

Cara Therapeutics, Inc.
Form 424B5
July 17, 2018
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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 JULY 17, 2018

PROSPECTUS SUPPLEMENT

(to Prospectus, dated March 24, 2017)

4,500,000 Shares

Common Stock

We are offering 4,500,000 shares of our common stock pursuant to this prospectus supplement. Our common stock is listed for trading on The Nasdaq Global Market under the symbol CARA. On July 16, 2018, the last reported sale price of our common stock on The Nasdaq Global Market was \$21.16 per share.

We are an emerging growth company as defined 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 risks. See Risk Factors beginning on page S-8 of this prospectus supplement.

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.

	PER SHARE	TOTAL
Public Offering Price	\$	\$
Underwriting Discounts and Commissions ⁽¹⁾	\$	\$
Proceeds to Cara Therapeutics, Inc. (before expenses)	\$	\$

(1) See "Underwriting" beginning on page S-15 of this prospectus supplement for a description of the compensation payable to the underwriters.

Delivery of the shares of common stock is expected to be made on or about _____, 2018. We have granted the underwriters an option for a period of 30 days to purchase an additional 675,000 shares of our common stock. If the underwriters exercise the option in full, the total underwriting discounts and commissions payable by us will be \$ _____, and the total proceeds to us, before expenses, will be \$ _____.

Jefferies
Piper Jaffray

BofA Merrill Lynch
Stifel

Canaccord Genuity

Needham & Company

H.C. Wainwright & Co.
Prospectus supplement dated _____

Janney Montgomery Scott
_____, 2018.

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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**.

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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**.

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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 pruritus and pain by selectively targeting kappa opioid receptors. We are developing a novel and proprietary class of product candidates, led by KORSUVA (CR845/difelikefalin), a first-in-class kappa opioid receptor agonist that targets the body's peripheral nervous system, as well as certain immune cells.

In Phase 2 trials, KORSUVA (CR845/difelikefalin) Injection has demonstrated statistically significant reductions in itch intensity and concomitant improvement in quality of life measures in hemodialysis patients with moderate-to-severe chronic kidney disease-associated pruritus, or CKD-aP, and is currently being investigated in Phase 3 trials in hemodialysis patients with CKD-aP. We have partnered with Vifor Fresenius Medical Care Renal Pharma Ltd., or VFMCRP, to commercialize KORSUVA (CR845/difelikefalin) Injection in dialysis patients with CKD-aP worldwide, excluding the United States, Japan (Maruishi Pharmaceutical Co. Ltd., or Maruishi), and South Korea (Chong Kun Dang Pharmaceutical Corp., or CKDP). We retain all rights in the United States, and will promote KORSUVA (CR845/difelikefalin) Injection, if approved, with VFMCRP in U.S. Fresenius Medical Care North America, or FMCNA, dialysis clinics under a profit share agreement. Additionally, CR845/difelikefalin has demonstrated efficacy in patients with moderate-to-severe pain, without inducing many of the undesirable side effects typically associated with currently available opioid pain therapeutics. We retain rights to all KORSUVA/ CR845 formulations and indications worldwide, excluding KORSUVA (CR845/difelikefalin) Injection in dialysis patients with CKD-aP under our agreement with VFMCRP for certain ex-U.S. territories and our other license agreements in Japan (Maruishi) and South Korea (CKDP).

The U.S. Food and Drug Administration, or FDA, has conditionally accepted KORSUVA as the trade name for CR845/difelikefalin Injection and its safety and efficacy have not been fully evaluated by any regulatory authority.

CR845/Difelikefalin

Our product candidate, CR845/difelikefalin, is a new chemical entity, which is designed to selectively stimulate kappa, rather than mu, and delta opioid receptors outside of the central nervous system, or CNS. CR845/difelikefalin has been designed with specific chemical characteristics to restrict its entry into the CNS and further limit its mechanism of action to kappa opioid receptors in the peripheral nervous system, or nerves outside of the brain and spinal cord and certain immune cells. In addition to the side effects associated with activation of mu opioid receptors in the CNS, activation of kappa receptors in the CNS is also known to result in some undesirable effects, including acute psychiatric disorders. CR845/difelikefalin is designed to target peripheral nervous system and certain immune cells to result in modulation of pain signals as well as relief from pruritus or itch associated with certain chronic diseases. Since CR845/difelikefalin is designed to modulate signals peripherally without any significant activation of mu or kappa opioid receptors in the CNS, it is generally not expected to produce the CNS-related side effects of mu

opioids (i.e. constipation, nausea/vomiting, drug abuse, respiratory depression) or centrally-active kappa opioids (i.e. dysphoria and

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hallucinations). CR845/difelikefalin has been administered to more than 2,000 human subjects in Phase 1, Phase 2, Phase 2/3 and Phase 3 clinical trials as an I.V. infusion, rapid intravenous injection or oral capsule or tablet, and thus far has been observed to be generally well tolerated in these clinical trials.

