss per share; price per share or dividends per share (or appreciation in or maintenance of such price or dividends); regulatory achievements or compliance; implementation, completion or attainment of objectives relating to research, development, regulatory, commercial or strategic milestones or developments; market share; economic value or economic value added models; division, group or corporate financial goals; customer satisfaction/growth; customer service; employee satisfaction; recruitment and maintenance of personnel; human resources management; supervision of litigation and other legal matters; strategic partnerships and transactions; financial ratios (including those measuring liquidity, activity, profitability or leverage); debt levels or reductions; sales-related goals; financing and other capital raising transactions; cash on hand; acquisition activity; investment sourcing activity; and marketing initiatives, any of which may be measured in absolute terms or as compared to any incremental increase or decrease. Such performance goals also may be based solely by reference to our performance or the performance of a subsidiary, division, business segment or business unit, or based upon performance relative to performance of other companies or upon comparisons of any of the indicators of performance relative to performance of other companies.

Provisions of the 2018 plan relating to director compensation

The 2018 Plan provides that the plan administrator may establish compensation for non-employee directors from time to time subject to the 2018 Plan's limitations. Prior to commencing this offering, our stockholders will approve the initial terms of our non-employee director compensation program, which is described below under the heading "—Director compensation." Our board of directors or its authorized committee may modify the non-employee director compensation program from time to time in the exercise of its business judgment, taking into account such factors, circumstances and considerations as it shall deem relevant from time to time, provided that the sum of any cash compensation or other compensation and the grant date fair value (as determined in accordance with ASC 718, or any successor thereto) of any equity awards granted as compensation for services as a non-employee director during any fiscal year may not exceed $750,000, increased to $1,000,000, in the fiscal year of a non-employee director's initial service as a non-employee director. The plan administrator may make exceptions to this limit for individual non-employee directors in extraordinary circumstances, as the plan administrator may determine in its discretion, provided that the non-employee director receiving such additional compensation may not participate in the decision to award such compensation or in other contemporaneous compensation decisions involving non-employee directors.

Certain transactions

In connection with certain transactions and events affecting our common stock, including a change in control, or change in any applicable laws or accounting principles, the plan administrator has broad discretion to take action under the 2018 Plan to prevent the dilution or enlargement of intended benefits, facilitate such transaction or event, or give effect to such change in applicable laws or accounting principles. This includes canceling awards in exchange for either an amount in cash or other property with a value equal to the amount that would have been obtained upon exercise or settlement of the vested portion of such award or realization of the participant's rights under the vested portion of such award, accelerating the vesting of awards, providing for the assumption or substitution of awards by a successor entity, adjusting the number and type of shares available, replacing awards with other rights or property or terminating awards under the 2018 Plan. In the event of a change in control where the acquirer does not assume awards granted under the 2018 Plan, awards issued under the 2018 Plan shall be subject to accelerated vesting such that 100% of the awards will become vested and exercisable or payable, as applicable, and which may be subject to such terms and conditions as apply generally to holders of common stock under the change in control documents. In addition, in the event of certain non-reciprocal transactions with our stockholders, or an "equity restructuring," the plan administrator will make equitable adjustments to the 2018 Plan and outstanding awards as it deems appropriate to reflect the equity restructuring.

For purposes of the 2018 Plan, a "change in control" means and includes each of the following: (1) a transaction or series of transactions (other than an offering of our common stock to the general public through a registration statement filed with the SEC or a transaction or series of transactions that meets the requirements of clauses (x) and (y) of clause (3) below) whereby any "person" or related "group" of "persons" (as such terms are used in Sections 13(d) and 14(d)(2) of the Exchange Act) (other than us, any of our subsidiaries, an employee benefit plan maintained by us or any of our subsidiaries or a "person" that, prior to such transaction, directly or indirectly controls, is controlled by, or is under common control with, us) directly or indirectly acquires beneficial ownership (within the meaning of Rule 13d-3 under the Exchange Act) of our securities possessing more than 50% of the total combined voting power of our securities outstanding immediately after such acquisition; or (2) during any period of two consecutive years, individuals who, at the beginning of such period, constitute the board of directors together with any new director(s) (other than a director designated by a person who shall have entered into an agreement with us to effect a transaction described in clauses (1) or (3)) whose election by the board of directors or nomination for election by our stockholders was approved by a vote of at least two-thirds of the directors then still in office who either were directors at the beginning of the two-year period or whose election or nomination for election was previously so approved, cease for any reason to constitute a majority thereof; or (3) the consummation by us (whether directly involving us or indirectly involving us through one or more intermediaries) of (a) a merger, consolidation, reorganization, or business combination or (b) a sale or other disposition of all or substantially all of our assets in any single transaction or series of related transactions or (c) the acquisition of assets or stock of another entity, in each case other than a transaction: (x) which results in our voting securities outstanding immediately before the transaction continuing to represent (either by remaining outstanding or by being converted into our voting securities or the voting securities of a successor entity, directly or indirectly, at least a majority of the combined voting power of our outstanding voting securities or the successor entity's outstanding voting securities immediately after the transaction, and (y) after which no person or group beneficially owns voting securities representing 50% or more of the combined voting power of us or the successor entity (provided that no person will be treated as beneficially owning 50% or more of the combined voting power of us or the successor entity for purposes of this clause (y) solely as a result of the voting power held in us prior to the consummation of the transaction).

Foreign participants, claw-back provisions, transferability and participant payments

With respect to foreign participants, the plan administrator may modify award terms, establish subplans and/or adjust other terms and conditions of awards, subject to the share limits described above. All awards will be subject

to the provisions of any claw-back policy implemented by our company to the extent set forth in such claw-back policy or in the applicable award agreement. With limited exceptions for estate planning, domestic relations orders, certain beneficiary designations and the laws of descent and distribution, awards under the 2018 Plan are generally non-transferable prior to vesting and are exercisable only by the participant. With regard to tax withholding obligations arising in connection with awards under the 2018 Plan and exercise price obligations arising in connection with the exercise of stock options under the 2018 Plan, the plan administrator may, in its discretion, accept cash, wire transfer, or check, shares of our common stock that meet specified conditions, a "market sell order" or such other consideration as it deems suitable or any combination of the foregoing.

Plan amendment and termination

Our board of directors may amend or terminate the 2018 Plan at any time; however, except in connection with certain changes in our capital structure, stockholder approval will be required for any amendment that increases the number of shares available under the 2018 Plan. The plan administrator will have the authority, without the approval of our stockholders, to amend any outstanding stock option or SAR to reduce its exercise price per share. No award may be granted pursuant to the 2018 Plan after the tenth anniversary of the date on which our board of directors adopts the 2018 Plan.

Securities laws

The 2018 Plan is intended to conform to all provisions of the Securities Act, and the Exchange Act and any and all regulations and rules promulgated by the SEC thereunder, including, without limitation, Rule 16b-3. The 2018 Plan will be administered, and awards will be granted and may be exercised, only in such a manner as to conform to such laws, rules and regulations.

Federal income tax consequences

The material federal income tax consequences of the 2018 Plan under current federal income tax law are summarized in the following discussion, which deals with the general tax principles applicable to the 2018 Plan. The following discussion is based upon laws, regulations, rulings and decisions now in effect, all of which are subject to change. Foreign, state and local tax laws, and employment, estate and gift tax considerations are not discussed due to the fact that they may vary depending on individual circumstances and from locality to locality.

Stock options and SARs. A 2018 Plan participant generally will not recognize taxable income and we generally will not be entitled to a tax deduction upon the grant of a stock option or SAR. The tax consequences of exercising a stock option and the subsequent disposition of the shares received upon exercise will depend upon whether the option qualifies as an ISO or an NSO. Upon exercising an NSO when the fair market value of our stock is higher than the exercise price of the option, a 2018 Plan participant generally will recognize taxable income at ordinary income tax rates equal to the excess of the fair market value of the stock on the date of exercise over the purchase price, and we (or our subsidiaries, if any) generally will be entitled to a corresponding tax deduction for compensation expense, in the amount equal to the amount by which the fair market value of the shares purchased exceeds the purchase price for the shares. Upon a subsequent sale or other disposition of the option shares, the participant will recognize a short-term or long-term capital gain or loss in the amount of the difference between the sales price of the shares and the participant's tax basis in the shares.

Upon exercising an ISO, a 2018 Plan participant generally will not recognize taxable income, and we will not be entitled to a tax deduction for compensation expense. However, upon exercise, the amount by which the fair market value of the shares purchased exceeds the purchase price will be an item of adjustment for alternative minimum tax purposes. The participant will recognize taxable income upon a sale or other taxable disposition of the option shares. For federal income tax purposes, dispositions are divided into two categories: qualifying and disqualifying. A qualifying disposition generally occurs if the sale or other disposition is made more than

two years after the date the option was granted and more than one year after the date the shares are transferred upon exercise. If the sale or disposition occurs before these two periods are satisfied, then a disqualifying disposition generally will result.

Upon a qualifying disposition of ISO shares, the participant will recognize long-term capital gain in an amount equal to the excess of the amount realized upon the sale or other disposition of the shares over their purchase price. If there is a disqualifying disposition of the shares, then the excess of the fair market value of the shares on the exercise date (or, if less, the price at which the shares are sold) over their purchase price will be taxable as ordinary income to the participant. If there is a disqualifying disposition in the same year of exercise, it eliminates the item of adjustment for alternative minimum tax purposes. Any additional gain or loss recognized upon the disposition will be recognized as a capital gain or loss by the participant.

We will not be entitled to any tax deduction if the participant makes a qualifying disposition of ISO shares. If the participant makes a disqualifying disposition of the shares, we should be entitled to a tax deduction for compensation expense in the amount of the ordinary income recognized by the participant.

Upon exercising or settling an SAR, a 2018 Plan participant will recognize taxable income at ordinary income tax rates, and we should be entitled to a corresponding tax deduction for compensation expense, in the amount paid or value of the shares issued upon exercise or settlement. Payments in shares will be valued at the fair market value of the shares at the time of the payment, and upon the subsequent disposition of the shares the participant will recognize a short-term or long-term capital gain or loss in the amount of the difference between the sales price of the shares and the participant's tax basis in the shares.

Restricted stock and RSUs. A 2018 Plan participant generally will not recognize taxable income at ordinary income tax rates and we generally will not be entitled to a tax deduction upon the grant of restricted stock or RSUs. Upon the termination of restrictions on restricted stock or the payment of RSUs, the participant will recognize taxable income at ordinary income tax rates, and we should be entitled to a corresponding tax deduction for compensation expense, in the amount paid to the participant or the amount by which the then fair market value of the shares received by the participant exceeds the amount, if any, paid for them. Upon the subsequent disposition of any shares, the participant will recognize a short-term or long-term capital gain or loss in the amount of the difference between the sales price of the shares and the participant's tax basis in the shares. However, a 2018 Plan participant granted restricted stock that is subject to forfeiture or repurchase through a vesting schedule such that it is subject to a "risk of forfeiture" (as defined in Section 83 of the Code) may make an election under Section 83(b) of the Code to recognize taxable income at ordinary income tax rates, at the time of the grant, in an amount equal to the fair market value of the shares of common stock on the date of grant, less the amount paid, if any, for such shares. We will be entitled to a corresponding tax deduction for compensation, in the amount recognized as taxable income by the participant. If a timely Section 83(b) election is made, the participant will not recognize any additional ordinary income on the termination of restrictions on restricted stock, and we will not be entitled to any additional tax deduction.

Other stock or cash-based awards. A 2018 Plan participant will not recognize taxable income and we will not be entitled to a tax deduction upon the grant of other stock or cash-based awards until cash or shares are paid or distributed to the participant. At that time, any cash payments or the fair market value of shares that the participant receives will be taxable to the participant at ordinary income tax rates and we should be entitled to a corresponding tax deduction for compensation expense. Payments in shares will be valued at the fair market value of the shares at the time of the payment, and upon the subsequent disposition of the shares, the participant will recognize a short-term or long-term capital gain or loss in the amount of the difference between the sales price of the shares and the participant's tax basis in the shares.

2015 Stock Incentive Plan

Our board of directors and stockholders approved the 2015 Plan, which originally became effective in February 2015 and was further amended and restated in October 2015. As of March 31, 2018, 667,185 shares of our common stock were available for issuance under future awards under the 2015 Plan and 1,457,952 shares of our common stock were subject to outstanding option awards under the 2015 Plan.

The 2015 Plan will be terminated on, and we will not make any further awards under the 2015 Plan following, the date the 2018 Plan becomes effective. However, any outstanding awards granted under the 2015 Plan will remain outstanding, subject to the terms of our 2015 Plan and award agreements, until such outstanding awards vest and are exercised (as applicable) or until they terminate or expire by their terms. The material terms of the 2015 Plan are summarized below.

Eligibility and administration

Our employees, consultants and directors, and employees and consultants of our affiliates, are eligible to receive awards under the 2015 Plan. The 2015 Plan is generally administered by our board of directors with respect to awards to non-employee directors and by our compensation committee with respect to other participants, each of which may delegate its duties and responsibilities to committees of our directors and/or officers (referred to collectively as the plan administrator below), subject to certain limitations that may be imposed under the 2015 Plan, Section 16 of the Exchange Act and/or stock exchange rules, as applicable. The plan administrator has the authority to make all determinations and interpretations under, prescribe all forms for use with, and adopt rules for the administration of, the 2015 Plan, subject to its express terms and conditions. The plan administrator also sets the terms and conditions of all awards under the 2015 Plan, including any vesting and vesting acceleration conditions.

Limitation on awards and shares available

As of March 31, 2018, an aggregate of 2,413,373 shares of our common stock were authorized for issuance under awards granted pursuant to the 2015 Plan. In May 2018, the board of directors approved an amendment to the 2015 Plan to (i) increase the share limit by 729,484 shares to a total of 3,142,857 shares and (ii) increase the number of shares that may be issued upon the exercise of incentive stock options under the 2015 Plan to 3,142,857 shares. The amendment was effective immediately. Shares issued under the 2015 Plan may be authorized but unissued shares, shares purchased in the open market or treasury shares. If an award under the 2015 Plan expires, lapses or is terminated, exchanged for cash, surrendered, repurchased, canceled without having been fully exercised or forfeited, any shares subject to such award will, as applicable, become or again be available for new grants under the 2015 Plan.

Awards

The 2015 Plan provides for the grant of stock options, including ISOs and NSOs, restricted stock and SARs. Certain awards under the 2015 Plan may constitute or provide for a deferral of compensation, subject to Section 409A of the Internal Revenue Code, which may impose additional requirements on the terms and conditions of such awards. All awards under the 2015 Plan will be set forth in award agreements, which will detail the terms and conditions of the awards, including any applicable vesting and payment terms and post-termination exercise limitations. A brief description of each award type follows.

Stock options. Stock options provide for the purchase of shares of our common stock in the future at an exercise price set on the grant date. ISOs, by contrast to NSOs, may provide tax deferral beyond exercise and favorable capital gains tax treatment to their holders if certain holding period and other requirements of the Internal Revenue Code are satisfied. The exercise price of a stock option will not be less than 100% of the fair

market value of the underlying share on the date of grant (or 110% in the case of ISOs granted to certain significant stockholders), except with respect to certain substitute options granted in connection with a corporate transaction. The term of a stock option may not be longer than ten years (or five years in the case of ISOs granted to certain significant stockholders). Vesting conditions determined by the plan administrator may apply to stock options and may include continued service, performance and/or other conditions. ISOs generally may be granted only to our employees and employees of our parent or subsidiary corporations, if any.

SARs. SARs entitle their holder, upon exercise, to receive from us an amount equal to the appreciation of the shares subject to the award between the grant date and the exercise date. The exercise price (base value) of a SAR will not be less than 100% of the fair market value of the underlying share on the date of grant (except with respect to certain substitute SARs granted in connection with a corporate transaction), and the term of a SAR may not be longer than ten years. Vesting conditions determined by the plan administrator may apply to SARs and may include continued service, performance and/or other conditions.

Restricted stock. Restricted stock is an award of shares of our common stock that remain forfeitable unless and until specified conditions are met, and which may be subject to a purchase price. Conditions applicable to restricted stock may be based on continuing service, the attainment of performance goals and/or such other conditions as the plan administrator may determine.

Certain transactions

In connection with certain transactions and events affecting our common stock, including a change in control (as defined below), or change in any applicable laws or accounting principles, the plan administrator has broad discretion to take action under the 2015 Plan to prevent the dilution or enlargement of intended benefits, facilitate such transaction or event, or give effect to such change in applicable laws or accounting principles. This includes canceling awards, accelerating the vesting of awards, providing for the assumption or substitution of awards by a successor entity, adjusting the number and type of shares available and replacing or terminating awards under the 2015 Plan. In the event of a change in control where the acquirer does not assume awards granted under the 2015 Plan, awards issued under the 2015 Plan shall be subject to accelerated vesting such that 100% of the awards will become vested and exercisable or payable, as applicable. In addition, in the event of certain non-reciprocal transactions with our stockholders, or an “equity restructuring,” the plan administrator will make equitable adjustments to the 2015 Plan and outstanding awards as it deems appropriate to reflect the equity restructuring.

