

Cara Therapeutics, Inc.
Form 424B5
March 29, 2017
Table of Contents

Filed Pursuant to Rule 424(b)(5)
Registration No. 333-216657

The information contained in this preliminary prospectus supplement and the accompanying prospectus is not complete and may be changed. A registration statement relating to the securities has been declared effective by the Securities and Exchange Commission. This preliminary prospectus supplement and the accompanying prospectus do not constitute an offer to sell these securities and we are not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

Subject to completion, dated March 29, 2017

PROSPECTUS SUPPLEMENT

To Prospectus dated March 24, 2017

\$80,000,000

CARA THERAPEUTICS, INC.

Common Stock

\$ per share

Cara Therapeutics, Inc. is offering \$80,000,000 of our common stock in this offering.

Our common stock is listed for trading on The NASDAQ Global Market under the symbol **CARA**. The closing price per share of our common stock on March 28, 2017 was \$19.09.

We are an emerging growth company as that term is used in the Jumpstart Our Business Startups Act of 2012 and, as such, have elected to comply with certain reduced public company reporting requirements for this prospectus supplement and future filings.

Investing in our common stock involves a high degree of risk. See **Risk Factors** beginning on page 7 and the documents incorporated by reference in this prospectus supplement.

	Per Share	Total
Public offering price	\$	\$
Underwriting discounts and commissions ⁽¹⁾	\$	\$
Proceeds, before expenses, to us	\$	\$

⁽¹⁾ We refer you to the section titled "Underwriting" beginning on page 14 of this prospectus supplement for additional information regarding total underwriter compensation.

We have granted the underwriters a 30-day option to purchase a total of up to \$12,000,000 of additional shares of our common stock on the same terms and conditions set forth above. The underwriters expect to deliver shares of our common stock to purchasers on _____, 2017.

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

Piper Jaffray

Stifel

The date of this prospectus supplement is _____, 2017.

Table of Contents

TABLE OF CONTENTS

	Page
Prospectus Supplement	
<u>About this Prospectus Supplement</u>	iii
<u>Summary</u>	S-1
<u>Risk Factors</u>	S-7
<u>Use of Proceeds</u>	S-8
<u>Dilution</u>	S-9
<u>Material U.S. Federal Income Tax Considerations to Non-U.S. Holders</u>	S-10
<u>Underwriting</u>	S-14
<u>Legal Matters</u>	S-21
<u>Experts</u>	S-21
<u>Where You Can Find More Information</u>	S-22
<u>Incorporation of Certain Information by Reference</u>	S-22
Prospectus	
<u>About this Prospectus</u>	1
<u>Summary</u>	2
<u>Risk Factors</u>	7
<u>Special Note Regarding Forward-Looking Statements</u>	8
<u>Ratio of Earnings (Loss) to Fixed Charges</u>	10
<u>Use of Proceeds</u>	11
<u>Description of Capital Stock</u>	12
<u>Description of Debt Securities</u>	17
<u>Description of Warrants</u>	24
<u>Legal Ownership of Securities</u>	26
<u>Plan of Distribution</u>	30
<u>Legal Matters</u>	32
<u>Experts</u>	32
<u>Where You Can Find More Information</u>	32
<u>Incorporation of Certain Information by Reference</u>	33
<u>Disclosure of Commission Position on Indemnification for Securities Act Liability</u>	34

Table of Contents

Neither we nor the underwriters have authorized anyone to provide any information or to make any representations other than those contained or incorporated by reference in this prospectus supplement, the accompanying prospectus or in any free writing prospectuses we have authorized for use in connection with this offering. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. This prospectus supplement and the accompanying prospectus together constitute an offer to sell only the securities offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. The information contained in this prospectus supplement, the accompanying prospectus and any free writing prospectuses that we have authorized for use in connection with this offering is current only as of its date. Our business, financial condition, results of operations and prospects may have changed since those dates. You should read this prospectus supplement, the accompanying prospectus, the documents incorporated by reference herein and therein, and any free writing prospectus that we have authorized for use in connection with this offering when making your investment decision. You should also read and consider the information in the documents we have referred you to in the section of the accompanying prospectus titled "Incorporation of Certain Information by Reference."

Table of Contents

ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus form part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission, or SEC, utilizing a shelf registration process. This document contains two parts. The first part consists of this prospectus supplement, which provides you with specific information about this offering. The second part, the accompanying prospectus, provides more general information, some of which may not apply to this offering. Generally, when we refer only to the prospectus, we are referring to both parts combined. This prospectus supplement may add, update or change information contained in the accompanying prospectus. To the extent that any statement we make in this prospectus supplement is inconsistent with statements made in the accompanying prospectus or any documents incorporated by reference herein or therein, the statements made in this prospectus supplement will be deemed to modify or supersede those made in the accompanying prospectus and such documents incorporated by reference herein and therein. You should read this prospectus supplement and the accompanying prospectus, including the information incorporated by reference herein and therein, and any related free writing prospectus that we have authorized for use in connection with this offering.

You should rely only on the information that we have included or incorporated by reference in this prospectus supplement, the accompanying prospectus and any related free writing prospectus that we may authorize to be provided to you. We have not authorized any dealer, salesman or other person to give any information or to make any representation other than those contained or incorporated by reference in this prospectus supplement, the accompanying prospectus or any related free writing prospectus that we may authorize to be provided to you. You must not rely upon any information or representation not contained or incorporated by reference in this prospectus supplement, the accompanying prospectus or any related free writing prospectus. This prospectus supplement, the accompanying prospectus and any related free writing prospectus do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the registered securities to which they relate, nor do this prospectus supplement, the accompanying prospectus or any related free writing prospectus constitute an offer to sell or the solicitation of an offer to buy securities in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation in such jurisdiction.

You should not assume that the information contained in this prospectus supplement, the accompanying prospectus or any related free writing prospectus is accurate on any date subsequent to the date set forth on the front of the document or that any information we have incorporated by reference herein or therein is correct on any date subsequent to the date of the document incorporated by reference, even though this prospectus supplement, accompanying prospectus or any related free writing prospectus is delivered, or securities are sold, on a later date.

This prospectus supplement contains or incorporates by reference summaries of certain provisions contained in some of the documents described herein, but reference is made to the actual documents for complete information. All of the summaries are qualified in their entirety by the actual documents. Copies of some of the documents referred to herein have been or will be filed or have been or will be incorporated by reference as exhibits to the registration statement of which this prospectus supplement forms a part, and you may obtain copies of those documents as described in this prospectus supplement under the heading **Where You Can Find More Information**.

Table of Contents

SUMMARY

This summary highlights information contained in other parts of this prospectus supplement. Because it is only a summary, it does not contain all of the information that you should consider before investing in shares of our common stock and it is qualified in its entirety by, and should be read in conjunction with, the more detailed information appearing elsewhere in this prospectus supplement, the accompanying prospectus, any applicable free writing prospectus and the documents incorporated by reference herein and therein. You should read all such documents carefully, especially the risk factors and our financial statements and the related notes included or incorporated by reference herein or therein, before deciding to buy shares of our common stock. Unless the context requires otherwise, references in this prospectus to Cara, we, us and our refer to Cara Therapeutics, Inc.

General

We are a clinical-stage biopharmaceutical company focused on developing and commercializing new chemical entities designed to alleviate pain and pruritus by selectively targeting kappa opioid receptors. We are developing a novel and proprietary class of product candidates that target the body's peripheral nervous system and have demonstrated efficacy in clinical trials of patients with moderate-to-severe pain without inducing many of the undesirable side effects typically associated with currently available pain therapeutics.

Our most advanced product candidate, CR845, is a new chemical entity that is designed to produce pain relief by specifically stimulating kappa, rather than mu, opioid receptors outside of the central nervous system. Intravenous, or I.V., CR845, has demonstrated significant pain relief and a favorable safety and tolerability profile in three Phase 2 clinical trials in patients with acute postoperative pain. In addition, in the fourth quarter of 2014, we successfully completed a Human Abuse Liability, or HAL, trial of I.V. CR845 in which I.V. CR845 met the trial's primary endpoint by demonstrating highly statistically significant lower drug liking scores as measured by visual analog scale (VAS) Emax ($p < 0.0001$) when compared to the approved Schedule IV opioid, pentazocine. We believe that the totality of the results from the HAL trial are supportive of the potential for CR845 to be the first non-scheduled or low (Schedule V) scheduled peripheral opioid for acute pain.

In September 2015, we initiated our Phase 3 program for I.V. CR845 in postoperative pain with the dosing of the first subjects in an adaptive pivotal trial in patients undergoing a range of abdominal surgeries. The trial protocol initially included three dose levels of I.V. CR845 (1.0 ug/kg, 2.0 ug/kg and 5.0 ug/kg), which were compared to placebo with an interim conditional power assessment to identify optimal doses to be used to complete the enrollment of this trial.

In June 2016, we modified the trial protocol and resumed the trial as a three-arm trial, testing two doses of CR845 (1.0 ug/kg and 0.5 ug/kg) versus placebo, based on a safety review by us, the trial's Independent Data Monitoring Committee and the U.S. Food and Drug Administration, or FDA, of unblinded safety data from the first 90 patients dosed. The safety review was conducted in response to a clinical hold that the FDA placed on the trial in February 2016 and removed in April 2016 following the safety review. The clinical hold was based on a pre-specified stopping rule related to elevated serum sodium levels of greater than 150 mmol/L that was included in the clinical trial protocol.

The revised trial is enrolling up to 450 patients undergoing a range of abdominal surgeries, all of which are associated with moderate-to-severe postoperative pain, within the United States. The primary efficacy measure is the Change in Pain Intensity over the 24-hour postoperative period, using the patient-reported Numeric Rating Scale, or NRS, score collected at pre-specified time points through 24 hours.

Table of Contents

Postoperative nausea and vomiting is also being evaluated as a secondary efficacy measure. The impact of I.V. CR845 treatment on inflammatory biomarkers is also being explored. An interim conditional power analysis of our adaptive Phase 3 trial of I.V. CR845 for postoperative pain is expected in the second quarter of 2017.

Based on previous guidance from the FDA, we believe we will require 1,500 total exposures to I.V. CR845, including all Phase 1, Phase 2 and Phase 3 trials, prior to submitting a new drug application, or NDA. We believe our planned and ongoing clinical trials and our clinical trials completed to date will result in a sufficient number of drug exposures to support an NDA.

We are also developing an oral version of CR845, or Oral CR845, for acute and chronic pain. In the second quarter of 2014, we initiated a Phase 1 trial of a tablet formulation of Oral CR845, for which we announced positive top-line data in the fourth quarter of 2014. In August 2015, we advanced our tablet formulation of Oral CR845 into a Phase 2a clinical trial in patients with osteoarthritis, or OA, of the knee or hip. The Phase 2a trial was a single-blind, randomized, multiple ascending dose trial designed to evaluate the safety, pharmacokinetics, or PK, and effectiveness of Oral CR845 tablets dosed over a two-week treatment period in 80 OA patients experiencing moderate-to-severe pain, defined as ≥ 4 on an 11-point NRS at baseline. In December 2015, we announced positive top-line results from this Phase 2a trial. The results showed a dose-related reduction in mean baseline pain score up to 34% after two weeks, and a post-hoc analysis of the data revealed a statistically significant reduction in mean rescue medication for the top 5.0 mg dose group, as compared to the other dose groups, of approximately 80%. The results of the Phase 2a clinical trial established therapeutic doses and a dosing regimen for a larger randomized, double-blind, placebo-controlled Phase 2b trial, which we initiated during the third quarter of 2016. The Phase 2b trial is a trial of three tablet strengths of CR845 (1.0 mg, 2.5 mg and 5.0 mg), dosed twice-daily over an eight-week treatment period in more than 450 OA patients (increased from the initial target of 330 patients) experiencing moderate-to-severe pain across the United States. The primary efficacy endpoint is the change from baseline at week eight, with respect to the weekly mean of the daily pain intensity score using an NRS. We expect to report top-line data from this trial in the second quarter of 2017.

CR845 has exhibited anti-pruritic, or anti-itch, potency in standard preclinical models. In the fourth quarter of 2014, we reported positive top-line dose-ranging PK and safety data from a Phase 1b clinical trial, which was Part A of a Phase 2 proof-of-concept trial of I.V. CR845 for the treatment of uremic pruritus, an intractable systemic itch condition with high prevalence in dialysis patients with chronic kidney disease, for which there are no approved therapeutics in the United States. In July 2015, we reported positive top-line efficacy results from Part B of this Phase 2 proof-of-concept trial, in which we observed that I.V. CR845 demonstrated statistically significant results on the primary endpoint of reducing worst itch intensity as well as the secondary endpoint of quality of life improvements. We also observed I.V. CR845 to have a favorable safety and tolerability profile in the trial.

Based on the results of this trial, during the fourth quarter of 2015 we completed a guidance meeting with the FDA. We incorporated the feedback we received from the FDA in this guidance meeting in the overall design of our Phase 3 clinical trial program for I.V. CR845 for the treatment of uremic pruritus. In June 2016, we initiated a two-part Phase 2/3 adaptive design trial of I.V. CR845 in dialysis patients suffering from moderate-to-severe uremic pruritus. As described below under Recent Developments, we recently announced top-line results from Part A of the trial, which was a randomized, double-blind, placebo-controlled trial in 174 patients of three doses of I.V. CR845 (0.5ug/kg, 1.0 ug/kg and 1.5 ug/kg) administered three times per week after dialysis over an eight-week treatment period.

We also initiated a PK safety trial of multiple doses of Oral CR845 in hemodialysis patients to define bioequivalent tablet strengths to inform our ability to develop an oral tablet formulation for moderate-to-severe uremic pruritus. We expect to announce data from this trial in the second quarter of 2017.

Table of Contents

We commenced operations in 2004, and our primary activities to date have been organizing and staffing our company, developing our product candidates, including conducting preclinical studies and clinical trials of CR845-based product candidates, and raising capital. To date, we have financed our operations primarily through sales of our equity and debt securities and payments from license agreements. We have no products currently available for sale, and substantially all of our revenue to date has been revenue from license agreements, although we have received nominal amounts of revenue under research grants.

Recent Developments

On March 28, 2017, we announced top-line data from Part A of our two-part Phase 2/3 adaptive design trial of I.V. CR845 in dialysis patients suffering from moderate-to-severe uremic pruritus. Uremic pruritus is an intractable systemic itch condition with high prevalence in dialysis patients with chronic kidney disease, for which there are no approved therapeutics in the United States. Pruritus is also associated with diseases such as atopic dermatitis, eczema, cholestatic liver disease and psoriasis, with the largest number of patients treated for pruritus being those suffering from atopic dermatitis or eczema, chronic kidney disease and cholestatic liver disease.

Part A of the trial, was a randomized, double-blind, placebo-controlled trial of three doses of I.V. CR845 (0.5ug/kg, 1.0 ug/kg and 1.5 ug/kg) administered three times per week after dialysis over an eight-week treatment period in 174 patients with moderate-to-severe uremic pruritus.

The primary endpoint of this trial was the change from baseline of the mean worst itching score for week eight (days 51-57) measured on a standard NRS. Patients receiving I.V. CR845 experienced a 68% greater reduction from baseline in worst itch scores than those receiving placebo ($p<0.0019$). The secondary endpoint of this trial focused on quality of life measures associated with pruritus using the Skindex-10 score, a validated self-assessment scale with higher scores indicating worse quality of life. Patients receiving I.V. CR845 experienced a 100% greater reduction from baseline in the average total Skindex-10 score at week eight than those receiving placebo ($p<0.0007$). The total average Skindex-10 score reflected statistically significant reductions in each of the three Skindex-10 domains: disease ($p=0.0001$), mood/emotional distress ($p=0.01$) and social functioning ($p=0.009$).