Based on the non-clinical and clinical studies we have completed to date, we believe that CR845/difelikefalin, if approved, would be attractive to both patients and physicians as a treatment for moderate-to-severe pain or pruritus associated with certain diseases such as CKD-aP, chronic liver diseases-associated pruritus, or CLD-aP, and others due to the following attributes:

novel, peripherally-acting, kappa opioid receptor agonist mechanism of action;

evidence of efficacy in completed clinical trials of pruritus and pain;

potential for reducing mu opioid use and opioid-related adverse events, or AEs, such as nausea and vomiting;

avoidance of mu opioid-related CNS side effects, such as respiratory depression and euphoria;

absence of euphoria, which lowers addiction or abuse potential;

avoidance of interactions with other drugs because, as a peptide composed of four non-natural D-amino acids that is not metabolized in the liver, CR845/difelikefalin does not interact with the liver enzymes responsible for the metabolism of most commonly used classes of drugs; and

availability in injectable form for acute pain treatment as well as for treatment of pruritus in CKD patients undergoing hemodialysis in the hospital and dialysis center settings and oral form for treatment of chronic pain or pruritus conditions in the outpatient setting.

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Our current CR845/difelikefalin programs are summarized in the table below:

Program	Product Candidate	Primary Indication	Status	Commercialization Rights
Pruritus	KORSUVA (CR845/difelikefalin) Injection	Pruritus Chronic Kidney Disease- Hemodialysis (CKD-HD)	Phase 3 U.S. efficacy trial ongoing.	Cara (United States); Maruishi (Japan); CKDP (South Korea); Vifor Fresenius (Worldwide, other than United States, Japan and South Korea)
			Phase 3 long-term safety trial ongoing.	
			Phase 2/3 adaptive trial completed.	
			End of Phase 2 meeting with FDA completed.	
			Breakthrough Therapy Designation granted by FDA in June 2017.	
	Oral KORSUVA (CR845/difelikefalin)	Pruritus Chronic Kidney Disease- Hemodialysis (CKD-HD)	Phase 1 safety and PK study completed.	Cara (Worldwide, other than Japan and South Korea); Maruishi (Japan); CKDP (South Korea)
	Oral KORSUVA (CR845/difelikefalin)	Pruritus CKD (Stage III - V) (non-hemodialysis)	Phase 2 efficacy trial ongoing.	Cara (Worldwide, other than Japan and South Korea); Maruishi (Japan); CKDP (South Korea)
		Phase 1 safety and PK study completed.		

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	Oral KORSUVA (CR845/difelikefalin)	Pruritus Chronic Liver Disease (CLD)	IND filed in 4Q 2017.	Cara (Worldwide, other than South Korea); CKDP (South Korea)
Pain			Phase 1 safety and PK trial ongoing.	
	CR845/difelikefalin Injection	Acute Post-Operative Pain	Adaptive Phase 2/3 trial completed. Top-line data released.	Cara (Worldwide, other than Japan and South Korea); Maruishi (Japan); CKDP (South Korea)
	Oral CR845/difelikefalin	Chronic Pain	Phase 2b osteoarthritis, or OA, clinical trial completed. Top-line data released.	Cara (Worldwide, other than South Korea); CKDP (South Korea)

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Recent Developments

Top-Line Data from Adaptive Phase 2/3 Trial of CR845/difelikefalin Injection

In June 2018, we announced top-line results from our adaptive Phase 2/3 trial of CR845/difelikefalin injection in patients undergoing abdominal surgeries. At the 1.0 mcg/kg dose, CR845/difelikefalin injection achieved the primary endpoint of reduced pain over the 0-24 hour period ($p=0.032$) and demonstrated statistically significant reductions in pain intensity compared to placebo at all other pre-specified post-operative periods of 0-6 hours ($p=0.001$); 0-12 hours ($p=0.004$) and 0-18 hours ($p=0.013$). Additionally, CR845/difelikefalin injection treatment resulted in statistically significant reductions in the incidence of post-operative nausea and vomiting over the 24-hour period post-surgery for both 0.5 and 1.0 mcg/kg doses ($p=0.006$; $p<0.0001$, respectively). Incidence of adverse events was generally low and similar between placebo and CR845 groups.