Under the 2015 Plan, “change in control” generally means the occurrence of any of the following: (1) a change in the effective control of our company which occurs on the date that a majority of members of our board of directors is replaced during any twelve (12) month period by directors whose appointment or election is not endorsed by a majority vote of the members of the board of directors before the date of the appointment or election; (2) the date that any one person, or more than one person acting as a group acquires ownership of our stock that, together with stock held by such person, constitutes more than 50% of the total fair market value or total voting power of our stock, provided that a change in control will not be deemed to occur (A) on account of the acquisition of our securities directly from us, (B) on account of the acquisition of our securities by an investor, any affiliate thereof or any other person that acquires our securities in a transaction or series of related transactions the primary purpose of which is to obtain financing for us through the issuance of equity securities or (C) solely because the level of ownership held by any person exceeds the designated percentage threshold of the outstanding voting securities as a result of a repurchase or other acquisition of voting securities by us reducing the number of shares outstanding, provided that if a change in control would occur (but for the operation of this sentence) as a result of the acquisition of voting securities by us, and after such share acquisition, the person becomes the owner of any additional voting securities that, assuming the repurchase or other acquisition had not occurred, increases the percentage of the then outstanding voting

securities owned by the person over the designated percentage threshold, then a change in control will be deemed to occur; or (3) a change in the ownership of a substantial portion of our assets which occurs on the date that any person acquires (or has acquired during the twelve (12) month period ending on the date of the most recent acquisition by such person) our assets and the assets of our subsidiaries (taken as a whole) that have a total gross fair market value equal to or more than 50% of the total gross fair market value of all of our assets the assets of our subsidiaries (taken as a whole) immediately prior to such acquisition or acquisitions.

Claw-back provisions, transferability and participant payments

Awards under the 2015 Plan are generally non-transferable prior to vesting and are exercisable only by the participant. With regard to tax withholding obligations arising in connection with awards under the 2015 Plan and exercise price obligations arising in connection with the exercise of stock options under the 2015 Plan, the plan administrator may, in its discretion, accept cash, wire transfer, or check, shares of our common stock that meet specified conditions, and/or such other consideration as it deems suitable or any combination of the foregoing.

Plan amendment and termination

Our board of directors has the authority to amend, suspend or terminate the 2015 Plan, provided that such action does not impair the existing rights of any participant without such participant's consent. As described above, the 2015 Plan is expected to terminate upon the effective date of the 2018 Plan.

Securities laws and federal income tax consequences

The 2015 Plan is designed to comply with applicable securities laws in the same manner described above in the description of the 2018 Plan under the heading "— 2018 Incentive Award Plan — Securities laws." The general federal tax consequences of awards under the 2015 Plan are the same as those described above in the description of the 2018 Plan under the heading "— 2018 Incentive Award Plan — Federal income tax consequences."

2018 Employee Stock Purchase Plan

Our board of directors and our stockholders have approved a 2018 Employee Stock Purchase Plan, or the ESPP, which became effective in connection with this offering. The material terms of the ESPP are summarized below.

Shares available; administration. A total of 250,000 shares of our common stock are initially reserved for issuance under our ESPP. In addition, the number of shares available for issuance under the ESPP will be annually increased on January 1 of each calendar year beginning in 2019 and ending in 2028, by an amount equal to the lesser of: (a) 1% of the shares outstanding on the final day of the immediately preceding calendar year and (b) such smaller number of shares as is determined by our board of directors. In no event will more than 4,000,000 shares of our common stock be available for issuance under the ESPP.

Our board of directors or its committee will have authority to interpret the terms of the ESPP and determine eligibility of participants. We expect that the compensation committee will be the initial administrator of the ESPP.

Eligibility. Our employees are eligible to participate in the ESPP if they meet the eligibility requirements under the ESPP established from time to time by the plan administrator. However, an employee may not be granted rights to purchase stock under our ESPP if such employee, immediately after the grant, would own (directly or through attribution) stock possessing 5% or more of the total combined voting power or value of all classes of our common or other class of stock.

Grant of rights. The ESPP is intended to qualify under Section 423 of the Internal Revenue Code and stock will be offered under the ESPP during offering periods. The length of the offering periods under the ESPP will be determined by the plan administrator and may be up to 27 months long. Employee payroll deductions will be

used to purchase shares on each purchase date during an offering period. The number of purchase periods within, and purchase dates during each offering period will be established by the plan administrator prior to the commencement of each offering period. Offering periods under the ESPP will commence when determined by the plan administrator. The plan administrator may, in its discretion, modify the terms of future offering periods.

The ESPP permits participants to purchase common stock through payroll deductions of up to 20% of their eligible compensation, which includes a participant's gross base compensation for services to us, including overtime payments and excluding sales commissions, incentive compensation, bonuses, expense reimbursements, fringe benefits and other special payments. The plan administrator will establish a maximum number of shares that may be purchased by a participant during any offering period or purchase period, which, in the absence of a contrary designation, will be 100,000 shares. In addition, no employee will be permitted to accrue the right to purchase stock under the ESPP at a rate in excess of $25,000 worth of shares during any calendar year during which such a purchase right is outstanding (based on the fair market value per share of our common stock as of the first day of the offering period).

On the first trading day of each offering period, each participant will automatically be granted an option to purchase shares of our common stock. The option will be exercised on the applicable purchase date(s) during the offering period, to the extent of the payroll deductions accumulated during the applicable purchase period. The purchase price of the shares, in the absence of a contrary determination by the plan administrator, will be 85% of the lower of the fair market value of our common stock on the first trading day of the offering period or on the applicable purchase date, which will be the final trading day of the applicable purchase period. Participants may voluntarily end their participation in the ESPP at any time at least one week prior to the end of the applicable offering period (or such shorter or longer period specified by the plan administrator), and will be paid their accrued payroll deductions that have not yet been used to purchase shares of common stock. Participation ends automatically upon a participant's termination of employment.

A participant may not transfer rights granted under the ESPP other than by will, the laws of descent and distribution or as otherwise provided under the ESPP.

Certain transactions. In the event of certain transactions or events affecting our common stock, such as any stock dividend or other distribution, change in control, reorganization, merger, consolidation or other corporate transaction, the plan administrator will make equitable adjustments to the ESPP and outstanding rights. In addition, in the event of the foregoing transactions or events or certain significant transactions, including a change in control, the plan administrator may provide for (1) either the replacement of outstanding rights with other rights or property or termination of outstanding rights in exchange for cash, (2) the assumption or substitution of outstanding rights by the successor or survivor corporation or parent or subsidiary thereof, if any, (3) the adjustment in the number and type of shares of stock subject to outstanding rights, (4) the use of participants' accumulated payroll deductions to purchase stock on a new purchase date prior to the next scheduled purchase date and termination of any rights under ongoing offering periods or (5) the termination of all outstanding rights. Under the ESPP, a change in control has the same definition as given to such term in the 2018 Plan.

Plan amendment; termination. The plan administrator may amend, suspend or terminate the ESPP at any time. However, stockholder approval of any amendment to the ESPP will be obtained for any amendment which increases the aggregate number or changes the type of shares that may be sold pursuant to rights under the ESPP, changes the corporations or classes of corporations whose employees are eligible to participate in the ESPP or changes the ESPP in any manner that would cause the ESPP to no longer be an employee stock purchase plan within the meaning of Section 423(b) of the Internal Revenue Code. The ESPP will terminate on the tenth anniversary of the date it is initially approved by our board of directors.

Securities laws. The ESPP has been designed to comply with various securities laws in the same manner as described above in the description of the 2018 Plan.

Federal income taxes. The material federal income tax consequences of the ESPP under current federal income tax law are summarized in the following discussion, which deals with the general tax principles applicable to the ESPP. The following discussion is based upon laws, regulations, rulings and decisions now in effect, all of which are subject to change. Foreign, state and local tax laws, and employment, estate and gift tax considerations are not discussed due to the fact that they may vary depending on individual circumstances and from locality to locality.

The ESPP, and the right of participants to make purchases thereunder, is intended to qualify under the provisions of Section 423 of the Code. Under the applicable Code provisions, no income will be taxable to a participant until the sale or other disposition of the shares purchased under the ESPP. This means that an eligible employee will not recognize taxable income on the date the employee is granted an option under the ESPP (i.e., the first day of the offering period). In addition, the employee will not recognize taxable income upon the purchase of shares. Upon such sale or disposition, the participant will generally be subject to tax in an amount that depends upon the length of time such shares are held by the participant prior to disposing of them. If the shares are sold or disposed of more than two years from the first day of the offering period during which the shares were purchased and more than one year from the date of purchase, or if the participant dies while holding the shares, the participant (or his or her estate) will recognize ordinary income measured as the lesser of: (1) the excess of the fair market value of the shares at the time of such sale or disposition over the purchase price; or (2) an amount equal to 15% of the fair market value of the shares as of the first day of the offering period. Any additional gain will be treated as long-term capital gain. If the shares are held for the holding periods described above but are sold for a price that is less than the purchase price, there is no ordinary income and the participating employee has a long-term capital loss for the difference between the sale price and the purchase price.

If the shares are sold or otherwise disposed of before the expiration of the holding periods described above, the participant will recognize ordinary income generally measured as the excess of the fair market value of the shares on the date the shares are purchased over the purchase price and we will be entitled to a tax deduction for compensation expense in the amount of ordinary income recognized by the employee. Any additional gain or loss on such sale or disposition will be long-term or short-term capital gain or loss, depending on how long the shares were held following the date they were purchased by the participant prior to disposing of them. If the shares are sold or otherwise disposed of before the expiration of the holding periods described above but are sold for a price that is less than the purchase price, the participant will recognize ordinary income equal to the excess of the fair market value of the shares on the date of purchase over the purchase price (and we will be entitled to a corresponding deduction), but the participant generally will be able to report a capital loss equal to the difference between the sales price of the shares and the fair market value of the shares on the date of purchase.

Director compensation

Historically, we have not paid cash compensation to directors for their service on our board of directors. We have occasionally compensated certain of our non-employee directors with equity awards.

In 2017, we did not grant any equity awards to the non-employee members of our board of directors. The aggregate number of shares subject to each non-employee director’s outstanding and unexercised option awards as of December 31, 2017 was as follows: Dr. Wierenga, 80,850 stock options (20,060 of which were granted outside of the 2015 Plan); Dr. Freeman, 54,711 stock options; and Dr. Kaldor, 54,711 options.

In February 2018, we appointed Matthew K. Fust to our board of directors and in connection with his appointment, in March 2018, Mr. Fust was awarded a stock option to purchase 45,592 shares of our common stock in March 2018 with a grant date fair value of $55,181, as determined in accordance with ASC 718, *Stock Compensation*. One-third of Mr. Fust's stock option will vest on the one-year anniversary of the vesting commencement date, February 16, 2018, with the remainder vesting in equal monthly installments over twenty-four months thereafter. Prior to his appointment, Mr. Fust served as a finance advisor to us and received a monthly cash retainer of $3,000 for his services and was awarded a bonus in September 2017 in the amount of $3,000 for an aggregate of $39,000 in cash compensation for fiscal 2017. Additionally, in connection with services he provided in 2017, Mr. Fust was awarded a stock option to purchase 6,079 shares of our common stock in November 2017 with a grant date fair value of $7,000, as determined in accordance with ASC 505-50, *Equity—Equity-Based Payments to Non-Employees*. Mr. Fust's stock option will vest in equal monthly installments over four years from the vesting commencement date, December 1, 2017.

We have reimbursed and will continue to reimburse all of our non-employee directors for their travel, lodging and other reasonable expenses incurred in attending meetings of our board of directors and committees of our board of directors.

In connection with this offering, we intend to adopt and ask our stockholders to approve the initial terms of our non-employee director compensation program. The material terms of the non-employee director compensation program policy are summarized below.

The non-employee director compensation program will provide for annual retainer fees and/or long-term equity awards for our non-employee directors. We expect each non-employee director will receive an annual retainer of $40,000, with an additional $30,000 annual retainer payable to the Chairman of the board of directors. Non- employee directors serving as the chairs of the audit, compensation and nominating and corporate governance committees will receive additional annual retainers of $15,000, $10,000 and $7,500, respectively. Non-employee directors serving as members of the audit, compensation and nominating and corporate governance committees will receive additional annual retainers of $7,500, $5,000 and $3,750, respectively. Each non-employee director who is initially elected or appointed to the board of directors after the consummation of this offering will receive an initial grant of options to purchase 25,000 shares of our common stock, vesting over three years in three equal annual installments on each of the first three anniversaries of the grant date, subject to continuous service as a director through each vesting date. Each non-employee director who is serving on the board of directors as of the date of any annual meeting of our stockholders following the consummation of this offering and has been serving as a non-employee director for at least 6 months as of the date of such meeting will be automatically granted an option to purchase 12,500 shares of common stock, vesting on the first to occur of the first anniversary of the date of grant or the next occurring annual meeting of our stockholders, subject to continuous service as a director through such vesting date.

Compensation under our non-employee director compensation policy will be subject to the annual limits on non-employee director compensation set forth in the 2018 Plan, as described above. Our board of directors or its authorized committee may modify the non-employee director compensation program from time to time in the exercise of its business judgment, taking into account such factors, circumstances and considerations as it shall deem relevant from time to time, subject to the annual limit on non-employee director compensation set forth in the 2018 Plan. As provided in the 2018 Plan, our board of directors or its authorized committee may make exceptions to this limit for individual non-employee directors in extraordinary circumstances, as the board of directors or its authorized committee may determine in its discretion, provided that the non-employee director receiving such additional compensation may not participate in the decision to award such compensation or in other compensation decisions involving non-employee directors.

Limitations of liability and indemnification matters

Our amended and restated certificate of incorporation and our amended and restated bylaws provide that we will indemnify our directors and officers to the fullest extent permitted by the Delaware General Corporation Law, which prohibits our amended and restated certificate of incorporation from limiting the liability of our directors for the following:

- any breach of the director's duty of loyalty to us or our stockholders;
- acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law;
- unlawful payment of dividends or unlawful stock repurchases or redemptions; or
- any transaction from which the director derived an improper personal benefit.

Our amended and restated certificate of incorporation and our amended and restated bylaws also provide that if Delaware law is amended to authorize corporate action further eliminating or limiting the personal liability of a director, then the liability of our directors will be eliminated or limited to the fullest extent permitted by Delaware law, as so amended. This limitation of liability does not apply to liabilities arising under the federal securities laws and does not affect the availability of equitable remedies such as injunctive relief or rescission.

Our amended and restated certificate of incorporation and our amended and restated bylaws also provide that we shall have the power to indemnify our employees and agents to the fullest extent permitted by law. Our amended and restated bylaws also permit us to secure insurance on behalf of any officer, director, employee or other agent for any liability arising out of his or her actions in this capacity, regardless of whether our amended and restated bylaws would permit indemnification. We have obtained directors' and officers' liability insurance.

We have entered into separate indemnification agreements with our directors and executive officers, in addition to indemnification provided for in our amended and restated certificate of incorporation and amended and restated bylaws. These agreements, among other things, provide for indemnification of our directors and executive officers for expenses, judgments, fines and settlement amounts incurred by this person in any action or proceeding arising out of this person's services as a director or executive officer or at our request. We believe that these provisions in our amended and restated certificate of incorporation and amended and restated bylaws and indemnification agreements are necessary to attract and retain qualified persons as directors and executive officers.

The above description of the indemnification provisions of our amended and restated certificate of incorporation, our amended and restated bylaws and our indemnification agreements is not complete and is qualified in its entirety by reference to these documents, each of which is filed as an exhibit to the registration statement of which this prospectus is a part.

The limitation of liability and indemnification provisions in our amended and restated certificate of incorporation and amended and restated bylaws may discourage stockholders from bringing a lawsuit against directors for breach of their fiduciary duties. They may also reduce the likelihood of derivative litigation against directors and officers, even though an action, if successful, might benefit us and our stockholders. A stockholder's investment may be harmed to the extent we pay the costs of settlement and damage awards against directors and officers pursuant to these indemnification provisions. Insofar as indemnification for liabilities under the Securities Act may be permitted to directors, officers or persons controlling us pursuant to the foregoing provisions, we have been informed that in the opinion of the SEC such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable. There is no pending litigation or proceeding naming any of our directors or officers as to which indemnification is being sought, nor are we aware of any pending or threatened litigation that may result in claims for indemnification by any director or officer.

Certain relationships and related person transactions

The following includes a summary of transactions since January 1, 2015 to which we have been a party in which the amount involved exceeded or will exceed $120,000, and in which any of our directors, executive officers or, to our knowledge, beneficial owners of more than 5% of our capital stock or any member of the immediate family of any of the foregoing persons had or will have a direct or indirect material interest, other than equity and other compensation, termination, change in control and other arrangements, which are described under "Executive and director compensation." We also describe below certain other transactions with our directors, executive officers and stockholders.

Preferred stock financings

Series A Convertible Preferred Stock Financings. In October 2015, we entered into a Series A preferred stock purchase agreement, pursuant to which we sold to investors in an initial closing and, upon the achievement of certain specified milestones, subsequent closings from October 2015 to December 2017 in private placements an aggregate of 28,763,179 shares of our Series A convertible preferred stock at a purchase price of $1.043 per share, for an aggregate purchase price of approximately $30.0 million.

Series B Convertible Preferred Stock Financings. In February 2018, we entered into a Series B preferred stock purchase agreement, pursuant to which we sold to investors in an initial closing and a subsequent closing in February and March 2018 in private placements an aggregate of 19,641,200 shares of our Series B convertible preferred stock at a purchase price of $3.233 per share, for an aggregate purchase price of approximately $63.5 million.

All purchasers of our convertible preferred stock are entitled to specified registration rights. See the section titled "Description of capital stock—Registration rights" for more information regarding these registration rights.

The following table sets forth the aggregate number of shares acquired by the listed directors, executive officers or holders of more than 5% of our capital stock, or their affiliates. Each share of preferred stock, including the shares identified in the following table, will convert into shares of common stock at a ratio of 3.29-to-one immediately prior to the closing of this offering.

Participants	Series A convertible preferred stock	Series B convertible preferred stock
5% or Greater Stockholders(1)		
Entities affiliated with 5AM Ventures(2)	9,587,727	1,546,551
Entities affiliated with Vivo Capital(3)	9,587,727	1,546,551
Entities affiliated with Versant Ventures(4)	9,587,725	1,546,551
Perceptive Life Sciences Master Fund, Ltd.(5)	—	6,186,205
OrbiMed Private Investments VI, LP	—	5,722,239
Entities affiliated with RA Capital Management, LLC(6)	—	3,093,103

(1) Additional details regarding these stockholders and their equity holdings are provided under "Principal stockholders."

