

Prospectus supplement

(To prospectus dated July 2, 2020)

3,488,373 Shares

Common Stock

We are offering 3,488,373 shares of our common stock.

Our common stock is listed on the Nasdaq Global Market under the symbol "KRTX." On August 9, 2022, the last reported sale price of our common stock on the Nasdaq Global Market was \$228.45 per share.

Our business and an investment in our common stock involve significant risks. These risks are described under the caption "[Risk Factors](#)" on page S-10 of this prospectus supplement, page 6 of the accompanying prospectus and in Item 1A "Risk Factors" included in our Annual Report on Form 10-K for the year ended December 31, 2021, which is incorporated herein by reference.

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

	Per Share	Total
Public offering price	\$ 215.00	\$ 750,000,195.00
Underwriting discounts and commissions ⁽¹⁾	\$ 10.75	\$ 37,500,009.75
Proceeds, before expenses, to Karuna Therapeutics, Inc.	\$ 204.25	\$ 712,500,185.25

(1) See "[Underwriting](#)" beginning on page S-16 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 August 12, 2022. We have granted the underwriters an option for a period of 30 days to purchase up to an additional 523,255 shares of our common stock. If the underwriters exercise the option in full, the total underwriting discounts and commissions payable by us will be approximately \$43.1 million and the total proceeds to us, before expenses, will be approximately \$819.4 million.

Goldman Sachs & Co. LLC**J.P. Morgan****Jefferies****Stifel
JMP Securities, a Citizens Company****Guggenheim Securities****RBC Capital Markets
Wedbush PacGrow**

Prospectus supplement dated August 9, 2022

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ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus are part of a “shelf” registration statement on Form S-3 (File No. 333-239657) that we filed with the Securities and Exchange Commission, or the SEC, on July 2, 2020 and which became effective upon filing.

This document is in two parts. The first part is this prospectus supplement, which describes the terms of this offering and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference into this prospectus supplement and the accompanying prospectus. The second part is the accompanying prospectus, which gives more general information about the shares of our common stock and other securities we may offer from time to time under our shelf registration statement, some of which does not apply to the securities offered by this prospectus supplement. To the extent there is a conflict between the information contained in this prospectus supplement, on the one hand, and the information contained in the accompanying prospectus or any document incorporated by reference herein or therein, on the other hand, you should rely on the information in this prospectus supplement.

You should read this prospectus supplement, the accompanying prospectus, the documents incorporated by reference in this prospectus supplement and the accompanying prospectus and any free writing prospectus that we have authorized for use in connection with this offering before making an investment decision. You should also read and consider the information in the documents referred to in the sections of this prospectus supplement entitled “Where You Can Find More Information” and “Information Incorporated by Reference.”

Neither we nor the underwriters have authorized anyone to provide you with any information or to make any representation, other than those contained or incorporated by reference in this prospectus supplement and the accompanying prospectus, which together we sometimes refer to generally as the prospectus, or in any free writing prospectus prepared by us or on our behalf or to which we have referred you. We take no responsibility for, and provide no assurance as to the reliability of, any other information that others may give you. This prospectus supplement and the accompanying prospectus are an offer to sell only the shares offered hereby, but only in circumstances and in jurisdictions where it is lawful to do so. The information contained or incorporated by reference in this prospectus supplement and the accompanying prospectus is accurate only as of its date, regardless of the time of delivery of this prospectus supplement and the accompanying prospectus or of any sale of our common stock.

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

This prospectus supplement and the accompanying prospectus do not constitute an offer to sell, or a solicitation of an offer to purchase, the securities offered by this prospectus supplement and the accompanying prospectus in any jurisdiction to or from any person to whom or from whom it is unlawful to make such offer or solicitation of an offer in such jurisdiction. We are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where offers and sales are permitted.

Unless otherwise mentioned or unless the context requires otherwise, all references in this prospectus supplement to “Karuna,” “we,” “us” and “our” or similar references refer to Karuna Therapeutics, Inc. and its consolidated subsidiary, unless otherwise specified or the context otherwise requires.

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This prospectus supplement, the accompanying prospectus and the information incorporated by reference herein and therein include trademarks, service marks and trade names owned by us or other companies. All trademarks, service marks and trade names included or incorporated by reference into this prospectus supplement are the property of their respective owners.

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights certain information about us, this offering and selected information contained elsewhere in or incorporated by reference into this prospectus supplement. This summary is not complete and does not contain all of the information that you should consider before deciding whether to invest in our common stock. Before making an investment decision, you should carefully read the entire prospectus supplement and the accompanying prospectus (including the documents incorporated by reference herein and therein), especially the risks of investing in our common stock discussed under the heading "Risk Factors" in this prospectus supplement and the accompanying prospectus, and in our Annual Report on Form 10-K for the year ended December 31, 2021, which is incorporated by reference into this prospectus supplement and the accompanying prospectus. You should also carefully read the information incorporated by reference into this prospectus supplement, including our financial statements, and the exhibits to the registration statement of which this prospectus supplement is a part.

Overview

We are a clinical-stage biopharmaceutical company driven to create and deliver transformative medicines for people living with psychiatric and neurological conditions. Our pipeline is built on the broad therapeutic potential of our lead product candidate, KarXT (xanomeline-trospium), an oral modulator of muscarinic receptors that are located both in the central nervous system, or CNS, and various peripheral tissues. KarXT is our proprietary product candidate that combines xanomeline, a novel muscarinic agonist, with trospium, an approved muscarinic antagonist, to preferentially stimulate muscarinic receptors in the CNS. In August 2022, we announced positive topline results from our second registrational clinical trial, EMERGENT-2, evaluating the efficacy, safety and tolerability of KarXT compared to placebo for the treatment of acute psychosis in adults with schizophrenia, and our plan to submit a New Drug Application, or NDA, for KarXT for the treatment of schizophrenia in mid-2023. In this Phase 3 trial, KarXT met its primary endpoint, demonstrating a statistically significant and clinically meaningful 9.6-point reduction in Positive and Negative Syndrome Scale, or PANSS, total score compared to placebo at Week 5 (Cohen's d effect size of 0.61). KarXT also demonstrated an early and sustained statistically significant reduction of symptoms, as assessed by PANSS total score, starting at Week 2 and maintained such reduction through all timepoints in the trial. KarXT also met key secondary endpoints, demonstrating a statistically significant 2.9-point reduction in the PANSS positive symptoms subscale, a 1.8-point reduction in PANSS negative symptoms subscale and a 2.2-point reduction in PANSS negative Marder factor subscale. We have not yet evaluated the exploratory cognitive endpoint in EMERGENT-2, and plan to provide these results in the future. KarXT was generally well tolerated in this trial.