VFMCRP Licensing Agreement

On May 17, 2018, we entered into a license agreement, or the VFMCRP Agreement, with VFMCRP, a joint venture between Vifor Pharma Group and Fresenius Medical Care, under which we granted VFMCRP a license to seek regulatory approval to commercialize, import, export, use, distribute, offer for sale, promote, sell and otherwise commercialize KORSUVA (CR845/ difelikefalin) Injection for all therapeutic uses to prevent, inhibit or treat itch associated with pruritus in hemodialysis and peritoneal-dialysis patients worldwide (excluding the United States, Japan and South Korea).

Upon entry into the VFMCRP Agreement, VFMCRP initiated a non-refundable, non-creditable \$50 million upfront payment to us and Vifor (International) Ltd., or Vifor, purchased 1,174,827 shares of our common stock for \$20 million, at a price of \$17.024 per share. In addition, we are eligible to receive from VFMCRP regulatory and commercial milestone payments in the aggregate of up to \$470 million, consisting of up to \$30 million in regulatory milestones and up to \$440 million in tiered commercial milestones, all of which are sales-related. We are also eligible to receive tiered double-digit royalty payments based on annual net sales, as defined, of KORSUVA (CR845/ difelikefalin) Injection in the licensed territories. We retain full development and commercialization rights for KORSUVA (CR845/ difelikefalin) Injection for the treatment of CKD-aP in the United States except in the dialysis clinics of FMCNA, where VFMCRP and Cara will promote KORSUVA (CR845/ difelikefalin) Injection under a profit-sharing arrangement (subject to the terms and conditions of the VFMCRP Agreement) based on net FMCNA clinic sales recorded by us.

Financial Update

As of June 30, 2018, we had approximately \$132.0 million of cash, cash equivalents and marketable securities. This amount is unaudited and preliminary, and does not present all information necessary for an understanding of our financial condition as of June 30, 2018. The review of our financial statements for the quarter ended June 30, 2018 is ongoing and could result in changes to this amount. Our financial statements for the quarter ended June 30, 2018 will not be available until after this offering is completed, and consequently will not be available to you prior to investing in this offering.

Corporate Information

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.

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

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Implications of Being an Emerging Growth Company

As a company with less than \$1.07 billion in revenue during our last fiscal year, we qualify as an emerging growth company as defined in the Jumpstart Our Business Startups Act 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 \$1.07 billion in annual revenues, have more than \$700 million in market value of our capital stock held by non-affiliates 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.

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THE OFFERING

Common stock offered by us	4,500,000 shares
Common stock outstanding immediately following this offering	38,374,770 shares
Option to purchase additional shares	We have granted to the underwriters the option, exercisable for 30 days from the date of this prospectus supplement, to purchase up to 675,000 additional shares of our common stock.
Use of proceeds	<p>We estimate that the net proceeds from this offering will be approximately \$ million, or approximately \$ million if the underwriters exercise their option to purchase additional shares in full, after deducting the 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 and submission of a new drug application, or NDA, to the FDA for KORSUVA (CR845/difelikefalin) Injection for the treatment of pruritus associated with CKD in hemodialysis patients, the advancement of Oral KORSUVA (CR845/difelikefalin) into Phase 2 trials for the treatment of pruritus associated with CKD in Stage III-V patients and CLD patients, the expansion of our Oral program into certain dermatologic conditions and the exploration of further development of CR845/difelikefalin injection in the post-operative setting after consultation with the FDA, as well as 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 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

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Unless otherwise indicated, all information in this prospectus supplement relating to the number of shares of our common stock to be outstanding immediately after this offering is based on 32,699,943 shares of common stock outstanding as of March 31, 2018, gives effect to the issuance and sale of 1,174,827 shares of our common stock to Vifor in May 2018 in connection with the VFMCRP Agreement, and excludes:

3,932,992 shares of our common stock issuable upon the exercise of options outstanding as of March 31, 2018, at a weighted-average exercise price of \$12.18 per share (of which, options to purchase an aggregate of 194,672 shares were exercised after March 31, 2018 with a weighted-average exercise price of \$8.55 per share);

83,791 shares of our common stock issuable upon the vesting of performance-based restricted stock units, or RSUs, outstanding as of March 31, 2018; and

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805,401 shares of our common stock reserved for future issuance under our 2014 Equity Incentive Plan as of March 31, 2018.