(2) Represents securities acquired by 5AM Ventures IV, L.P. and 5AM Co-Investors IV, L.P. Mason Freeman, M.D., a member of our board of directors, is a venture partner at 5AM Venture Management, LLC, which is an affiliate of 5AM Partners IV, LLC.

(3) Represents securities acquired by Vivo Capital Fund VIII, L.P. and Vivo Capital Surplus Fund VIII, L.P. Jack B. Nielsen, M.Sc., a member of our board of directors, is a Managing Director at Vivo Capital.

(4) Represents securities acquired by Versant Venture Capital V, L.P., Versant Affiliates Fund V, L.P., Versant Ophthalmic Affiliates Fund I, L.P. and Versant Venture Capital V (Canada) LP.

(5) Weston Nichols, Ph.D., a member of our board of directors, is an analyst at Perceptive Advisors, LLC, an affiliate of Perceptive Life Sciences Master Fund, Ltd.

(6) Represents securities acquired by RA Capital Healthcare Fund, L.P. and Blackwell Partners LLC—Series A.

Investor rights agreement

We entered into an investor rights agreement in October 2015, which was amended in February 2018, with the holders of our convertible preferred stock, including entities with which certain of our directors are affiliated. This agreement provides for certain rights relating to the registration of their shares of common stock issuable upon conversion of their convertible preferred stock and certain additional covenants made by us. Except for the registration rights (including the related provisions pursuant to which we have agreed to indemnify the parties to the investor rights agreement), all rights under this agreement will terminate upon closing of this offering. The registration rights will continue following this offering and will terminate three years following the closing of this offering. See “Description of capital stock—Registration rights” for additional information.

Voting agreement

We entered into a voting agreement in October 2015, which was amended in February 2018, with certain of our stockholders, pursuant to which the following directors were each elected to serve as members on our board of directors and, as of the date of this prospectus, continue to so serve: Drs. Freeman, Kaldor, Struthers, Nichols, and Wierenga and Messrs. Fust and Nielsen. Pursuant to the voting agreement, Dr. Struthers, as our Chief Executive Officer, was initially selected to serve on our board of directors as a representative of holders of our common stock, as designated by a majority of our common stockholders. Dr. Wierenga and Mr. Fust were initially selected to serve on our board of directors as representatives of holders of our common stock and preferred stock, as designated by a majority of our common and preferred stockholders, voting together as a single class. Drs. Freeman and Kaldor and Mr. Nielsen were initially selected to serve on our board of directors as representatives of holders of our Series A convertible preferred stock, as designated by 5AM Ventures, Versant Ventures and Vivo Capital, respectively. Dr. Nichols was initially selected to serve on our board of directors as a representative of holders of our Series B convertible preferred stock, as designated by Perceptive Life Sciences Master Fund, Ltd.

The voting agreement will terminate upon the closing of this offering, and members previously elected to our board of directors pursuant to this agreement will continue to serve as directors until they resign, are removed or their successors are duly elected by holders of our common stock. The composition of our board of directors after this offering is described in more detail under “Management—Board composition and election of directors.”

Employment agreements

We have entered into employment agreements with our executive officers. For more information regarding these employment agreements, see the section in this prospectus entitled “Executive and director compensation—Narrative disclosure to compensation tables—Employment agreements with our executive officers.”

Director and officer indemnification

We have entered into indemnification agreements with each of our directors and executive officers. These agreements, among other things, require us or will require us to indemnify each director (and in certain cases their related venture capital funds) and executive officer to the fullest extent permitted by Delaware law, including indemnification of expenses such as attorneys’ fees, judgments, fines and settlement amounts

incurred by the director or executive officer in any action or proceeding, including any action or proceeding by or in right of us, arising out of the person's services as a director or executive officer.

Our amended and restated certificate of incorporation and our amended and restated bylaws provide that we will indemnify each of our directors and officers to the fullest extent permitted by the Delaware General Corporation Law. Further, we have purchased a policy of directors' and officers' liability insurance that insures our directors and officers against the cost of defense, settlement or payment of a judgment under certain circumstances. For further information, see "Executive and director compensation—Limitations of liability and indemnification matters."

Stock option grants to executive officers and directors

We have granted stock options to our executive officers and certain of our directors as more fully described in the section entitled "Executive and director compensation."

Participation in this offering

Certain of our principal stockholders, including entities affiliated with certain of our directors, have indicated an interest in purchasing an aggregate of approximately $30.0 million in shares of our common stock in this offering at the initial public offering price per share and on the same terms as the other purchasers in this offering. However, because these indications of interest are not binding agreements or commitments to purchase, the underwriters may determine to sell more, less or no shares in this offering to any or all of these stockholders, or any or all of these stockholders may determine to purchase more, less or no shares in this offering. The underwriters will receive the same underwriting discount on any shares purchased by these stockholders as they will on any other shares sold to the public in this offering.

Policies and procedures for related person transactions

Our board of directors will adopt a written related person transaction policy, to be effective upon the closing of this offering, setting forth the policies and procedures for the review and approval or ratification of related-person transactions. This policy will cover, with certain exceptions set forth in Item 404 of Regulation S-K under the Securities Act, any transaction, arrangement or relationship, or any series of similar transactions, arrangements or relationships in which we were or are to be a participant, where the amount involved exceeds $120,000 and a related person had or will have a direct or indirect material interest, including, without limitation, purchases of goods or services by or from the related person or entities in which the related person has a material interest, indebtedness, guarantees of indebtedness and employment by us of a related person. In reviewing and approving any such transactions, our audit committee is tasked to consider all relevant facts and circumstances, including, but not limited to, whether the transaction is on terms comparable to those that could be obtained in an arm's length transaction and the extent of the related person's interest in the transaction. All of the transactions described in this section occurred prior to the adoption of this policy.

Principal stockholders

The following table sets forth information with respect to the beneficial ownership of our common stock as of June 30, 2018, and as adjusted to reflect the sale of shares of common stock in this offering, by:

- each of our named executive officers;
- each of our directors;
- all of our executive officers and directors as a group; and
- each person or group of affiliated persons known by us to beneficially own more than 5% of our common stock.

The number of shares beneficially owned by each stockholder is determined under rules issued by the SEC. Under these rules, beneficial ownership includes any shares as to which a person has sole or shared voting power or investment power. Applicable percentage ownership is based on 17,195,957 shares of common stock outstanding on June 30, 2018, which gives effect to the automatic conversion of all outstanding shares of our preferred stock into 14,712,571 shares of our common stock and includes 139,025 shares subject to repurchase. In computing the number of shares beneficially owned by a person and the percentage ownership of that person, shares of common stock subject to options or other rights held by such person that are currently exercisable or will become exercisable within 60 days of June 30, 2018 are considered outstanding, although these shares are not considered outstanding for purposes of computing the percentage ownership of any other person.

Unless otherwise indicated, the address of each beneficial owner listed below is c/o Crinetics Pharmaceuticals, Inc., 10222 Barnes Canyon Road, Bldg. #2, San Diego, California 92121. We believe, based on information provided to us, that each of the stockholders listed below has sole voting and investment power with respect to the shares beneficially owned by the stockholder unless noted otherwise, subject to community property laws where applicable.

Certain of our principal stockholders, including entities affiliated with certain of our directors, have indicated an interest in purchasing an aggregate of approximately $30.0 million in shares of our common stock in this offering at the initial public offering price. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters may determine to sell more, less or no shares in this offering to any or all of these stockholders, or any or all of these stockholders may determine to purchase more, less or no shares in this offering. The following table does not reflect any such potential purchases by these stockholders or their affiliated entities. If any shares are purchased by these stockholders, the number of shares of common stock beneficially owned after this offering and the percentage of common stock beneficially owned after this offering would increase from that set forth in the table below.

Name of beneficial owner	Shares beneficially owned before and after the offering	Percentage of shares beneficially owned	
		Before offering	After offering
5% or Greater Stockholders			
Entities affiliated with Vivo Capital(1)	3,438,989	20.0%	14.8%
Entities affiliated with 5AM Ventures(2)	3,384,278	19.7%	14.6%
Entities affiliated with Versant Ventures(3)	3,384,276	19.7%	14.6%
Perceptive Life Sciences Master Fund, Ltd.(4)	1,880,305	10.9%	8.1%
OrbiMed Private Investments VI, LP(5)	1,739,282	10.1%	7.5%
Entities affiliated with RA Capital Management, LLC(6)	940,152	5.5%	4.1%
Named Executive Officers and Directors			
R. Scott Struthers, Ph.D.(7)	1,257,597	7.3%	5.4%
Jack B. Nielsen, M.Sc.(1)	0	*	*
Mason Freeman, M.D.(2)(8)	37,613	*	*
Matthew K. Fust(9)	58,762	*	*
Stephen Kaldor, Ph.D.(3)(10)	52,810	*	*
Weston Nichols, Ph.D.(4)	0	*	*
Wendell Wierenga, Ph.D(11)	80,849	*	*
All executive officers and directors as a group (9 persons)(12)	1,605,032	9.2%	6.8%

* Less than 1%.

(1) Consists of (1) 2,973,653 shares of common stock held by Vivo Capital Fund VIII, L.P., or Vivo Capital, (2) 410,625 shares of common stock held by Vivo Capital Surplus Fund VIII, L.P., or Vivo Surplus, and (3) 54,711 shares of common stock held by Vivo Capital LLC, including 18,237 shares of common stock subject to repurchase by us. Vivo Capital VIII, LLC is the general partner of both Vivo Capital and Vivo Capital Surplus. Vivo Capital LLC is the management company of Vivo Capital VIII, LLC. The voting members of each of Vivo Capital LLC and Vivo Capital VIII, LLC are Frank Kung, Albert Cha, Edgar Engleman, Chen Yu and Shan Fu, none of whom has individual voting or investment power with respect to these shares. Jack B. Nielsen, M.Sc., a member of our board of directors, is a Managing Director at Vivo Capital LLC. Each of the above-listed individuals disclaims beneficial ownership of such shares. The address for Vivo Capital VIII, LLC and Vivo Capital LLC is 505 Hamilton Avenue, Suite 207, Palo Alto, California 94301.

(2) Consists of (1) 3,248,908 shares of common stock held by 5AM Ventures IV, L.P and (2) 135,370 shares of common stock held by 5AM Co-Investors IV, L.P. Dr. John D. Diekman, Andrew Schwab, and Dr. Scott M. Rocklage are managing members of 5AM Partners IV, LLC, the general partner of 5AM Ventures IV, L.P. and 5AM Co-Investors IV, L.P., and as such, share voting and investment authority over the shares held by 5AM Ventures IV, L.P. and 5AM Co-Investors IV, L.P. Mason Freeman, M.D., a member of our board of directors, is a venture partner at 5AM Venture Management, LLC, which is an affiliate of 5AM Partners IV, LLC. Each of 5AM Partners IV, LLC, Dr. Diekman, Mr. Schwab, Dr. Rocklage, and Dr. Freeman disclaim beneficial ownership of such shares except to the extent of its or their pecuniary interest therein. The address of 5AM Ventures is 501 2nd Street, Suite 350, San Francisco, CA 94107.

(3) Consists of (1) 2,969,926 shares of common stock held by Versant Venture Capital V, L.P., or VVC V, (2) 89,336 shares of common stock held by Versant Affiliates Fund V, L.P., or VAF V, (3) 98,989 shares of common stock held by Versant Ophthalmic Affiliates Fund I, L.P., or VOA, and (4) 226,025 shares of common stock held by Versant Venture Capital V (Canada) LP, or VVC CAN. Versant Ventures V, LLC, or VV V, serves as the sole general partner of VOA, VAF V and VVC V and owns no shares directly. Versant Ventures V (Canada) GP-GP, Inc. or VV V CAN GP, serves as the sole general partner of Versant Ventures V (Canada), L.P., or VV V CAN, which serves as the sole general partner of VVC CAN and owns no shares directly. Samuel D. Colella, William J. Link, Bradley Bolzon, Ph.D., Robin L. Praeger, Kirk G. Nielson and Thomas Woiwode, Ph.D. are managing directors of VV V and directors of VV V CAN GP and share voting and dispositive power over the shares held by VOA, VAF V, VVC V and VVC CAN. Each of the above-listed individuals disclaim beneficial ownership of the shares held by VOA, VAF V, VVC V and VVC CAN, except

to the extent of their pecuniary interests therein. The address for each of the Versant Ventures entities is One Sansome Street, Suite 3630, San Francisco, CA 94104.

(4) Consists of 1,880,305 shares of common stock. Perceptive Advisors LLC serves as the investment manager to Perceptive Life Sciences Master Fund, Ltd. and may be deemed to beneficially own such shares. Joseph Edelman is the managing member of Perceptive Advisors LLC and may be deemed to beneficially own such shares. Weston Nichols, Ph.D., a member of our board of directors, is an analyst at Perceptive Advisors LLC. Both Mr. Edelman and Mr. Nichols disclaim beneficial ownership of these shares except to the extent of their pecuniary interest therein. The principal business address of these persons and entities is 51 Astor Place, 10th Floor, New York, NY 10003.

(5) Consists of 1,739,282 shares of common stock. OrbiMed Capital GP VI LLC, or GP VI, is the sole general partner of OrbiMed Private Investments VI, LP, or OPI VI. OrbiMed Advisors LLC, or OrbiMed Advisors, is the managing member of GP VI. By virtue of such relationships, GP VI and OrbiMed Advisors may be deemed to have voting and investment power with respect to the shares held by OPI VI and as a result may be deemed to have beneficial ownership of such shares. OrbiMed Advisors exercises investment and voting power through a management committee comprised of Carl L. Gordon, Sven H. Borho and Jonathan T. Silverstein. Each of GP VI, OrbiMed Advisors and Carl L. Gordon, Sven H. Borho and Jonathan T. Silverstein disclaims beneficial ownership of the shares held by OPI VI, except to the extent of its or his pecuniary interest therein if any. The address of these entities is 601 Lexington Avenue, 54th floor, New York, New York 10022.

(6) Consists of (1) 758,703 shares of common stock held by RA Capital Healthcare Fund, L.P. and (2) 181,449 shares of common stock held by Blackwell Partners LLC—Series A. Peter Kolchinsky, as sole member of RA Capital Management, LLC, which is the general partner of RA Capital Healthcare Fund, L.P. and the investment advisor of Blackwell Partners LLC—Series A, has voting and investment power over the shares held by Blackwell Partners LLC—Series A and RA Capital Healthcare Fund, L.P. RA Capital Management, LLC and Dr. Kolchinsky may be deemed to have shared voting and dispositive power over the shares directly owned by RA Capital Healthcare Fund, L.P. and Blackwell Partners, LLC—Series A. Dr. Kolchinsky and RA Capital Management, LLC disclaim beneficial ownership over all shares held by Blackwell Partners LLC—Series A and RA Capital Healthcare Fund, LP, except to the extent of any pecuniary interest in such shares. The notice address for RA Capital Healthcare Fund, L.P. is 20 Park Plaza, Suite 1200, Boston, MA 02116. The notice address for Blackwell Partners LLC—Series A is 280 S. Mangum Street, Suite 210, Durham, NC 27701.

(7) Includes 1,215,805 shares of common stock and 41,792 shares of common stock underlying options held by Dr. Struthers that are exercisable as of June 30, 2018 or that will become exercisable within 60 days after such date.

(8) Includes 37,613 shares of common stock underlying options held by Dr. Freeman that are exercisable as of June 30, 2018 or that will become exercisable within 60 days after such date.

(9) Includes 12,536 shares of common stock and 46,226 shares of common stock underlying options held by Mr. Fust that are exercisable as of June 30, 2018 or that will become exercisable within 60 days after such date.

(10) Includes 52,810 shares of common stock underlying options held by Dr. Kaldor that are exercisable as of June 30, 2018 or that will become exercisable within 60 days after such date.

(11) Includes 74,517 shares of common stock, including 16,622 shares of common stock subject to repurchase by us, and 6,332 shares of common stock underlying options held by Dr. Wierenga that are exercisable as of June 30, 2018 or that will become exercisable within 60 days after such date.

(12) Consists of shares of common stock and shares of common stock issuable upon exercise of outstanding options which are exercisable as of June 30, 2018 or that will become exercisable within 60 days after such date, as set forth in previous footnotes. Also includes 55,851 shares of common stock subject to repurchase by us and 61,550 shares of common stock underlying options that are exercisable as of June 30, 2018 or that will become exercisable within 60 days after such date, in each case, held by Marc Wilson, our Chief Financial Officer.

Description of capital stock

General

The following description summarizes some of the terms of our amended and restated certificate of incorporation and amended and restated bylaws, the amended and restated investor rights agreement and of the Delaware General Corporation Law. Because it is only a summary, it does not contain all the information that may be important to you. For a complete description you should refer to our amended and restated certificate of incorporation, amended and restated bylaws, and amended and restated investor rights agreement, copies of which have been filed or incorporated by reference as exhibits to the registration statement of which the prospectus is a part, as well as the relevant provisions of the Delaware General Corporation Law.

Following the closing of this offering, our authorized capital stock will consist of 200,000,000 shares of common stock, $0.001 par value per share, and 10,000,000 shares of preferred stock, $0.001 par value per share.

Common stock

As of March 31, 2018, there were 17,007,961 shares of our common stock outstanding and held of record by 27 stockholders, assuming the automatic conversion of all outstanding shares of our convertible preferred stock into shares of common stock, which will automatically occur immediately prior to the closing of this offering. 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. See below under “—Anti-takeover effects of Delaware law and our certificate of incorporation and bylaws—Amendment of charter provisions.”

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.

Preferred stock

Upon completion of this offering, all of our previously outstanding shares of convertible preferred stock will have been converted into common stock, there will be no authorized shares of our previously convertible preferred stock and we will have no shares of preferred stock outstanding. Under the terms of our amended and restated certificate of incorporation, which will become effective immediately prior to the closing of this offering, 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 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.