Overall, I.V. CR845 was observed to be well tolerated over the eight-week treatment period and the unblinded Drug Safety Monitoring Board did not report any significant drug-related events during the course of the trial. The most common adverse events were transient paresthesia, primarily mid-facial tingling or numbness, somnolence and dizziness, as reported in previous clinical studies of I.V. CR845.

We plan to meet with the FDA for an end-of-Phase 2 meeting to review the results of Part A of this trial to determine an optimal dose to take into Part B of this Phase 2/3 adaptive design trial, and define the broader path towards approval. Pending discussions with the FDA, Part B of the study is intended to be a randomized, double-blind, placebo-controlled trial of I.V. CR845 administered three times per week after dialysis over a 12-week treatment period in up to 240 patients with moderate-to-severe uremic pruritus.

Corporate Information

Information concerning the Company is contained in the documents that we file with the SEC as a reporting company under the Securities Exchange Act of 1934, as amended, which are accessible at www.sec.gov. Our website address is www.caratherapeutics.com. The information contained on, or that can be accessed through, our website is not a part of this prospectus. Investors should not rely on any such information in deciding whether to purchase our common stock. We have included our website address in this prospectus solely as an inactive textual reference.

Table of Contents

Our mailing address is 4 Stamford Plaza, 107 Elm Street, 9th Floor, Stamford, Connecticut 06902. Our telephone number is (203) 406-3700.

Implications of Being an Emerging Growth Company

As a company with less than \$1 billion in revenue during our last fiscal year, we qualify as an emerging growth company as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from specified 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 may take advantage of these provisions until December 31, 2019, or until such earlier time that we are no longer an emerging growth company. We would cease to be an emerging growth company if we have more than \$1 billion in annual revenues, have more than \$700 million in market value of our capital stock held by nonaffiliates or issue more than \$1 billion of non-convertible debt over a three-year period. We may choose to take advantage of some, but not all, of the available exemptions. We have taken advantage of some reduced reporting burdens in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein. Accordingly, such information may be different than the information you receive from other public companies in which you hold stock.

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 provision allows an emerging growth company to delay the adoption of some accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

Table of Contents

THE OFFERING

Common stock offered by us	\$80,000,000 of shares
Total common stock to be outstanding after this offering	31,487,538 shares, or 32,116,139 shares if the underwriters exercise their option to purchase additional shares in full, based on an aggregate offering of \$80,000,000 of our common stock at an assumed public offering price of \$19.09 per share (the last reported sale price of our common stock on The NASDAQ Global Market on March 28, 2017).
Price per share	\$
Underwriters' option	The underwriters have an option for a period of 30 days to purchase up to 628,601 additional shares of our common stock, based on an aggregate offering of \$80,000,000 of our common stock at an assumed public offering price of \$19.09 per share (the last reported sale price of our common stock on The NASDAQ Global Market on March 28, 2017).
Use of proceeds	<p>We estimate that the net proceeds from this offering will be approximately \$74.7 million, or approximately \$86.0 million if the underwriters exercise their option to purchase additional shares in full, based on an assumed public offering price of \$19.09 per share (the last reported sale price of our common stock on The NASDAQ Global Market on March 28, 2017), after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.</p> <p>We intend to use the net proceeds of this offering to fund our clinical and research development activities, including the completion of our Phase 3 program for I.V. CR845 in uremic pruritus, two Phase 3 trials of I.V. CR845 in acute pain and a Phase 2b trial of Oral CR845 in osteoarthritis pain, and for working capital and other general corporate purposes, including in-licensing and acquisitions. We may also use a portion of the net proceeds to invest in or acquire businesses or technologies that we believe are complementary to our own, although we have no current plans, commitments or agreements with respect to any acquisitions as of the date of this prospectus supplement. See "Use of Proceeds."</p>
Risk factors	You should read the "Risk Factors" section of this prospectus supplement and the documents referred to therein for a discussion of factors to consider carefully before deciding to invest in shares of our common stock.
NASDAQ Global Market symbol	CARA

S-5

Table of Contents

The number of shares of our common stock to be outstanding after this offering is based on 27,296,863 shares of our common stock outstanding as of December 31, 2016, and excludes 3,225,199 shares of common stock reserved for issuance under our 2004 Stock Incentive Plan and our 2014 Equity Incentive Plan as of December 31, 2016, consisting of 2,548,408 shares of common stock subject to outstanding awards and 676,791 shares of common stock that remain available under our 2014 Equity Incentive Plan for future grants. Except as otherwise indicated herein, all information in this prospectus supplement, including the number of shares that will be outstanding after this offering, does not assume or give effect to the exercise of the underwriters' option to purchase additional shares in this offering and assumes no exercise of outstanding options subsequent to December 31, 2016.

S-6

Table of Contents

RISK FACTORS

An investment in our common stock involves a high degree of risk. Before deciding whether to invest in our common stock, you should carefully consider the risks described below and those discussed under the section titled "Risk Factors" contained in our Annual Report on Form 10-K for the year ended December 31, 2016, which is incorporated by reference in this prospectus supplement and the accompanying prospectus, together with other information in this prospectus supplement, the accompanying prospectus, the information and documents incorporated by reference herein and therein, and in any free writing prospectus that we have authorized for use in connection with this offering. If any of these risks actually occurs, our business, financial condition, results of operations or cash flow could be seriously harmed. This could cause the trading price of our common stock to decline, resulting in a loss of all or part of your investment.

Risks Related to This Offering

Management will have broad discretion as to the use of the proceeds from this offering, and we may not use the proceeds effectively.

Our management will have broad discretion with respect to the use of proceeds of this offering, including for any of the purposes described in the section of this prospectus supplement titled "Use of Proceeds." You will be relying on the judgment of our management regarding the application of the proceeds of this offering. The results and effectiveness of the use of proceeds are uncertain, and we could spend the proceeds in ways that you do not agree with or that do not improve our results of operations or enhance the value of our common stock. Our failure to apply these funds effectively could have a material adverse effect on our business, delay the development of our product candidates and cause the price of our common stock to decline.

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

Since the public offering price for our common stock in this offering is substantially higher than the net tangible book value per share of our common stock outstanding prior to this offering, you will suffer immediate and substantial dilution in the net tangible book value of the common stock you purchase in this offering. Based on the assumed public offering price of \$19.09 per share (the last reported sale price of our common stock on The NASDAQ Global Market on March 28, 2017), if you purchase shares in this offering, you will suffer immediate dilution of \$15.11 per share in the net tangible book value of the common stock. If the underwriters exercise their option to purchase additional shares, you will experience additional dilution. See the section titled "Dilution" below for a more detailed discussion of the dilution you will incur if you purchase shares in this offering.

Changes in tax law may affect the U.S. federal tax considerations of the purchase, ownership and disposition of our common stock.

Potential tax reform in the United States may result in significant changes to United States federal income taxation law, including changes to the U.S. federal income taxation of corporations (including the Company) and/or changes to the U.S. federal income taxation of stockholders in U.S. corporations, including investors in our common stock. We are currently unable to predict whether such changes will occur and, if so, the impact of such changes, including on the U.S. federal income tax considerations relating to the purchase, ownership and disposition of our common stock, as discussed below in the section titled "Material U.S. Federal Income Tax Considerations to Non-U.S. Holders."

Table of Contents

USE OF PROCEEDS

We estimate that the net proceeds from our issuance and sale of 4,190,675 shares of our common stock in this offering will be approximately \$74.7 million, or approximately \$86.0 million if the underwriters exercise their option to purchase additional shares in full, based on an assumed public offering price of \$19.09 per share (the last reported sale price of our common stock on The NASDAQ Global Market on March 28, 2017), after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

We intend to use the net proceeds of this offering to fund our clinical and research development activities, including the completion of our Phase 3 program for I.V. CR845 in uremic pruritus, two Phase 3 trials of I.V. CR845 in acute pain and a Phase 2b trial of Oral CR845 in osteoarthritis pain, and for working capital and other general corporate purposes, including in-licensing and acquisitions. We may also use a portion of the net proceeds to invest in or acquire businesses or technologies that we believe are complementary to our own, although we have no current plans, commitments or agreements with respect to any acquisitions as of the date of this prospectus supplement. Pending these uses, we plan to invest these net proceeds in investment-grade, interest bearing securities.

These expected uses represent our intentions based upon our current plans and business conditions, which could change in the future as our plans and business conditions evolve. We currently anticipate that the net proceeds from this offering, together with our existing cash resources, will be sufficient to fund our currently anticipated operating expenses and capital expenditures into 2019. The amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including the progress of our development, the status of and results from clinical trials, as well as any new collaborations that we may enter into with third parties for our product candidates, and any unforeseen cash needs. As a result, our management will have broad discretion in the application of the net proceeds from this offering, and investors will be relying on the judgment of our management regarding the application of the net proceeds from this offering. The timing and amount of our actual expenditures will be based on many factors, including cash flows from operations and the anticipated growth of our business.

Table of Contents

DILUTION

If you invest in our common stock, your interest will be diluted immediately to the extent of the difference between the public offering price per share you will pay in this offering and the as adjusted net tangible book value per share of our common stock after this offering. Net tangible book value per share represents our total tangible assets less total liabilities, divided by the number of shares of our common stock outstanding.

As of December 31, 2016, our net tangible book value was \$50.7 million, or \$1.86 per share of common stock. After giving effect to our issuance and sale of 4,190,675 shares of our common stock in this offering at the assumed public offering price of \$19.09 per share (the last reported sale price of our common stock on The NASDAQ Global Market on March 28, 2017), after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us, the as adjusted net tangible book value as of December 31, 2016 would have been \$125.4 million, or \$3.98 per share. This represents an immediate increase in as adjusted net tangible book value to existing stockholders of \$2.12 per share and an immediate dilution to new investors purchasing common stock in this offering of \$15.11 per share.

The following table illustrates this per share dilution to the new investors purchasing shares of our common stock in this offering:

Assumed public offering price per share	\$ 19.09
Net tangible book value per share as of December 31, 2016	\$ 1.86
Increase in net tangible book value per share attributable to new investors purchasing shares in this offering	2.12
As adjusted net tangible book value per share after this offering	3.98
Dilution per share to new investors purchasing shares in this offering	\$ 15.11

Each \$1.00 increase or decrease in the assumed public offering price of \$19.09 per share would increase or decrease, as applicable, our as adjusted net tangible book value by approximately \$0.13 per share, and would increase or decrease, as applicable, dilution per share to new investors in this offering by \$0.87 per share, assuming that the aggregate dollar amount of the shares offered by us remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. The foregoing as adjusted information is illustrative only and will be adjusted based on the actual public offering price of this offering determined at pricing.

If the underwriters exercise their option to purchase additional shares in full, at the assumed public offering price of \$19.09 per share (the last reported sale price of our common stock on The NASDAQ Global Market on March 28, 2017), the as adjusted net tangible book value will increase to \$4.26

per share, representing an immediate increase in net tangible book value to existing stockholders of \$2.40 per share and an immediate dilution in net tangible book value of \$14.83 per share to new investors.

The foregoing table and calculations are based on 27,296,863 shares of our common stock outstanding as of December 31, 2016, and exclude 3,225,199 shares of common stock reserved for issuance under our 2004 Stock Incentive Plan and our 2014 Equity Incentive Plan as of December 31, 2016, consisting of 2,548,408 shares of common stock subject to outstanding awards and 676,791 shares of common stock that remain available under our 2014 Equity Incentive Plan for future grants.

Table of Contents

MATERIAL U.S. FEDERAL INCOME TAX CONSIDERATIONS TO NON-U.S. HOLDERS

The following is a general discussion of the material U.S. federal income tax considerations relating to the acquisition, ownership and disposition of our common stock by Non-U.S. Holders (as defined below). This discussion is a summary for general information purposes only and does not consider all aspects of U.S. federal income taxation that may be relevant to particular Non-U.S. Holders in light of their individual circumstances or to certain types of Non-U.S. Holders subject to special tax rules under the Internal Revenue Code of 1986, as amended, or the Code, including partnerships or other pass-through entities for U.S. federal income tax purposes, banks, financial institutions or other financial services entities, broker-dealers, insurance companies, tax-exempt organizations, regulated investment companies, real estate investment trusts, foreign governments, pension plans, controlled foreign corporations, passive foreign investment companies, corporations that accumulate earnings to avoid U.S. federal income tax, persons who use or are required to use mark-to-market accounting, persons that hold our shares as part of a straddle, a hedge or a conversion transaction, certain former citizens or permanent residents of the U.S., investors in pass-through entities, or persons who hold or receive shares of our common stock pursuant to the exercise of an employee stock option or otherwise as compensation. In addition, this summary does not address the effects of any applicable gift or estate tax, and this summary does not address the potential application of the alternative minimum tax or the Medicare contribution tax or any tax considerations that may apply to Non-U.S. Holders of our common stock under state, local or non-U.S. tax laws and any other U.S. federal tax laws. This discussion does not take into account or address changes to United States tax law that may result from tax reforms that may be enacted in 2017 or thereafter.

This summary is based on the Code, and applicable Treasury Regulations, rulings, administrative pronouncements and decisions as of the date of this registration statement, all of which are subject to change or differing interpretations at any time with possible retroactive effect. We have not sought, and will not seek, any ruling from the Internal Revenue Service, or the IRS, with respect to the tax consequences discussed herein, and there can be no assurance that the IRS will not take a position contrary to the tax consequences discussed below or that any position taken by the IRS would not be sustained. This discussion assumes that a Non-U.S. Holder will hold our common stock as a capital asset within the meaning of Section 1221 of the Code (generally, property held for investment).

For purposes of this discussion, the term Non-U.S. Holder means a beneficial owner of our shares that is not a partnership (or entity or arrangement treated as a partnership for U.S. federal income tax purposes) and is not, for U.S. federal income tax purposes:

an individual who is a citizen or resident of the United States;

a corporation created or organized in the U.S. or under the laws of the U.S. or of 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 if (1) a U.S. court can exercise primary supervision over the trust's administration and one or more U.S. persons have the authority to control all of the trust's substantial decisions or (2) the trust has a valid election in effect under applicable U.S. Treasury Regulations to be treated as a U.S. person.

If a partnership (or entity or arrangement treated as a partnership for U.S. federal income tax purposes) or an entity that is treated as a disregarded entity for U.S. federal income tax purposes (regardless of its place of organization or formation) is a beneficial owner of our common stock, the tax treatment of a partner in the partnership or the owner of the disregarded entity will generally depend upon the status of the partner or the owner of the disregarded entity and the activities of the partnership or the disregarded

Table of Contents

entity. If you are a partner of a partnership holding our common stock or the owner of a disregarded entity holding our common stock, you should consult your tax advisor regarding the tax consequences of the purchase, ownership, and disposition of our common stock.

THIS SUMMARY IS NOT INTENDED TO BE TAX ADVICE. PROSPECTIVE INVESTORS SHOULD CONSULT THEIR TAX ADVISORS REGARDING THE PARTICULAR U.S. FEDERAL INCOME TAX CONSEQUENCES TO THEM OF ACQUIRING, OWNING AND DISPOSING OF OUR COMMON STOCK, AS WELL AS ANY TAX CONSEQUENCES ARISING UNDER ANY STATE, LOCAL OR FOREIGN TAX LAWS AND ANY OTHER U.S. FEDERAL TAX LAWS.

Distributions on Our Common Stock

In general, subject to the discussions below under the headings Information Reporting and Backup Withholding and Foreign Accounts, distributions, if any, paid on our common stock to a Non-U.S. Holder (to the extent paid out of our current or accumulated earnings and profits, as determined under U.S. federal income tax principles) will constitute dividends and be subject to U.S. withholding tax at a rate equal to 30% of the gross amount of the dividend, or a lower rate prescribed by an applicable income tax treaty, unless the dividends are effectively connected with a trade or business carried on by the Non-U.S. Holder within the United States. The portion of any distribution not constituting a dividend (because such distribution exceeds our current and accumulated earnings and profits) will be treated first as reducing the Non-U.S. Holder's basis in its shares of our common stock, but not below zero, and to the extent it exceeds the Non-U.S. Holder's basis, as capital gain and will be treated as described below under Gain on Sale, Exchange or Other Disposition of Our Common Stock.