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 or vesting of outstanding RSUs subsequent to March 31, 2018.

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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, 2017, 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 public offering price of \$ per share, investors purchasing shares of common stock in this offering will incur immediate dilution of \$ per share in the pro forma as adjusted net tangible book value. 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.

New or future changes to tax laws could materially adversely affect our company.

On December 22, 2017, President Trump signed into law the Tax Cuts and Jobs Act, or TCJA, which significantly amends the Internal Revenue Code of 1986. The TCJA, among other things, reduces the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, limits the tax deduction for interest expense to 30% of adjusted taxable income, eliminates net operating loss carrybacks, limits the deduction for net operating losses carried forward from taxable years beginning after December 31, 2017 to 80% of taxable income, imposes a one-time tax on offshore earnings at reduced rates regardless of whether they are repatriated, allows immediate deductions for certain new investments instead of deductions for depreciation expense over time, and modifies or repeals many business deductions and credits. We continue to examine the impact these changes may have on our business. Notwithstanding the reduction in the corporate income tax rate, the overall impact of the TCJA is uncertain and our business and financial condition could be adversely affected. The impact of the TCJA on holders of our common stock is also

uncertain and could be adverse.

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USE OF PROCEEDS

We estimate that the net proceeds to us from this offering, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us, will be approximately \$ million (or approximately \$ million if the underwriters exercise their option to purchase additional shares in full).

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 and submission of an NDA to the FDA for KORSUVA (CR845/difelikefalin) Injection for the treatment of pruritus associated with CKD in hemodialysis patients, the advancement of Oral KORSUVA (CR845/difelikefalin) into Phase 2 trials for the treatment of pruritus associated with CKD in Stage III-V patients and CLD patients, the expansion of our Oral program into certain dermatologic conditions and the exploration of further development of CR845/difelikefalin injection in the post-operative setting after consultation with the FDA, as well as 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 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 2021. 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.

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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 pro forma 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 March 31, 2018, our net tangible book value was \$72.1 million, or \$2.20 per share of common stock. After giving effect to our issuance and sale of (1) 1,174,827 shares of our common stock to Vifor for \$20 million, at a price of \$17.024 per share, in May 2018 and (2) our issuance and sale of 4,500,000 shares of our common stock in this offering at the public offering price of \$ per share, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us, our pro forma as adjusted net tangible book value as of March 31, 2018 would have been \$ million, or \$ per share of common stock. This represents an immediate increase in pro forma as adjusted net tangible book value of \$ per share to our existing stockholders and an immediate dilution of \$ per share to investors participating in this offering at the public offering price.

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

Public offering price per share	\$
Net tangible book value per share as of March 31, 2018	\$ 2.20
Increase in net tangible book value per common share attributable to the sale of shares to Vifor in May 2018	
Increase in net tangible book value per share attributable to new investors purchasing shares in this offering	
Pro forma as adjusted net tangible book value per share after this offering	
Dilution per share to new investors purchasing shares in this offering	\$

If the underwriters exercise their option to purchase 675,000 additional shares in full, at public offering price of \$ per share, the pro forma as adjusted net tangible book value will increase to \$ per share, representing an immediate increase in net tangible book value to existing stockholders of \$ per share and an immediate dilution in net tangible book value of \$ per share to new investors.

The table and discussion above is based on 32,699,943 shares of common stock outstanding as of March 31, 2018, gives effect to the issuance and sale of 1,174,827 shares of our common stock to Vifor in May 2018 in connection with the VFMCRP Agreement, unless otherwise indicated, and excludes:

3,932,992 shares of our common stock issuable upon the exercise of options outstanding as of March 31, 2018, at a weighted-average exercise price of \$12.18 per share (of which, options to purchase an aggregate of 194,672 shares were exercised after March 31, 2018 with a weighted-average exercise price of \$8.55 per share);

83,791 shares of our common stock issuable upon the vesting of performance-based RSUs outstanding as of March 31, 2018; and

805,401 shares of our common stock reserved for future issuance under our 2014 Equity Incentive Plan as of March 31, 2018.

To the extent that any options are exercised, any RSUs vest and are settled, new equity awards are issued under our 2014 Equity Incentive Plan, or we otherwise issue additional shares of common stock in the future (including shares issued in connection with strategic and other transactions), there will be further dilution to new investors.