Options

As of March 31, 2018, options to purchase 1,457,952 shares of our common stock were outstanding, of which 377,520 were vested and 564,826 were exercisable as of that date. For additional information regarding the terms of this plan, see “Executive compensation—Incentive award plans—2015 Stock Option Plan.”

Registration rights

As of March 31, 2018, upon the closing of this offering holders of 14,712,571 shares of our common stock, which includes all of the shares of common stock issuable upon the automatic conversion of our convertible preferred stock immediately prior to the closing of this offering, will be entitled to the following rights with respect to the registration of such shares for public resale under the Securities Act, pursuant to the amended and restated investor rights agreement by and among us and certain of our stockholders. The registration of shares of common stock as a result of the following rights being exercised would enable holders to trade these shares without restriction under the Securities Act when the applicable registration statement is declared effective.

Demand registration rights

Form S-1. If at any time beginning six months following the effective date of the registration statement of which this prospectus forms a part, the holders of at least 30% of the registrable securities request in writing that we effect a registration with respect to their shares in an offering, we may be required to register their shares. We are obligated to effect at most two registrations for the holders of registrable securities in response to these demand registration rights, subject to certain exceptions.

Form S-3. If at any time we become entitled under the Securities Act to register our shares on Form S-3, the holders of at least 30% of the registrable securities request in writing that we register their shares for public resale on Form S-3 and the price to the public of the offering is $2.0 million or more, we will be required to provide notice to all holders of registrable securities and to use all reasonable efforts to effect such registration; provided, however, that we will not be required to effect such a registration if, within the preceding 12 months, we have already effected two registrations on Form S-3 for the holders of registrable securities.

In the case of an S-1 registration, if the holders requesting registration intend to distribute their shares by means of an underwriting, the underwriter of such offering will have the right to limit the numbers of shares to be underwritten for reasons related to the marketing of the shares.

Piggyback registration rights

If at any time following the closing of this offering we propose to register any shares of our common stock under the Securities Act, subject to certain exceptions, the holders of registrable securities will be entitled to notice of the registration and to include their shares of registrable securities in the registration. If our proposed registration involves an underwriting, the managing underwriter of such offering will have the right to limit the number of shares to be underwritten for reasons related to the marketing of the shares.

Indemnification

Our investor rights agreement contains customary cross indemnification provisions, under which we are obligated to indemnify holders of registrable securities in the event of material misstatements or omissions in the registration statement attributable to us, and they are obligated to indemnify us for material misstatements or omissions attributable to them.

Expenses

Ordinarily, other than underwriting discounts and commissions, we will be required to pay all expenses incurred by us related to any registration effected pursuant to the exercise of these registration rights. These expenses may include all registration and filing fees, printing expenses, fees and disbursements of our counsel, reasonable fees and disbursements of a counsel for the selling securityholders, blue sky fees and expenses and the expenses of any special audits incident to the registration.

Termination of registration rights

The registration rights terminate upon the earlier of three years after the closing of this offering or upon the closing of an acquisition of our company.

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, 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.

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

Our board of directors is divided into three classes. The directors in each class will serve for a three-year term (other than the directors initially assigned to Class I whose term shall expire at our first annual meeting of stockholders), one class being elected each year by our stockholders. For more information on the classified board, see “Management—Board composition and election of directors.” 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. Our 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 provision contained in our restated certificate of incorporation is inapplicable or unenforceable if it is 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 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.

Transfer agent and registrar

The transfer agent and registrar for our common stock is Computershare Trust Company, N.A. The transfer agent and registrar's address is 250 Royall Street, Canton, Massachusetts 02021.

The Nasdaq Global Select Market Listing

Our common stock has been approved for listing on the Nasdaq Global Select Market under the symbol "CRNX."

Limitations of liability and indemnification matters

For a discussion of liability and indemnification, see "Executive and director compensation—Limitations of liability and indemnification matters."

Shares eligible for future sale

Immediately prior to this offering, there was no public market for our common stock. Future sales of substantial amounts of common stock in the public market, or the perception that such sales may occur, could adversely affect the market price of our common stock. Although our common stock has been approved for listing on the Nasdaq Global Select Market, we cannot assure you that there will be an active public market for our common stock.

Based on the number of shares of our common stock outstanding as of March 31, 2018, and assuming (1) the issuance of 6,000,000 shares in this offering, (2) the automatic conversion of all outstanding shares of our convertible preferred stock into 14,712,571 shares of our common stock, which will occur automatically immediately prior to the closing of the offering, (3) no exercise of the underwriters' option to purchase additional shares of common stock and (4) no exercise of outstanding options, we will have outstanding an aggregate of approximately 23,007,961 shares of common stock.

Of these shares, all shares sold in this offering will be freely tradable without restriction or further registration under the Securities Act, except for any shares purchased by our "affiliates," as that term is defined in Rule 144 under the Securities Act, and shares purchased in this offering by participants in our directed share program, who have signed lock-up agreements or are otherwise restricted from reselling such shares by Rule 144 of the Securities Act. Shares purchased by our affiliates would be subject to the Rule 144 resale restrictions described below, other than the holding period requirement.

The remaining 17,007,961 shares of common stock will be "restricted securities," as that term is defined in Rule 144 under the Securities Act. These restricted securities are eligible for public sale only if they are registered under the Securities Act or if they qualify for an exemption from registration under Rule 144 or 701 under the Securities Act, each of which is summarized below. We expect that substantially all of these shares will be subject to the 180-day lock-up period under the lock-up agreements described below.

In addition, of the 1,457,952 shares of our common stock that were subject to stock options outstanding as of March 31, 2018, options to purchase 377,520 of such shares of common stock were vested as of such date and, upon exercise, these shares will be eligible for sale subject to the lock–up agreements described below and Rules 144 and 701 under the Securities Act.

Lock-up agreements

We, along with our directors, executive officers and substantially all of our other stockholders and optionholders, have agreed with the underwriters that for a period of 180 days, after the date of this prospectus, subject to specified exceptions, we or they will not 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 sale of, or otherwise dispose of or transfer any shares of common stock or any securities convertible into or exercisable or exchangeable for shares of common stock, request or demand that we file a registration statement related to our common stock or enter into any swap or other agreement that transfers to another, in whole or in part, directly or indirectly, the economic consequence of ownership of the common stock. Upon expiration of the lock-up period, certain of our stockholders will have the right to require us to register their shares under the Securities Act. See "—Registration rights" below and "Description of capital stock—Registration rights."

J.P. Morgan Securities LLC, Leerink Partners LLC and Piper Jaffray & Co. may, in their sole discretion and at any time or from time to time before the termination of the lock-up period, in certain cases without public notice, release all or any portion of the securities subject to lock-up agreements. There are no existing agreements

between the underwriters and any of our stockholders who will execute a lock-up agreement providing consent to the sale of shares prior to the expiration of the lock-up period.

Upon the expiration of the lock-up period, substantially all of the shares subject to such lock-up restrictions will become eligible for sale, subject to the limitations discussed above.

Rule 10b5-1 trading plans

Following the completion of this offering, certain of our officers, directors and significant stockholders may adopt written plans, known as Rule 10b5-1 trading plans, in which they will contract with a broker to buy or sell shares of our common stock on a periodic basis to diversify their assets and investments. Under these 10b5-1 trading plans, a broker may execute trades pursuant to parameters established by the officer, director or stockholder when entering into the plan, without further direction from such officer, director or stockholder. Such sales would not commence until the expiration of the applicable lock-up agreements entered into by such officer, director or stockholder in connection with this offering.

Rule 144

Affiliate resales of restricted securities

In general, beginning 90 days after the effective date of the registration statement of which this prospectus is a part, a person who is an affiliate of ours, or who was an affiliate at any time during the 90 days before a sale, who has beneficially owned shares of our common stock for at least six months would be entitled to sell in “broker’s transactions” or certain “riskless principal transactions” or to market makers, a number of shares within any three-month period that does not exceed the greater of:

- 1% of the number of shares of our common stock then outstanding, which will equal approximately 230,079 shares immediately after this offering; or
- the average weekly trading volume in our common stock on the Nasdaq Global Select Market during the four calendar weeks preceding the filing of a notice on Form 144 with respect to such sale.

Affiliate resales under Rule 144 are also subject to the availability of current public information about us. In addition, if the number of shares being sold under Rule 144 by an affiliate during any three-month period exceeds 5,000 shares or has an aggregate sale price in excess of $50,000, the seller must file a notice on Form 144 with the SEC and the Nasdaq Global Select Market concurrently with either the placing of a sale order with the broker or the execution of a sale directly with a market maker.

Non-affiliate resales of restricted securities

In general, beginning 90 days after the effective date of the registration statement of which this prospectus is a part, a person who is not an affiliate of ours at the time of sale, and has not been an affiliate at any time during the three months preceding a sale, and who has beneficially owned shares of our common stock for at least six months but less than a year, is entitled to sell such shares subject only to the availability of current public information about us. If such person has held our shares for at least one year, such person can resell under Rule 144(b)(1) without regard to any Rule 144 restrictions, including the 90-day public company requirement and the current public information requirement.

Non-affiliate resales are not subject to the manner of sale, volume limitation or notice filing provisions of Rule 144.

Rule 701

In general, under Rule 701, any of an issuer's employees, directors, officers, consultants or advisors who purchases shares from the issuer in connection with a compensatory stock or option plan or other written agreement before the effective date of a registration statement under the Securities Act is entitled to sell such shares 90 days after such effective date in reliance on Rule 144. An affiliate of the issuer can resell shares in reliance on Rule 144 without having to comply with the holding period requirement, and non-affiliates of the issuer can resell shares in reliance on Rule 144 without having to comply with the current public information and holding period requirements.

Equity plans

We intend to file one or more registration statements on Form S-8 under the Securities Act to register all shares of common stock subject to outstanding stock options and common stock issued or issuable under our equity incentive plans and employee stock purchase plan. We expect to file the registration statement covering shares offered pursuant to these stock plans shortly after the date of this prospectus, permitting the resale of such shares by non-affiliates in the public market without restriction under the Securities Act and the sale by affiliates in the public market subject to compliance with the resale provisions of Rule 144.

Registration rights

As of March 31, 2018, upon the closing of this offering holders of 14,712,571 shares of our common stock, which includes all of the shares of common stock issuable upon the automatic conversion of our convertible preferred stock immediately prior to the closing of this offering, or their transferees will be entitled to various rights with respect to the registration of these shares under the Securities Act upon the closing of this offering. Registration of these shares under the Securities Act would result in these shares becoming fully tradable without restriction under the Securities Act immediately upon the effectiveness of the registration, except for shares purchased by affiliates. See "Description of capital stock—Registration rights" for additional information. Shares covered by a registration statement will be eligible for sale in the public market upon the expiration or release from the terms of the lock-up agreement.

Material U.S. federal income tax consequences to Non-U.S. Holders

The following discussion is a summary of the material U.S. federal income tax consequences to Non-U.S. Holders (as defined below) of the purchase, ownership and disposition of our common stock issued pursuant to this offering, but does not purport to be a complete analysis of all potential tax effects. The effects of other U.S. federal tax laws, such as estate and gift tax laws, and any applicable state, local or non-U.S. tax laws are not discussed. This discussion is based on the U.S. Internal Revenue Code of 1986, as amended, or the Code, Treasury Regulations promulgated thereunder, judicial decisions, and published rulings and administrative pronouncements of the U.S. Internal Revenue Service, or the IRS, in each case in effect as of the date hereof. These authorities may change or be subject to differing interpretations. Any such change or differing interpretation may be applied retroactively in a manner that could adversely affect a Non-U.S. Holder of our common stock. We have not sought and will not seek any rulings from the IRS regarding the matters discussed below. There can be no assurance the IRS or a court will not take a contrary position to that discussed below regarding the tax consequences of the purchase, ownership and disposition of our common stock.

This discussion is limited to Non-U.S. Holders that hold our common stock as a "capital asset" within the meaning of Section 1221 of the Code (generally, property held for investment). This discussion does not address all U.S. federal income tax consequences relevant to a Non-U.S. Holder's particular circumstances, including the impact of the alternative minimum tax or the Medicare contribution tax on net investment income. In addition, it does not address consequences relevant to Non-U.S. Holders subject to special rules, including, without limitation:

- U.S. expatriates and former citizens or long-term residents of the United States;
- persons holding our common stock as part of a hedge, straddle or other risk reduction strategy or as part of a conversion transaction or other integrated investment;
- banks, insurance companies, and other financial institutions;
- brokers, dealers or traders in securities;
- "controlled foreign corporations," "passive foreign investment companies," and corporations that accumulate earnings to avoid U.S. federal income tax;
- partnerships or other entities or arrangements treated as partnerships for U.S. federal income tax purposes (and investors therein);
- tax-exempt organizations or governmental organizations;
- persons deemed to sell our common stock under the constructive sale provisions of the Code;
- persons who hold or receive our common stock pursuant to the exercise of any employee stock option or otherwise as compensation;
- persons subject to special tax accounting rules as a result of any item of gross income with respect to our common stock being taken into account in an "applicable financial statement" (as defined in the Code);
- tax-qualified retirement plans; and
- "qualified foreign pension funds" as defined in Section 897(l)(2) of the Code and entities all of the interests of which are held by qualified foreign pension funds.

If an entity treated as a partnership for U.S. federal income tax purposes holds our common stock, the tax treatment of a partner in the partnership will depend on the status of the partner, the activities of the

partnership and certain determinations made at the partner level. Accordingly, partnerships holding our common stock and the partners in such partnerships should consult their tax advisors regarding the U.S. federal income tax consequences to them.

THIS DISCUSSION IS FOR INFORMATION PURPOSES ONLY AND IS NOT TAX ADVICE. INVESTORS SHOULD CONSULT THEIR TAX ADVISORS WITH RESPECT TO THE APPLICATION OF THE U.S. FEDERAL INCOME TAX LAWS TO THEIR PARTICULAR SITUATIONS AS WELL AS ANY TAX CONSEQUENCES OF THE PURCHASE, OWNERSHIP AND DISPOSITION OF OUR COMMON STOCK ARISING UNDER THE U.S. FEDERAL ESTATE OR GIFT TAX LAWS OR UNDER THE LAWS OF ANY STATE, LOCAL OR NON-U.S. TAXING JURISDICTION OR UNDER ANY APPLICABLE INCOME TAX TREATY.

Definition of a Non-U.S. Holder

For purposes of this discussion, a “Non-U.S. Holder” is any beneficial owner of our common stock that is neither a “U.S. person” nor an entity treated as a partnership for U.S. federal income tax purposes. A U.S. person is any person that, for U.S. federal income tax purposes, is or is treated as any of the following:

- an individual who is a citizen or resident of the United States;
- a corporation created or organized under the laws of the United States, any state thereof, or the District of Columbia;
- an estate, the income of which is subject to U.S. federal income tax regardless of its source; or
- a trust that (1) is subject to the primary supervision of a U.S. court and the control of one or more “United States persons” (within the meaning of Section 7701(a)(30) of the Code), or (2) has a valid election in effect to be treated as a United States person for U.S. federal income tax purposes.

Distributions

As described in the section entitled “Dividend policy,” we do not anticipate declaring or paying dividends to holders of our common stock in the foreseeable future. However, if we do make distributions of cash or property on our common stock, such distributions will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. Amounts not treated as dividends for U.S. federal income tax purposes will constitute a return of capital and first be applied against and reduce a Non-U.S. Holder’s adjusted tax basis in its common stock, but not below zero. Any excess will be treated as capital gain and will be treated as described below under “—Sale or other taxable disposition.”

Subject to the discussion below on effectively connected income, dividends paid to a Non-U.S. Holder of our common stock will be subject to U.S. federal withholding tax at a rate of 30% of the gross amount of the dividends (or such lower rate specified by an applicable income tax treaty, provided the Non-U.S. Holder furnishes a valid IRS Form W-8BEN or W-8BEN-E (or other applicable documentation) certifying qualification for the lower treaty rate). If a Non-U.S. Holder holds the stock through a financial institution or other agent acting on the Non-U.S. Holder’s behalf, the Non-U.S. Holder will be required to provide appropriate documentation to the agent, who then will be required to provide certification to the applicable withholding agent, either directly or through other intermediaries. A Non-U.S. Holder that does not timely furnish the required documentation, but that qualifies for a reduced treaty rate, may obtain a refund of any excess amounts withheld by timely filing an appropriate claim for refund with the IRS. Non-U.S. Holders should consult their tax advisors regarding their entitlement to benefits under any applicable income tax treaty.

If dividends paid to a Non-U.S. Holder are effectively connected with the Non-U.S. Holder's conduct of a trade or business within the United States (and, if required by an applicable income tax treaty, the Non-U.S. Holder maintains a permanent establishment in the United States to which such dividends are attributable), the Non-U.S. Holder will be exempt from the U.S. federal withholding tax described above. To claim the exemption, the Non-U.S. Holder must furnish to the applicable withholding agent a valid IRS Form W-8ECI, certifying that the dividends are effectively connected with the Non-U.S. Holder's conduct of a trade or business within the United States.

Any such effectively connected dividends will be subject to U.S. federal income tax on a net income basis at the regular graduated rates. A Non-U.S. Holder that is a corporation also may be subject to a branch profits tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty) on such effectively connected dividends, as adjusted for certain items. Non-U.S. Holders should consult their tax advisors regarding any applicable tax treaties that may provide for different rules.

Sale or other taxable disposition

A Non-U.S. Holder will not be subject to U.S. federal income tax on any gain realized upon the sale or other taxable disposition of our common stock unless:

- the gain is effectively connected with the Non-U.S. Holder's conduct of a trade or business within the United States (and, if required by an applicable income tax treaty, the Non-U.S. Holder maintains a permanent establishment in the United States to which such gain is attributable);
- the Non-U.S. Holder is a nonresident alien individual present in the United States for 183 days or more during the taxable year of the disposition and certain other requirements are met; or
- our common stock constitutes a U.S. real property interest, or USRPI, by reason of our status as a U.S. real property holding corporation, or USRPHC, for U.S. federal income tax purposes.