A Non-U.S. Holder who claims the benefit of an applicable income tax treaty generally will be required to satisfy certain certification and other requirements prior to the distribution date. Such Non-U.S. Holder must generally provide the withholding agent with a properly executed IRS Form W-8BEN, IRS Form W-8BEN-E or other appropriate form claiming an exemption from or reduction in withholding under an applicable income tax treaty. This certification must be provided before dividends on our common stock are paid and must be updated periodically. If a Non-U.S. Holder holds our common 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 us or our paying agent, either directly or through other intermediaries. If tax is withheld in an amount in excess of the amount applicable under an income tax treaty, a refund of the excess amount may generally be obtained 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 an applicable income tax treaty.

Dividends that are effectively connected with a Non-U.S. Holder's conduct of a U.S. trade or business (and, if required by an applicable income tax treaty, attributable to a U.S. permanent establishment or fixed base of the Non-U.S. Holder) generally will not be subject to the 30% U.S. federal withholding tax if the Non-U.S. Holder provides the withholding agent with the required forms, including IRS Form W-8ECI, but instead generally will be subject to U.S. federal income tax on a net income basis at the regular graduated rates in the same manner as if the Non-U.S. Holder were a resident of the U.S. This certification must be provided before dividends on our common stock are paid and must be updated periodically. A corporate Non-U.S. Holder that receives effectively connected dividends may also be subject to an additional branch profits tax at a rate of 30% (or a lower rate prescribed by an applicable income tax treaty) of its effectively connected earnings and profits for the taxable year, as adjusted for certain items.

Table of Contents

Gain on Sale, Exchange or Other Disposition of Our Common Stock

In general, a Non-U.S. holder will not be subject to any U.S. federal income tax or withholding tax on any gain realized upon such holder's sale, exchange or other disposition of shares of our common stock unless:

- (i) the gain is effectively connected with a trade or business carried on by the Non-U.S. Holder within the United States (and, if required by an applicable income tax treaty, attributable to a U.S. permanent establishment or fixed base of the Non-U.S. Holder);
- (ii) the Non-U.S. Holder is an individual who is present in the United States for 183 days or more in the taxable year of disposition and certain other conditions are met; or
- (iii) we are or have been a United States real property holding corporation for U.S. federal income tax purposes at any time during the shorter of the five-year period ending on the date of disposition or the period that the Non-U.S. Holder held the common stock, and, in the case where shares of our common stock are regularly traded on an established securities market, the Non-U.S. Holder owns, or is treated as owning, more than five percent of our common stock at any time during the foregoing period.

Net gain realized by a Non-U.S. Holder described in clause (i) above generally will be subject to U.S. federal income tax in the same manner as if the Non-U.S. Holder were a U.S. person. Any gains of a corporate Non-U.S. Holder described in clause (i) above may also be subject to an additional branch profits tax at a 30% rate, or such lower rate as may be specified by an applicable income tax treaty.

Gain realized by an individual Non-U.S. Holder described in clause (ii) above will be subject to a flat 30% (or such lower rate specified by an applicable income tax treaty) tax, which gain may be offset by certain U.S. source capital losses, even though the individual is not considered a resident of the United States, provided that the Non-U.S. Holder has timely filed U.S. federal income tax returns with respect to such losses.

For purposes of clause (iii) above, a corporation is a United States real property holding corporation if the fair market value of its U.S. real property interests equals or exceeds 50% of the sum of the fair market value of its worldwide real property interests plus its other assets used or held for use in a trade or business. We believe that we are not, and we do not anticipate that we will become, a United States real property holding corporation. However, because the determination of whether we are a United States real property holding corporation depends on the fair market value of our U.S. real property interests relative to the fair market value of our other business assets, there can be no assurance that we will not become a United States real property holding corporation in the future. If we become a United States real property holding corporation, as long as our common stock is regularly traded on an established securities market, our common stock will be treated as a U.S. real property interest only with respect to a Non-U.S. Holder that actually or constructively held more than 5% of our common stock at any time during the shorter of the two periods described in clause (iii), above. If we are a U.S. real property holding corporation and either our common stock is not regularly traded on an established securities market or a Non-U.S. Holder holds, or is treated as holding, more than 5% of our outstanding common stock, directly or indirectly, during the applicable testing period, such Non-U.S. Holder will generally be taxed on any gain in the same manner as gain that is effectively connected with the conduct of a U.S. trade or business, except that the branch profits tax generally will not apply. If we are a U.S. real property holding corporation and our common stock is not regularly traded on an established securities market, a Non-U.S. Holder's proceeds received on the disposition of shares will also generally be subject to withholding at a rate of 15%. Prospective investors are encouraged to consult their own tax advisors regarding the possible consequences to them if we are, or were to become, a USRPHC.

Table of Contents

Information Reporting and Backup Withholding

Generally, we must report annually to the IRS and to each Non-U.S. Holder the amount of dividends paid, the name and address of the recipient, and the amount, if any, of tax withheld. These information reporting requirements apply even if withholding was not required because the dividends were effectively connected with the Non-U.S. Holder's conduct of a trade or business within the United States or withholding was reduced by an applicable income tax treaty. Under applicable income tax treaties or other agreements, the IRS may make its reports available to the tax authorities in the Non-U.S. Holder's country of residence.

Dividends paid to a Non-U.S. Holder that is not an exempt recipient generally will be subject to backup withholding, currently at a rate of 28%, unless the Non-U.S. Holder certifies to the withholding agent as to its foreign status, which certification may generally be made on IRS Form W-8BEN, Form W-8BEN-E or other appropriate version of IRS Form W-8. Notwithstanding the foregoing, backup withholding may apply if either we or our paying agent has actual knowledge, or reason to know, that the holder is a U.S. person that is not an exempt recipient.

Proceeds from the sale or other disposition of common stock by a Non-U.S. Holder effected by or through a U.S. office of a broker will generally be subject to information reporting and backup withholding, currently at a rate of 28%, unless the Non-U.S. Holder certifies to the withholding agent under penalties of perjury as to, among other things, its name, address and status as a Non-U.S. Holder or otherwise establishes an exemption. Payment of disposition proceeds effected outside the United States by or through a non-U.S. office of a non-U.S. broker generally will not be subject to information reporting or backup withholding if the payment is not received in the U.S. Information reporting, but generally not backup withholding (provided the broker does not have actual knowledge or reason to know that the holder is a U.S. person that is not an exempt recipient), will apply to such a payment if the broker has certain connections with the United States unless the broker has documentary evidence in its records that the beneficial owner thereof is a Non-U.S. Holder and specified conditions are met or an exemption is otherwise established.

Backup withholding is not an additional tax. Any amount withheld under the backup withholding rules from a payment to a Non-U.S. Holder that results in an overpayment of taxes generally will be refunded, or credited against the holder's U.S. federal income tax liability, if any, provided that the required information is timely furnished to the IRS.

Foreign Accounts

The Foreign Account Tax Compliance Act, or FATCA, generally imposes a 30% withholding tax on dividends on, and gross proceeds from the sale or disposition of, our common stock if paid to a foreign entity unless (i) if the foreign entity is a foreign financial institution, the foreign entity undertakes certain due diligence, reporting, withholding, and certification obligations, (ii) if the foreign entity is not a foreign financial institution, the foreign entity identifies certain U.S. holders of debt or equity interests in such foreign entity or (iii) the foreign entity is otherwise exempt from FATCA.

Withholding under FATCA generally (1) applies to payments of dividends on our common stock and (2) will apply to payments of gross proceeds from a sale or other disposition of our common stock made after December 31, 2018. An intergovernmental agreement between the United States and an applicable foreign country may modify the requirements described in this section. Under certain circumstances, a Non-U.S. Holder may be eligible for refunds or credits of the tax. Non-U.S. Holders should consult their own tax advisors regarding the possible implications of FATCA on their investment in our common stock.

Table of Contents**UNDERWRITING**

Subject to the terms and conditions set forth in an underwriting agreement, each of the underwriters named below has severally agreed to purchase from us the aggregate number of shares of common stock set forth opposite their respective names below:

Name	Number of Shares
Piper Jaffray & Co.	
Stifel, Nicolaus & Company, Incorporated	
Total	

The underwriting agreement provides that the obligations of the several underwriters are subject to various conditions, including approval of legal matters by counsel. The nature of the underwriters' obligations commits them to purchase and pay for all of the shares of common stock listed above if any are purchased. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

The underwriters expect to deliver the shares of common stock to purchasers on or about _____, 2017.

Option to Purchase Additional Shares

We have granted a 30-day option to the underwriters to purchase up to a total of _____ additional shares of our common stock from us, at the public offering price, less the underwriting discounts and commissions payable by us, as set forth on the cover page of this prospectus supplement. If the underwriters exercise this option in whole or in part, then each of the underwriters will be separately committed, subject to the conditions described in the underwriting agreement, to purchase the additional shares of our common stock in proportion to their respective commitments set forth in the table above.

Commissions and Discounts

The underwriters propose to offer the shares of common stock directly to the public at the public offering price set forth on the cover page of this prospectus, and at this price less a concession not in excess of \$ _____ per share of common stock to other dealers specified in a master agreement among underwriters who are members of the Financial Industry Regulatory Authority, Inc. The underwriters may allow, and the other dealers specified may reallow, concessions not in excess of \$ _____ per share of common stock to these other dealers. After this offering, the offering price, concessions, and other selling terms may be changed by the underwriters. Our common stock is offered subject to receipt and acceptance by the underwriters and to the other conditions, including the right to reject orders in whole or in part.

The following table summarizes the compensation to be paid to the underwriters by us and the proceeds, before expenses, payable to us:

	Per Share	Total Without option exercise	With full option exercise
Public offering price	\$	\$	\$
Underwriting discounts and commissions	\$	\$	\$
Proceeds, before expenses, to us	\$	\$	\$

Table of Contents

The expenses of this offering that are payable by us are estimated to be approximately \$500,000 (excluding underwriting discounts and commissions). We have agreed to reimburse the underwriters for certain of their expenses in an amount not to exceed \$ _____, including expenses of up to \$ _____ in connection with the clearance of this offering with the Financial Industry Regulatory Authority, as set forth in the underwriting agreement.

Indemnification of Underwriters

We will indemnify the underwriters against some civil liabilities, including liabilities under the Securities Act and liabilities arising from breaches of our representations and warranties contained in the underwriting agreement. If we are unable to provide this indemnification, we will contribute to payments the underwriters may be required to make in respect of those liabilities.

No Sale of Similar Securities

We and each of our directors and executive officers have agreed that we and they will not, without the prior written consent of each of Piper Jaffray & Co. and Stifel, Nicolaus & Company, Incorporated, directly or indirectly:

offer, sell, contract to sell (including any short sale), pledge, hypothecate transfer, establish an open put equivalent position within the meaning of Rule 16a-1(h) under the Exchange Act, grant any option, right or warrant for the sale of, purchase any option or contract to sell, sell any option or contract to purchase any shares of our common stock or securities convertible into or exchangeable or exercisable for any shares of our common stock;

otherwise encumber, dispose of or transfer, or grant any rights with respect to, directly or indirectly, any shares of our common stock or securities convertible into or exchangeable or exercisable for any shares of our common stock, enter into a transaction which would have the same effect, or enter into any swap, hedge or other arrangement that transfers, in whole or in part, any of the economic consequences of ownership of our common stock, whether any such aforementioned transaction is to be settled by delivery of our common stock or other securities, in cash or otherwise; or

publicly announce an intention to do any of the foregoing, for a period of 90 days after the date of this prospectus supplement. However, these lock-up restrictions will not apply to: (a) bona fide gifts made by the holder, (b) transfers of our securities to a trust for the direct or indirect benefit of the holder or the immediate family of the holder in a transaction not involving a disposition for value, (c) transfers of securities by will or intestate succession upon the death of the holder, (d) transfers or distributions to stockholders, members, partners, beneficiaries, or other equity holders of the securities holder, (e) the surrender or forfeiture of shares of common stock to us to satisfy tax withholding obligations upon exercise or vesting of stock options or warrants, (f) transfers of securities to the company in connection with the repurchase of shares pursuant to employee benefit plans, (g) a *bona fide* third party tender offer, merger, consolidation, or other similar transaction made to all holders of our common stock, (h) transfers pursuant to operation of law, including pursuant to a domestic order or negotiated divorce settlement, (i) the exercise of any option to purchase of our common stock granted under an equity incentive plan or stock purchase plan, or warrant to purchase our securities, provided that underlying shares received continue to be subject to the lock-up agreement, or (j) the entry into or activation following prior suspension of a trading plan established pursuant to Rule 10b5-1 under the Exchange Act, provided that such plan does not provide for any sales or other dispositions of shares of common stock during the 90-day restricted period. Any transferee under the excepted transfers described above in (a), (b) or (d) must agree in writing, prior to the transfer, to be bound by the applicable lock-up agreement.

Table of Contents

Piper Jaffray & Co. and Stifel, Nicolaus & Company, Incorporated may, in their sole discretion and at any time or from time to time before the termination of the 90-day period, 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 directors, officers or stockholders who will execute a lock-up agreement providing consent to the sale of shares prior to the expiration of the restricted period.

NASDAQ Market Listing

Our common stock is listed for trading on The NASDAQ Global Market under the symbol CARA.

Short Sales, Stabilizing Transactions, and Penalty Bids

In order to facilitate this offering, persons participating in this offering may engage in transactions that stabilize, maintain, or otherwise affect the price of our common stock during and after this offering. Specifically, the underwriters may engage in the following activities in accordance with the rules of the Securities and Exchange Commission.

Short sales. Short sales involve the sales by the underwriters of a greater number of shares than they are required to purchase in the offering. Covered short sales are short sales made in an amount not greater than the underwriters' option to purchase additional shares from us in this offering. The underwriters may close out any covered short position by either exercising their option to purchase shares or purchasing shares in the open market. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the option. Naked short sales are any short sales in excess of such option. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market after pricing that could adversely affect investors who purchase in this offering.

Stabilizing transactions. The underwriters may make bids for or purchases of the shares for the purpose of pegging, fixing, or maintaining the price of the shares, so long as stabilizing bids do not exceed a specified maximum.

Penalty bids. If the underwriters purchase shares in the open market in a stabilizing transaction or syndicate covering transaction, they may reclaim a selling concession from the underwriters and selling group members who sold those shares as part of this offering. Stabilization and syndicate covering transactions may cause the price of the shares to be higher than it would be in the absence of these transactions. The imposition of a penalty bid might also have an effect on the price of the shares if it discourages resales of the shares.

The transactions above may occur on the NASDAQ Global Market or otherwise. Neither we nor the underwriters make any representation or prediction as to the effect that the transactions described above may have on the price of the shares. If these transactions are commenced, they may be discontinued without notice at any time.

Electronic Distribution

A prospectus in electronic format may be made available on the internet sites or through other online services maintained by one or more of the underwriters participating in this offering, or by their affiliates. Other than the prospectus in electronic format, the information on any underwriter's web site and any information contained in any other web site maintained by an underwriter is not part of the prospectus or the registration statement of which this prospectus forms a part, has not been approved and/or endorsed by us or any underwriter in its capacity as underwriter and should not be relied upon by investors.

Table of Contents

Relationships

Certain of the underwriters or their affiliates may in the future provide investment banking, lending, financial advisory and other related services to us and our affiliates for which they may receive customary fees and commissions.