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

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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 purchased in this offering 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, accrual method taxpayers subject to special accounting rules under Section 451(b) of the Code, 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 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 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.

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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 U.S. person. 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.

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.

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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 tax 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 United States real property holding corporation.

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 24%, 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 24%, 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.

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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 withheld. Non-U.S. Holders should consult their own tax advisors regarding the possible implications of FATCA on their investment in our common stock.

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Subject to the terms and conditions set forth in the underwriting agreement, dated _____, 2018 among us and Jefferies LLC and Merrill Lynch, Pierce, Fenner & Smith Incorporated, as the representatives of the underwriters named below and the joint book-running managers of this offering, we have agreed to sell to the underwriters, and each of the underwriters has agreed, severally and not jointly, to purchase from us, the respective number of shares of common stock shown opposite its name below:

UNDERWRITER	NUMBER OF SHARES
Jefferies LLC	
Merrill Lynch, Pierce, Fenner & Smith Incorporated	
Piper Jaffray & Co.	
Stifel, Nicolaus & Company, Incorporated	
Canaccord Genuity LLC	
Needham & Company, LLC	
H.C. Wainwright & Co., LLC	
Janney Montgomery Scott LLC	
Total	

The underwriting agreement provides that the obligations of the several underwriters are subject to certain conditions precedent such as the receipt by the underwriters of officers' certificates and legal opinions and approval of certain legal matters by their counsel. The underwriting agreement provides that the underwriters will purchase all of the shares of common stock if any of them are purchased. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the nondefaulting underwriters may be increased or the underwriting agreement may be terminated. We have agreed to indemnify the underwriters and certain of their controlling persons against certain liabilities, including liabilities under the Securities Act, and to contribute to payments that the underwriters may be required to make in respect of those liabilities.

The underwriters have advised us that, following the completion of this offering, they currently intend to make a market in the common stock as permitted by applicable laws and regulations. However, the underwriters are not obligated to do so, and the underwriters may discontinue any market-making activities at any time without notice in their sole discretion. Accordingly, no assurance can be given as to the liquidity of the trading market for the common stock, that you will be able to sell any of the common stock held by you at a particular time or that the prices that you receive when you sell will be favorable.

The underwriters are offering the shares of common stock subject to their acceptance of the shares of common stock from us and subject to prior sale. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Commission and Expenses

The underwriters have advised us that they propose to offer the shares of common stock to the public at the public offering price set forth on the cover page of this prospectus and to certain dealers, which may include the underwriters, at that price less a concession not in excess of \$ per share of common stock. The underwriters may allow, and certain dealers may reallocate, a discount from the concession not in excess of \$ per share of common stock to certain brokers and dealers. After the offering, the public offering price, concession and reallocation to dealers may be reduced by the representatives. No such reduction will change the amount of proceeds to be received by us as set forth on the cover page of this prospectus.

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The following table shows the public offering price, the underwriting discounts and commissions that we are to pay the underwriters and the proceeds, before expenses, to us in connection with this. Such amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase additional shares.

	PER SHARE		TOTAL	
	WITHOUT OPTION TO PURCHASE ADDITIONAL SHARES	WITH OPTION TO PURCHASE ADDITIONAL SHARES	WITHOUT OPTION TO PURCHASE ADDITIONAL SHARES	WITH OPTION TO PURCHASE ADDITIONAL SHARES
Public offering price	\$	\$	\$	\$
Underwriting discounts and commissions paid by us	\$	\$	\$	\$
Proceeds to us, before expenses	\$	\$	\$	\$

We estimate expenses payable by us in connection with this offering, other than the underwriting discounts and commissions referred to above, will be approximately \$. We have also agreed to reimburse the underwriters for certain of their expenses in an amount up to \$50,000.

Listing

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

Stamp Taxes

If you purchase shares of common stock offered in this prospectus, you may be required to pay stamp taxes and other charges under the laws and practices of the country of purchase, in addition to the offering price listed on the cover page of this prospectus.

Option to Purchase Additional Shares

We have granted to the underwriters an option, exercisable for 30 days from the date of this prospectus, to purchase, from time to time, in whole or in part, up to an aggregate of shares from us at the public offering price set forth on the cover page of this prospectus, less underwriting discounts and commissions. If the underwriters exercise this option, each underwriter will be obligated, subject to specified conditions, to purchase a number of additional shares proportionate to that underwriter's initial purchase commitment as indicated in the table above.