We are initially developing KarXT for the treatment of acute psychosis in patients with schizophrenia. KarXT combines xanomeline, a muscarinic receptor agonist that preferentially stimulates M1 and M4 muscarinic receptors, and trospium, an approved muscarinic receptor antagonist that does not measurably cross the blood-brain barrier, confining its effects to peripheral tissues. M1 and M4 muscarinic receptors are the receptor subtypes believed to mediate the antipsychotic and procognitive effects of xanomeline and other muscarinic agonists. Results from preclinical studies and clinical trials conducted by third parties support the hypothesis that xanomeline can reduce psychosis and improve cognition. To our knowledge, xanomeline is the only muscarinic orthosteric agonist that has demonstrated therapeutic benefit in clinical trials in both schizophrenia and Alzheimer's Disease, or AD. Like all muscarinic receptor agonists studied to date, however, xanomeline's tolerability has been limited by side effects arising from muscarinic receptor stimulation in peripheral tissues, leading to nausea, vomiting, diarrhea and increased salivation and sweating, collectively referred to as cholinergic adverse events. Trospium is a muscarinic receptor antagonist approved in the United States and Europe for the treatment of overactive bladder that inhibits all five muscarinic receptor subtypes in peripheral tissues. We believe that the combination of xanomeline and trospium in KarXT has the potential to preferentially stimulate M1 and M4 muscarinic receptors in the brain without stimulating muscarinic receptors in peripheral tissues in order to achieve meaningful therapeutic benefit in patients with psychotic and cognitive disorders.

The EMERGENT program is our clinical program evaluating KarXT for the treatment of schizophrenia, and includes the completed positive Phase 2 EMERGENT-1 and Phase 3 EMERGENT-2 trials and three ongoing Phase 3 trials (EMERGENT-3, EMERGENT-4, and EMERGENT-5). Following the positive results of EMERGENT-1 in November 2019, we had an End-of-Phase 2 meeting with the U.S. Food and Drug Administration, or FDA, in which the FDA indicated that our completed Phase 2 EMERGENT-1 trial, along with one successful Phase 3 efficacy and safety trial, and additional safety data to meet regulatory requirements, would be acceptable to support an NDA submission in schizophrenia. As a result of the recently completed Phase 3 EMERGENT-2 trial, we plan to submit our NDA for KarXT for the treatment of schizophrenia to the FDA in mid-2023. We define mid-year as the second and third quarters of a calendar year.

Given the unique mechanism of action of KarXT in comparison to existing standard of care therapies, we believe there is the potential for therapeutic benefit as both a monotherapy and as an adjunctive therapy for the treatment of schizophrenia. In November 2021, we initiated our Phase 3 ARISE trial evaluating the efficacy and safety of KarXT compared to placebo as an adjunctive treatment in adults with schizophrenia who have an inadequate response to their current antipsychotic therapy. This six-week, 1:1 randomized, double-blind, placebo-controlled Phase 3 trial is designed to enroll approximately 400 adults with schizophrenia who have not achieved an adequate response to their current atypical antipsychotic treatment. The primary outcome measure of the trial is change in PANSS total score of KarXT compared to placebo at week 6. Upon completion of the trial at week 6, participants will have the opportunity to enroll in a 52-week outpatient, open-label extension trial evaluating the long-term safety and tolerability of KarXT when dosed with atypical antipsychotic treatment. We anticipate topline data from the ARISE trial in the first half of 2024. In addition, we initiated the open-label extension of ARISE in the first half of 2022.

We are also developing KarXT as a potential treatment for dementia-related psychosis, or DRP, with an initial focus on psychosis related to AD. The ADEPT program, which is the clinical program evaluating KarXT as a potential treatment for psychosis related to AD, will consist of three Phase 3 trials: ADEPT-1, ADEPT-2 and ADEPT-3. The Phase 3 ADEPT-1 trial, which we plan to initiate in the third quarter of 2022, will evaluate the efficacy and safety of KarXT compared to placebo in adults with moderate to severe psychosis related to AD. This trial will consist of a 12-week, single-blind treatment period, followed by a 26-week, double-blind, randomized withdrawal period in which subjects who meet the response criteria will be randomized to receive KarXT or placebo. The single-blind treatment period is designed to enroll approximately 400 adults with AD, between 55 and 90 years old, with moderate to severe hallucinations or delusions, who are living at home or at an assisted living facility. The primary objective of this trial is to evaluate relapse prevention as measured by time from randomization to relapse during the 26-week, double-blind period.

In addition, in 2023 we plan to initiate our Phase 3 ADEPT-2 and ADEPT-3 trials. ADEPT-2 will be a 12-week, flexible-dose, double-blind, placebo-controlled trial evaluating the efficacy and safety of KarXT versus placebo, and ADEPT-3 will be an open-label extension trial of ADEPT-1 and ADEPT-2 evaluating the long-term safety of KarXT, in adults with psychosis related to AD. We expect to complete both the ADEPT-1 and ADEPT-2 trials in 2025. Our initial focus on the AD dementia subtype of DRP reflects various strategic development, regulatory and commercial considerations, and we remain interested in exploring KarXT in other dementia subtypes in future development programs.

We have assembled a team whose members have extensive expertise in the research, development and commercialization of numerous CNS agents, as well as deep familiarity with the biology of neuropsychiatric disorders, such as schizophrenia and DRP, including the role of muscarinic receptors in potential treatment of these diseases. We plan to leverage this expertise to develop a pipeline of product candidates targeting a broad range of psychiatric and neurological conditions.

Pipeline

We are advancing a pipeline of therapeutic programs to address the positive, negative and cognitive symptoms associated with schizophrenia and psychosis related to AD. We are leveraging our expertise and experience to explore the development of KarXT for additional CNS disorders, as well as advance our other muscarinic-targeted drug candidates and a target-agnostic drug discovery program through our collaboration with PsychoGenics, Inc.