Notice to Prospective Investors in the European Economic Area

In relation to each member state of the European Economic Area that 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 (the relevant implementation date), an offer of securities described in this prospectus may not be made to the public in that relevant member state other than:

to any legal entity which is a qualified investor as defined in the Prospectus Directive;

to fewer than 100 or, if the relevant member state has implemented the relevant provision of the 2010 PD Amending Directive, 150, natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the representatives for any such offer; or

in any other circumstances that do not require the publication of a prospectus pursuant to Article 3 of the Prospectus Directive, provided that no such offer of securities shall require us or any underwriter to publish a prospectus pursuant to Article 3 of the Prospectus Directive. For purposes of this provision, the expression an offer of securities to the public in any relevant member state means the communication in any form and by any means of sufficient information on the terms of the offer and the securities to be offered so as to enable an investor to decide to purchase or subscribe the securities, as the expression may be varied in that member state by any measure implementing the Prospectus Directive in that member state, and the expression Prospectus Directive means Directive 2003/71/EC (and amendments thereto, including the 2010 PD Amending Directive) and includes any relevant implementing measure in each relevant member state, and the expression 2010 PD Amending Directive means Directive 2010/73/EU.

We have not authorized and do not authorize the making of any offer of securities through any financial intermediary on their behalf, other than offers made by the underwriters with a view to the final placement of the securities as contemplated in this prospectus. Accordingly, no purchaser of the securities, other than the underwriters, is authorized to make any further offer of the securities on behalf of us or the underwriters.

Notice to Prospective Investors in the United Kingdom

This prospectus is only being distributed to, and is only directed at, persons in the United Kingdom that are qualified investors within the meaning of Article 2(1)(e) of the Prospectus Directive (Qualified Investors) that are also (i) investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 (the Order) or (ii) high net worth entities, and other persons to whom it may lawfully be communicated, falling within Article 49(2)(a) to (d) of the Order (all such persons together being referred to as relevant persons). This prospectus and its contents are confidential and should not be distributed, published or reproduced (in whole or in part) or disclosed by recipients to any other persons in the United Kingdom. Any person in the United Kingdom that is not a relevant person should not act or rely on this document or any of its contents.

Table of Contents

Notice to Prospective Investors in Canada

This prospectus supplement constitutes an exempt offering document as defined in and for the purposes of applicable Canadian securities laws. No prospectus has been filed with any securities commission or similar regulatory authority in Canada in connection with the offer and sale of the common stock. No securities commission or similar regulatory authority in Canada has reviewed or in any way passed upon this prospectus supplement or on the merits of the common stock and any representation to the contrary is an offence.

Canadian investors are advised that this prospectus supplement has been prepared in reliance on section 3A.3 of National Instrument 33-105 *Underwriting Conflicts* (NI 33-105). Pursuant to section 3A.3 of NI 33-105, this prospectus supplement is exempt from the requirement that the Company and the underwriter(s) provide investors with certain conflicts of interest disclosure pertaining to connected issuer and/or related issuer relationships that may exist between the Company and the underwriter(s) as would otherwise be required pursuant to subsection 2.1(1) of NI 33-105.

Resale Restrictions

The offer and sale of the common stock in Canada is being made on a private placement basis only and is exempt from the requirement that the Company prepares and files a prospectus under applicable Canadian securities laws. Any resale of the common stock acquired by a Canadian investor in this offering must be made in accordance with applicable Canadian securities laws, which may vary depending on the relevant jurisdiction, and which may require resales to be made in accordance with Canadian prospectus requirements, pursuant to a statutory exemption from the prospectus requirements, in a transaction exempt from the prospectus requirements or otherwise under a discretionary exemption from the prospectus requirements granted by the applicable local Canadian securities regulatory authority. These resale restrictions may under certain circumstances apply to resales of the common stock outside of Canada.

Representations of Purchasers

Each Canadian investor who purchases the common stock will be deemed to have represented to the Company and the underwriter(s) that the investor (i) is purchasing the common stock as principal, or is deemed to be purchasing as principal in accordance with applicable Canadian securities laws, for investment only and not with a view to resale or redistribution; (ii) is an accredited investor as such term is defined in section 1.1 of National Instrument 45-106 *Prospectus Exemptions* (NI 45-106) or, in Ontario, as such term is defined in section 73.3(1) of the *Securities Act* (Ontario); and (iii) is a permitted client as such term is defined in section 1.1 of National Instrument 31-103 *Registration Requirements, Exemptions and Ongoing Registrant Obligations*.

Taxation and Eligibility for Investment

Any discussion of taxation and related matters contained in this prospectus supplement does not purport to be a comprehensive description of all of the tax considerations that may be relevant to a Canadian investor when deciding to purchase the common stock and, in particular, does not address any Canadian tax considerations. No representation or warranty is hereby made as to the tax consequences to a resident, or deemed resident, of Canada of an investment in the common stock or with respect to the eligibility of the common stock for investment by such investor under relevant Canadian federal and provincial legislation and regulations.

Rights of Action for Damages or Rescission

Securities legislation in certain of the Canadian jurisdictions provides certain purchasers of securities pursuant to an offering memorandum (such as this prospectus supplement), including where the

Table of Contents

distribution involves an eligible foreign security as such term is defined in Ontario Securities Commission Rule 45-501 *Ontario Prospectus and Registration Exemptions* and in Multilateral Instrument 45-107 *Listing Representation and Statutory Rights of Action Disclosure Exemptions*, as applicable, with a remedy for damages or rescission, or both, in addition to any other rights they may have at law, where the offering memorandum, or other offering document that constitutes an offering memorandum, and any amendment thereto, contains a misrepresentation as defined under applicable Canadian securities laws. These remedies, or notice with respect to these remedies, must be exercised or delivered, as the case may be, by the purchaser within the time limits prescribed under, and are subject to limitations and defences under, applicable Canadian securities legislation. In addition, these remedies are in addition to and without derogation from any other right or remedy available at law to the investor.

Language of Documents

Upon receipt of this document, each Canadian investor hereby confirms that it has expressly requested that all documents evidencing or relating in any way to the sale of the securities described herein (including for greater certainty any purchase confirmation or any notice) be drawn up in the English language only. *Par la réception de ce document, chaque investisseur Canadien confirme par les présentes qu'il a expressément exigé que tous les documents faisant foi ou se rapportant de quelque manière que ce soit à la vente des valeurs mobilières décrites aux présentes (incluant, pour plus de certitude, toute confirmation d'achat ou tout avis) soient rédigés en anglais seulement.*

Notice to Prospective Investors in France

This prospectus has not been prepared in the context of a public offering of financial securities in France within the meaning of Article L.411-1 of the French Code Monétaire et Financier and Title I of Book II of the Règlement Général of the Autorité des marchés financiers (the AMF) and therefore has not been and will not be filed with the AMF for prior approval or submitted for clearance to the AMF. Consequently, the shares of our common stock may not be, directly or indirectly, offered or sold to the public in France and offers and sales of the shares of our common stock may only be made in France to qualified investors (investisseurs qualifiés) acting for their own, as defined in and in accordance with Articles L.411-2 and D.411-1 to D.411-4, D.734-1, D.744-1, D.754-1 and D.764-1 of the French Code Monétaire et Financier. Neither this prospectus nor any other offering material may be released, issued or distributed to the public in France or used in connection with any offer for subscription on sale of the shares of our common stock to the public in France. The subsequent direct or indirect retransfer of the shares of our common stock to the public in France may only be made in compliance with Articles L.411-1, L.411-2, L.412-1 and L.621-8 through L.621-8-3 of the French Code Monétaire et Financier.

Notice to Residents of Germany

Each person who is in possession of this prospectus is aware of the fact that no German securities prospectus (wertpapierprospekt) within the meaning of the securities prospectus act (wertpapier-prospektgesetz, or the Act) of the Federal Republic of Germany has been or will be published with respect to the shares of our common stock. In particular, each underwriter has represented that it has not engaged and has agreed that it will not engage in a public offering in the Federal Republic of Germany (öffentliches Angebot) within the meaning of the Act with respect to any of the shares of our common stock otherwise than in accordance with the act and all other applicable legal and regulatory requirements.

Notice to Residents of Switzerland

The securities which are the subject of the offering contemplated by this prospectus may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange, or SIX, or on any other stock exchange or regulated trading facility in Switzerland. This prospectus has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of

Table of Contents

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. None of this prospectus or any other offering or marketing material relating to the securities or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

None of this prospectus or any other offering or marketing material relating to the offering, us or the securities have been or will be filed with or approved by any Swiss regulatory authority. In particular, this prospectus will not be filed with, and the offer of securities will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA and the offer of securities has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes, or CISA. The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of the securities.

Notice to Residents of the Netherlands

The offering of the shares of our common stock is not a public offering in The Netherlands. The shares of our common stock may not be offered or sold to individuals or legal entities in The Netherlands unless (i) a prospectus relating to the offer is available to the public, which has been approved by the Dutch Authority for the Financial Markets (Autoriteit Financiële Markten) or by the competent supervisory authority of another state that is a member of the European Union or party to the Agreement on the European Economic Area, as amended or (ii) an exception or exemption applies to the offer pursuant to Article 5:3 of The Netherlands Financial Supervision Act (Wet op het financieel toezicht) or Article 53 paragraph 2 or 3 of the Exemption Regulation of the Financial Supervision Act, for instance due to the offer targeting exclusively qualified investors (gekwalficeerde beleggers) within the meaning of Article 1:1 of The Netherlands Financial Supervision Act.

Notice to Residents of Japan

The underwriters will not offer or sell any of the shares of our common stock directly or indirectly in Japan or to, or for the benefit of any Japanese person or to others, for re-offering or re-sale directly or indirectly in Japan or to any Japanese person, except in each case pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the Financial Instruments and Exchange Law of Japan and any other applicable laws and regulations of Japan. For purposes of this paragraph, Japanese person means any person resident in Japan, including any corporation or other entity organized under the laws of Japan.

Notice to Residents of Hong Kong

The underwriters and each of their affiliates have not (1) offered or sold, and will not offer or sell, in Hong Kong, by means of any document, any shares of our common stock other than (a) to professional investors within the meaning of 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 Ordinance (Cap. 32) of Hong Kong or which do not constitute an offer to the public within the meaning of that Ordinance; and (2) issued or had in its possession for the purposes of issue, and will not issue or have in its possession for the purposes of issue, whether in Hong Kong or elsewhere any advertisement, invitation or document relating to the shares of our common stock which is directed at, or the contents of which are likely to be accessed or read by, the public in Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to the shares of our common stock which are or are intended to be disposed of only to persons outside Hong Kong or only to professional investors within the meaning of the Securities and Futures Ordinance and any rules made under that Ordinance. The contents of this document have not been reviewed by any regulatory authority in Hong Kong. You are advised to exercise caution in relation to the offer. If you are in any doubt about any of the contents of this document, you should obtain independent professional advice.

Table of Contents

Notice to Residents of Singapore

This document has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this document and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of shares of our common stock may not be circulated or distributed, nor may shares of our common stock 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 (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore (the "Securities and Futures Act"), (ii) to a relevant person, or any person pursuant to Section 275(1A), and in accordance with the conditions, specified in Section 275 of the Securities and Futures Act or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the Securities and Futures Act.

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

- (a) a corporation (which is not an accredited investor) 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 is an accredited investor, shares, debentures and units of shares and debentures of that corporation or the beneficiaries' rights and interest in that trust shall not be transferable for six months after that corporation or that trust has acquired the shares of our common stock under Section 275 except:
 - (1) to an institutional investor or to a relevant person, or to any person pursuant to an offer that is made on terms that such rights or interest are acquired at a consideration of not less than \$200,000 (or its equivalent in a foreign currency) for each transaction, whether such amount is to be paid for in cash or by exchange of securities or other assets;
 - (2) where no consideration is given for the transfer; or
 - (3) by operation of law.

LEGAL MATTERS

The validity of the common stock being offered in this offering will be passed upon for us by Cooley LLP, New York, New York. Certain legal matters related to this offering will be passed upon for the underwriters by Latham & Watkins LLP.

EXPERTS

The financial statements of Cara Therapeutics, Inc., appearing in Cara Therapeutics, Inc. Annual Report (Form 10-K) for the year ended December 31, 2016 have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon, included therein, and incorporated herein by reference. Such financial statements are incorporated herein by reference in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

Table of Contents

WHERE YOU CAN FIND MORE INFORMATION

This prospectus supplement and the accompanying prospectus form part of a registration statement on Form S-3 that we filed with the SEC. This prospectus supplement and the accompanying prospectus do not contain all of the information set forth in the registration statement and the exhibits to the registration statement or the documents incorporated by reference herein and therein. For further information with respect to us and the securities that we are offering under this prospectus supplement, we refer you to the registration statement and the exhibits and schedules filed as a part of the registration statement and the documents incorporated by reference herein and therein. You should rely only on the information contained in this prospectus supplement or the accompanying prospectus or incorporated by reference herein or therein. We have not authorized anyone else to provide you with different information. We are not making an offer of these securities in any state where the offer is not permitted. You should not assume that the information in this prospectus is accurate as of any date other than the date on the front page of this prospectus supplement, regardless of the time of delivery of this prospectus supplement or any sale of the securities offered hereby.

We file annual, quarterly and current reports, proxy statements and other information with the SEC. You may read and copy the registration statement, as well as any other document filed by us with the SEC, at the SEC's Public Reference Room at 100 F Street NE, Washington, D.C. 20549. You can also request copies of these documents by writing to the SEC and paying a fee for the copying cost. You may obtain information on the operation of the Public Reference Room by calling the SEC at (800) SEC-0330. The SEC maintains a website that contains reports, proxy statements and other information regarding issuers that file electronically with the SEC, including Cara Therapeutics. The address of the SEC website is www.sec.gov.

We maintain a website at www.caratherapeutics.com. Information contained in or accessible through our website does not constitute a part of this prospectus.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference information into this prospectus supplement, which means that we can disclose important information to you by referring you to another document filed separately with the SEC. The SEC file number for the documents incorporated by reference in this prospectus is 001-36279. The documents incorporated by reference into this prospectus supplement contain important information that you should read about us.

The following documents are incorporated by reference into this document:

our Annual Report on Form 10-K for the fiscal year ended December 31, 2016 filed with the SEC on March 10, 2017;

our Current Report on Form 8-K filed with the SEC on March 28, 2017; and

the description of our common stock, which is registered under Section 12 of the Exchange Act, in our registration statement on Form 8-A, filed with the SEC on January 27, 2014, including any amendments or reports filed for the purpose of updating such description.

We also incorporate by reference into this prospectus all documents (other than current reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items) that are filed by us with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of this prospectus supplement but prior to the termination of the offering. These documents include periodic reports, such as Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q and Current Reports on Form 8-K, as well as proxy statements.

Table of Contents

We will provide to each person, including any beneficial owner, to whom a prospectus is delivered, without charge upon written or oral request, a copy of any or all of the documents that are incorporated by reference into this prospectus but not delivered with the prospectus, including exhibits which are specifically incorporated by reference into such documents. Requests should be directed to: Cara Therapeutics, Inc., Attn: Investor Relations, 4 Stamford Plaza, 107 Elm Street, 9th Floor, Stamford, Connecticut 06902, telephone: (203) 406-3700.

Any statement contained herein or in a document incorporated or deemed to be incorporated by reference into this document will be deemed to be modified or superseded for purposes of the document to the extent that a statement contained in this document or any other subsequently filed document that is deemed to be incorporated by reference into this document modifies or supersedes the statement.

S-23

Table of Contents

PROSPECTUS

\$250,000,000

Common Stock

Preferred Stock

Debt Securities

Warrants

From time to time, we may offer up to \$250,000,000 of any combination of the securities described in this prospectus. We may also offer securities as may be issuable upon conversion, redemption, repurchase, exchange or exercise of any securities registered hereunder, including any applicable antidilution provisions.

This prospectus provides a general description of the securities we may offer. Each time we offer securities, we will provide specific terms of the securities offered in a supplement to this prospectus. We may also authorize one or more free writing prospectuses to be provided to you in connection with these offerings. The prospectus supplement and any related free writing prospectus may also add, update or change information contained in this prospectus. You should carefully read this prospectus, the applicable prospectus supplement and any related free writing prospectus, as well as any documents incorporated by reference, before you invest in any of the securities being offered.