No Sales of Similar Securities

We, our officers and our directors have agreed, subject to specified exceptions, not to directly or indirectly:

sell, offer, contract or grant any option to sell (including any short sale), pledge, transfer, establish an open put equivalent position within the meaning of Rule 16a-1(h) under the Securities Exchange Act of 1934, as amended, or

otherwise dispose of any shares of common stock, options or warrants to acquire shares of common stock, or securities exchangeable or exercisable for or convertible into shares of common stock currently or hereafter owned either of record or beneficially, or

publicly announce an intention to do any of the foregoing for a period of 90 days after the date of this prospectus without the prior written consent of Jefferies LLC and Merrill Lynch, Pierce, Fenner & Smith Incorporated.

This restriction terminates after the close of trading of the common stock on and including the 90th day after the date of this prospectus.

Jefferies LLC and Merrill Lynch, Pierce, Fenner & Smith 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 shareholders who will execute a lock-up agreement, providing consent to the sale of shares prior to the expiration of the lock-up period.

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Stabilization

The underwriters have advised us that they, pursuant to Regulation M under the Securities Exchange Act of 1934, as amended, certain persons participating in the offering may engage in short sale transactions, stabilizing transactions, syndicate covering transactions or the imposition of penalty bids in connection with this offering. These activities may have the effect of stabilizing or maintaining the market price of the common stock at a level above that which might otherwise prevail in the open market. Establishing short sales positions may involve either covered short sales or naked short sales.

Covered short sales are sales made in an amount not greater than the underwriters' option to purchase additional shares of our common stock in this offering. The underwriters may close out any covered short position by either exercising their option to purchase additional shares of our common stock or purchasing shares of our common stock in the open market. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the option to purchase additional shares.

Naked short sales are sales in excess of the option to purchase additional shares of our common stock. 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 shares of our common stock in the open market after pricing that could adversely affect investors who purchase in this offering.

A stabilizing bid is a bid for the purchase of shares of common stock on behalf of the underwriters for the purpose of fixing or maintaining the price of the common stock. A syndicate covering transaction is the bid for or the purchase of shares of common stock on behalf of the underwriters to reduce a short position incurred by the underwriters in connection with the offering. Similar to other purchase transactions, the underwriter's purchases to cover the syndicate short sales may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock may be higher than the price that might otherwise exist in the open market. A penalty bid is an arrangement permitting the underwriters to reclaim the selling concession otherwise accruing to a syndicate member in connection with the offering if the common stock originally sold by such syndicate member are purchased in a syndicate covering transaction and therefore have not been effectively placed by such syndicate member.

Neither we, nor any of the underwriters make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our common stock. The underwriters are not obligated to engage in these activities and, if commenced, any of the activities may be discontinued at any time.

The underwriters may also engage in passive market making transactions in our common stock on The Nasdaq Global Market in accordance with Rule 103 of Regulation M during a period before the commencement of offers or sales of shares of our common stock in this offering and extending through the completion of distribution. A passive market maker must display its bid at a price not in excess of the highest independent bid of that security. However, if all independent bids are lowered below the passive market maker's bid, that bid must then be lowered when specified purchase limits are exceeded.

Electronic Distribution

A prospectus in electronic format may be made available by e-mail or on the web sites or through online services maintained by one or more of the underwriters or their affiliates. In those cases, prospective investors may view

offering terms online and may be allowed to place orders online. The underwriters may agree with us to allocate a specific number of shares of common stock for sale to online brokerage account holders. Any such allocation for online distributions will be made by the underwriters on the same basis as other allocations. Other than the prospectus in electronic format, the information on the underwriters' web sites and any information contained in any other web site maintained by any of the underwriters is not part of this prospectus, has not been approved and/or endorsed by us or the underwriters and should not be relied upon by investors.

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Other Activities and Relationships

The underwriter and certain of its affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. The underwriter and certain of its affiliates have, from time to time, performed, and may in the future perform, various commercial and investment banking and financial advisory services for us and our affiliates, for which they received or will receive customary fees and expenses.