PROGRAM	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	STATUS / UPCOMING MILESTONE
Schizophrenia	EMERGENT-1				Complete
	EMERGENT-2				Complete*
	EMERGENT-3				Topline data Q1 2023
	EMERGENT-4 (open-label extension)				Enrolling
	EMERGENT-5				Enrolling
Schizophrenia (adjunctive) Psychosis in adults with an inadequate response to standard of care	ARISE				Topline data 1H 2024
	ARISE (open-label extension)				Enrolling
Psychosis in Alzheimer's disease	ADEPT-1				Planned initiation 3Q '22
	ADEPT-2				Planned initiation 2023
	ADEPT-3 (open-label extension)				Planned initiation 2023

* Additional analysis ongoing

Our Programs

Our Ongoing EMERGENT program for the Treatment of Acute Psychosis in Adults with Schizophrenia

The EMERGENT program is our clinical program evaluating KarXT for the treatment of schizophrenia, and includes the completed positive Phase 2 EMERGENT-1 and Phase 3 EMERGENT-2 trials and three ongoing Phase 3 trials (EMERGENT-3, EMERGENT-4, and EMERGENT-5).

Completed Phase 3 EMERGENT-2 Clinical Trial

In August 2022, we announced positive topline results from our Phase 3 EMERGENT-2 trial evaluating the efficacy, safety and tolerability of KarXT compared to placebo for the treatment of acute psychosis in adults with schizophrenia. KarXT met the primary endpoint, demonstrating a statistically significant and clinically meaningful 9.6-point reduction in PANSS total score compared to placebo (-21.2 KarXT vs. -11.6 placebo, $p < 0.0001$) at Week 5 (Cohen's d effect size of 0.61). KarXT also demonstrated an early and sustained statistically significant reduction of symptoms, as assessed by PANSS total score, starting at Week 2 and maintained such reduction through all timepoints in the trial. KarXT also met key secondary endpoints, demonstrating a statistically significant 2.9-point reduction in the PANSS positive symptoms subscale (-6.8 KarXT vs. -3.9 placebo, $p < 0.0001$), a 1.8-point reduction in PANSS negative symptoms subscale (-3.4 KarXT vs. -1.6 placebo, $p = 0.0055$) and a 2.2-point reduction in PANSS negative Marder factor subscale (-4.2 KarXT vs. -2.0 placebo, $p = 0.022$). We have not yet evaluated the exploratory cognitive endpoint in EMERGENT-2, and plan to provide these results in the future.

KarXT was generally well tolerated in this trial. Overall discontinuation rates were similar between KarXT and placebo groups (25% vs. 21%). The overall treatment-emergent adverse events, or TEAEs, rate for KarXT and placebo was 75% and 58%, respectively. Discontinuation rates related to TEAEs were similar between KarXT (7%)

and placebo (6%). Equal rates of serious TEAEs were observed between KarXT and placebo (2% in each group) and included suicidal ideation, worsening of schizophrenia symptoms, and appendicitis. None of the serious TEAEs were determined to be drug related. The most common TEAEs ($\geq 5\%$) in the KarXT arm were all mild to moderate in severity and included constipation, dyspepsia, nausea, vomiting, headache, increases in blood pressure, dizziness, gastroesophageal reflux disease (acid reflux), abdominal discomfort, and diarrhea. Mean blood pressure measures were similar between KarXT and placebo throughout the trial, and no syncopal events were observed. In the subset of patients with a TEAE of increases in blood pressure, mean blood pressure at endpoint was similar to baseline and did not lead to trial discontinuation. Similar to prior trials, an increase in heart rate was associated with KarXT treatment and decreased in magnitude by the end of the trial. Consistent with EMERGENT-1, KarXT was not associated with common problematic side effects of current treatments, including sedation (somnolence), weight gain, and extrapyramidal symptoms. In the trial, 81% of patients on KarXT compared to 90% on placebo titrated to the highest dose level.

Completed Phase 2 EMERGENT-1 Clinical Trial

In November 2019, we announced the positive results of our Phase 2 EMERGENT-1 trial evaluating KarXT for the treatment of acute psychosis in adults with schizophrenia. In this trial, KarXT met the trial's primary endpoint with a statistically significant ($p < 0.0001$) and clinically meaningful 11.6 point mean reduction in total PANSS scores over placebo at week 5 (-17.4 KarXT vs. -5.9 placebo). We also observed a statistically significant 3.2 point mean reduction from baseline in the PANSS-positive subscale (-5.6 KarXT vs. -2.4 placebo) and a statistically significant 2.3 point mean reduction from baseline in the PANSS-negative subscale (-3.2 KarXT vs. -0.9 placebo) at week five ($p < 0.0001$ and $p < 0.001$, respectively). The total PANSS, PANSS-positive subscale, and the PANSS-negative subscale had statistically significant separation at every assessment throughout the trial. We also analyzed additional pre-specified secondary endpoints, including PANSS negative Marder factor subscale, clinical global impression, or CGI-S, frequency counts and percentage of CGI-S responders, defined as a CGI-S rating of either 1 or 2 at week five. We observed a statistically significant 2.5 point mean reduction from baseline in the PANSS negative Marder factor subscale (-3.9 KarXT v. -1.3 placebo) at week five ($p < 0.001$). The PANSS negative Marder factor subscale had statistically significant separation at every assessment point through the trial. We also observed statistically significant different CGI-S frequency counts for KarXT compared to placebo at week five ($p < 0.001$). A 4:1 ratio of CGI-S responders (5.6% KarXT v. 1.4% placebo) was also observed, however this result was not statistically significant ($p = 0.151$).

KarXT was observed to be well tolerated in the Phase 2 EMERGENT-1 trial. The overall discontinuation rate in the KarXT treatment arm was similar to placebo (20% on KarXT vs. 21% on placebo) and the number of discontinuations due to treatment emergent adverse events was equal in the two arms ($n = 2$ on KarXT and $n = 2$ on placebo). No patients discontinued treatment due to cholinergic adverse events in either arm of the trial. The overall treatment emergent adverse event rate was 54% on KarXT and 43% on placebo. Occurrences of drowsiness, extrapyramidal side effects, such as tremors or slurred speech, or weight gain, which are adverse effects generally associated with current antipsychotic drugs, were similar to placebo. The most common adverse events were constipation, nausea, dry mouth, dyspepsia, and vomiting, all of which were mild or moderate in severity and transient in nature. Placebo-adjusted rates of nausea, vomiting and dry mouth all decreased over time during the trial. There was no syncope, and there was no mean change in blood pressure. One patient in the KarXT group discontinued due to elevated gamma-glutamyl transferase. There was a 5.5 beats per minute peak mean placebo adjusted resting heart rate increase in the KarXT group, with a downward trend after week 2. One serious adverse event was observed in the KarXT treatment group, in which a patient discontinued and sought hospital care for worsening psychosis, meeting the regulatory definition of serious adverse event. The clinical trial administrator was not able to rule out that the serious adverse event was drug related, and as such, the serious adverse event was classified as being "possibly-drug related." All other treatment emergent adverse events were mild or moderate.