Gain described in the first bullet point above generally will be subject to U.S. federal income tax on a net income basis at the regular graduated rates. A Non-U.S. Holder that is a corporation also may be subject to a branch profits tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty) on such effectively connected gain, as adjusted for certain items.

Gain described in the second bullet point above will be subject to U.S. federal income tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty), which may be offset by U.S. source capital losses of the Non-U.S. Holder (even though the Non-U.S. Holder is not considered a resident of the United States), provided the Non-U.S. Holder has timely filed U.S. federal income tax returns with respect to such losses.

With respect to the third bullet point above, we believe we currently are not, and do not anticipate becoming, a USRPHC. Because the determination of whether we are a USRPHC depends, however, on the fair market value of our USRPIs relative to the fair market value of our non-U.S. real property interests and our other business assets, there can be no assurance we currently are not a USRPHC or will not become one in the future. Even if we are or were to become a USRPHC, gain arising from the sale or other taxable disposition by a Non-U.S. Holder of our common stock will not be subject to U.S. federal income tax if our common stock is "regularly traded," as defined by applicable Treasury Regulations, on an established securities market, and such Non-U.S. Holder owned, actually or constructively, 5% or less of our common stock throughout the shorter of the five-year period ending on the date of the sale or other taxable disposition or the Non-U.S. Holder's holding period.

Non-U.S. Holders should consult their tax advisors regarding potentially applicable income tax treaties that may provide for different rules.

Information reporting and backup withholding

Payments of dividends on our common stock will not be subject to backup withholding, provided the applicable withholding agent does not have actual knowledge or reason to know the holder is a United States person and the holder either certifies its non-U.S. status, such as by furnishing a valid IRS Form W-8BEN, W-8BEN-E or W-8ECI, or otherwise establishes an exemption. However, information returns are required to be filed with the IRS in connection with any dividends on our common stock paid to the Non-U.S. Holder, regardless of whether any tax was actually withheld. In addition, proceeds of the sale or other taxable disposition of our common stock within the United States or conducted through certain U.S.-related brokers generally will not be subject to backup withholding or information reporting, if the applicable withholding agent receives the certification described above and does not have actual knowledge or reason to know that such holder is a United States person, or the holder otherwise establishes an exemption. Proceeds of a disposition of our common stock conducted through a non-U.S. office of a non-U.S. broker generally will not be subject to backup withholding or information reporting.

Copies of information returns that are filed with the IRS may also be made available under the provisions of an applicable treaty or agreement to the tax authorities of the country in which the Non-U.S. Holder resides or is established.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules may be allowed as a refund or a credit against a Non-U.S. Holder's U.S. federal income tax liability, provided the required information is timely furnished to the IRS.

Additional withholding tax on payments made to foreign accounts

Withholding taxes may be imposed under Sections 1471 to 1474 of the Code (such Sections are commonly referred to as the Foreign Account Tax Compliance Act, or FATCA) on certain types of payments made to non-U.S. financial institutions and certain other non-U.S. entities. Specifically, a 30% withholding tax may be imposed on dividends on, or gross proceeds from the sale or other disposition of, our common stock paid to a "foreign financial institution" or a "non-financial foreign entity" (each as defined in the Code), unless (1) the foreign financial institution undertakes certain diligence and reporting obligations, (2) the non-financial foreign entity either certifies it does not have any "substantial United States owners" (as defined in the Code) or furnishes identifying information regarding each substantial United States owner, or (3) the foreign financial institution or non-financial foreign entity otherwise qualifies for an exemption from these rules. If the payee is a foreign financial institution and is subject to the diligence and reporting requirements in (1) above, it must enter into an agreement with the U.S. Department of the Treasury requiring, among other things, that it undertake to identify accounts held by certain "specified United States persons" or "United States-owned foreign entities" (each as defined in the Code), annually report certain information about such accounts, and withhold 30% on certain payments to non-compliant foreign financial institutions and certain other account holders. Foreign financial institutions located in jurisdictions that have an intergovernmental agreement with the United States governing FATCA may be subject to different rules.

Under the applicable Treasury Regulations and administrative guidance, withholding under FATCA generally applies to payments of dividends on our common stock and will apply to payments of gross proceeds from the sale or other disposition of such stock on or after January 1, 2019.

Prospective investors should consult their tax advisors regarding the potential application of withholding under FATCA to their investment in our common stock.

Underwriting

We are offering the shares of common stock described in this prospectus through a number of underwriters. J.P. Morgan Securities LLC, Leerink Partners LLC and Piper Jaffray & 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, 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	2,850,000
Leerink Partners LLC	1,800,000
Piper Jaffray & Co.	1,350,000
Total	6,000,000

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 initial public offering price set forth on the cover page of this prospectus and to certain dealers at that price less a concession not in excess of $0.714 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 initial public offering price, the underwriters may change the offering price and the other selling terms. Sales of shares made outside of the United States may be made by affiliates of the underwriters.

The underwriters have an option to buy up to 900,000 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 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.

Certain of our principal stockholders, including entities affiliated with certain of our directors, have indicated an interest in purchasing an aggregate of approximately $30.0 million in shares of our common stock in this offering at the initial public offering price. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters may determine to sell more, less or no shares in this offering to any or all of these stockholders, and any or all of these stockholders may determine to purchase more, less or no shares in this offering. The underwriters will receive the same underwriting discount on any shares purchased by these stockholders as they will on any other shares sold to the public in this offering.

At our request, the underwriters have reserved for sale, at the initial public offering price, up to 2% of the shares offered hereby for employees, directors and other persons associated with us who have expressed an interest in purchasing common stock in the offering. Our officers and directors who are participating in this program have agreed that any shares purchased through this program will be subject to a 180-day lock-up restriction. The number of shares available for sale to the general public in the offering will be reduced to the

extent these persons purchase the reserved shares. Any reserved shares not so purchased will be offered by the underwriters to the general public on the same terms as the other shares.

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 $1.19 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 option to purchase additional shares exercise	With full option to purchase additional shares exercise
Per Share	$ 1.19	$ 1.19
Total	$ 7,140,000	$ 8,211,000

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 $2.8 million. 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 $35,000.

A 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 (1) offer, pledge, announce the intention to sell, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase or otherwise dispose of, directly or indirectly, or file with the SEC a registration statement under the Securities Act relating to, any shares of our common stock or securities convertible into or exchangeable or exercisable for any shares of our common stock, or publicly disclose the intention to make any offer, sale, pledge, disposition or filing, or (2) enter into any swap or other arrangement that transfers all or a portion of the economic consequences associated with the ownership of any shares of common stock or any such other securities (regardless of whether any of these transactions are to be settled by the delivery of shares of common stock or such other securities, in cash or otherwise), in each case without the prior written consent of J.P. Morgan Securities LLC, Leerink Partners LLC and Piper Jaffray & Co. for a period of 180 days after the date of this prospectus, subject to certain exceptions.

Our directors and executive officers, and substantially all of our securityholders have entered into lock-up agreements with the underwriters prior to the commencement of this offering pursuant to which each of these persons or entities, with limited exceptions, for a period of 180 days after the date of this prospectus, may not, without the prior written consent of J.P. Morgan Securities LLC, Leerink Partners LLC and Piper Jaffray & Co., (1) offer, pledge, announce the intention to sell, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, 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 directors, executive officers, managers and members in accordance with the rules and regulations of the SEC and securities which may be issued upon exercise of a stock option or warrant) or (2) enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of the common stock or such other securities, whether

any such transaction described in clause (1) or (2) above is to be settled by delivery of common stock or such other securities, in cash or otherwise, or (3) make any demand for or exercise any right with respect to the registration of any shares of our common stock or any security convertible into or exercisable or exchangeable for our common stock.

The restrictions described in the immediately preceding paragraph do not apply to, among other items:

(1) the securities to be sold by the securityholder pursuant to the underwriting agreement;

(2) transfers of shares of common stock as a bona fide gift or gifts;

(3) distributions of shares of common stock to limited or general partners, members or stockholders of the securityholder;

(4) transfers to an immediate family member or trust for the direct or indirect benefit of the securityholder or an immediate family member;

(5) transfers to any corporation, partnership, limited liability company or other entity all of the beneficial ownership interests of which are held by the securityholder;

(6) transfers by will, other testamentary document or intestate succession to the legal representative, heir, beneficiary or a member of the immediate family of the securityholder;

(7) transfers pursuant to a court or regulatory agency order, a qualified domestic order or in connection with a divorce settlement;

(8) transfers to us in connection with the “net” or “cashless” exercise of options or other rights to purchase shares of common stock granted pursuant to an equity incentive plan, stock purchase plan or other arrangement described in this prospectus in satisfaction of any tax withholding obligations through cashless surrender or otherwise, provided, that, any shares of common stock issued upon exercise of such option or other rights shall continue to be subject to the restrictions set forth herein until the expiration of the restricted period;

(9) if the securityholder is an investment company registered under the Investment Company Act of 1940, as amended, 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;

(10) transfers to any affiliate (as defined in Rule 405 promulgated under the Securities Act) of the securityholder or any investment fund or other entity controlled or managed by the securityholder or under common management or control with the securityholder;

(11) in connection with the conversion of our outstanding shares of preferred stock into common stock as described in this prospectus, or any reclassification or conversion of the common stock, provided that any common stock received upon such conversion or reclassification will be subject to the lockup agreement;

(12) a transfer of securities to us in connection with any contractual arrangement in effect on the date of this prospectus that provides for the repurchase of the securityholder’s shares by us in connection with the termination of the securityholder’s employment or other services with us is permitted, provided that no filing under Section 16 of the Exchange Act or other public filing, report or announcement reporting a reduction in beneficial ownership of shares of common stock shall be required or shall be voluntarily made during the restricted period within 60 days after the date the securityholder ceases to provide services to us, and after such 60th day, if the securityholder is required to file a report under Section 16 of the Exchange Act reporting a

reduction in beneficial ownership of shares of common stock during the restricted period, the securityholder shall clearly indicate in the footnotes thereto that the filing relates to the termination of the securityholder's employment or other services;

(13) a transfer of securities pursuant to a *bona fide* third-party tender offer, merger, consolidation or other similar transaction made to all holders of our securities involving a change of control of our company, in each case that is approved by the independent members of our board of directors, provided that in the event that such tender offer, merger, consolidation or other such transaction is not completed, such securities held by the securityholder shall remain subject to the lockup agreement;

(14) the establishment of a 10b5-1 trading plan that complies with Rule 10b5-1 under the Exchange Act, provided that (A) there are no sales of securities under such plan during the restricted period, (B) the establishment of such plan is not required to be reported in any public report or filing with the SEC, or otherwise, and (C) the securityholder does not otherwise voluntarily effect any public filing or report or any public announcement regarding the establishment of such plan; and

(15) the sale of securities purchased by the securityholder in this offering or in the open market following the date of this prospectus if and only if (A) such securities are not required to be reported in any public report or filing with the SEC, or otherwise and (B) the securityholder does not otherwise voluntarily effect any public filing or report regarding such sales,

provided that, in the case of any transfer or distribution pursuant to clauses (2), (3), (4), (5), (6), (7), (9) or (10), each transferee, donee or distributee shall execute and deliver to the representatives a lock-up; provided, further, that in the case of any transfer or distribution pursuant to clauses (3), (4), (5), (6), (7) and (10), such transfer shall not involve a disposition for value; and provided, further, that in the case of any transfer or distribution pursuant to clauses (2) through (10), no filing by any party (donor, donee, transferor or transferee) under the Exchange Act, or other public announcement shall be required or shall be made voluntarily in connection with such transfer or distribution (other than a filing on a Form 5 made after the expiration of the restricted period referred to above). If the securityholder is an officer or director of our company, the securityholder further agrees that the foregoing provisions shall be equally applicable to any issuer-directed securities the securityholder may purchase in this offering.

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

Our common stock has been approved for listing 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 the 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 the Nasdaq Global Select Market, in the over-the-counter market or otherwise.

Prior to this offering, there has been no public market for our common stock. The initial public offering price was determined by negotiations between us and the representatives of the underwriters. In determining the initial public offering price, we and the representatives of the underwriters considered a number of factors including:

- the information set forth in this prospectus and otherwise available to the representatives;
- our prospects and the history and prospects for the industry in which we compete;
- an assessment of our management;
- our prospects for future earnings;
- the general condition of the securities markets at the time of this offering;
- the recent market prices of, and demand for, publicly traded common stock of generally comparable companies; and
- other factors deemed relevant by the underwriters and us.

Neither we nor the underwriters can assure investors that an active trading market will develop for our common shares, or that the shares will trade in the public market at or above the initial public offering price.

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.

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 in any jurisdiction where action for that purpose is required.

The securities offered by this prospectus may not be offered or sold, directly or indirectly, nor may this 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 comes are advised to inform themselves about and to observe any restrictions relating to the offering and the distribution of this prospectus. This prospectus does not constitute an offer to sell or a solicitation of an offer to buy any securities offered by this 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 which has implemented the Prospectus Directive (each, a "Relevant Member State"), with effect from and including the date on which the Prospectus Directive is implemented in that Relevant Member State, no offer of shares may be made to the public in that Relevant Member State other than:

a) to any legal entity which is a qualified investor as defined in the Prospectus Directive;

b) to fewer than 150 natural or legal persons (other than qualified investors as defined in the Prospectus Directive), subject to obtaining the prior consent of the underwriters; or

c) in any other circumstances falling within Article 3(2) of the Prospectus Directive,

provided that no such offer of shares shall require the Company or any underwriter to publish a prospectus pursuant to Article 3 of the Prospectus Directive or supplement a prospectus pursuant to Article 16 of the Prospectus Directive and each person who initially acquires any shares 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 the law in that Relevant Member State implementing Article 2(1)(e) of the Prospectus Directive.

In the case of any shares being offered to a financial intermediary as that term is used in Article 3(2) of the Prospectus Directive, each such financial intermediary will be deemed to have represented, acknowledged and agreed that the shares 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 to the public other than their offer or resale in a Relevant Member State to qualified investors as so defined or in circumstances in which the prior consent of the representatives has been obtained to each such proposed offer or resale.

For the purposes of this provision, the expression an "offer of shares to the public" in relation to any shares in any Relevant Member State means the communication in any form and by means of sufficient information on the terms of the offer and the shares to be offered so as to enable an investor to decide to purchase shares, as the same may be varied in that Member State by any measure implementing the Prospectus Directive in that Member State, the expression "Prospectus Directive" means Directive 2003/71/EC (as amended, including by Directive 2010/73/EU), and includes any relevant implementing measure in the Relevant Member State.

Notice to prospective investors in the United Kingdom

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 Directive) (1) 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 (the

"Order") and/or (2) 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 may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 Prospectus Exemptions or subsection 73.3(1) of the Securities Act (Ontario), and are permitted clients, as defined in National Instrument 31-103 Registration Requirements, Exemptions and Ongoing Registrant Obligations. Any resale of the shares must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus (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 ("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 or the shares has 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 (FINMA), and the offer of shares has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes ("CISA"). 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 ("DIFC")

This document relates to an Exempt Offer in accordance with the Markets Rules 2012 of the Dubai Financial Services Authority ("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 DIFC) other than in compliance with the laws of the United Arab Emirates (and the DIFC) governing the issue, offering and sale of securities. Further, this prospectus does not constitute a public offer of securities in the United Arab Emirates (including the DIFC) and is not intended to be a public offer. This prospectus has not been approved by or filed with the Central Bank of the United Arab Emirates, the Securities and Commodities Authority or the DFSA.

Notice to prospective investors in Australia

This prospectus:

- does not constitute a product disclosure document or a prospectus under Chapter 6D.2 of the Corporations Act 2001 (Cth) (the “Corporations Act”);
- has not been, and will not be, lodged with the Australian Securities and Investments Commission (“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 under Chapter 6D.2 of the Corporations Act;
- does not constitute or involve a recommendation to acquire, an offer or invitation for issue or sale, an offer or invitation to arrange the issue or sale, or an issue or sale, of interests to a “retail client” (as defined in section 761G of the Corporations Act and applicable regulations) in Australia; 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, or Exempt Investors, available under section 708 of the Corporations Act.

The shares may not be directly or indirectly offered for subscription or purchased or sold, and no invitations to subscribe for or buy the shares may be issued, and no draft or definitive offering memorandum, advertisement or other offering material relating to any shares 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, you represent and warrant to us that you are an Exempt Investor.

As any offer of shares under this document 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 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 securities 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 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 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 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 Hong Kong and any rules made under that Ordinance; 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 which do not constitute an offer to the public within the meaning of that Ordinance. No advertisement, invitation or document relating to the shares has been or may be issued or has been or may 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 shares which are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" as defined in the Securities and Futures Ordinance and any rules made under that Ordinance.

Notice to prospective investors in Singapore

This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of 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 Singapore other than (1) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore (the "SFA"), (2) to a relevant person pursuant to Section 275(1), or any person pursuant to Section 275(1A), and in accordance with the conditions specified in Section 275 of the SFA, or (3) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

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

a) 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

b) 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 (as defined in Section 239(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 pursuant to an offer made under Section 275 of the SFA except:

i) to an institutional investor or to a relevant person defined in Section 275(2) of the SFA, 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 32 of the Securities and Futures (Offers of Investments) (Shares and Debentures) Regulations 2005 of Singapore.

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 ("CMA") pursuant to resolution number 2-11-2004 dated 4 October 2004 as amended by resolution number 1-28-2008, as amended (the "CMA Regulations"). 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 authorised 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 Company may be offered to companies incorporated under the BVI Business Companies Act, 2004 (British Virgin Islands) ("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. This prospectus has not been, and will not be, registered with the Financial Services Commission of the British Virgin Islands. No registered prospectus has been or will be prepared in respect of the shares for the purposes of the Securities and Investment Business Act, 2010 ("SIBA") or the Public Issuers Code of the British Virgin Islands.