This prospectus may not be used to consummate a sale of any securities unless accompanied by a prospectus supplement.

Our common stock is traded on the Nasdaq Global Market under the symbol CARA. On March 10, 2017, the last reported sales price of our common stock was \$15.84 per share. The applicable prospectus supplement will contain information, where applicable, as to any other listing on the Nasdaq Global Market or any securities market or other exchange of the securities, if any, covered by the prospectus supplement.

We will sell these securities directly to investors, through agents designated from time to time or to or through underwriters or dealers, on a continuous or delayed basis. For additional information on the methods of sale, you should refer to the section entitled Plan of Distribution in this prospectus. If any agents or underwriters are involved in the sale of any securities with respect to which this prospectus is being delivered, the names of such agents or underwriters and any applicable fees, commissions, discounts or over-allotment options will be set forth in a prospectus supplement. The price to the public of such securities and the net proceeds we expect to receive from such sale will also be set forth in a prospectus supplement.

Investing in our securities involves a high degree of risk. You should review carefully the risks and uncertainties described under the heading Risk Factors contained in the applicable prospectus supplement and any related

free writing prospectus, and under similar headings in the other documents that are incorporated by reference into this prospectus.

NEITHER THE SECURITIES AND EXCHANGE COMMISSION NOR ANY STATE SECURITIES COMMISSION HAS APPROVED OR DISAPPROVED OF THESE SECURITIES OR DETERMINED IF THIS PROSPECTUS IS TRUTHFUL OR COMPLETE. ANY REPRESENTATION TO THE CONTRARY IS A CRIMINAL OFFENSE.

The date of this prospectus is March 24, 2017.

Table of Contents

TABLE OF CONTENTS

<u>ABOUT THIS PROSPECTUS</u>	1
<u>SUMMARY</u>	2
<u>RISK FACTORS</u>	7
<u>SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS</u>	8
<u>RATIO OF EARNINGS (LOSS) TO FIXED CHARGES</u>	10
<u>USE OF PROCEEDS</u>	11
<u>DESCRIPTION OF CAPITAL STOCK</u>	12
<u>DESCRIPTION OF DEBT SECURITIES</u>	17
<u>DESCRIPTION OF WARRANTS</u>	24
<u>LEGAL OWNERSHIP OF SECURITIES</u>	26
<u>PLAN OF DISTRIBUTION</u>	30
<u>LEGAL MATTERS</u>	32
<u>EXPERTS</u>	32
<u>WHERE YOU CAN FIND MORE INFORMATION</u>	32
<u>INCORPORATION OF CERTAIN INFORMATION BY REFERENCE</u>	33
<u>DISCLOSURE OF COMMISSION POSITION ON INDEMNIFICATION FOR SECURITIES ACT LIABILITY</u>	34

Table of Contents

ABOUT THIS PROSPECTUS

This prospectus is a part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission, or SEC, utilizing a shelf registration process. Under this shelf registration process, we may sell any combination of the securities described in this prospectus in one or more offerings up to a total dollar amount of \$250,000,000. This prospectus provides you with a general description of the securities we may offer.

Each time we sell securities under this prospectus, we will provide a prospectus supplement that will contain specific information about the terms of that offering. We may also authorize one or more free writing prospectuses to be provided to you that may contain material information relating to these offerings. The prospectus supplement and any related free writing prospectus that we may authorize to be provided to you may also add, update or change information contained in this prospectus or in any documents that we have incorporated by reference into this prospectus. You should read this prospectus, any applicable prospectus supplement and any related free writing prospectus, together with the information incorporated herein by reference as described under the heading **Incorporation of Certain Information By Reference**, before investing in any of the securities offered.

THIS PROSPECTUS MAY NOT BE USED TO CONSUMMATE A SALE OF SECURITIES UNLESS IT IS ACCOMPANIED BY A PROSPECTUS SUPPLEMENT.

You should rely only on the information that we have provided or incorporated by reference in this prospectus, any applicable prospectus supplement and any related free writing prospectus that we may authorize to be provided to you. We have not authorized any dealer, salesman or other person to give any information or to make any representation other than those contained or incorporated by reference in this prospectus, any applicable prospectus supplement or any related free writing prospectus that we may authorize to be provided to you. You must not rely upon any information or representation not contained or incorporated by reference in this prospectus, any applicable prospectus supplement or any related free writing prospectus. This prospectus, any applicable supplement to this prospectus or any related free writing prospectus do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the registered securities to which they relate, nor do this prospectus, any applicable supplement to this prospectus or any related free writing prospectus constitute an offer to sell or the solicitation of an offer to buy securities in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation in such jurisdiction.

You should not assume that the information contained in this prospectus, any applicable prospectus supplement or any related free writing prospectus is accurate on any date subsequent to the date set forth on the front of the document or that any information we have incorporated by reference is correct on any date subsequent to the date of the document incorporated by reference, even though this prospectus, any applicable prospectus supplement or any related free writing prospectus is delivered, or securities are sold, on a later date.

This prospectus contains summaries of certain provisions contained in some of the documents described herein, but reference is made to the actual documents for complete information. All of the summaries are qualified in their entirety by the actual documents. Copies of some of the documents referred to herein have been filed, will be filed or will be incorporated by reference as exhibits to the registration statement of which this prospectus is a part, and you may obtain copies of those documents as described below under the heading **Where You Can Find More Information**.

Table of Contents

SUMMARY

This summary highlights selected information from this prospectus and does not contain all of the information that you need to consider in making your investment decision. You should carefully read the entire prospectus, the applicable prospectus supplement and any related free writing prospectus, including the risks of investing in our securities discussed under the heading **Risk Factors** contained in the applicable prospectus supplement and any related free writing prospectus, and under similar headings in the other documents that are incorporated by reference into this prospectus. You should also carefully read the information incorporated by reference into this prospectus, including our financial statements, and the exhibits to the registration statement of which this prospectus is a part.

Unless the context indicates otherwise, as used in this prospectus, the terms **Cara Therapeutics**, **Cara**, **the Company**, **we**, **us** and **our** refer to Cara Therapeutics, Inc., a Delaware corporation. We use Cara Therapeutics as a trademark in the United States. All other trademarks or trade names referred to in this prospectus are the property of their respective owners.

Our Company

We are a clinical-stage biopharmaceutical company focused on developing and commercializing new chemical entities designed to alleviate pain and pruritus by selectively targeting kappa opioid receptors. We are developing a novel and proprietary class of product candidates that target the body's peripheral nervous system and have demonstrated efficacy in patients with moderate-to-severe pain without inducing many of the undesirable side effects typically associated with currently available pain therapeutics.

Our most advanced product candidate is based on our new chemical entity, CR845, which is designed to produce pain relief by specifically stimulating kappa, rather than mu, opioid receptors outside of the central nervous system. Intravenous, or I.V., CR845, has demonstrated significant pain relief and a favorable safety and tolerability profile in three Phase 2 clinical trials in patients with acute postoperative pain. In addition, in the fourth quarter of 2014, we successfully completed a Human Abuse Liability, or HAL, trial of I.V. CR845 in which I.V. CR845 met the trial's primary endpoint by demonstrating highly statistically significant lower drug liking scores as measured by visual analog scale (VAS) Emax ($p < 0.0001$) when compared to the approved Schedule IV opioid, pentazocine. We believe that the totality of the results from the HAL trial are supportive of the potential for CR845 to be the first non-scheduled or low (Schedule V) scheduled peripheral opioid for acute pain.

In September 2015, we initiated our Phase 3 program for I.V. CR845 in postoperative pain with the dosing of the first subjects in an adaptive pivotal trial in patients undergoing a range of abdominal surgeries. The trial protocol initially included three dose levels of I.V. CR845 (1.0 ug/kg, 2.0 ug/kg and 5.0 ug/kg), which were compared to placebo with an interim conditional power assessment to identify optimal doses to be used to complete the enrollment of this trial.

In June 2016, we modified the trial protocol and resumed the trial as a three-arm trial, testing two doses of CR845 (1.0 ug/kg and 0.5 ug/kg) versus placebo, based on a safety review by us, the trial's Independent Data Monitoring Committee and the U.S. Food and Drug Administration, or FDA, of unblinded safety data from the first 90 patients dosed. The safety review was conducted in response to a clinical hold that the FDA placed on the trial in February 2016 and removed in April 2016 following the safety review. The clinical hold was based on a pre-specified stopping rule related to elevated serum sodium levels of greater than 150 mmol/L that was included in the clinical trial protocol.

The revised trial is enrolling up to 450 patients undergoing a range of abdominal surgeries, all of which are associated with moderate-to-severe postoperative pain, within the United States. The primary efficacy measure is

Table of Contents

the Change in Pain Intensity over the 24-hour postoperative period, using the patient-reported Numeric Rating Scale, or NRS, score collected at pre-specified time points through 24 hours. Postoperative nausea and vomiting is also being evaluated as a secondary efficacy measure. The impact of I.V. CR845 treatment on inflammatory biomarkers is also being explored. An interim conditional power analysis of our adaptive Phase 3 trial of I.V. CR845 for postoperative pain is expected in the second quarter of 2017.

Based on previous guidance from the FDA, we believe we will require 1,500 total exposures to I.V. CR845, including all Phase 1, Phase 2 and Phase 3 trials, prior to submitting a new drug application, or NDA. We believe our planned clinical trials and our clinical trials completed to date will result in a sufficient number of drug exposures to support an NDA.

We are also developing an oral version of CR845, or Oral CR845, for acute and chronic pain. In the second quarter of 2014, we initiated a Phase 1 trial of a tablet formulation of Oral CR845, for which we announced positive top-line data in the fourth quarter of 2014. In August 2015, we advanced our tablet formulation of Oral CR845 into a Phase 2a clinical trial in patients with osteoarthritis, or OA, of the knee or hip. The Phase 2a trial was a single-blind, randomized, multiple ascending dose trial designed to evaluate the safety, pharmacokinetics, or PK, and effectiveness of Oral CR845 tablets dosed over a two-week treatment period in 80 OA patients experiencing moderate-to-severe pain, defined as >4 on an 11-point NRS at baseline. In December 2015, we announced positive top-line results from this Phase 2a trial. The results showed a dose-related reduction in mean baseline pain score up to 34% after two weeks, with a statistically significant reduction in mean rescue medication for the top 5.0 mg dose group of approximately 80%. The results of the Phase 2a clinical trial established therapeutic doses and a dosing regimen for a larger randomized, double-blind, placebo-controlled Phase 2b trial, which we initiated during the third quarter of 2016. The Phase 2b trial is a trial of three tablet strengths of CR845, 1.0 mg, 2.5 mg and 5.0 mg, dosed twice-daily over an eight-week treatment period in approximately 330 OA patients experiencing moderate-to-severe pain across the United States. The primary efficacy endpoint is the change from baseline at week eight, with respect to the weekly mean of the daily pain intensity score using an NRS. We expect to report top-line data in the second quarter of 2017.

CR845 has exhibited anti-pruritic, or anti-itch, potency in standard preclinical models. In the fourth quarter of 2014, we reported positive top-line dose-ranging pharmacokinetic, or PK, and safety data from a Phase 1b clinical trial, which was part A of a Phase 2 proof-of-concept trial of I.V. CR845 for the treatment of uremic pruritus, an intractable systemic itch condition with high prevalence in dialysis patients with chronic kidney disease, for which there are no approved therapeutics in the United States. In July 2015, we reported positive top-line efficacy results from Part B of this Phase 2 proof-of-concept trial, in which we observed that I.V. CR845 demonstrated statistically significant results on the primary endpoint of reducing worst itch intensity as well as the secondary endpoint of quality of life improvements. We also observed I.V. CR845 to have a favorable safety and tolerability profile in the trial.

Based on the results of this trial, during the fourth quarter of 2015 we completed a guidance meeting with the FDA. We have incorporated the feedback we received from the FDA in this guidance meeting in the overall design of our Phase 3 clinical trial program for I.V. CR845 for the treatment of uremic pruritus. In June 2016, we initiated a two-part Phase 2/3 adaptive design trial of I.V. CR845 in dialysis patients suffering from moderate-to-severe uremic pruritus. Part A of the trial, is a randomized, double-blind, placebo-controlled trial in approximately 160 patients of three doses of I.V. CR845 (0.5ug/kg, 1.0 ug/kg and 1.5 ug/kg) administered three times per week after dialysis over an 8-week period. Part B will be a randomized double-blind placebo-controlled trial in up to 240 patients of one optimized dose of I.V. CR845 administered three times per week after dialysis over a 12-week treatment period. The primary endpoint will be reduction in worst itching scores from baseline values measured on a standard NRS alongside secondary quantitative quality of life endpoints. We expect to report top-line data from Part A of this trial in the first quarter of 2017.

We have also initiated a PK safety trial of multiple doses of Oral CR845 in hemodialysis patients to define bioequivalent tablet strengths to inform our ability to develop an oral tablet formulation for moderate-to-severe

Table of Contents

uremic pruritus. We expect to complete this trial in the first quarter of 2017, with data readout expected in the second quarter of 2017.

To date, we have financed our operations primarily through sales of our equity and debt securities and payments from license agreements. We have no products currently available for sale, and substantially all of our revenue to date has been revenue from license agreements, although we have received nominal amounts of revenue under research grants.

Since our inception and through December 31, 2016, we have raised an aggregate of approximately \$237.6 million to fund our operations, including (1) proceeds of \$75.2 million, net of underwriting discounts and commissions and offering expenses paid by us from the sale of approximately 4.33 million shares of our common stock in our follow-on offering of our common stock, which closed in August 2015; (2) proceeds of \$56.3 million, net of underwriting discounts and commissions and offering expenses paid by us, from the sale of 5.75 million shares of our common stock in our initial public offering, which closed in February 2014; (3) proceeds of \$65.9 million from the sale of shares of our convertible preferred stock prior to our initial public offering; (4) net proceeds of \$7.4 million from debt financings; and (5) aggregate payments of \$32.6 million pursuant to license agreements, primarily with Maruishi Pharmaceutical Co., Ltd. in Japan and Chong Kun Dang Pharmaceutical Corporation in South Korea, related to CR845 and an earlier product candidate for which development efforts ceased in 2007.

Corporate Information

Cara commenced operations in 2004, and our primary activities to date have been organizing and staffing our company, developing our product candidates, including conducting preclinical studies and clinical trials of CR845-based product candidates, and raising capital. Additional information concerning the Company is contained in the documents we file with the SEC, as described above. We maintain a website at www.caratherapeutics.com which contains information about Cara. Information contained in or accessed through our website is not part of or incorporated into this prospectus and should not be considered part of any offering documents.

Our mailing address is 4 Stamford Plaza, 107 Elm Street, Stamford, Connecticut 06902 (telephone number (203) 406-3700) where our principal executive offices are located and all of our operations are conducted. Our website is located at <http://www.caratherapeutics.com>. We do not incorporate by reference into this prospectus the information on, or accessible through, our website, and you should not consider it as part of this prospectus.

The Securities We May Offer

We may offer shares of our common stock and preferred stock, various series of debt securities and warrants to purchase any of such securities, with a total value of up to \$250,000,000 from time to time under this prospectus, together with any applicable prospectus supplement and any related free writing prospectus, at prices and on terms to be determined by market conditions at the time of the offering. This prospectus provides you with a general description of the securities we may offer. Each time we offer a type or series of securities under this prospectus, we will provide a prospectus supplement that will describe the specific amounts, prices and other important terms of the securities, including, to the extent applicable:

designation or classification;

aggregate principal amount or aggregate offering price;

maturity, if applicable;

original issue discount, if any;

Table of Contents

rates and times of payment of interest or dividends, if any;

redemption, conversion, exchange or sinking fund terms, if any;

conversion or exchange prices or rates, if any, and, if applicable, any provisions for changes to or adjustments in the conversion or exchange prices or rates and in the securities or other property receivable upon conversion or exchange;

ranking;

restrictive covenants, if any;

voting or other rights, if any; and

important United States federal income tax considerations.