Ongoing EMERGENT Clinical Trials and NDA Plans

Following the positive results of EMERGENT-1, we had an End-of-Phase 2 meeting with the FDA in which the FDA indicated that our completed EMERGENT-1 trial, along with one successful Phase 3 efficacy and safety trial, and additional safety data to meet regulatory requirements, would be acceptable to support an NDA submission in schizophrenia. As a result of the recently completed EMERGENT-2 trial, we plan to submit our NDA to the FDA in mid-2023.

In addition to the completed Phase 2 EMERGENT-1 and Phase 3 EMERGENT-2 trials, we are currently enrolling the following trials as part of our EMERGENT program:

- **EMERGENT-3:** A five-week inpatient trial evaluating the efficacy and safety of KarXT compared to placebo in 246 adults with schizophrenia conducted in the United States and Ukraine. We anticipate topline data in the first quarter of 2023. We continue to enroll patients at clinical trial sites in the United States.
- **EMERGENT-4:** A 52-week outpatient, open-label extension trial evaluating the long-term safety and tolerability of KarXT in adults with schizophrenia who completed EMERGENT-2 or EMERGENT-3.
- **EMERGENT-5:** A 52-week outpatient, open-label trial conducted in the United States and Puerto Rico evaluating the long-term safety and tolerability of KarXT in adults with schizophrenia who were not enrolled in EMERGENT-2 or EMERGENT-3.

Our Ongoing ARISE program for KarXT as Adjunctive Therapy in Adults with Schizophrenia

Given the unique mechanism of action of KarXT in comparison to existing standard of care therapies, we believe there is the potential for therapeutic benefit as both a monotherapy and as an adjunctive therapy for the treatment of schizophrenia. In November 2021, we initiated our Phase 3 ARISE trial to evaluate the safety and efficacy of KarXT compared to placebo as an adjunctive treatment in adults with schizophrenia who have an inadequate response to their current antipsychotic therapy. This six-week, 1:1 randomized, double-blind, placebo-controlled Phase 3 trial is designed to enroll approximately 400 adults with schizophrenia who have not achieved an adequate response to their current atypical antipsychotic treatment. Participants in this trial will continue their currently prescribed atypical antipsychotic therapy at the same dose or regimen schedule as prior to entry in the study, and will receive a flexible dose of KarXT or placebo based on tolerability and clinical response as determined by a clinician. The primary outcome measure of the trial is change in PANSS total score of KarXT compared to placebo at week 6. Upon completion of the trial at week 6, participants will have the opportunity to enroll in a 52-week outpatient, open-label extension trial evaluating the long-term safety and tolerability of KarXT when dosed with atypical antipsychotic treatment. We anticipate topline data from the ARISE trial in the first half of 2024. In addition, we initiated the open-label extension of ARISE in the first half of 2022.

Our Planned ADEPT program for the Treatment of Psychosis Related to Alzheimer's Disease

We are also developing KarXT as a potential treatment for DRP, with an initial focus on psychosis related to AD. In June 2021, we announced results from our multi-cohort, placebo-controlled Phase 1b trial evaluating the safety and tolerability of KarXT in healthy elderly volunteers. Results from the trial suggest that potentially therapeutic doses of KarXT can be administered to elderly adults while maintaining a favorable tolerability profile, and support the advancement of KarXT into a Phase 3 program.

The ADEPT program, which is the clinical program evaluating KarXT as a potential treatment for psychosis related to AD, will consist of three Phase 3 trials: ADEPT-1, ADEPT-2 and ADEPT-3. The Phase 3 ADEPT-1 trial, which we plan to initiate in the third quarter of 2022, will evaluate the efficacy and safety of KarXT compared to placebo in adults with moderate to severe psychosis related to AD. This trial will consist of a 12-week, single-blind treatment period, followed by a 26-week, double-blind, randomized withdrawal period in which subjects who meet the response criteria will be randomized to receive KarXT or placebo. The single-blind

treatment period is designed to enroll approximately 400 adults with AD, between 55 and 90 years old, with moderate to severe hallucinations or delusions, who are living at home or at an assisted living facility. The primary objective of this trial is to evaluate relapse prevention as measured by time from randomization to relapse during the 26-week, double-blind period.

In addition, in 2023 we plan to initiate our Phase 3 ADEPT-2 and ADEPT-3 trials. ADEPT-2 will be a 12-week, flexible-dose, double-blind, placebo-controlled trial evaluating the efficacy and safety of KarXT versus placebo, and ADEPT-3 will be an open-label extension trial of ADEPT-1 and ADEPT-2 evaluating the long-term safety of KarXT, in adults with psychosis related to AD. We expect to complete both the ADEPT-1 and ADEPT-2 trials in 2025. Our initial focus on the AD dementia subtype of DRP reflects various strategic development, regulatory and commercial considerations, and we remain interested in exploring KarXT in other dementia subtypes in future development programs.

Corporate Information

We were incorporated under the laws of the State of Delaware in July 2009 under the name Karuna Pharmaceuticals, Inc. and changed our name to Karuna Therapeutics, Inc. in March 2019. Our principal corporate office is located at 99 High Street, Floor 26, Boston, Massachusetts 02110, and our telephone number is (857) 299-2244. Our website address is www.karunatx.com. The information contained on, or that can be accessed through, our website is not a part of this prospectus supplement. We have included our website address in this prospectus supplement solely as an inactive textual reference.

THE OFFERING

Common stock offered by us	3,488,373 shares of our common stock.
Option to purchase additional shares	The underwriters have a 30-day option to purchase up to an additional 523,255 shares of our common stock.
Common stock to be outstanding immediately after this offering	33,421,476 shares (33,944,731 shares if the underwriters exercise their option to purchase additional shares in full).
Use of Proceeds	We estimate that the net proceeds to us from this offering will be \$711.9 million (or \$818.8 million if the underwriters exercise their option to purchase additional shares in full). We currently intend to use the net proceeds from this offering, together with our existing cash, cash equivalents and available-for-sale investments, to fund our ongoing and planned clinical trials of KarXT and other research and development, to support the potential commercialization of KarXT for psychosis in schizophrenia, and for working capital and general corporate purposes. See “Use of Proceeds” on page S-14 of this prospectus supplement.
Risk Factors	Investing in our securities involves a high degree of risk. See “Risk Factors” beginning on page S-10 of this prospectus supplement, page 6 of the accompanying prospectus, and Item 1A “Risk Factors” included in our Annual Report on Form 10-K for the year ended December 31, 2021 filed with the SEC on February 24, 2022 and other information included and incorporated by reference in this prospectus supplement and the accompanying prospectus for a discussion of factors that you should carefully consider before deciding to invest in our common stock.
Nasdaq Global Market symbol	“KRTX”

The number of shares of common stock shown above to be outstanding after this offering is based on 29,933,103 shares of common stock outstanding as of June 30, 2022, and excludes the following:

- 5,912,840 shares of common stock issuable upon the exercise of stock options outstanding as of June 30, 2022, at a weighted-average exercise price of \$58.32 per share;
- 1,568,533 shares of common stock reserved for future issuance under our 2019 Stock Option and Incentive Plan as of June 30, 2022; and
- 1,041,445 shares of common stock reserved for future issuance under our 2019 Employee Stock Purchase Plan as of June 30, 2022.