Notice to prospective investors in China

This prospectus does not constitute a public offer of shares, whether by sale or subscription, in the People's Republic of China (the "PRC"). The shares are not being offered or sold directly or indirectly in the PRC to or for the benefit of, legal or natural persons of the PRC.

Further, no legal or natural persons of the PRC may directly or indirectly purchase any of the shares or any beneficial interest therein without obtaining all prior PRC's governmental approvals that are required, whether statutorily or otherwise. Persons who come into possession of this document are required by the issuer and its representatives to observe these restrictions.

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 (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 (the "FETL"). 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 ("Commission") for the Commission's approval pursuant to the Capital Markets and Services Act 2007. Accordingly, this prospectus 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 (1) a closed end fund approved by the Commission; (2) a holder of a Capital Markets Services Licence; (3) 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; (4) 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; (5) an individual who has a gross annual income exceeding RM300,000 (or its equivalent in foreign currencies) per annum in the preceding twelve months; (6) 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; (7) a corporation with total net assets exceeding RM10 million (or its equivalent in a foreign currencies) based on the last audited accounts; (8) a partnership with total net assets exceeding RM10 million (or its equivalent in foreign currencies); (9) a bank licensee or insurance licensee as defined in the Labuan Financial Services and Securities Act 2010; (10) an Islamic bank licensee or takaful licensee as defined in the Labuan Financial Services and Securities Act 2010; and (11) any other person as may be specified by the Commission; provided that, in the each of the preceding categories (1) to (11), the distribution of the shares is made by a holder of a Capital Markets Services Licence who carries on the business of dealing in securities. The distribution in Malaysia of this prospectus is subject to Malaysian laws. This prospectus 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 authorised 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, 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 applies:

a) the offer, transfer, sale, renunciation or delivery is to:

i) persons 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 (c), (d) or (e), acting as agent in the capacity of an authorised portfolio manager for a pension fund or collective investment scheme (in each case duly registered as such under South African law); or

vii) any combination of the person in (i) to (vii); or

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.

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) (the “South African Companies Act”)) in South Africa is being made in connection with the issue of the shares. 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. Any issue or offering of the shares in South Africa constitutes an offer of the shares in South Africa for subscription or sale in South Africa only to persons who fall within the exemption from “offers to the public” set out in section 96(1)(a) of the South African Companies Act. Accordingly, this document must not be acted on or relied on by persons in South Africa who do not fall within section 96(1)(a) of the South African Companies Act (such persons being referred to as “SA Relevant Persons”). Any investment or investment activity to which this document relates is available in South Africa only to SA Relevant Persons and will be engaged in South Africa only with SA relevant persons.

Legal matters

The validity of the shares of common stock offered hereby will be passed upon for us by Latham & Watkins LLP, San Diego, California. The underwriters are being represented by Cooley LLP, San Diego, California.

Experts

The consolidated financial statements as of December 31, 2016 and 2017 and for each of the two years in the period ended December 31, 2017, included in this prospectus and in the registration statement have been so included in reliance on the report of BDO USA, LLP, an independent registered public accounting firm appearing elsewhere herein and in the registration statement, given on the authority of said firm as experts in auditing and accounting.

Where you can find more information

We have filed with the SEC a registration statement on Form S-1 under the Securities Act with respect to the shares of common stock offered hereby. This prospectus, which constitutes a part of the registration statement, does not contain all of the information set forth in the registration statement or the exhibits and schedules filed therewith. For further information about us and the common stock offered hereby, we refer you to the registration statement and the exhibits and schedules filed thereto. Statements contained in this prospectus regarding the contents of any contract or any other document that is filed as an exhibit to the registration statement are not necessarily complete, and each such statement is qualified in all respects by reference to the full text of such contract or other document filed as an exhibit to the registration statement. Upon the closing of this offering, we will be required to file periodic reports, proxy statements and other information with the SEC pursuant to the Exchange Act. You may read and copy this information at the Public Reference Room of the SEC, 100 F Street, N.E., Room 1580, Washington, D.C. 20549. You may obtain information on the operation of the public reference rooms by calling the SEC at 1-800-SEC-0330. The SEC also maintains an Internet website that contains reports, proxy statements and other information about registrants, like us, that file electronically with the SEC. The address of that site is *www.sec.gov*.

Upon the completion of this offering, we will become subject to the information and periodic reporting requirements of the Exchange Act and, in accordance therewith, will file periodic reports, proxy statements and other information with the SEC. Such periodic reports, proxy statements and other information will be available for inspection and copying at the public reference room and website of the SEC referred to above. We maintain a website at www.crinetics.com. Upon the completion of this offering, you may access our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act with the SEC free of charge at our website as soon as reasonably practicable after such material is electronically filed with, or furnished to, the SEC. The reference to our website address does not constitute incorporation by reference of the information contained on our website, and you should not consider the contents of our website in making an investment decision with respect to our common stock.

Crinetics Pharmaceuticals, Inc.

Index to Consolidated Financial Statements

Report of Independent Registered Public Accounting Firm

Board of Directors and Stockholders
Crinetics Pharmaceuticals, Inc.

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of Crinetics Pharmaceuticals, Inc. (the "Company") and subsidiary as of December 31, 2017 and 2016, the related consolidated statements of operations, convertible preferred stock and stockholders' equity (deficit), and cash flows for each of the two years in the period ended December 31, 2017, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company and subsidiaries at December 31, 2017 and 2016, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2017, in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's consolidated financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) ("PCAOB") and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ BDO USA, LLP
We have served as the Company's auditor since 2016.
San Diego, California
May 2, 2018, except for the "Reverse Stock Split" paragraph of Note 7, as to which the date is July 9, 2018

Crinetics Pharmaceuticals, Inc.

Consolidated Balance Sheets
(in thousands, except share and par value data)

	December 31, 2016	December 31, 2017	March 31, 2018 (unaudited)	Pro Forma Stockholders' Equity March 31, 2018 (unaudited)
Assets				
Current assets:				
Cash and cash equivalents	$12,152	$ 14,192	$ 73,740	
Prepaid expenses and other current assets	213	973	991	
Total current assets	12,365	15,165	74,731	
Property and equipment, net	224	400	476	
Restricted cash	–	–	500	
Other assets	10	33	622	
Total assets	$12,599	$ 15,598	$ 76,329	
Liabilities, convertible preferred stock and stockholders' equity (deficit)				
Current liabilities:				
Accounts payable	$ 340	$ 403	$ 1,335	
Accrued expenses	501	494	1,801	
Current portion of long-term debt	49	–	–	
Total current liabilities	890	897	3,136	
Long-term debt, net of current portion	163	–	–	
Deferred rent	5	20	22	
Unvested stock liability	5	3	172	
Commitments and contingencies (Note 3)				
Convertible preferred stock, $0.001 par value; authorized shares – 38,350,914 at December 31, 2016 and 2017 and 48,868,345 at March 31, 2018 (unaudited); issued and outstanding shares – 17,257,911, 28,763,179 and 48,404,379 at December 31, 2016 and 2017 and March 31, 2018 (unaudited), respectively; liquidation preference of $18,000, $30,000 and $93,500 at December 31, 2016 and 2017 and March 31, 2018 (unaudited), respectively; no shares issued and outstanding, pro forma (unaudited)	17,740	29,700	92,975	$ -
Stockholders' equity (deficit):				
Common stock, $0.001 par value; authorized shares – 50,500,000 at December 31, 2016 and 2017 and 65,000,000 at March 31, 2018 (unaudited); issued shares – 1,978,592, 2,076,171 and 2,295,390 at December 31, 2016 and 2017 and March 31, 2018 (unaudited), respectively; outstanding shares – 1,164,762, 1,549,575 and 2,191,035 at December 31, 2016 and 2017 and March 31, 2018 (unaudited), respectively; 17,007,961 shares issued and 16,903,606 shares outstanding, pro forma (unaudited)	1	1	2	17
Additional paid-in capital	903	1,242	1,751	94,711
Accumulated deficit	(7,108)	(16,265)	(21,729)	(21,729)
Total stockholders' equity (deficit)	(6,204)	(15,022)	(19,976)	$ 72,999
Total liabilities, convertible preferred stock and stockholders' equity (deficit)	$12,599	$ 15,598	$ 76,329	

See accompanying notes.

Crinetics Pharmaceuticals, Inc.

Consolidated Statements of Operations
(in thousands, except share and per share data)

	Years Ended December 31,		Three Months Ended March 31,	
	2016	2017	2017	2018
			(unaudited)	
Grant revenues	$ 589	$ 2,045	$ 45	$ 442
Operating expenses:				
Research and development	5,100	9,233	2,065	4,720
General and administrative	1,533	1,939	589	1,248
Total operating expenses	6,633	11,172	2,654	5,968
Loss from operations	(6,044)	(9,127)	(2,609)	(5,526)
Other income (expense):				
Interest income	37	26	7	64
Interest expense	(11)	(8)	(2)	–
Other expense	(1)	(48)	(2)	(2)
Total other income (expense)	25	(30)	3	62
Net loss	$ (6,019)	$ (9,157)	$ (2,606)	$ (5,464)
Net loss per share, basic and diluted	$ (5.96)	$ (6.68)	$ (2.18)	$ (2.92)
Weighted-average shares of common stock outstanding, basic and diluted	1,010,510	1,370,578	1,197,711	1,869,576
Pro forma net loss per share, basic and diluted (unaudited)		$ (1.18)		$ (0.39)
Pro forma weighted-average shares of common stock outstanding, basic and diluted (unaudited)		7,746,089		13,878,156

See accompanying notes.

Crinetics Pharmaceuticals, Inc.

Consolidated Statements of Convertible Preferred Stock and Stockholders' Equity (Deficit)
(in thousands, except share data)

	Convertible Preferred Stock		Common Stock		Additional Paid-In Capital	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount			
Balance at December 31, 2015	17,257,911	$ 17,740	876,611	$ 1	$ 625	$ (1,089)	$ (463)
Vesting of shares of common stock subject to repurchase	–	–	287,234	–	8	–	8
Exercise of common stock options	–	–	917	–	–	–	–
Stock-based compensation expense	–	–	–	–	270	–	270
Net loss	–	–	–	–	–	(6,019)	(6,019)
Balance at December 31, 2016	17,257,911	17,740	1,164,762	1	903	(7,108)	(6,204)
Issuance of Series A convertible preferred stock, net of issuance costs of $40	11,505,268	11,960	–	–	–	–	–
Vesting of shares of common stock subject to repurchase	–	–	287,234	–	2	–	2
Exercise of common stock options	–	–	97,579	–	66	–	66
Stock-based compensation expense	–	–	–	–	271	–	271
Net loss	–	–	–	–	–	(9,157)	(9,157)
Balance at December 31, 2017	28,763,179	29,700	1,549,575	1	1,242	(16,265)	(15,022)
Issuance of Series B convertible preferred stock, net of issuance costs of $225 (unaudited)	19,641,200	63,275	–	–	–	–	–
Vesting of shares of common stock subject to repurchase (unaudited)	–	–	526,723	1	2	–	3
Exercise of common stock options (unaudited)	–	–	114,737	–	81	–	81
Stock-based compensation (unaudited)	–	–	–	–	426	–	426
Net loss (unaudited)	–	–	–	–	–	(5,464)	(5,464)
Balance at March 31, 2018 (unaudited)	48,404,379	$ 92,975	2,191,035	$ 2	$ 1,751	$ (21,729)	$ (19,976)

See accompanying notes.

Crinetics Pharmaceuticals, Inc.

Consolidated Statements of Cash Flows
(in thousands)

	Years Ended December 31,		Three Months Ended March 31,	
	2016	2017	2017	2018
			(unaudited)	
Cash flows from operating activities				
Net loss	$ (6,019)	$ (9,157)	$ (2,606)	$ (5,464)
Adjustments to reconcile net loss to net cash used in operating activities:				
Depreciation and amortization	92	128	27	48
Stock-based compensation	270	271	56	426
Changes in operating assets and liabilities:				
Prepaid expenses and other assets	(116)	(783)	32	(290)
Accounts payable and accrued expenses	300	47	163	1,871
Deferred rent	5	15	2	2
Net cash used in operating activities	(5,468)	(9,479)	(2,326)	(3,407)
Cash flows from investing activities				
Purchases of property and equipment	(190)	(304)	(20)	(57)
Net cash used in investing activities	(190)	(304)	(20)	(57)
Cash flows from financing activities				
Proceeds from issuance of convertible preferred stock, net of issuance costs	(5)	11,969	–	63,393
Proceeds from exercise of common stock options	–	66	63	253
Repayment of long-term debt	(48)	(212)	(12)	–
Payment of initial public offering costs	–	–	–	(134)
Net cash provided by (used in) financing activities	(53)	11,823	51	63,512
Net increase (decrease) in cash, cash equivalents and restricted cash	(5,711)	2,040	(2,295)	60,048
Cash, cash equivalents and restricted cash, beginning of period	17,863	12,152	12,152	14,192
Cash, cash equivalents and restricted cash, end of period	$12,152	$14,192	$ 9,857	$74,240
Supplemental disclosure of cash flow information				
Cash paid for interest	$ 11	$ 8	$ 2	$ –
Supplemental disclosure of non-cash investing and financing activities				
Change in unvested stock liability	$ 8	$ 2	$ –	$ (3)
Change in accrued preferred stock issuance costs and initial public offering costs	$ –	$ 9	$ –	$ 301
Change in accrued property and equipment purchases	$ –	$ –	$ –	$ 67

See accompanying notes.

Crinetics Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements
(Information as of March 31, 2018 and thereafter and for the three months ended March 31, 2017 and 2018 is unaudited)

1. Organization and Summary of Significant Accounting Policies

Description of Business

Crinetics Pharmaceuticals, Inc. (the "Company") is a clinical stage pharmaceutical company incorporated in Delaware on November 18, 2008 and based in San Diego, California. The Company is focused on the discovery, development and commercialization of novel therapeutics for rare endocrine diseases and endocrine-related tumors. In January 2017, the Company established a wholly-owned Australian subsidiary, Crinetics Australia Pty Ltd ("CAPL"), in order to conduct various preclinical and clinical activities for its development candidates.

Liquidity and Going Concern

From its inception through March 31, 2018, the Company has devoted substantially all of its efforts to drug discovery and development and conducting preclinical studies and clinical trials. The Company has a limited operating history and the sales and income potential of the Company's business and market are unproven. Successful transition to attaining profitable operations is dependent upon achieving a level of revenues adequate to support the Company's cost structure. As of December 31, 2017 and March 31, 2018, the Company had $14.2 million and $73.7 million, respectively, in cash and cash equivalents. The Company believes it has sufficient cash to meet its funding requirements for the foreseeable future. However, the Company has experienced net losses and negative cash flows from operating activities since its inception, and had an accumulated deficit of $16.3 million and $21.7 million, respectively, as of December 31, 2017 and March 31, 2018. The Company expects to continue to incur net losses into the foreseeable future and that it will need to raise substantial additional capital to accomplish its business plan over the next several years. The Company plans to continue to fund its losses from operations and capital funding needs through a combination of equity offerings, debt financings or other sources, including potentially collaborations, licenses and other similar arrangements. If the Company is not able to secure adequate additional funding, the Company may be forced to make reductions in spending, extend payment terms with suppliers, liquidate assets where possible, or suspend or curtail planned programs. Any of these actions could materially harm the Company's business, results of operations and future prospects. There can be no assurance as to the availability or terms upon which such financing and capital might be available in the future.

Principles of Consolidation and Foreign Currency Transactions

The consolidated financial statements include the accounts of the Company and CAPL. All intercompany accounts and transactions have been eliminated in consolidation. The functional currency of both the Company and CAPL is the U.S. dollar. The Company's assets and liabilities that are not denominated in the functional currency are remeasured into U.S. dollars at foreign currency exchange rates in effect at the balance sheet date except for nonmonetary assets, which are remeasured at historical foreign currency exchange rates in effect at the date of transaction. Net realized and unrealized gains and losses from foreign currency transactions and remeasurement are reported in other income (expense), in the consolidated statements of operations and were not material for all periods presented.

Use of Estimates

The Company's consolidated financial statements are prepared in accordance with accounting principles generally accepted in the United States of America ("U.S. GAAP"). The preparation of the Company's consolidated financial statements requires it to make estimates and assumptions that impact the reported amounts of assets, liabilities, revenues and expenses and the disclosure of contingent assets and liabilities in

the Company's consolidated financial statements and accompanying notes. The most significant estimates in the Company's consolidated financial statements relate to revenue recognition, accrued amounts receivable under the Australian research and development tax incentive program, accrued expenses, and the fair value of stock-based compensation. Although these estimates are based on the Company's knowledge of current events and actions it may undertake in the future, actual results may ultimately materially differ from these estimates and assumptions.

Unaudited Interim Financial Information

The accompanying interim consolidated balance sheet as of March 31, 2018, the consolidated statements of operations and cash flows for the three months ended March 31, 2017 and 2018 and the consolidated statement of convertible preferred stock and stockholders' equity (deficit) for the three months ended March 31, 2018 and the related consolidated footnote disclosures are unaudited. In management's opinion, the unaudited interim financial statements have been prepared on the same basis as the audited financial statements and include all adjustments, which include only normal recurring adjustments, necessary for the fair presentation of the Company's financial position as of March 31, 2018 and its results of operations and cash flows for the three months ended March 31, 2017 and 2018 in accordance with U.S. GAAP. The results for the three months ended March 31, 2018 are not necessarily indicative of the results expected for the full fiscal year or any other interim period.

Unaudited Pro Forma Balance Sheet Information

The unaudited pro forma balance sheet information as of March 31, 2018 assumes the conversion of all outstanding shares of convertible preferred stock into 14,712,571 shares of the Company's common stock and the related reclassification of the carrying value of the convertible preferred stock to permanent equity upon completion of the Company's planned initial public offering ("IPO"). Shares of common stock issued in the IPO and any related net proceeds are excluded from the pro forma information.