In the ordinary course of their various business activities, the underwriter and certain of its affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers, and such investment and securities activities may involve securities and/or instruments issued by us and our affiliates. If the underwriters or their respective affiliates have a lending relationship with us, they routinely hedge their credit exposure to us consistent with their customary risk management policies. The underwriters and their respective affiliates may hedge such exposure by entering into transactions which consist of either the purchase of credit default swaps or the creation of short positions in our securities or the securities of our affiliates, including potentially the common stock offered hereby. Any such short positions could adversely affect future trading prices of the common stock offered hereby. The underwriters and certain of their respective affiliates may also communicate independent investment recommendations, market color or trading ideas and/or publish or express independent research views in respect of such securities or instruments and may at any time hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

Disclaimers About Non-U.S. Jurisdictions

European Economic Area

In relation to each member state of the European Economic Area, no offer of ordinary shares which are the subject of the offering has been, or will be made to the public in that Member State, other than under the following exemptions under the Prospectus Directive:

- (a) to any legal entity which is a qualified investor as defined in the Prospectus Directive;
- (b) to fewer than 150 natural or legal persons (other than qualified investors as defined in the Prospectus Directive), subject to obtaining the prior consent of the Representatives for any such offer; or
- (c) in any other circumstances falling within Article 3(2) of the Prospectus Directive, *provided* that no such offer of ordinary shares referred to in (a) to (c) above shall result in a requirement for the Company or any Representative to publish a prospectus pursuant to Article 3 of the Prospectus Directive, or supplement a prospectus pursuant to Article 16 of the Prospectus Directive.

Each person located in a Member State to whom any offer of ordinary shares is made or who receives any communication in respect of an offer of ordinary shares, or who initially acquires any ordinary shares will be deemed to have represented, warranted, acknowledged and agreed to and with each Representative and the Company that (1) it

is a qualified investor within the meaning of the law in that Member State implementing Article 2(1)(e) of the Prospectus Directive; and (2) in the case of any ordinary shares acquired by it as a financial intermediary as that term is used in Article 3(2) of the Prospectus Directive, the ordinary shares acquired by it in the offer have not been acquired on behalf of, nor have they been acquired with a view to their offer or resale to, persons in any Member State other than qualified investors, as that term is defined in the Prospectus Directive, or in circumstances in which the prior consent of the Representatives has been given to the offer or resale; or where ordinary shares have been acquired by it on behalf of persons in any Member State other than qualified investors, the offer of those ordinary shares to it is not treated under the Prospectus Directive as having been made to such persons.

The Company, the Representatives and their respective affiliates will rely upon the truth and accuracy of the foregoing representations, acknowledgments and agreements.

This prospectus has been prepared on the basis that any offer of shares in any Member State will be made pursuant to an exemption under the Prospectus Directive from the requirement to publish a prospectus for offers of shares.

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Accordingly any person making or intending to make an offer in that Member State of shares which are the subject of the offering contemplated in this prospectus may only do so in circumstances in which no obligation arises for the Company or any of the Representatives to publish a prospectus pursuant to Article 3 of the Prospectus Directive in relation to such offer. Neither the Company nor the Representatives have authorized, nor do they authorize, the making of any offer of shares in circumstances in which an obligation arises for the Company or the Representatives to publish a prospectus for such offer.

For the purposes of this provision, the expression an offer of ordinary shares to the public in relation to any ordinary shares in any Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the ordinary shares to be offered so as to enable an investor to decide to purchase or subscribe the ordinary shares, as the same may be varied in that Member State by any measure implementing the Prospectus Directive in that Member State, the expression Prospectus Directive means Directive 2003/71/EC (as amended) and includes any relevant implementing measure in each Member State.

The above selling restriction is in addition to any other selling restrictions set out below.

Notice to Prospective Investors in the United Kingdom

In addition, in the United Kingdom, this document is being distributed only to, and is directed only at, and any offer subsequently made may only be directed at persons who are qualified investors (as defined in the Prospectus Directive) (i) who have professional experience in matters relating to investments falling within Article 19 (5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended (the Order) and/or (ii) who are high net worth companies (or persons to whom it may otherwise be lawfully communicated) falling within Article 49(2)(a) to (d) of the Order (all such persons together being referred to as relevant persons). This document must not be acted on or relied on in the United Kingdom by persons who are not relevant persons. In the United Kingdom, any investment or investment activity to which this document relates is only available to, and will be engaged in with, relevant persons.

Notice to Prospective Investors in Switzerland

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

Neither this document nor any other offering or marketing material relating to the offering, the Company, the shares have been or will be filed with or approved by any Swiss regulatory authority. In particular, this document will not be filed with, and the offer of shares will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA, and the offer of shares 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 shares.