Unless otherwise indicated, all information in this prospectus supplement assumes no exercise of the underwriters’ option to purchase additional shares of common stock from us, no exercise of outstanding stock options after June 30, 2022 and no sales under our Equity Distribution Agreement with Goldman Sachs & Co. LLC after June 30, 2022.

RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risk factors described below, together with the risks under the heading “Risk Factors” beginning on page 6 of the accompanying prospectus and under Part I, Item A of our Annual Report on Form 10-K for the fiscal year ended December 31, 2021, filed with the SEC on February 24, 2022, and all other information contained or incorporated by reference into this prospectus supplement and the accompanying prospectus, including our financial statements and the related notes, as updated by our subsequent filings under the Securities Exchange Act of 1934, as amended, or the Exchange Act, and in any free writing prospectus that we have authorized for use in connection with this offering before acquiring any of our common stock. These risks could have a material and adverse impact on our business, results of operations, financial condition and growth prospects, which may cause the trading price of our common stock to decline and you could lose all or part of your investment.

Risks Related to this Offering and Ownership of our Common Stock

If you purchase shares of common stock in this offering, you will suffer immediate and substantial dilution of your investment.

The public offering price of our common stock is substantially higher than the net tangible book value per share of our common stock. Therefore, if you purchase shares of our common stock in this offering, you will pay a price per share that substantially exceeds our net tangible book value per share after this offering. Based on the public offering price of \$215.00 per share, you will experience immediate dilution of \$181.58 per share, representing the difference between our as adjusted net tangible book value per share as of June 30, 2022, after giving effect to this offering, and the public offering price. Furthermore, if the underwriters exercise their option to purchase additional shares or we issue additional shares, whether upon exercise of our previously issued options, pursuant to our Equity Distribution Agreement with Goldman Sachs & Co. LLC, or otherwise, you will experience further dilution. For additional information on the dilution that you will experience immediately after this offering, see the section titled “Dilution.”

The trading price of our common stock is likely to be highly volatile, which could result in substantial losses for purchasers of our common stock in this offering. Securities class action or other litigation involving our company or members of our management team could also substantially harm our business, financial condition and results of operations.

Our stock price has historically been volatile. The stock market in general and the market for pharmaceutical and biotechnology companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, you may not be able to sell your common stock at or above the public offering price and you may lose some or all of your investment. The market price for our common stock may be influenced by many factors, including:

- the success of existing or new competitive products or technologies;
- regulatory actions with respect to our product candidates or our competitors’ products and product candidates;
- announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures, collaborations or capital commitments;
- the timing and results of clinical trials of KarXT and any other product candidates;
- commencement or termination of collaborations for our development programs;
- failure or discontinuation of any of our development programs;
- results of clinical trials of product candidates of our competitors;

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- regulatory, legal or political developments in the United States and other countries;
- volatility resulting from the economic turmoil caused by the COVID-19 pandemic;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our product candidates or clinical development programs;
- the extent to which we in-license, acquire or invest in other indications or product candidates;
- the results of our efforts to develop additional product candidates or products;
- actual or anticipated changes in estimates as to financial results or development timelines;
- announcement or expectation of additional financing efforts;
- sales of our common stock by us, our insiders or other stockholders;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in estimates or recommendations by securities analysts, if any, that cover us;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors; and
- general economic, industry and market conditions, including inflation and fluctuations in interest rates.

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for pharmaceutical and biotechnology companies, which have experienced significant stock price volatility in recent years.

We have broad discretion in the use of the net proceeds from this offering and may invest or spend the proceeds in ways with which you do not agree and in ways that may not yield a return on your investment.

Although we currently intend to use the net proceeds from this offering in the manner described in the section titled “Use of Proceeds” in this prospectus supplement, our management will have broad discretion in the application of the net proceeds from this offering and could spend the proceeds in ways that do not improve our results of operations or enhance the value of our common stock. You will not have the opportunity to influence our decisions on how to use the net proceeds from this offering. The failure by our management to apply these funds effectively could result in financial losses that could harm our business, cause the price of our common stock to decline and delay the development of our product candidates. Pending their use, we may invest the net proceeds from this offering in a manner that does not produce income or that loses value.

You may experience future dilution as a result of future equity offerings.

In order to raise additional capital, we may in the future offer additional shares of our common stock or other securities convertible into or exchangeable for our common stock at prices that may not be the same as the price per share in this offering. We may sell shares or other securities in any other offering at a price per share that is less than the price per share paid by investors in this offering, and investors purchasing shares or other securities in the future could have rights superior to existing stockholders. If we sell common stock, convertible securities, or other equity securities, investors may be materially diluted by subsequent sales.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA

This prospectus supplement, the accompanying prospectus and the information incorporated by reference herein and therein, as well as any free writing prospectus that we have authorized for use in connection with this offering, contain express or implied forward-looking statements that are based on our management's belief and assumptions and on information currently available to our management. Although we believe that the expectations reflected in these forward-looking statements are reasonable, these statements relate to future events or our future operational or financial performance, and involve known and unknown risks, uncertainties, and other factors that may cause our actual results, performance, or achievements to be materially different from any future results, performance, or achievements expressed or implied by these forward-looking statements. These forward-looking statements include, but are not limited to, statements about the following, among other things:

- the timing, progress and results of preclinical studies and clinical trials for KarXT in our current indications and other product candidates, including statements regarding the timing of initiation and completion of studies or trials and related preparatory work and the period during which the results of the trials will become available;
- our research and development plans, including our plans to explore the therapeutic potential of KarXT in additional indications;
- our plans to develop and commercialize KarXT and other product candidates;
- the timing of and our ability to obtain and maintain marketing approvals for our product candidates;
- the rate and degree of market acceptance and clinical utility of any product candidates for which we receive marketing approval;
- our commercialization, marketing and manufacturing capabilities and strategy;
- our intellectual property position and strategy;
- our ability to identify additional product candidates with significant commercial potential;
- the ability and efforts of our licensee, Zai Lab (Shanghai) Co., Ltd., to successfully develop and commercialize KarXT, if approved, in mainland China, Hong Kong, Macau, and Taiwan, under the terms and conditions of our license agreement;
- our plans to enter into collaborations for the development and commercialization of product candidates and the potential benefits of any future collaboration;
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- our ability to raise additional capital in sufficient amounts or on terms acceptable to us;
- our ability to retain the continued service of our key professionals and to identify, hire and retain additional qualified professionals;
- developments relating to our competitors and our industry;
- the impact of government laws and regulations; and
- the anticipated use of proceeds from this offering.