Fair Value Measurements

The accounting guidance defines fair value, establishes a consistent framework for measuring fair value and expands disclosure for each major asset and liability category measured at fair value on either a recurring or non-recurring basis. Fair value is defined as an exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. As such, fair value is a market-based measurement that should be determined based on assumptions that market participants would use in pricing an asset or liability. As a basis for considering such assumptions, the accounting guidance establishes a three-tier fair value hierarchy, which prioritizes the inputs used in measuring fair value as follows:

Level 1: Observable inputs such as quoted prices in active markets.

Level 2: Inputs, other than the quoted prices in active markets that are observable either directly or indirectly.

Level 3: Unobservable inputs in which there is little or no market data, which require the reporting entity to develop its own assumptions.

The carrying amounts of the Company's current financial assets, restricted cash and current financial liabilities are considered to be representative of their respective fair values because of the short-term nature of

those instruments. The fair value of the long-term debt as of December 31, 2016 approximates its carrying value due to the market rate of interest. As of December 31, 2016 and 2017 and March 31, 2018, the Company had no financial assets measured at fair value on a recurring basis and none of the Company's non-financial assets and liabilities were recorded at fair value on a non-recurring basis. No transfers between levels have occurred for the periods presented.

Cash, Cash Equivalents and Restricted Cash

The Company considers all highly liquid investments with maturities of three months or less when purchased to be cash equivalents. Cash and cash equivalents include cash in readily available checking accounts and a money market account.

Restricted cash represents cash held as collateral for the Company's facility lease and is reported as a long-term asset in the accompanying consolidated balance sheets. Cash, cash equivalents and restricted cash presented in the accompanying consolidated statements of cash flows consist of the following (in thousands):

	December 31,		March 31,	
	2016	2017	2017	2018
Cash and cash equivalents	$12,152	$14,192	$9,857	$73,740
Restricted cash	–	–	–	500
	$12,152	$14,192	$9,857	$74,240

Concentrations of Credit Risk

Financial instruments that potentially subject the Company to significant concentrations of credit risk consist primarily of cash and cash equivalents. The Company maintains deposits in federally insured financial institutions in excess of federally insured limits. The Company has not experienced any losses in such accounts and believes it is not exposed to significant risk on its cash balances due to the financial position of the depository institution in which those deposits are held. Additionally, the Company established guidelines regarding approved investments and maturities of investments, which are designed to maintain safety and liquidity.

Property and Equipment, Net

Property and equipment, which consist of lab equipment, computer and software and office equipment, are stated at cost and depreciated on a straight-line basis over the estimated useful life of the related assets (generally three to five years). Leasehold improvements are stated at cost and amortized on a straight-line basis over the lesser of the remaining lease term of the related lease or the estimated useful life of the leasehold improvements. Repairs and maintenance costs are charged to expense as incurred and expenditures that materially extend the useful lives of assets are capitalized.

Impairment of Long-Lived Assets

Long-lived assets consist of property and equipment. An impairment loss is recorded if and when events and circumstances indicate that assets might be impaired and the undiscounted cash flows estimated to be generated by those assets are less than the carrying amount of those assets. The Company has not recognized any impairment losses through March 31, 2018.

Crinetics Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements—(Continued)
(Information as of March 31, 2018 and thereafter and for the three months ended March 31, 2017 and 2018 is unaudited)

Deferred Rent

Rent expense is recorded on a straight-line basis over the term of the Company's facility lease. The difference between rent expense and amounts paid under the lease are recorded as deferred rent in the accompanying consolidated balance sheets.

Revenue Recognition

The Company's revenues are derived from Small Business Innovation Research ("SBIR") grants from the National Institutes of Health. The Company recognizes SBIR grant revenue as reimbursable grant costs are incurred. The costs associated with these reimbursements are reflected as a component of research and development expense in the accompanying consolidated statements of operations.

Australian Research and Development Tax Incentive

CAPL is eligible to obtain a cash refund from the Australian Taxation Office for eligible research and development expenditures under the Australian Research and Development Tax Incentive Program (the "Australian Tax Incentive"). The Australian Tax Incentive is recognized as a reduction to research and development expense when there is reasonable assurance that the Australian Tax Incentive will be received, the relevant expenditure has been incurred, and the amount can be reliably measured. As of December 31, 2017 and March 31, 2018, the Company had an Australian Tax Incentive receivable of $0.5 million and $0.8 million, respectively, and recognized reductions to research and development expense of $0.5 million and $0.3 million, respectively, for the year ended December 31, 2017 and the three months ended March 31, 2018. No Australian Tax Incentive was recognized for the year ended December 31, 2016 and the three months ended March 31, 2017.

Research and Development Expenses

The Company's research and development expenses consist primarily of salaries, payroll taxes, employee benefits and stock-based compensation charges for those individuals involved in research and development efforts, as well as consulting expenses, third-party research and development expenses, laboratory supplies, clinical materials and overhead, including facilities and depreciation costs, offset by the Australian Tax Incentive discussed above. Research and development expenses are charged to expense as incurred. Payments made prior to the receipt of goods or services to be used in research and development are capitalized until the goods or services are received.

Stock-Based Compensation

Stock-based compensation expense represents the cost of the grant date fair value of employee awards over the requisite service period of the awards (usually the vesting period) on a straight-line basis. For stock awards for which vesting is subject to performance-based milestones, the expense is recorded over the remaining service period after the point when the achievement of the milestone is probable or the performance condition has been achieved. The Company accounts for awards to nonemployees using the fair value method. Awards to nonemployees are subject to periodic revaluation over their vesting terms. The Company estimates the fair value of all stock option grants using the Black-Scholes option pricing model and recognizes forfeitures as they occur.

Income Taxes

The Company accounts for income taxes under the asset and liability method, which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have

been included in the consolidated financial statements. Under this method, deferred tax assets and liabilities are determined on the basis of the differences between the consolidated financial statements and tax basis of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. The effect of a change in tax rates on deferred tax assets and liabilities is recognized in income in the period that includes the enactment date.

The Company recognizes net deferred tax assets to the extent that the Company believes these assets are more likely than not to be realized. In making such a determination, management considers all available positive and negative evidence, including future reversals of existing taxable temporary differences, projected future taxable income, tax-planning strategies, and results of recent operations. If management determines that the Company would be able to realize its deferred tax assets in the future in excess of their net recorded amount, management would make an adjustment to the deferred tax asset valuation allowance, which would reduce the provision for income taxes.

The Company records uncertain tax positions on the basis of a two-step process whereby (1) management determines whether it is more likely than not that the tax positions will be sustained on the basis of the technical merits of the position and (2) for those tax positions that meet the more-likely-than-not recognition threshold, management recognizes the largest amount of tax benefit that is more than 50% likely to be realized upon ultimate settlement with the related tax authority. The Company recognizes interest and penalties related to unrecognized tax benefits within income tax expense. Any accrued interest and penalties are included within the related tax liability.

Comprehensive Loss

Comprehensive loss is defined as a change in equity during a period from transactions and other events and circumstances from non-owner sources. There have been no items qualifying as other comprehensive loss and, therefore, for all periods presented, the Company's comprehensive loss was the same as its reported net loss.

Net Loss Per Share

Basic net loss per share is computed by dividing the net loss by the weighted-average number of common shares outstanding for the period, without consideration for potentially dilutive securities. Diluted net loss per share is computed by dividing the net loss by the weighted-average number of shares of common stock and dilutive common stock equivalents outstanding for the period determined using the treasury-stock and if-converted methods. Dilutive common stock equivalents are comprised of convertible preferred stock, common stock subject to repurchase, and options outstanding under the Company's stock option plan. For all periods presented, there is no difference in the number of shares used to calculate basic and diluted shares outstanding as inclusion of the potentially dilutive securities would be antidilutive.

Crinetics Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements—(Continued)
(Information as of March 31, 2018 and thereafter and for the three months ended March 31, 2017 and 2018 is unaudited)

Potentially dilutive securities not included in the calculation of diluted net loss per share because to do so would be anti-dilutive are as follows (in common stock equivalent shares):

	December 31,		March 31,	
	2016	2017	2017	2018
Convertible preferred stock	5,245,562	8,742,597	5,245,562	14,712,571
Common stock options	856,217	838,276	706,673	1,457,952
Common stock subject to repurchase	813,830	526,596	742,021	104,355
Total	6,915,609	10,107,469	6,694,256	16,274,878

Unaudited Pro Forma Net Loss Per Share

The following table summarizes the Company's unaudited pro forma net loss per share (in thousands, except share and per share data):

	Year Ended December 31, 2017	Three Months Ended March 31, 2018
Numerator		
Net loss and pro forma net loss	$ (9,157)	$ (5,464)
Denominator		
Shares used to compute net loss per share, basic and diluted	1,370,578	1,869,576
Pro forma adjustments to reflect assumed weighted-average effect of conversion of convertible preferred stock	6,375,511	12,008,580
Shares used to compute pro forma net loss per share, basic and diluted	7,746,089	13,878,156
Pro forma net loss per share, basic and diluted	$ (1.18)	$ (0.39)

Segment Reporting

Operating segments are identified as components of an enterprise about which separate discrete financial information is available for evaluation by the chief operating decision-maker in making decisions regarding resource allocation and assessing performance. The Company views its operations and manages its business in one operating segment.

Recent Accounting Pronouncements

In May 2014, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") 2014-09, *Revenue from Contracts with Customers*, which converges the FASB and the International Accounting Standards Board standard on revenue recognition. Areas of revenue recognition that will be affected include, but are not limited to, transfer of control, variable consideration, allocation of transfer pricing, licenses, time value of money, contract costs and disclosures. This guidance is effective for the fiscal years and

Crinetics Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements—(Continued)
(Information as of March 31, 2018 and thereafter and for the three months ended March 31, 2017 and 2018 is unaudited)

interim reporting periods beginning after December 15, 2017. The Company adopted ASU 2014-09 on January 1, 2018. The Company does not currently have any contracts with customers and, as such, the adoption had no material impact on its financial position and results of operations.

In February 2016, the FASB issued ASU 2016-02, *Leases*, which outlines a comprehensive lease accounting model and supersedes the current lease guidance. The new accounting standard requires lessees to recognize lease liabilities and corresponding right-of-use assets for all leases with lease terms of greater than twelve months. It also changes the definition of a lease and expands the disclosure requirements of lease arrangements. The new accounting standard must be adopted using the modified retrospective approach and is effective for public entities for annual reporting periods beginning after December 15, 2018 with early adoption permitted. Although the Company is in the process of evaluating the impact of adoption of the ASU on its financial statements, the Company currently believes the most significant changes will be related to the recognition of lease liabilities on the Company's consolidated balance sheets for real estate operating leases.

Recently Adopted Accounting Pronouncements

In November 2016, the FASB issued ASU No. 2016-18, *Restricted Cash*, which requires entities to show the changes in the total of cash, cash equivalents, restricted cash and restricted cash equivalents in the statement of cash flows. As a result, entities will no longer present transfers between cash and cash equivalents and restricted cash and restricted cash equivalents in the statement of cash flows. The adoption of this standard, in the first quarter of 2018, changed the presentation of the Company's statement of cash flows to include its restricted cash balance with non-restricted cash balances. The new guidance did not have a material impact on the Company's consolidated financial statements.

2. Balance Sheet Details

Prepaid expenses and other current assets consist of the following (in thousands):

	December 31,		March 31,
	2016	2017	2018
Grant receivable	$ 72	$231	$243
Prepaid research and development	98	141	27
Australian tax incentive receivable	-	503	495
Other	43	98	226
Total	$213	$973	$991

Property and equipment consist of the following (in thousands):

	December 31,		March 31,
	2016	2017	2018
Laboratory equipment	$ 360	$ 640	$ 645
Computers and software	27	27	27
Office equipment	19	19	19
Leasehold improvements	-	18	18
Construction in progress	-	-	119
	406	704	828
Less accumulated depreciation and amortization	(182)	(304)	(352)
Total	$ 224	$ 400	$ 476

Crinetics Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements—(Continued)
(Information as of March 31, 2018 and thereafter and for the three months ended March 31, 2017 and 2018 is unaudited)

Other assets consist of the following (in thousands):

	December 31,		March 31,
	2016	2017	2018
Long-term portion of Australian tax incentive receivable	$ -	$ -	$ 288
Deferred initial public offering costs	-	-	317
Other	10	33	17
	$ 10	$ 33	$ 622

Accrued expenses consist of the following (in thousands):

	December 31,		March 31,
	2016	2017	2018
Accrued compensation	$272	$315	$ 610
Accrued research and development	180	126	1,009
Other accrued expenses	49	53	182
Total	$501	$494	$1,801

3. Commitments and Contingencies

2013 Operating Lease

In July 2013, as amended in 2015 and March 2017, the Company entered into a non-cancelable operating lease for laboratory facilities and office space in San Diego, California. The lease expires in April 2020 and is subject to charges for common area maintenance and other costs. The Company has an early termination option subject to at least five months prior written notice and a termination fee of two months base rent and the unamortized portion of any leasing costs, abated rent and any other lease concessions. In addition, the Company has an option to extend the term of the lease for two years. Rent expense is being recognized on a straight-line basis over the term of the lease. Rent expense was $0.1 million, $0.2 million, $33,000 and $44,000 for the years ended December 31, 2016 and 2017 and the three months ended March 31, 2017 and 2018, respectively.

2018 Operating Lease

In February 2018, the Company entered into a non-cancelable operating lease for its new facility in San Diego, California. The lease has an initial term of seven years and the Company has an option to extend the term of the lease for an additional five years and has a termination option subject to early termination fees. The lease is subject to base lease payments and additional charges for common area maintenance and other costs and includes certain lease incentives and tenant improvement allowances. Under the terms of the lease agreement, the Company provided the lessor with an irrevocable letter of credit in the amount of $0.5 million. The lessor is entitled to draw on the letter of credit in the event of any default by the Company under the terms of the lease.

Crinetics Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements—(Continued)
(Information as of March 31, 2018 and thereafter and for the three months ended March 31, 2017 and 2018 is unaudited)

As of March 31, 2018, future minimum payments under the non-cancelable operating leases were as follows (in thousands):

Nine months ended December 31, 2018	$ 405
Years ended December 31,	
2019	1,296
2020	1,195
2021	1,176
2022	1,211
Thereafter	3,292
	$8,575

Litigation

From time to time, the Company may be subject to various claims and suits arising in the ordinary course of business. The Company does not expect that the resolution of these matters will have a material adverse effect on its financial position or results of operations.

4. Convertible Preferred Stock and Stockholders' Deficit

The authorized, issued and outstanding shares of convertible preferred stock as of March 31, 2018 consist of the following (in thousands, except share amounts):

	Shares Authorized	Shares Issued and Outstanding	Liquidation Preference	Carrying Value
Series A	28,763,179	28,763,179	$ 30,000	$ 29,700
Series B	20,105,166	19,641,200	63,500	63,275
Total	48,868,345	48,404,379	$ 93,500	$ 92,975

The authorized, issued and outstanding shares of convertible preferred stock as of December 31, 2017 consist of the following (in thousands, except share amounts):

	Shares Authorized	Shares Issued and Outstanding	Liquidation Preference	Carrying Value
Series A	38,350,914	28,763,179	$ 30,000	$ 29,700

The authorized, issued and outstanding shares of convertible preferred stock as of December 31, 2016 consist of the following (in thousands, except share amounts):

	Shares Authorized	Shares Issued and Outstanding	Liquidation Preference	Carrying Value
Series A	38,350,914	17,257,911	$ 18,000	$ 17,740

Crinetics Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements—(Continued)
(Information as of March 31, 2018 and thereafter and for the three months ended March 31, 2017 and 2018 is unaudited)

The convertible preferred stock is classified outside of stockholders' equity (deficit) because the shares contain certain redemption features that are not solely within the control of the Company.

Description of Securities

Dividends

Holders of Series A convertible preferred stock and Series B convertible preferred stock (collectively, "Series Preferred"), in preference to the holders of common stock, shall be entitled to receive, but only out of funds that are legally available therefor, cash dividends at the annual per share rate of $0.27452 per share and $0.85093 per share, respectively. Such dividends shall be payable only when, as and if declared by the Company's board of directors and shall be non-cumulative. No dividends have been declared as of March 31, 2018.

Liquidation

Holders of Series A convertible preferred stock and Series B convertible preferred stock are entitled to receive a liquidation preference at the rate of $3.43147 per share and $10.63657 per share, respectively, plus all declared and unpaid dividends. Liquidation payments to the holders of Series Preferred have priority and are made in preference to any payments to the holders of common stock. After full payment of the liquidation preference to the holders of the Series Preferred, the remaining assets, if any, will be distributed ratably to the holders of the common stock and Series Preferred on an as-if-converted to common stock basis until the holders of Series A convertible preferred stock and Series B convertible preferred stock have received an aggregate amount per share equal to $10.29441 and $21.27314, respectively, plus all declared and unpaid dividends thereon; thereafter, the remaining assets of the Company legally available for distribution, if any, shall be distributed ratably to the holders of the common stock.

Conversion

The shares of Series Preferred are convertible into shares of common stock at a ratio of 3.29-to-one, at the option of the holder, subject to certain anti-dilution adjustments. Each share of Series Preferred is automatically converted into common stock, (A) at any time upon the affirmative election of the holders of at least a majority of the outstanding shares of the both Series A convertible preferred and Series B convertible preferred, or (B) immediately upon the closing of a firmly underwritten public offering pursuant to an effective registration statement under the Securities Act of 1933, as amended, covering the offer and sale of common stock for the account of the Company in which (i) the per share price is at least $15.9549 (ii) the gross cash proceeds to the Company are at least $50 million and (iii) the Company's shares have been listed for trading on the NYSE or Nasdaq.

Voting Rights

The holder of each share of Series Preferred is entitled to one vote for each share of common stock into which it would convert and to vote as one class with the common stockholders on all matters.