The prospectus supplement and any related free writing prospectus that we may authorize to be provided to you may also add, update or change information contained in this prospectus or in documents we have incorporated by reference. However, no prospectus supplement or free writing prospectus will offer a security that is not registered and described in this prospectus at the time of the effectiveness of the registration statement of which this prospectus is a part.

This prospectus may not be used to consummate a sale of securities unless it is accompanied by a prospectus supplement.

We may sell the securities directly to investors or through underwriters, dealers or agents. We, and our underwriters or agents, reserve the right to accept or reject all or part of any proposed purchase of securities. If we do offer securities through underwriters or agents, we will include in the applicable prospectus supplement:

the names of those underwriters or agents;

applicable fees, discounts and commissions to be paid to them;

details regarding over-allotment options, if any; and

the estimated net proceeds to us.

Common Stock. We may issue shares of our common stock from time to time. The holders of our common stock are entitled to one vote for each share held of record on all matters submitted to a vote of stockholders and do not have

cumulative voting rights. Subject to preferences that may be applicable to any outstanding shares of preferred stock, the holders of our common stock are entitled to receive ratably such dividends as may be declared by our board of directors out of legally available funds. Upon our liquidation, dissolution or winding up, holders of our common stock are entitled to share ratably in all assets remaining after payment of liabilities and the liquidation preferences of any then outstanding shares of preferred stock. Our common stock does not carry any preemptive rights enabling a holder to subscribe for, or receive shares of, any class of our common stock or any other securities convertible into shares of any class of our common stock, or any redemption rights.

Preferred Stock. We may issue shares of our preferred stock from time to time, in one or more series. Under our certificate of incorporation, our board of directors has the authority, without further action by the stockholders (unless such stockholder action is required by applicable law or the rules of any stock exchange or market on which our securities are then traded), to designate up to 5,000,000 shares of preferred stock in one or more series and to determine the designations, voting powers, preferences and rights of each series of the preferred stock, as well as the qualifications, limitations or restrictions thereof, including dividend rights, conversion rights, preemptive rights, terms of redemption or repurchase, liquidation preferences, sinking fund terms and the number of shares constituting any series or the designation of any series, any or all of which may be greater than the rights of the common stock. Any convertible preferred stock we may issue will be convertible into our common stock or exchangeable for our other securities. Conversion may be mandatory or at the holder's option and would be at prescribed conversion rates.

Table of Contents

If we sell any series of preferred stock under this prospectus, we will fix the designations, voting powers, preferences and rights of such series of preferred stock, as well as the qualifications, limitations or restrictions thereof, in the certificate of designation relating to that series. We will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of any certificate of designation that describes the terms of the series of preferred stock that we are offering before the issuance of the related series of preferred stock. We urge you to read the applicable prospectus supplement (and any free writing prospectus that we may authorize to be provided to you) related to the series of preferred stock being offered, as well as the complete certificate of designation that contains the terms of the applicable series of preferred stock.

Debt Securities. We may issue debt securities from time to time, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. The senior debt securities will rank equally with any other unsecured and unsubordinated debt. The subordinated debt securities will be subordinate and junior in right of payment, to the extent and in the manner described in the instrument governing the debt, to all of our senior indebtedness. Convertible debt securities will be convertible into or exchangeable for our common stock or preferred stock. Conversion may be mandatory or at the holder's option and would be at prescribed conversion rates.

The debt securities will be issued under one or more documents called indentures, which are contracts between us and a national banking association or other eligible party, as trustee. In this prospectus, we have summarized certain general features of the debt securities. We urge you, however, to read the applicable prospectus supplement (and any free writing prospectus that we may authorize to be provided to you) related to the series of debt securities being offered, as well as the complete indentures that contain the terms of the debt securities. Forms of indentures have been filed as exhibits to the registration statement of which this prospectus is a part, and supplemental indentures and forms of debt securities containing the terms of the debt securities being offered will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the SEC.

Warrants. We may issue warrants for the purchase of common stock, preferred stock and/or debt securities in one or more series. We may issue warrants independently or together with common stock, preferred stock and/or debt securities, and the warrants may be attached to or separate from these securities. In this prospectus, we have summarized certain general features of the warrants. We urge you, however, to read the applicable prospectus supplement (and any free writing prospectus that we may authorize to be provided to you) related to the particular series of warrants being offered, as well as the complete warrant agreements and warrant certificates that contain the terms of the warrants. Forms of the warrant agreements and forms of warrant certificates containing the terms of the warrants being offered have been filed as exhibits to the registration statement of which this prospectus is a part, and supplemental warrant agreements and forms of warrant certificates will be filed as exhibits to the registration statement or will be incorporated by reference from reports that we file with the SEC.

We will evidence each series of warrants by warrant certificates that we will issue. Warrants may be issued under an applicable warrant agreement that we enter into with a warrant agent. We will indicate the name and address of the warrant agent, if applicable, in the prospectus supplement relating to the particular series of warrants being offered.

Table of Contents

RISK FACTORS

Investing in our securities involves a high degree of risk. You should carefully review the risks and uncertainties described under the heading "Risk Factors" contained in the applicable prospectus supplement and any related free writing prospectus, and under similar headings in the other documents that are incorporated by reference into this prospectus, before deciding whether to purchase any of the securities being registered pursuant to the registration statement of which this prospectus is a part. Each of the risk factors could adversely affect our business, operating results and financial condition, as well as adversely affect the value of an investment in our securities, and the occurrence of any of these risks might cause you to lose all or part of your investment. Additional risks not presently known to us or that we currently believe are immaterial may also significantly impair our business operations.

Table of Contents

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

Certain statements contained or incorporated by reference in this prospectus, any accompanying prospectus supplement and any related free writing prospectus constitute forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 and releases issued by the SEC and within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. In some cases, you can identify forward-looking statements by the words anticipate, believe, continue, could, estimate, expect, intend, may, might, objective, predict, project, potential, should, will, or would, and or the negative of these terms, or other comparable terms intended to identify statements about the future. From time to time, we publish forward-looking statements relating to matters such as anticipated financial performance, business prospects, technological developments, new products, research and development activities and other aspects of our present and future business operations as well as similar matters.

Forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause our or our industry's actual results, levels of activity, performance or achievements to be materially different from any future results, levels of activity, performance or achievements expressed or implied by such forward-looking statements. Although we believe that we have a reasonable basis for each forward-looking statement contained in this prospectus, we caution you that these statements are based on a combination of facts and factors currently known by us and our expectations of the future, about which we cannot be certain. While it is impossible to identify or predict all such matters, these differences may result from, among other things:

the success and timing of our clinical trials, including our clinical trial programs for I.V. CR845 in acute pain and uremic pruritus and Oral CR845 in acute and chronic pain, and the reporting of clinical trial results;

the potential regulatory development pathway for I.V. CR845 in uremic pruritus, including the potential request for breakthrough therapy designation;

our plans to develop and commercialize I.V. CR845, Oral CR845 and our other product candidates;

the potential results of ongoing and planned preclinical studies and clinical trials and future regulatory and development milestones for our product candidates;

the size and growth of the potential markets for pain management, including the postoperative and chronic pain markets, and for our other product candidates and our ability to serve those markets;

our ability to obtain and maintain regulatory approval of our product candidates, including I.V. and Oral CR845, and the labeling under any approval we may obtain;

the anticipated commercial launch of our lead product candidate, I.V. CR845;

the potential of future scheduling of I.V. CR845 by the United States Drug Enforcement Administration, or DEA, if regulatory approval is received;

the performance of our current and future collaborators, including Maruishi Pharmaceuticals Co. Ltd. and Chong Kun Dang Pharmaceutical Corp. and our ability to maintain such collaborations;

our ability to establish additional collaborations for our product candidates;

the continued service of our key scientific or management personnel;

our ability to establish commercialization and marketing capabilities;

regulatory developments in the United States and foreign countries;

the rate and degree of market acceptance of any approved products;

our ability to obtain and maintain coverage and adequate reimbursement from third-party payers for any approved products;

Table of Contents

our planned use of our cash and cash equivalents and marketable securities and the clinical milestones we expect to fund with such proceeds;

the accuracy of our estimates regarding expenses, future revenues and capital requirements;

our ability to obtain funding for our operations;

our ability to obtain and maintain intellectual property protection for our product candidates and our ability to operate our business without infringing on the intellectual property rights of others;

the success of competing drugs that are or may become available; and

the performance of third-party manufacturers and clinical research organizations.

In evaluating such forward-looking statements, you should specifically consider various factors, including the risks outlined under the heading **Risk Factors** contained in this prospectus, any accompanying prospectus supplement and any related free writing prospectus, and in our most recent Annual Report on Form 10-K and in our most recent Quarterly Report on Form 10-Q or Current Reports on Form 8-K filed with the SEC. The discussion of risks and uncertainties set forth in those filings is not necessarily a complete or exhaustive list of all risks facing us at any particular point in time. As a result of these factors, we cannot assure you that the forward-looking statements in this prospectus will prove to be accurate. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame or at all. We undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law. Forward-looking statements represent our estimates and assumptions only as of the date such forward-looking statements are made. You should carefully read this prospectus, any accompanying prospectus supplement and any related free writing prospectus, together with the information incorporated herein or therein by reference, and with the understanding that our actual future results may materially differ from what we expect. We qualify all of our forward-looking statements by these cautionary statements.

Table of Contents**RATIO OF EARNINGS (LOSS) TO FIXED CHARGES**

The following table sets forth our ratio of earnings (loss) to fixed charges for each of the periods indicated. We do not have any preferred stock outstanding as of the date of this prospectus and did not have any preferred stock with required dividend payments during any of the periods presented below. Therefore, there are no preferred dividends included in our calculation of these ratios. The following table is qualified by the more detailed information appearing in the computation table set forth in Exhibit 12.1 to the registration statement of which this prospectus is part and our historical financial statements, including the notes to those financial statements, incorporated by reference in this prospectus.

	Year Ended December 31,				
	2016	2015	2014	2013	2012
	(in thousands)				
Pre-tax loss	\$ (57,748)	\$ (25,087)	\$ (17,946)	\$ (3,993)	\$ (6,302)
Ratio of earnings to fixed charges (1)	N/A	N/A	N/A	N/A	N/A
Coverage deficiency	\$ 57,748	\$ 25,087	\$ 17,946	\$ 3,993	\$ 6,302

- (1) We did not record earnings for the years ended 2012 through 2016. Accordingly, our earnings were insufficient to cover fixed charges for such periods and we are unable to disclose a ratio of earnings to fixed charges for such periods.

Table of Contents

USE OF PROCEEDS

We will retain broad discretion over the use of the net proceeds from the sale of the securities offered hereby. Except as described in any applicable prospectus supplement or in any free writing prospectuses that we may authorize to be provided to you in connection with a specific offering, we currently intend to use the net proceeds from the sale of the securities offered hereby to conduct planned clinical trials of I.V. CR845 and Oral CR845, to fund the research and development of our preclinical pipeline, including drug discovery, and for working capital and other general corporate purposes. We may also use a portion of the net proceeds to invest in or acquire businesses or technologies that we believe are complementary to our own, although we have no current plans, commitments or agreements with respect to any acquisitions as of the date of this prospectus. We will set forth in the applicable prospectus supplement or free writing prospectus our intended use for the net proceeds received from the sale of any securities sold pursuant to the prospectus supplement or free writing prospectus. Pending these uses, we intend to invest the net proceeds in investment-grade, interest-bearing securities.

Table of Contents

DESCRIPTION OF CAPITAL STOCK

As of the date of this prospectus, our certificate of incorporation authorizes us to issue 100,000,000 shares of common stock, par value \$0.001 per share, and 5,000,000 shares of preferred stock, par value \$0.001 per share. As of December 31, 2016, 27,296,863 shares of common stock were outstanding and no shares of preferred stock were outstanding.

The following summary description of our capital stock is based on the provisions of our certificate of incorporation, as well as our bylaws and the applicable provisions of the Delaware General Corporation Law. This information is qualified entirely by reference to the applicable provisions of our certificate of incorporation, bylaws and the Delaware General Corporation Law. For information on how to obtain copies of our certificate of incorporation and bylaws, which are exhibits to the registration statement of which this prospectus is a part, see [Where You Can Find Additional Information](#).

Common Stock

The holders of our common stock are entitled to one vote for each share held of record on all matters submitted to a vote of stockholders. The holders of our common stock do not have cumulative voting rights in the election of directors. Subject to preferences that may be applicable to any outstanding shares of preferred stock, the holders of common stock are entitled to receive ratably such dividends as may be declared by our board of directors out of legally available funds. Upon our liquidation, dissolution or winding up, holders of our common stock are entitled to share ratably in all assets remaining after payment of liabilities and the liquidation preferences of any outstanding shares of preferred stock. Holders of common stock have no preemptive rights and no right to convert their common stock into any other securities. There are no redemption or sinking fund provisions applicable to our common stock.

Additional shares of authorized common stock may be issued, as authorized by our board of directors from time to time, without stockholder approval, except as may be required by applicable stock exchange requirements.

The rights of the holders of our common stock are subject to, and may be adversely affected by, the rights of holders of shares of any preferred stock that we may designate and issue in the future.

Registration Rights

We and some of the holders of our common stock have entered into an investor rights agreement. The registration rights provisions of this agreement provide those holders with demand, piggyback and Form S-3 registration rights with respect to the shares of our common stock currently held by them.

Demand Registration Rights

The holders of at least 20% of the registrable securities, as defined under the investor rights agreement, have the right to make up to two demands that we file a registration statement to register all or a portion of their shares so long as the aggregate offering price of securities requested to be sold under such registration statement is at least \$10,000,000, net of underwriting discounts and commissions and subject to specified exceptions.

Piggyback Registration Rights

If we register any securities for public sale, holders of registrable securities, as defined under the investor rights agreement, are entitled to written notice of the registration and will have the right to include their shares in the

registration statement. The underwriters of any offering will have the right to limit the number of shares having registration rights to be included in the registration statement provided such registration does not include

Table of Contents

shares of any other selling stockholders, in which case any and all shares held by selling stockholders may be excluded from the offering.

Registration on Form S-3

If we are eligible to file a registration statement on Form S-3, the holders of at least 10% of the registrable securities, as defined under the investor rights agreement, have the right to demand up to twice per year that we file registration statements on Form S-3 so long as the aggregate offering price of the securities to be sold under the registration statement on Form S-3 is at least \$5,000,000, net of underwriting discounts and commissions, and subject to specified exceptions.

Expenses of Registration; Indemnification

Generally, we are required to bear all registration expenses incurred in connection with the demand, Form S-3 and piggyback registrations described above, other than underwriting discounts and commissions. The investor rights agreement contains customary indemnification provisions with respect to registration rights.

Termination of Registration Rights

The demand, Form S-3 and piggyback registration rights discussed above will terminate if all of the holder's registrable securities may be sold without restriction under Rule 144 of the Securities Act.

Preferred Stock

Pursuant to our amended and restated certificate of incorporation, or the Restated Certificate, our board of directors has the authority, without further action by the stockholders (unless such stockholder action is required by applicable law or stock exchange listing rules), to designate and issue up to 5,000,000 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 designations, powers, preferences, privileges and relative participating, optional or special rights and the qualifications, limitations or restrictions thereof, including dividend rights, conversion rights, voting rights, terms of redemption and liquidation preferences, any or all of which may be greater than the rights of the common stock, 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.

The board of directors, without stockholder approval, can issue preferred stock with voting, conversion or other rights that could adversely affect the voting power and other rights of the holders of common stock. Preferred stock could be issued quickly with terms designed to delay or prevent a change in control of our company or make removal of management more difficult. Additionally, the issuance of preferred stock may have the effect of decreasing the market price of the common stock and may adversely affect the voting power of holders of common stock and reduce the likelihood that common stockholders will receive dividend payments and payments upon liquidation.