In some cases, forward-looking statements can be identified by terminology such as “may,” “should,” “expects,” “intends,” “plans,” “anticipates,” “believes,” “estimates,” “predicts,” “potential,” “continue,” or the negative of these terms or other comparable terminology. These statements are only predictions. You should not place undue reliance on forward-looking statements because they involve known and unknown risks, uncertainties, and other factors, which are, in some cases, beyond our control and which could materially affect results. Factors that may cause actual results to differ materially from current expectations include, among other

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things, those listed under the section entitled “Risk Factors” and elsewhere in this prospectus supplement, the accompanying prospectus and any related free writing prospectus, and in our Annual Report on Form 10-K for the year ended December 31, 2021, which is incorporated by reference herein. Any forward-looking statement in this prospectus supplement reflects our current view with respect to future events and is subject to these and other risks, uncertainties and assumptions relating to our operations, results of operations, industry and future growth. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future. If one or more of these risks or uncertainties occur, or if our underlying assumptions prove to be incorrect, actual events or results may vary significantly from those expressed or implied by the forward-looking statements. No forward-looking statement is a guarantee of future performance.

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

Any forward-looking statement represents our views as of the date of this prospectus supplement or the accompanying prospectus, as applicable. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we have no current intention of doing so except to the extent required by applicable law. You should therefore not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this prospectus supplement.

This prospectus supplement and the accompanying prospectus include statistical and other industry and market data that we obtained from industry publications and research, surveys, and studies conducted by third parties. Industry publications and third-party research, surveys, and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. Although we are responsible for the disclosure contained in this prospectus supplement and we believe the information from industry publications and other third-party sources included in this prospectus supplement is reliable, such information is inherently imprecise. Industry publications and third-party research, surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. While we believe that our internal assumptions are reasonable, no independent source has verified such assumptions.

USE OF PROCEEDS

We estimate that the net proceeds from our issuance and sale of 3,488,373 shares of our common stock in this offering will be approximately \$711.9 million (or \$818.8 million if the underwriters exercise their option to purchase additional shares in full), after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

We currently estimate that we will use the net proceeds from this offering, together with our existing cash, cash equivalents and available-for-sale investments, to fund our ongoing and planned clinical trials of KarXT and other research and development, to support the potential commercialization of KarXT for psychosis in schizophrenia, and for working capital and general corporate purposes.

This expected use of the net proceeds from this offering along with our existing cash, cash equivalents and available-for-sale investments represents our intentions based upon our current plans and business conditions, which could change in the future as our plans and business conditions evolve. For example, we may use a portion of the net proceeds for the acquisition of businesses or technologies to continue to build our pipeline, our research and development capabilities and our intellectual property position, although we currently have no agreements, commitments or understandings with respect to any such transaction. The amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including the progress of our development and commercialization efforts, the status of and results from clinical trials, any collaborations that we may enter into with third parties for our product candidates and any unforeseen cash needs. Moreover, our estimates of the costs to fund our trials are based on the current designs of the trials. If we were to modify the design of any of these trials, for instance, to increase the number of patients in the trials, our costs to fund the trials could increase. As a result, our management will retain broad discretion over the allocation of the net proceeds from this offering.

Based on our current operating plan, we believe that the net proceeds from this offering, together with our existing cash, cash equivalents and available-for-sale investments, will enable us to fund our planned operating expenses and capital expenditures through the end of 2025. We have based this estimate on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we currently expect.

Pending our use of the net proceeds from this offering, we intend to invest the net proceeds in a variety of capital preservation investments, including short-term, investment-grade, interest-bearing instruments and U.S. government securities.

DILUTION

If you invest in our common stock in this offering, your ownership interest will be diluted to the extent of the difference between the public offering price per share of our common stock in this offering and the as adjusted net tangible book value per share of our common stock immediately after this offering. Our net tangible book value as of June 30, 2022 was \$404.9 million, or \$13.53 per share. Net tangible book value per share is determined by dividing our total tangible assets, less total liabilities, by the number of shares of our common stock outstanding as of June 30, 2022. Dilution with respect to net tangible book value per share represents the difference between the amount per share paid by purchasers of shares of common stock in this offering and the net tangible book value per share of our common stock immediately after this offering.

After giving effect to the sale of 3,488,373 shares of our common stock in this offering at a public offering price of \$215.00 per share, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of June 30, 2022 would have been \$1.117 billion, or \$33.42 per share. This represents an immediate increase in net tangible book value of \$19.89 per share to existing stockholders and immediate dilution of \$181.58 per share to investors purchasing our common stock in this offering. The following table illustrates this dilution on a per share basis:

Public offering price per share	\$215.00
Net tangible book value per share as of June 30, 2022	\$13.53
Increase in net tangible book value per share attributable to this offering	<u>\$19.89</u>
As adjusted net tangible book value per share as of June 30, 2022, after giving effect to this offering	\$ 33.42
Dilution per share to investors purchasing our common stock in this offering	\$ 181.58

The above discussion and table are based on 29,993,103 shares of common stock outstanding as of June 30, 2022, and excludes the following:

- 5,912,840 shares of common stock issuable upon the exercise of stock options outstanding as of June 30, 2022, at a weighted-average exercise price of \$58.32 per share;
- 1,568,533 shares of common stock reserved for future issuance under our 2019 Stock Option and Incentive Plan as of June 30, 2022; and
- 1,041,445 shares of common stock reserved for future issuance under our 2019 Employee Stock Purchase Plan as of June 30, 2022.

To the extent that outstanding options as of June 30, 2022 have been or may be exercised or other shares are issued, investors purchasing our common stock in this offering may experience further dilution. In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that 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.