Convertible Preferred Stock Transactions

In April and December 2017, pursuant to a Series A preferred stock purchase agreement entered into in October 2015 which called for an initial closing and, upon the achievement of certain specified milestones, subsequent closings, the Company issued an aggregate of 11,505,268 shares of Series A convertible preferred stock at $1.043 per share for cash proceeds of $12.0 million, net of $40,000 of offering costs.

Crinetics Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements—(Continued)
(Information as of March 31, 2018 and thereafter and for the three months ended March 31, 2017 and 2018 is unaudited)

In February and March 2018, pursuant to a Series B stock purchase agreement entered into in February 2018 which called for an initial closing and a subsequent closing, the Company issued an aggregate of 19,641,200 shares of its Series B convertible preferred stock at a purchase price of $3.233 per share, for aggregate gross proceeds of $63.5 million. The Company incurred $0.2 million of issuance costs in connection with the Series B financing.

Shares of Common Stock Subject to Repurchase

In October 2015, in connection with the issuance of Series A convertible preferred stock, certain of the Company's founders entered into stock restriction agreements, whereby 1,914,893 of previously unrestricted shares of common stock became subject to repurchase by the Company upon the stockholder's termination of employment or service to the Company. Any shares subject to repurchase by the Company are not deemed, for accounting purposes, to be outstanding until those shares vest. The Company's repurchase rights lapsed as to 765,957 shares of common stock in October 2015 and lapse 23,936 shares per month thereafter, such that the shares of common stock will be fully vested in October 2019. However, the shares of common stock are subject to accelerated vesting upon certain events, and became fully vested upon the closing of the Company's Series B preferred stock financing in February 2018 (see Note 7). The stock restriction agreements resulted in the deemed cancellation and reissuance of common shares. As such, the Company recognizes the measurement date fair value of the restricted stock over the vesting period as compensation expense. As of October 2015, the aggregate fair value of the common shares subject to repurchase was $1.4 million. For of the years ended December 31, 2016 and 2017 and the three months ended March 31, 2017 and 2018, the Company recognized stock-based compensation for these awards of $0.2 million, $0.2 million, $0.1 million and $0.4 million, respectively. As of December 31, 2016 and 2017 and March 31, 2018, 813,830 shares, 526,596 shares and no shares of common stock, respectively, were subject to repurchase by the Company. As of December 31, 2016 and 2017 and March 31, 2018, the unvested stock liability related to these awards was $5,000 and $3,000 and $0, respectively.

Stock Incentive Plan

In February 2015, the Company adopted the Crinetics Pharmaceuticals, Inc. 2015 Stock Incentive Plan (the "Plan"), which provides for the issuance of incentive stock options, non-statutory stock options, restricted stock awards, restricted stock unit awards and other stock awards to its employees, members of its board of directors and consultants. The Plan expires in February 2025 and, in general, the options issued under the Plan expire ten years from the date of grant and vest over a four-year period. The Plan allows for early exercise of stock options, and early exercised options and restricted stock awards may be subject to repurchase by the Company until they become fully vested. As of December 31, 2016 and 2017, no awards under the Plan were subject to repurchase by the Company. As of March 31, 2018, there were 104,355 shares issued and subject to repurchase as a result of the early exercise of stock options, resulting in an unvested stock liability of $0.2 million. As of December 31, 2016 and 2017 and March 31, 2018, 1,653,495 shares, 1,653,495 shares and 2,413,373 shares, respectively, were authorized for issuance under the Plan, of which 825,844 shares, 746,205 shares and 667,185 shares, respectively, remained available for future issuance.

Crinetics Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements—(Continued)
(Information as of March 31, 2018 and thereafter and for the three months ended March 31, 2017 and 2018 is unaudited)

Prior to adoption of the Plan, stock options to purchase 47,717 shares of common stock were granted. As of December 31, 2017 and March 31, 2018, options to purchase 23,099 shares of common stock remained outstanding outside of the Plan and are included in the table below.

A summary of the Company's stock option activity is as follows (in thousands, expect share and per share data):

	Number of Outstanding Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value
Balance at December 31, 2016	856,217	$0.69	8.89	$ 38
Granted	147,407	1.34		
Cancelled	(67,768)	0.73		
Exercised	(97,580)	0.68		
Balance at December 31, 2017	838,276	0.80	8.25	$ 549
Granted	838,898	1.83		
Exercised	(219,222)	1.15		
Balance at March 31, 2018	1,457,952	$1.34	8.98	$ 839
Vested and expected to vest at December 31, 2017	838,276	$0.80	8.25	$ 549
Exercisable at December 31, 2017	351,041	$0.65	7.72	$ 283
Vested and expected to vest at March 31, 2018	1,457,952	$1.34	8.98	$ 839
Exercisable at March 31, 2018	564,826	$1.01	8.33	$ 512

The Company received cash from the exercise of stock options of $0, $0.1 million, $0.1 million and $0.3 million for the years ended December 31, 2016 and 2017 and the three months ended March 31, 2017 and 2018, respectively. The total intrinsic value of stock options exercised was $0, $5,000, $0 and $0.1 million for the years ended December 31, 2016 and 2017 and the three months ended March 31, 2017 and 2018, respectively.

Stock-Based Compensation Expense

The assumptions used in the Black-Scholes option pricing model to determine the fair value of employee stock option grants were as follows:

	Years Ended December 31,		Three Months Ended March 31,	
	2016	2017	2017	2018
Risk-free interest rate	1.49%	1.89% – 2.14%	2.06%	2.45% – 2.70%
Expected volatility	63.78%	65.61% – 73.45%	67.35%	70.1%
Expected term (in years)	6.08	6.02 – 6.08	6.08	5.52 – 6.08
Expected dividend yield	0.0%	0.0%	0.0%	0.0%

Crinetics Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements—(Continued)
(Information as of March 31, 2018 and thereafter and for the three months ended March 31, 2017 and 2018 is unaudited)

Risk-free interest rate. The risk-free interest rate is based on the U.S. Treasury yield in effect at the time of grant for zero coupon U.S. Treasury notes with maturities approximately equal to the expected term of the awards.

Expected volatility. Since the Company is not yet a public company and does not have a trading history for its common stock, the expected volatility assumption is based on volatilities of a peer group of similar companies whose share prices are publicly available. The peer group was developed based on companies in the biotechnology industry. The Company will continue to apply this process until a sufficient amount of historical information regarding the volatility of its own stock price becomes available

Expected term. The expected term represents the period of time that options are expected to be outstanding. Because the Company does not have historical exercise behavior, it determines the expected life assumption using the simplified method, for employees, which is an average of the contractual term of the option and its vesting period.

Expected dividend yield. The Company bases the expected dividend yield assumption on the fact that it has never paid cash dividends and has no present intention to pay cash dividends, therefore, the Company used an expected dividend yield of zero.

Stock-based compensation expense recognized for all equity awards has been reported in the consolidated statements of operations as follows (in thousands):

	Years Ended December 31,		Three Months Ended March 31,	
	2016	2017	2017	2018
Research and development	$108	$122	$ 27	$ 161
General and administrative	162	149	29	265
Total	$270	$271	$ 56	$ 426

The weighted-average grant date fair value of employee option grants for the years ended December 31, 2016 and 2017 and the three months ended March 31, 2017 and 2018 was $0.43 per share, $0.85 per share $0.45 per share and $1.17 per share, respectively. As of December 31, 2017 and March 31, 2018, total unrecognized stock-based compensation costs related employee awards was $0.2 million and $1.1 million, respectively, which is expected to be recognized over a remaining weighted-average period of approximately 3.0 years and 3.6 years, respectively.

Common Stock Reserved for Future Issuance

Common stock reserved for future issuance is as follows:

	December 31, 2017	March 31, 2018
Conversion of preferred stock	8,742,597	14,712,571
Common stock options issued and outstanding	838,276	1,457,952
Common stock options available for future issuance	746,205	667,185
Total	10,327,078	16,837,708

Crinetics Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements—(Continued)
(Information as of March 31, 2018 and thereafter and for the three months ended March 31, 2017 and 2018 is unaudited)

5. Income Taxes

The Company's loss before benefit for income taxes for the years ended December 31, 2016 and 2017 were generated in the following jurisdictions (in thousands):

	Years Ended December 31,	
	2016	2017
Domestic	$(6,019)	$(8,141)
Foreign	-	(1,016)
Consolidated net loss	$(6,019)	$(9,157)

A reconciliation of income tax expense to the amount computed by applying the statutory federal income tax rate to the loss from operations is summarized for the years ended December 31, 2016 and 2017 as follows (in thousands):

	Years Ended December 31,	
	2016	2017
Expected tax benefit at statutory rate	$(2,046)	$(3,113)
State income taxes, net of federal benefit	(327)	(474)
Tax effect of:		
Change in valuation allowance	2,511	2,112
Federal rate change	-	1,602
Research and development credit	(342)	(525)
Australian Tax Incentive	-	176
Other	204	222
Total	$ -	$ -

Significant components of the Company's net deferred tax assets as of December 31, 2016 and 2017 are as follows (in thousands):

	December 31,	
	2016	2017
Deferred tax assets:		
Tax loss carryforwards	$ 2,378	$ 1,863
Capitalized research expenses	-	2,127
Research and development and other tax credits	333	829
Other, net	35	39
Total deferred tax assets	2,746	4,858
Less valuation allowance	(2,746)	(4,858)
Net deferred tax assets	$ -	$ -

At December 31, 2017, the Company had federal, state, and foreign net operating loss carryforwards of approximately $6.2 million, $6.4 million and $0.4 million, respectively. The federal and state loss carryforwards

will begin expiring in 2035, unless previously utilized. The foreign loss carryforwards do not expire. The Company also has federal and California research and development credit carryforwards totaling $0.6 million and $0.4 million, respectively. The federal research and development credit carryforwards will begin to expire in 2030, unless previously utilized. The California research credits do not expire.

Management assesses the available positive and negative evidence to estimate if sufficient future taxable income will be generated to use the existing deferred tax assets. Based on the weight of all evidence including a history of operating losses, management has determined that it is more likely than not that the net deferred tax assets will not be realized. A valuation allowance of $4.9 million as of December 31, 2017 has been established to offset the deferred tax assets as realization of such assets is uncertain.

Future utilization of the Company's net operating loss and research and development credit carryforwards to offset future taxable income may be subject to an annual limitation, pursuant to Internal Revenue Code ("IRC") Sections 382 and 383, as a result of ownership changes that may have occurred or that could occur in the future. An ownership change occurs when a cumulative change in ownership of more than 50% occurs within a three-year period. The Company has not completed an IRC Section 382/383 analysis regarding the limitation of net operating loss and research and development credit carryforwards. When this analysis is finalized, the Company plans to update its unrecognized tax benefits accordingly.

The Company has not provided for deferred taxes on the outside basis difference of its Australian subsidiary. The deficit in earnings would result in a deferred tax asset, and it is not apparent that this temporary difference will reverse in the foreseeable future.

The Tax Cuts and Jobs Act ("the Act") was enacted on December 22, 2017. The Act includes a number of changes to existing U.S. tax laws that impact the Company, most notably a reduction of the U.S. federal corporate tax rate from a maximum of 35% to a flat 21%, effective January 1, 2018, and a one-time transition tax on unremitted foreign earnings. In conjunction with the tax law changes, the Securities and Exchange Commission staff issued Staff Accounting Bulletin 118 ("SAB 118") to address the application of U.S. GAAP in situations when a registrant does not have the necessary information available, prepared, or analyzed (including computations) in reasonable detail to complete the accounting for certain income tax effects of the Act. In these instances, a Company can record provisional amounts in its consolidated financial statements for the income tax effects for which a reasonable estimate can be determined. For items for which a reasonable estimate cannot be determined, a company should continue to apply ASC 740 based on the provisions of the tax laws that were in effect immediately prior to the Act being enacted.

As a result of the new law, the Company has remeasured its deferred tax assets based on the rates at which they are expected to reverse in the future, resulting in a reduction in the deferred tax asset balance of $1.6 million which was offset by a reduction in the valuation allowance by a corresponding amount. The one-time transition tax is based on the total post-1986 earnings and profits (E&P) previously deferred from U.S. income taxes. As the Company has a deficit in post-1986 E&P from its foreign subsidiary, there was no increase in income tax expense as a result of the one-time transition tax. This impact is considered to be a provisional amount as the Company is still analyzing certain aspects of the Act and refining its calculations. The ultimate impact may differ from this provisional amount, due to, among other things, additional analysis, changes in interpretations and assumptions the Company has made, additional regulatory guidance that may be issued, and actions the Company may take as a result of the Act.

Crinetics Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements—(Continued)
(Information as of March 31, 2018 and thereafter and for the three months ended March 31, 2017 and 2018 is unaudited)

The following table summarized the changes to the Company's unrecognized tax benefits for the years ended December 31, 2016 and 2017 (in thousands)

	2016	2017
Beginning balance	$ -	$ 68
Increases related to current year positions	68	91
Ending balance	$68	$159

The Company's unrecognized tax benefits as of December 31, 2016 and 2017 were $0.1 million and $0.2 million, respectively. Due to the existence of the valuation allowance, future changes in unrecognized tax benefits would have no effect on the Company's effective tax rate. The Company's policy is to recognize interest and penalties related to income tax matters in income tax expense. For the years ended December 31, 2016 and 2017, the Company has not recorded any interest or penalties related to income tax matters. The Company does not foresee any material changes to unrecognized tax benefits within the next twelve months.

The Company is subject to taxation in the United States federal and state jurisdictions as well as Australia. Generally, the Company's federal income tax returns from 2014 and forward and state income tax returns from 2013 and forward are subject to examination by tax authorities; however, the Company's tax attribute carryforwards such as net operating losses and research tax credits generated in closed years are also subject to examination. The Australian tax returns are subject to examination beginning in 2017. The Company is not currently under audit by any tax authority.

6. 401(k) Plan

The Company maintains a defined contribution 401(k) plan available to eligible employees. Employee contributions are voluntary and are determined on an individual basis, limited to the maximum amount allowable under federal tax regulations. The Company, at its discretion, may make certain matching contributions to the 401(k) plan. As of December 31, 2017 and March 31, 2018, the Company had not made any matching contributions.

7. Subsequent Events

The Company has completed an evaluation of all subsequent events through May 2, 2018 for the consolidated financial statements as of and for the years ended December 31, 2016 and 2017 and through July 9, 2018 for the interim consolidated financial statements as of and for the three months ended March 31, 2018, to ensure that these consolidated financial statements include appropriate disclosure of events both recognized in the consolidated financial statements and events which occurred but were not recognized in the consolidated financial statements. Except as described below, the Company has concluded that no subsequent event has occurred that requires disclosure.

2015 Stock Incentive Plan

In May 2018, the shares reserved for issuance under the 2015 Stock Incentive Plan were increased by 729,484 shares to a total of 3,142,857 shares.

In May and June 2018, certain employees and consultants of the Company were granted options to purchase an aggregate of 1,027,196 shares of common stock at exercise prices ranging from $9.28 to $12.01 per share.

Crinetics Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements—(Continued)
(Information as of March 31, 2018 and thereafter and for the three months ended March 31, 2017 and 2018 is unaudited)

SBIR Grants

In the second quarter of 2018, the Company was awarded two SBIR grants for an aggregate of $2.4 million. The grants will fund the continued research and development of the Company's nonpeptide, oral somatostatin agonists for acromegaly and congenital hyperinsulinemias.

Approval of the 2018 Equity Incentive Award Plan

In July 2018, the Company's board of directors and stockholders approved and adopted the 2018 Incentive Award Plan (the "2018 Plan"). The 2018 Plan will become effective on the day prior to the effectiveness of the IPO. Under the 2018 Plan, the Company may grant stock options, stock appreciation rights, restricted stock, restricted stock units, and other stock or cash-based awards to individuals who are then employees, officers, directors or consultants of the Company, and employees and consultants of the Company's subsidiaries. A total of 1,600,000 shares of common stock were approved to be initially reserved for issuance under the 2018 Plan. The number of shares reserved that are remaining under the 2015 Plan as of the effective date of the 2018 Plan will be added to the shares initially reserved under the 2018 Plan upon its effectiveness. In addition, the number of shares of common stock available for issuance under the 2018 Plan will be automatically increased on the first day of each calendar year during the ten-year term of the 2018 Plan, beginning with January 1, 2019, by an amount equal to 5% of the outstanding number of shares of the Company's common stock on December 31st of the preceding calendar year or such lesser amount as determined by the Company's board of directors.

Approval of the 2018 Employee Stock Purchase Plan

In July 2018, the Company's board of directors and stockholders approved and adopted the 2018 Employee Stock Purchase Plan (the "ESPP"). The ESPP will become effective on the day prior to the effectiveness of the IPO. The ESPP permits participants to purchase common stock through payroll deductions of up to 20% of their eligible compensation. A total of 250,000 shares of common stock were approved to be initially reserved for issuance under the ESPP. In addition, the number of shares of common stock available for issuance under the ESPP will be automatically increased on the first day of each calendar year during the ten-year term of the ESPP, beginning with January 1, 2019, by an amount equal to 1% of the outstanding number of shares of the Company's common stock on December 31st of the preceding calendar year or such lesser amount as determined by the Company's board of directors.

Increase in Authorized Common Stock

In July 2018, the Company increased the number of shares of its authorized common stock from 65,000,000 shares to 67,400,000 shares.

Reverse Stock Split

On July 6, 2018, the Company effected a 1-for-3.29 reverse stock split of its common stock. The par value and the authorized shares of the common stock were not adjusted as a result of the reverse stock split. The reverse stock split resulted in an adjustment to the Series A and B preferred stock conversion prices to reflect a proportional decrease in the number of shares of common stock to be issued upon conversion. The accompanying consolidated financial statements and notes to the consolidated financial statements give retroactive effect to the reverse stock split for all periods presented.

Table of Contents

6,000,000 shares

Common stock

Prospectus

J.P. Morgan **Leerink Partners** **Piper Jaffray**

July 17, 2018