Our board of directors will fix the designations, voting powers, preferences and rights of each series, as well as the qualifications, limitations or restrictions thereof, of the preferred stock of each series that we offer under this prospectus and applicable prospectus supplements in the certificate of designation relating to that series. We will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of any certificate of designation that describes the terms of the series of preferred stock we are offering before the issuance of that series of preferred stock. This description will include:

the title and stated value;

the number of shares we are offering;

Table of Contents

the liquidation preference per share;

the purchase price per share;

the dividend rate per share, dividend period and payment dates and method of calculation for dividends;

whether dividends will be cumulative or non-cumulative and, if cumulative, the date from which dividends will accumulate;

our right, if any, to defer payment of dividends and the maximum length of any such deferral period;

the procedures for any auction and remarketing, if any;

the provisions for a sinking fund, if any;

the provisions for redemption or repurchase, if applicable, and any restrictions on our ability to exercise those redemption and repurchase rights;

any listing of the preferred stock on any securities exchange or market;

whether the preferred stock will be convertible into our common stock or other securities of ours, including depositary shares and warrants, and, if applicable, the conversion period, the conversion price, or how it will be calculated, and under what circumstances it may be adjusted;

whether the preferred stock will be exchangeable into debt securities, and, if applicable, the exchange period, the exchange price, or how it will be calculated, and under what circumstances it may be adjusted;

voting rights, if any, of the preferred stock;

preemption rights, if any;

restrictions on transfer, sale or other assignment, if any;

whether interests in the preferred stock will be represented by depositary shares;

a discussion of any material or special United States federal income tax considerations applicable to the preferred stock;

the relative ranking and preferences of the preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs;

any limitations on issuances of any class or series of preferred stock ranking senior to or on a parity with the series of preferred stock being issued as to dividend rights and rights if we liquidate, dissolve or wind up our affairs; and

any other specific terms, rights, preferences, privileges, qualifications or restrictions of the preferred stock. The General Corporation Law of the State of Delaware, the state of our incorporation, provides that the holders of preferred stock will have the right to vote separately as a class (or, in some cases, as a series) on an amendment to our certificate of incorporation if the amendment would change the par value or, unless the certificate of incorporation provided otherwise, the number of authorized shares of the class or change the powers, preferences or special rights of the class or series so as to adversely affect the class or series, as the case may be. This right is in addition to any voting rights that may be provided for in the applicable certificate of designation.

Antitakeover Effects of Provisions of Charter Documents and Delaware Law

Charter Documents. Our Restated Certificate and Amended and Restated Bylaws, or Bylaws, each as amended to date, include a number of provisions that may have the effect of deterring hostile takeovers or

Table of Contents

delaying or preventing changes in control or management of our company. First, our board of directors is classified into three classes of directors. Under Delaware law, directors of a corporation with a classified board may be removed only for cause unless the corporation's certificate of incorporation provides otherwise. Our Restated Certificate does not provide otherwise. In addition, the Restated Certificate provides that all stockholder action must be effected at a duly called meeting of stockholders and not by a consent in writing. Further, our Bylaws limit who may call special meetings of the stockholders. Our Restated Certificate does not include a provision for cumulative voting for directors. Under cumulative voting, a minority stockholder holding a sufficient percentage of a class of shares may be able to ensure the election of one or more directors. Finally, our Bylaws establish procedures, including advance notice procedures, with regard to the nomination of candidates for election as directors and stockholder proposals. These and other provisions of our Restated Certificate and Bylaws and Delaware law could discourage potential acquisition proposals and could delay or prevent a change in control or management of our company.

Delaware Takeover Statute. We are subject to Section 203 of the General Corporation Law of the State of Delaware, or DGCL, which regulates acquisitions of some Delaware corporations. Section 203 generally prohibits a publicly held Delaware corporation from engaging in a business combination with an interested stockholder for a period of three years following the date of the transaction in which the person became an interested stockholder, unless:

the board of directors of the corporation approved the business combination or the other transaction in which the person became an interested stockholder prior to the date of the business combination or other transaction;

upon consummation of the transaction that resulted in the person becoming an interested stockholder, the person owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding shares owned by persons who are directors and also officers of the corporation and shares issued under employee stock plans under which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or

on or subsequent to the date the person became an interested stockholder, the board of directors of the corporation approved the business combination and the stockholders of the corporation authorized the business combination at an annual or special meeting of stockholders by the affirmative vote of at least 66-2/3% of the outstanding stock of the corporation not owned by the interested stockholder.

Section 203 of the DGCL defines a business combination to include any of the following:

any merger or consolidation involving the corporation and the interested stockholder;

any sale, transfer, pledge or other disposition of 10% or more of the corporation's assets or outstanding stock involving the interested stockholder;

subject to exceptions, any transaction that results in the issuance or transfer by the corporation of any of its stock to the interested stockholder;

any transaction involving the corporation that has the effect of increasing the proportionate share of its stock owned by the interested stockholder; or

the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

In general, Section 203 defines an "interested stockholder" as any person who, together with the person's 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.

Table of Contents

Section 203 of the DGCL could depress our stock price and delay, discourage or prohibit transactions not approved in advance by our board of directors, such as takeover attempts that might otherwise involve the payment to our stockholders of a premium over the market price of our common stock.

Transfer Agent And Registrar

The transfer agent and registrar for our common stock is American Stock Transfer & Trust Company, and its address is 6201 15th Street, Brooklyn, NY 11219. The transfer agent for any series of preferred stock that we may offer under this prospectus will be named and described in the prospectus supplement for that series.

Listing on the Nasdaq Global Market

Our common stock is listed on the Nasdaq Global Market under the symbol CARA.

Table of Contents

DESCRIPTION OF DEBT SECURITIES

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

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

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

General

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

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

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

the title of the series of debt securities;

any limit upon the aggregate principal amount that may be issued;

the maturity date or dates;

the form of the debt securities of the series;

the applicability of any guarantees;

whether or not the debt securities will be secured or unsecured, and the terms of any secured debt;

whether the debt securities rank as senior debt, senior subordinated debt, subordinated debt or any combination thereof, and the terms of any subordination;

Table of Contents

if the price (expressed as a percentage of the aggregate principal amount thereof) at which such debt securities will be issued is a price other than the principal amount thereof, the portion of the principal amount thereof payable upon declaration of acceleration of the maturity thereof, or if applicable, the portion of the principal amount of such debt securities that is convertible into another security or the method by which any such portion shall be determined;

the interest rate or rates, which may be fixed or variable, or the method for determining the rate and the date interest will begin to accrue, the dates interest will be payable and the regular record dates for interest payment dates or the method for determining such dates;

our right, if any, to defer payment of interest and the maximum length of any such deferral period;

if applicable, the date or dates after which, or the period or periods during which, and the price or prices at which, we may, at our option, redeem the series of debt securities pursuant to any optional or provisional redemption provisions and the terms of those redemption provisions;

the date or dates, if any, on which, and the price or prices at which we are obligated, pursuant to any mandatory sinking fund or analogous fund provisions or otherwise, to redeem, or at the holder's option to purchase, the series of debt securities and the currency or currency unit in which the debt securities are payable;

the denominations in which we will issue the series of debt securities, if other than denominations of \$1,000 and any integral multiple thereof;

any and all terms, if applicable, relating to any auction or remarketing of the debt securities of that series and any security for our obligations with respect to such debt securities and any other terms which may be advisable in connection with the marketing of debt securities of that series;

whether the debt securities of the series shall be issued in whole or in part in the form of a global security or securities; the terms and conditions, if any, upon which such global security or securities may be exchanged in whole or in part for other individual securities; and the depositary for such global security or securities;

if applicable, the provisions relating to conversion or exchange of any debt securities of the series and the terms and conditions upon which such debt securities will be so convertible or exchangeable, including the conversion or exchange price, as applicable, or how it will be calculated and may be adjusted, any mandatory or optional (at our option or the holders' option) conversion or exchange features, the applicable conversion or exchange period and the manner of settlement for any conversion or exchange;

if other than the full principal amount thereof, the portion of the principal amount of debt securities of the series which shall be payable upon declaration of acceleration of the maturity thereof;

additions to or changes in the covenants applicable to the particular debt securities being issued, including, among others, the consolidation, merger or sale covenant;

additions to or changes in the events of default with respect to the securities and any change in the right of the trustee or the holders to declare the principal, premium, if any, and interest, if any, with respect to such securities to be due and payable;

additions to or changes in or deletions of the provisions relating to covenant defeasance and legal defeasance;

additions to or changes in the provisions relating to satisfaction and discharge of the indenture;

additions to or changes in the provisions relating to the modification of the indenture both with and without the consent of holders of debt securities issued under the indenture;

the currency of payment of debt securities if other than U.S. dollars and the manner of determining the equivalent amount in U.S. dollars;

Table of Contents

whether interest will be payable in cash or additional debt securities at our or the holders' option and the terms and conditions upon which the election may be made;

the terms and conditions, if any, upon which we will pay amounts in addition to the stated interest, premium, if any and principal amounts of the debt securities of the series to any holder that is not a United States person for federal tax purposes;

any restrictions on transfer, sale or assignment of the debt securities of the series; and

any other specific terms, preferences, rights or limitations of, or restrictions on, the debt securities, any other additions or changes in the provisions of the indenture, and any terms that may be required by us or advisable under applicable laws or regulations.

Conversion or Exchange Rights

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

Consolidation, Merger or Sale

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

Events of Default under the Indenture

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

if we fail to pay any installment of interest on any series of debt securities, as and when the same shall become due and payable, and such default continues for a period of 90 days; provided, however, that a valid extension of an interest payment period by us in accordance with the terms of any indenture supplemental thereto shall not constitute a default in the payment of interest for this purpose;

if we fail to pay the principal of, or premium, if any, on any series of debt securities as and when the same shall become due and payable whether at maturity, upon redemption, by declaration or otherwise, or in any payment required by any sinking or analogous fund established with respect to such series; provided, however, that a valid extension of the maturity of such debt securities in accordance with the terms of any

indenture supplemental thereto shall not constitute a default in the payment of principal or premium, if any;

if we fail to observe or perform any other covenant or agreement contained in the debt securities or the indenture, other than a covenant specifically relating to another series of debt securities, and our failure continues for 90 days after we receive written notice of such failure, requiring the same to be remedied and stating that such is a notice of default thereunder, from the trustee or holders of at least 25% in aggregate principal amount of the outstanding debt securities of the applicable series; and

if specified events of bankruptcy, insolvency or reorganization occur.

Table of Contents

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

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

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

the direction so given by the holder is not in conflict with any law or the applicable indenture; and

subject to its duties under the Trust Indenture Act, the trustee need not take any action that might involve it in personal liability or might be unduly prejudicial to the holders not involved in the proceeding.

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

the holder has given written notice to the trustee of a continuing event of default with respect to that series;

the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series have made written request,

such holders have offered to the trustee indemnity satisfactory to it against the costs, expenses and liabilities to be incurred by the trustee in compliance with the request; and

the trustee does not institute the proceeding, and does not receive from the holders of a majority in aggregate principal amount of the outstanding debt securities of that series other conflicting directions within 90 days after the notice, request and offer.

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

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

Modification of Indenture; Waiver

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

to cure any ambiguity, defect or inconsistency in the indenture or in the debt securities of any series;

to comply with the provisions described above under Description of Debt Securities Consolidation, Merger or Sale;

Table of Contents

to provide for uncertificated debt securities in addition to or in place of certificated debt securities;

to add to our covenants, restrictions, conditions or provisions such new covenants, restrictions, conditions or provisions for the benefit of the holders of all or any series of debt securities, to make the occurrence, or the occurrence and the continuance, of a default in any such additional covenants, restrictions, conditions or provisions an event of default or to surrender any right or power conferred upon us in the indenture;

to add to, delete from or revise the conditions, limitations, and restrictions on the authorized amount, terms, or purposes of issue, authentication and delivery of debt securities, as set forth in the indenture;

to make any change that does not adversely affect the interests of any holder of debt securities of any series in any material respect;

to provide for the issuance of and establish the form and terms and conditions of the debt securities of any series as provided above under **Description of Debt Securities General** to establish the form of any certifications required to be furnished pursuant to the terms of the indenture or any series of debt securities, or to add to the rights of the holders of any series of debt securities;

to evidence and provide for the acceptance of appointment under any indenture by a successor trustee; or

to comply with any requirements of the SEC in connection with the qualification of any indenture under the Trust Indenture Act.

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

extending the fixed maturity of any debt securities of any series;

reducing the principal amount, reducing the rate of or extending the time of payment of interest, or reducing any premium payable upon the redemption of any series of any debt securities; or

reducing the percentage of debt securities, the holders of which are required to consent to any amendment, supplement, modification or waiver.

Discharge

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

provide for payment;

register the transfer or exchange of debt securities of the series;

replace stolen, lost or mutilated debt securities of the series;

pay principal of and premium and interest on any debt securities of the series;

maintain paying agencies;

hold monies for payment in trust;

recover excess money held by the trustee;

compensate and indemnify the trustee; and

appoint any successor trustee.

Table of Contents

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

Form, Exchange and Transfer

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

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

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

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

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

issue, register the transfer of, or exchange any debt securities of that series during a period beginning at the opening of business 15 days before the day of mailing of a notice of redemption of any debt securities that may be selected for redemption and ending at the close of business on the day of the mailing; or

register the transfer of or exchange any debt securities so selected for redemption, in whole or in part, except the unredeemed portion of any debt securities we are redeeming in part.

Information Concerning the Trustee

The trustee, other than during the occurrence and continuance of an event of default under an indenture, undertakes to perform only those duties as are specifically set forth in the applicable indenture. Upon an event of default under an

indenture, the trustee must use the same degree of care as a prudent person would exercise or use in the conduct of his or her own affairs. Subject to this provision, the trustee is under no obligation to exercise any of the powers given it by the indenture at the request of any holder of debt securities unless it is offered reasonable security and indemnity against the costs, expenses and liabilities that it might incur.

Table of Contents

Payment and Paying Agents

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

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

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

Governing Law

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

Table of Contents

DESCRIPTION OF WARRANTS

The following description, together with the additional information we may include in any applicable prospectus supplements and free writing prospectuses, summarizes the material terms and provisions of the warrants that we may issue under this prospectus, which may consist of warrants to purchase common stock, preferred stock or debt securities and may be issued in one or more series. Warrants may be issued independently or together with common stock, preferred stock or debt securities offered by any prospectus supplement, and may be attached to or separate from those securities. While the terms we have summarized below will apply generally to any warrants that we may offer under this prospectus, we will describe the particular terms of any series of warrants that we may offer in more detail in the applicable prospectus supplement and any applicable free writing prospectus. The terms of any warrants offered under a prospectus supplement may differ from the terms described below. However, no prospectus supplement will fundamentally change the terms that are set forth in this prospectus or offer a security that is not registered and described in this prospectus at the time of its effectiveness.

We have filed forms of the warrant agreements and forms of warrant certificates containing the terms of the warrants being offered as exhibits to the registration statement of which this prospectus is a part. We will file as exhibits to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of warrant agreement, if any, including a form of warrant certificate, that describes the terms of the particular series of warrants we are offering before the issuance of the related series of warrants. The following summaries of material provisions of the warrants and the warrant agreements are subject to, and qualified in their entirety by reference to, all the provisions of the warrant agreement and warrant certificate applicable to the particular series of warrants that we may offer under this prospectus. We urge you to read the applicable prospectus supplements related to the particular series of warrants that we may offer under this prospectus, as well as any related free writing prospectuses, and the complete warrant agreements and warrant certificates that contain the terms of the warrants.