UNDERWRITING

We and the underwriters named below have entered into an underwriting agreement with respect to the shares being offered. Subject to certain conditions, each underwriter has severally agreed to purchase the number of shares indicated in the following table. Goldman Sachs & Co. LLC and J.P. Morgan Securities LLC are the representatives of the underwriters.

<u>Underwriters</u>	<u>Number of Shares</u>
Goldman Sachs & Co. LLC	1,273,257
J.P. Morgan Securities LLC	1,029,070
Jefferies LLC	383,721
Stifel, Nicolaus & Company, Incorporated	244,186
Guggenheim Securities, LLC	244,186
RBC Capital Markets, LLC	174,419
JMP Securities LLC	69,767
Wedbush Securities Inc.	69,767
Total	<u>3,488,373</u>

The underwriters are committed to take and pay for all of the shares being offered, if any are taken, other than the shares covered by the option described below unless and until this option is exercised.

The underwriters have an option to buy up to an additional 523,255 shares of common stock from us. They may exercise that option for 30 days. If any shares are purchased pursuant to this option, the underwriters will severally purchase shares in approximately the same proportion as set forth in the table above.

The following table shows the per share and total underwriting discounts and commissions to be paid to the underwriters by us. Such amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase additional shares.

<u>Paid by Us</u>	<u>No Exercise</u>	<u>Full Exercise</u>
<u>Per Share</u>	\$ 10.75	\$ 10.75
Total	\$ 37,500,009.75	\$ 43,125,001.00

We estimate that our total expenses of the offering, excluding underwriting discounts and commissions, will be approximately \$600,000. We have agreed to reimburse the underwriters for expenses of up to \$20,000 related to the clearance of this offering with the Financial Industry Regulatory Authority, Inc.

Shares sold by the underwriters to the public will initially be offered at the public offering price set forth on the cover of this prospectus supplement. Any shares sold by the underwriters to securities dealers may be sold at a discount of up to \$6.45 per share from the public offering price. After the initial offering of the shares, the representatives may change the offering price and the other selling terms. The offering of the shares by the underwriters is subject to receipt and acceptance and subject to the underwriters' right to reject any order in whole or in part.

We, our executive officers and our directors have agreed with the underwriters, subject to certain exceptions, not to dispose of or hedge any of our common stock or securities convertible into or exchangeable for shares of our common stock during the period from the date of this prospectus supplement continuing through the date 90 days, in our case, and 45 days, in the case of our executive officers and our directors, after the date of this prospectus supplement, except with the prior written consent of Goldman Sachs & Co. LLC and J.P. Morgan Securities LLC. This agreement does not apply to any existing employee benefit plans.

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Our common stock is listed on The Nasdaq Global Market under the symbol “KRTX.”

In connection with the offering, the underwriters may purchase and sell shares of our common stock in the open market. These transactions may include short sales, stabilizing transactions and purchases to cover positions created by short sales. Short sales involve the sale by the underwriters of a greater number of shares than they are required to purchase in the offering, and a short position represents the amount of such sales that have not been covered by subsequent purchases. A “covered short position” is a short position that is not greater than the amount of additional shares for which the underwriters’ option described above may be exercised. The underwriters may cover any covered short position by either exercising their option to purchase additional shares or purchasing shares in the open market. In determining the source of shares to cover 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 additional shares pursuant to the option described above. “Naked” short sales are any short sales that create a short position greater than the amount of additional shares for which the option described above may be exercised. The underwriters must cover any such naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of our common stock in the open market after pricing that could adversely affect investors who purchase in the offering. Stabilizing transactions consist of various bids for or purchases of our common stock made by the underwriters in the open market prior to the completion of the offering.

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

Purchases to cover a short position and stabilizing transactions, as well as other purchases by the underwriters for their own accounts, may have the effect of preventing or retarding a decline in the market price of our common stock, and together with the imposition of the penalty bid, may stabilize, maintain or otherwise affect the market price of our common stock. As a result, the price of the common stock may be higher than the price that otherwise might exist in the open market. The underwriters are not required to engage in these activities and may end any of these activities at any time. These transactions may be effected on The Nasdaq Global Market, in the over-the-counter market or otherwise.

We have agreed to indemnify the several underwriters against certain liabilities, including liabilities under the Securities Act of 1933, as amended, or the Securities Act.

The underwriters and their respective affiliates are full service financial institutions engaged in various activities, which may include sales and trading, commercial and investment banking, advisory, investment management, investment research, principal investment, hedging, market making, brokerage and other financial and non-financial activities and services. Certain of the underwriters and their respective affiliates have provided, and may in the future provide, a variety of these services to us and to persons and entities with relationships with us, for which they received or will receive customary fees and expenses. For example, Goldman Sachs & Co. LLC is the agent under an Equity Distribution Agreement dated as of July 2, 2020, with us. Under the Equity Distribution Agreement, we may offer and sell, from time to time, shares of our common stock through Goldman Sachs & Co. LLC through an “at the market offering” as defined in Rule 415(a)(4) promulgated under the Securities Act.

In the ordinary course of their various business activities, the underwriters and their respective affiliates, officers, directors and employees may purchase, sell or hold a broad array of investments and actively trade securities, derivatives, loans, commodities, currencies, credit default swaps and other financial instruments for their own account and for the accounts of their customers, and such investment and trading activities may involve or relate to our assets, securities and/or instruments (directly, as collateral securing other obligations or otherwise) and/or persons and entities with relationships with us. The underwriters and their respective affiliates

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may also communicate independent investment recommendations, market color or trading ideas and/or publish or express independent research views in respect of such assets, securities or instruments and may at any time hold, or recommend to clients that they should acquire, long and/or short positions in such assets, securities and instruments.

Notice to Prospective Investors in the European Economic Area

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

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

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

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

Each person in a Relevant Member State who receives any communication in respect of, or who acquires any shares under, the offering contemplated hereby will be deemed to have represented, warranted and agreed to and with each of the Underwriters and their affiliates and the Company that:

- a) it is a qualified investor within the meaning of the Prospectus Regulation; and
- b) in the case of any Shares acquired by it as a financial intermediary, as that term is used in Article 5 of the Prospectus Regulation, (i) the shares acquired by it in the offering have not been acquired on a non-discretionary basis on behalf of, nor have they been acquired with a view to their offer or resale to, persons in any Relevant Member State other than qualified investors, as that term is defined in the Prospectus Regulation, or have been acquired in other circumstances falling within the points (a) to (d) of Article 1(4) of the Prospectus Regulation and the prior consent of the representatives has been given to the offer or resale; or (ii) where the Shares have been acquired by it on behalf of persons in any Relevant Member State other than qualified investors, the offer of those Shares to it is not treated under the Prospectus Regulation as having been made to such persons.