Notice to Prospective Investors in the Dubai International Financial Centre

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

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Notice to Prospective Investors in Australia

No placement document, prospectus, product disclosure statement or other disclosure document has been lodged with the Australian Securities and Investments Commission (ASIC), in relation to the offering. This prospectus does not constitute a prospectus, product disclosure statement or other disclosure document under the Corporations Act 2001, or the Corporations Act, and does not purport to include the information required for a prospectus, product disclosure statement or other disclosure document under the Corporations Act.

Any offer in Australia of the shares may only be made to persons (the Exempt Investors) who are sophisticated investors (within the meaning of section 708(8) of the Corporations Act), professional investors (within the meaning of section 708(11) of the Corporations Act) or otherwise pursuant to one or more exemptions contained in section 708 of the Corporations Act so that it is lawful to offer the shares without disclosure to investors under Chapter 6D of the Corporations Act.

The shares applied for by Exempt Investors in Australia must not be offered for sale in Australia in the period of 12 months after the date of allotment under the offering, except in circumstances where disclosure to investors under Chapter 6D of the Corporations Act would not be required pursuant to an exemption under section 708 of the Corporations Act or otherwise or where the offer is pursuant to a disclosure document which complies with Chapter 6D of the Corporations Act. Any person acquiring shares must observe such Australian on-sale restrictions.

This prospectus contains general information only and does not take account of the investment objectives, financial situation or particular needs of any particular person. It does not contain any securities recommendations or financial product advice. Before making an investment decision, investors need to consider whether the information in this prospectus is appropriate to their needs, objectives and circumstances, and, if necessary, seek expert advice on those matters.

Notice to Prospective Investors in Hong Kong

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

Notice to Prospective Investors in Japan

The securities have not been and will not be registered under the Financial Instruments and Exchange Law of Japan (Law No. 25 of 1948, as amended) and, accordingly, will not be offered or sold, directly or indirectly, in Japan, or for the benefit of any Japanese Person or to others for re-offering or resale, directly or indirectly, in Japan or to any Japanese Person, except in compliance with all applicable laws, regulations and ministerial guidelines promulgated by relevant Japanese governmental or regulatory authorities in effect at the relevant time. For the purposes of this paragraph, Japanese Person shall mean any person resident in Japan, including any corporation or other entity organized under the laws of Japan.

Notice to Prospective Investors in Singapore

This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of Non-CIS Securities may not be circulated or distributed, nor may the Non-CIS Securities 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, or the SFA, (ii) to a relevant person pursuant to Section 275(1), or any person pursuant to Section 275(1A), and in accordance with the conditions specified in Section 275, of the SFA, or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

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Where the Non-CIS Securities are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

(a) a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or

(b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor, securities (as defined in Section 239(1) of the SFA) of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the Non-CIS Securities pursuant to an offer made under Section 275 of the SFA except:

(a) to an institutional investor or to a relevant person defined in Section 275(2) of the SFA, or to any person arising from an offer referred to in Section 275(1A) or Section 276(4)(i)(B) of the SFA;

(b) where no consideration is or will be given for the transfer;

(c) where the transfer is by operation of law;

(d) as specified in Section 276(7) of the SFA; or

(e) as specified in Regulation 32 of the Securities and Futures (Offers of Investments) (Shares and Debentures) Regulations 2005 of Singapore.

Notice to Prospective Investors in Canada

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

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

Pursuant to section 3A.3 (or, in the case of securities issued or guaranteed by the government of a non-Canadian jurisdiction, section 3A.4) of National Instrument 33-105 *Underwriting Conflicts* (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

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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.

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EXPERTS

The financial statements of Cara Therapeutics, Inc., appearing in Cara Therapeutics, Inc. Annual Report (Form 10-K) for the year ended December 31, 2017 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.

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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.

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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, 2017 filed with the SEC on March 15, 2018;

the information specifically incorporated by reference in our Annual Report on Form 10-K for the year ended December 31, 2017 from our Definitive Proxy Statement on Schedule 14A relating to our 2018 Annual Meeting of Stockholders, which was filed with the SEC on April 26, 2018;

our Quarterly Report on Form 10-Q for the fiscal quarter ended March 31, 2018 filed with the SEC on May 9, 2018;

our Current Reports on Form 8-K filed with the SEC on June 27, 2018, June 8, 2018, May 23, 2018 and March 12, 2018; 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.

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.

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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.

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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**.

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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

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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

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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;

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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.

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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.

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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.

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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;

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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.

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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