General

We will describe in the applicable prospectus supplement the terms relating to a series of warrants being offered, including:

the offering price and aggregate number of warrants offered;

the currency for which the warrants may be purchased;

if applicable, the designation and terms of the securities with which the warrants are issued and the number of warrants issued with each such security or each principal amount of such security;

if applicable, the date on and after which the warrants and the related securities will be separately transferable;

in the case of warrants to purchase debt securities, the principal amount of debt securities purchasable upon exercise of one warrant and the price at which, and currency in which, this principal amount of debt

securities may be purchased upon such exercise;

in the case of warrants to purchase common stock or preferred stock, the number of shares of common stock or preferred stock, as the case may be, purchasable upon the exercise of one warrant and the price at which, and the currency in which, these shares may be purchased upon such exercise;

the effect of any merger, consolidation, sale or other disposition of our business on the warrant agreements and the warrants;

the terms of any rights to redeem or call the warrants;

the terms of any rights to force the exercise of the warrants;

any provisions for changes to or adjustments in the exercise price or number of securities issuable upon exercise of the warrants;

Table of Contents

the dates on which the right to exercise the warrants will commence and expire;

the manner in which the warrant agreements and warrants may be modified;

a discussion of any material or special United States federal income tax consequences of holding or exercising the warrants;

the terms of the securities issuable upon exercise of the warrants; and

any other specific terms, preferences, rights or limitations of or restrictions on the warrants.

Before exercising their warrants, holders of warrants will not have any of the rights of holders of the securities purchasable upon such exercise, including:

in the case of warrants to purchase debt securities, the right to receive payments of principal of, or premium, if any, or interest on, the debt securities purchasable upon exercise or to enforce covenants in the applicable indenture; or

in the case of warrants to purchase common stock or preferred stock, the right to receive dividends, if any, or, payments upon our liquidation, dissolution or winding up or to exercise voting rights, if any.

Exercise of Warrants

Each warrant will entitle the holder to purchase the securities that we specify in the applicable prospectus supplement at the exercise price that we describe in the applicable prospectus supplement. Unless we otherwise specify in the applicable prospectus supplement, holders of the warrants may exercise the warrants at any time up to the specified time on the expiration date that we set forth in the applicable prospectus supplement. After the close of business on the expiration date, unexercised warrants will become void.

Unless we otherwise specify in the applicable prospectus supplement, holders of the warrants may exercise the warrants by delivering the warrant certificate representing the warrants to be exercised together with specified information, and paying the required amount to the warrant agent in immediately available funds, as provided in the applicable prospectus supplement. We will set forth on the reverse side of the warrant certificate and in the applicable prospectus supplement the information that the holder of the warrant will be required to deliver to the warrant agent in connection with the exercise of the warrant.

Upon receipt of the required payment and the warrant certificate properly completed and duly executed at the corporate trust office of the warrant agent or any other office indicated in the applicable prospectus supplement, we will issue and deliver the securities purchasable upon such exercise. If fewer than all of the warrants represented by the warrant certificate are exercised, then we will issue a new warrant certificate for the remaining amount of warrants. If we so indicate in the applicable prospectus supplement, holders of the warrants may surrender securities as all or part of the exercise price for warrants.

Governing Law

Unless we provide otherwise in the applicable prospectus supplement, the warrants and warrant agreements will be governed by and construed in accordance with the laws of the State of New York.

Enforceability of Rights by Holders of Warrants

Each warrant agent will act solely as our agent under the applicable warrant agreement and will not assume any obligation or relationship of agency or trust with any holder of any warrant. A single bank or trust company may act as warrant agent for more than one issue of warrants. A warrant agent will have no duty or responsibility in case of any default by us under the applicable warrant agreement or warrant, including any duty or responsibility to initiate any proceedings at law or otherwise, or to make any demand upon us. Any holder of a warrant may, without the consent of the related warrant agent or the holder of any other warrant, enforce by appropriate legal action its right to exercise, and receive the securities purchasable upon exercise of, its warrants.

Table of Contents

LEGAL OWNERSHIP OF SECURITIES

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

Book-Entry Holders

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

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

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

Street Name Holders

We may terminate a global security or issue securities that are not issued in global form. In these cases, investors may choose to hold their securities in their own names or in street name. Securities held by an investor in street name would be registered in the name of a bank, broker or other financial institution that the investor chooses, and the investor would hold only a beneficial interest in those securities through an account he or she maintains at that institution.

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

Legal Holders

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

Table of Contents

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

Special Considerations for Indirect Holders

If you hold securities through a bank, broker or other financial institution, either in book-entry form because the securities are represented by one or more global securities or in street name, you should check with your own institution to find out:

how it handles securities payments and notices;

whether it imposes fees or charges;

how it would handle a request for the holders' consent, if ever required;

whether and how you can instruct it to send you securities registered in your own name so you can be a holder, if that is permitted in the future;

how it would exercise rights under the securities if there were a default or other event triggering the need for holders to act to protect their interests; and

if the securities are in book-entry form, how the depositary's rules and procedures will affect these matters.

Global Securities

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

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

A global security may not be transferred to or registered in the name of anyone other than the depositary, its nominee or a successor depositary, unless special termination situations arise. We describe those situations below under **Special Situations When A Global Security Will Be Terminated**. As a result of these arrangements, the depositary, or its

nominee, will be the sole registered owner and legal holder of all securities represented by a global security, and investors will be permitted to own only beneficial interests in a global security. Beneficial interests must be held by means of an account with a broker, bank or other financial institution that in turn has an account with the depository or with another institution that does. Thus, an investor whose security is represented by a global security will not be a legal holder of the security, but only an indirect holder of a beneficial interest in the global security.

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

Table of Contents

Special Considerations For Global Securities

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

If securities are issued only as global securities, an investor should be aware of the following:

an investor cannot cause the securities to be registered in his or her name, and cannot obtain non-global certificates for his or her interest in the securities, except in the special situations we describe below;

an investor will be an indirect holder and must look to his or her own bank or broker for payments on the securities and protection of his or her legal rights relating to the securities, as we describe above;

an investor may not be able to sell interests in the securities to some insurance companies and to other institutions that are required by law to own their securities in non-book-entry form;

an investor may not be able to pledge his or her interest in the global security in circumstances where certificates representing the securities must be delivered to the lender or other beneficiary of the pledge in order for the pledge to be effective;

the depositary's policies, which may change from time to time, will govern payments, transfers, exchanges and other matters relating to an investor's interest in the global security;

we and any applicable trustee have no responsibility for any aspect of the depositary's actions or for its records of ownership interests in the global security, nor will we or any applicable trustee supervise the depositary in any way;

the depositary may, and we understand that DTC will, require that those who purchase and sell interests in the global security within its book-entry system use immediately available funds, and your broker or bank may require you to do so as well; and

financial institutions that participate in the depositary's book-entry system, and through which an investor holds its interest in the global security, may also have their own policies affecting payments, notices and other matters relating to the securities.

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

Special Situations When A Global Security Will Be Terminated

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

A global security will terminate when the following special situations occur:

if the depositary notifies us that it is unwilling, unable or no longer qualified to continue as depositary for that global security and we do not appoint another institution to act as depositary within 90 days;

if we notify any applicable trustee that we wish to terminate that global security; or

if an event of default has occurred with regard to securities represented by that global security and has not been cured or waived.

Table of Contents

The applicable prospectus supplement may also list additional situations for terminating a global security that would apply only to the particular series of securities covered by the prospectus supplement. When a global security terminates, the depositary, and neither we nor any applicable trustee, is responsible for deciding the names of the institutions that will be the initial direct holders.

Table of Contents

PLAN OF DISTRIBUTION

We may sell the securities from time to time pursuant to underwritten public offerings, negotiated transactions, block trades or a combination of these methods. We may sell the securities to or through underwriters or dealers, through agents, or directly to one or more purchasers. We may distribute securities from time to time in one or more transactions:

at a fixed price or prices, which may be changed;

at market prices prevailing at the time of sale;

at prices related to such prevailing market prices; or

at negotiated prices.

We may also sell equity securities covered by this registration statement in an at the market offering as defined in Rule 415 under the Securities Act. Such offering may be made into an existing trading market for such securities in transactions at other than a fixed price, either:

on or through the facilities of the Nasdaq Global Market or any other securities exchange or quotation or trading service on which such securities may be listed, quoted or traded at the time of sale; and/or

to or through a market maker otherwise than on the Nasdaq Global Market or such other securities exchanges or quotation or trading services.

Such at-the-market offerings, if any, may be conducted by underwriters acting as principal or agent.

A prospectus supplement or supplements (and any related free writing prospectus that we may authorize to be provided to you) will describe the terms of the offering of the securities, including, to the extent applicable:

the name or names of any underwriters, if any;

the purchase price of the securities and the proceeds we will receive from the sale;

any over-allotment options under which underwriters may purchase additional securities from us;

any agency fees or underwriting discounts and other items constituting agents or underwriters compensation;

any public offering price;

any discounts or concessions allowed or reallocated or paid to dealers; and

any securities exchange or market on which the securities may be listed.

Only underwriters named in the prospectus supplement are underwriters of the securities offered by the prospectus supplement.

If underwriters are used in the sale, they will acquire the securities for their own account and may resell the securities from time to time in one or more transactions at a fixed public offering price or at varying prices determined at the time of sale. The obligations of the underwriters to purchase the securities will be subject to the conditions set forth in the applicable underwriting agreement. We may offer the securities to the public through underwriting syndicates represented by managing underwriters or by underwriters without a syndicate. Subject to certain conditions, the underwriters will be obligated to purchase all of the securities offered by the prospectus supplement. Any public offering price and any discounts or concessions allowed or reallocated or paid to dealers may change from time to time. We may use underwriters with whom we have a material relationship. We will describe in the prospectus supplement, naming the underwriter, the nature of any such relationship.

Table of Contents

We may sell securities directly or through agents we designate from time to time. We will name any agent involved in the offering and sale of securities, and we will describe any commissions we will pay the agent in the prospectus supplement. Unless the prospectus supplement states otherwise, our agent will act on a best-efforts basis for the period of its appointment.

We may authorize agents or underwriters to solicit offers by certain types of institutional investors to purchase securities from us at the public offering price set forth in the prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. We will describe the conditions to these contracts and the commissions we must pay for solicitation of these contracts in the prospectus supplement.

We may provide agents and underwriters with indemnification against civil liabilities related to this offering, including liabilities under the Securities Act, or contribution with respect to payments that the agents or underwriters may make with respect to these liabilities. Agents and underwriters may engage in transactions with, or perform services for, us in the ordinary course of business.

All securities we offer, other than common stock, will be new issues of securities with no established trading market. Any underwriters may make a market in these securities, but will not be obligated to do so and may discontinue any market making at any time without notice. We cannot guarantee the liquidity of the trading markets for any securities.

Any underwriter may engage in overallotment, stabilizing transactions, short covering transactions and penalty bids in accordance with Regulation M under the Exchange Act. Overallotment involves sales in excess of the offering size, which create a short position. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum. Short covering transactions involve purchases of the securities in the open market after the distribution is completed to cover short positions. Penalty bids permit the underwriters to reclaim a selling concession from a dealer when the securities originally sold by the dealer are purchased in a stabilizing or covering transaction to cover short positions. Those activities may cause the price of the securities to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of the activities at any time.

Any underwriters who are qualified market makers on the Nasdaq Global Market may engage in passive market making transactions in the securities on the Nasdaq Global Market in accordance with Rule 103 of Regulation M, during the business day prior to the pricing of the offering, before the commencement of offers or sales of the securities. Passive market makers must comply with applicable volume and price limitations and must be identified as passive market makers. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for such security; if all independent bids are lowered below the passive market maker's bid, however, the passive market maker's bid must then be lowered when certain purchase limits are exceeded. Passive market making may stabilize the market price of the securities at a level above that which might otherwise prevail in the open market and, if commenced, may be discontinued at any time.

In compliance with guidelines of the Financial Industry Regulatory Authority, or FINRA, the maximum consideration or discount to be received by any FINRA member or independent broker dealer may not exceed 8% of the aggregate amount of the securities offered pursuant to this prospectus and any applicable prospectus supplement.

Table of Contents

LEGAL MATTERS

Unless otherwise indicated in the applicable prospectus supplement, certain legal matters in connection with the offering and the validity of the securities offered by this prospectus, and any supplement thereto, will be passed upon by Cooley LLP.

EXPERTS

The financial statements of Cara Therapeutics, Inc. appearing in Cara Therapeutics, Inc.'s Annual Report (Form 10-K) for the year ended December 31, 2016 have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon, included therein, and incorporated herein by reference. Such financial statements are incorporated herein by reference in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus is part of a registration statement we filed with the Securities and Exchange Commission, or SEC. This prospectus does not contain all of the information set forth in the registration statement and the exhibits to the registration statement. For further information with respect to us and the securities we are offering under this prospectus, we refer you to the registration statement and the exhibits and schedules filed as a part of the registration statement. You should rely only on the information contained in this prospectus or incorporated by reference. We have not authorized anyone else to provide you with different information. We are not making an offer of these securities in any state where the offer is not permitted. You should not assume that the information in this prospectus is accurate as of any date other than the date on the front page of this prospectus, regardless of the time of delivery of this prospectus or any sale of the securities offered by this prospectus.

We file annual, quarterly and current reports, proxy statements and other information with the SEC. You may read and copy the registration statement, as well as any other document filed by us with the SEC, at the SEC's Public Reference Room at 100 F Street NE, Washington, D.C. 20549. You can also request copies of these documents by writing to the SEC and paying a fee for the copying cost. You may obtain information on the operation of the Public Reference Room by calling the SEC at (800) SEC-0330. The SEC maintains a website that contains reports, proxy statements and other information regarding issuers that file electronically with the SEC, including Cara Therapeutics. The address of the SEC website is www.sec.gov.

We maintain a website at www.caratherapeutics.com. Information contained in or accessible through our website does not constitute a part of this prospectus.

Table of Contents

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference information into this prospectus, which means that we can disclose important information to you by referring you to another document filed separately with the SEC. The SEC file number for the documents incorporated by reference in this prospectus is 001-36279. The documents incorporated by reference into this prospectus contain important information that you should read about us.

The following documents are incorporated by reference into this document:

our Annual Report on Form 10-K for the fiscal year ended December 31, 2016 and filed with the SEC on March 10, 2017; and

the description of our common stock, which is registered under Section 12 of the Exchange Act, in our registration statement on Form 8-A, filed with the SEC on January 27, 2014, including any amendments or reports filed for the purpose of updating such description.

We also incorporate by reference into this prospectus all documents (other than current reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items) that are filed by us with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act (i) after the date of the initial filing of the registration statement of which this prospectus forms a part and prior to effectiveness of the registration statement, or (ii) after the date of this prospectus but prior to the termination of the offering. These documents include periodic reports, such as Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q and Current Reports on Form 8-K, as well as proxy statements.

We will provide to each person, including any beneficial owner, to whom a prospectus is delivered, without charge upon written or oral request, a copy of any or all of the documents that are incorporated by reference into this prospectus but not delivered with the prospectus, including exhibits which are specifically incorporated by reference into such documents. Requests should be directed to: Cara Therapeutics, Inc., Attn: Investor Relations, 4 Stamford Plaza, 107 Elm Street, Stamford, Connecticut 06902, telephone: (203) 406-3700.

Any statement contained herein or in a document incorporated or deemed to be incorporated by reference into this document will be deemed to be modified or superseded for purposes of the document to the extent that a statement contained in this document or any other subsequently filed document that is deemed to be incorporated by reference into this document modifies or supersedes the statement.

Table of Contents

**DISCLOSURE OF COMMISSION POSITION ON INDEMNIFICATION FOR
SECURITIES ACT LIABILITY**

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers or persons controlling the registrant pursuant to the foregoing provisions, the registrant has 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.

Table of Contents

\$80,000,000

CARA THERAPEUTICS, INC.

Common Stock

PRELIMINARY PROSPECTUS

Piper Jaffray

Stifel

, 2017