The Company, the underwriters and their affiliates, and others will rely upon the truth and accuracy of the foregoing representation, acknowledgement and agreement. Notwithstanding the above, a person who is not a qualified investor and who has notified the representatives of such fact in writing may, with the prior consent of the representatives, be permitted to acquire shares in the offering.

Notice to Prospective Investors in the United Kingdom

This prospectus supplement and any other material in relation to the common shares described herein is only being distributed to, and is only directed at, and any investment or investment activity to which this prospectus supplement relates is available only to, and will be engaged in only with persons who are (i) persons having professional experience in matters relating to investments who fall within the definition of investment professionals in Article 19(5) of the FPO; or (ii) high net worth entities falling within Article 49(2)(a) to (d) of the FPO; (iii) outside the UK; or (iv) persons to whom an invitation or inducement to engage in investment activity (within the meaning of Section 21 of the FSMA) in connection with the issue or sale of any Shares may otherwise lawfully be communicated or caused to be communicated, (all such persons together being referred to as “Relevant Persons”). The shares are only available in the UK to, and any invitation, offer or agreement to purchase or otherwise acquire the shares will be engaged in only with, the Relevant Persons. This prospectus supplement and its contents are confidential and should not be distributed, published or reproduced (in whole or in part) or disclosed by recipients to any other person in the UK. Any person in the UK that is not a Relevant Person should not act or rely on this prospectus supplement or any of its contents.

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

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

provided that no such offer of the shares shall require us and/or any underwriters or any of their affiliates to publish a prospectus pursuant to Section 85 of the FSMA or supplement a prospectus pursuant to Article 23 of the UK Prospectus Regulation. For the purposes of this provision, the expression an “offer to the public” in relation to the shares in the United Kingdom means the communication in any form and by any means of sufficient information on the terms of the offer and any shares to be offered so as to enable an investor to decide to purchase or subscribe for any shares and the expression “UK Prospectus Regulation” means Regulation (EU) 2017/1129 as it forms part of domestic law by virtue of the European Union (Withdrawal) Act 2018.

Each person in the UK who acquires any shares in the offering or to whom any offer is made will be deemed to have represented, acknowledged and agreed to and with us, the underwriters and their affiliates that it meets the criteria outlined in this section.

Notice to Prospective Investors in Canada

The securities may be sold in Canada 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 securities must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

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

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

Notice to Prospective Investors in Hong Kong

The shares may not be offered or sold in Hong Kong by means of any document other than (i) in circumstances which do not constitute an offer to the public within the meaning of the Companies (Winding Up and Miscellaneous Provisions) Ordinance (Cap. 32 of the Laws of Hong Kong) (“Companies (Winding Up and Miscellaneous Provisions) Ordinance”) or which do not constitute an invitation to the public within the meaning of the Securities and Futures Ordinance (Cap. 571 of the Laws of Hong Kong) (“Securities and Futures Ordinance”), or (ii) to “professional investors” as defined in the Securities and Futures Ordinance and any rules made thereunder, or (iii) in other circumstances which do not result in the document being a “prospectus” as defined in the Companies (Winding Up and Miscellaneous Provisions) Ordinance, and no advertisement, invitation or document relating to the shares may be issued or may be in the possession of any person for the purpose of issue (in each case 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 in Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to shares which are or are intended to be disposed of only to persons outside Hong Kong or only to “professional investors” in Hong Kong as defined in the Securities and Futures Ordinance and any rules made thereunder.

Notice to Prospective Investors in Singapore

This prospectus supplement has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus supplement and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares may not be circulated or distributed, nor may the shares be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor (as defined under Section 4A of the Securities and Futures Act, Chapter 289 of Singapore (the “SFA”)) under Section 274 of the SFA, (ii) to a relevant person (as defined in Section 275(2) of the SFA) pursuant to Section 275(1) of the SFA, or any person pursuant to Section 275(1A) of the SFA, and in accordance with the conditions specified in Section 275 of the SFA or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA, in each case subject to conditions set forth in the SFA.

Where the shares are subscribed or purchased under Section 275 of the SFA by a relevant person which is 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, the securities (as defined in Section 239(1) of the SFA) of that corporation shall not be transferable for 6 months after that corporation has acquired the shares under Section 275 of the SFA except: (1) to an institutional investor under Section 274 of the SFA or to a relevant person (as defined in Section 275(2) of the SFA), (2) where such transfer arises from an offer in that corporation’s securities pursuant to Section 275(1A) of the SFA, (3) where no consideration is or will be given for the transfer, (4) where the transfer is by operation of law, (5) as specified in Section 276(7) of the SFA, or (6) as specified in Regulation 32 of the Securities and Futures (Offers of Investments) (Shares and Debentures) Regulations 2005 of Singapore (“Regulation 32”).

Where the shares are subscribed or purchased under Section 275 of the SFA by a relevant person which is a trust (where the trustee is not an accredited investor (as defined in Section 4A of the SFA)) whose sole purpose is to hold investments and each beneficiary of the trust is an accredited investor, the beneficiaries’ rights and interest (howsoever described) in that trust shall not be transferable for 6 months after that trust has acquired the shares under Section 275 of the SFA except: (1) to an institutional investor under Section 274 of the SFA or to a relevant person (as defined in Section 275(2) of the SFA), (2) where such transfer arises from an offer that is made on terms

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that such rights or interest are acquired at a consideration of not less than S\$200,000 (or its equivalent in a foreign currency) for each transaction (whether such amount is to be paid for in cash or by exchange of securities or other assets), (3) where no consideration is or will be given for the transfer, (4) where the transfer is by operation of law, (5) as specified in Section 276(7) of the SFA, or (6) as specified in Regulation 32.

Notice to Prospective Investors in Japan

The securities have not been and will not be registered under the Financial Instruments and Exchange Act of Japan (Act No. 25 of 1948, as amended), or the FIEA. The securities may not be offered or sold, directly or indirectly, in Japan or to or for the benefit of any resident of Japan (including any person resident in Japan or any corporation or other entity organized under the laws of Japan) or to others for reoffering or resale, directly or indirectly, in Japan or to or for the benefit of any resident of Japan, except pursuant to an exemption from the registration requirements of the FIEA and otherwise in compliance with any relevant laws and regulations of Japan.

Notice to Prospective Investors in Australia

No prospectus or other disclosure document, as defined in the Corporations Act 2001 (“Cth”) of Australia, or the Corporations Act, in relation to our shares has been or will be lodged with the Australian Securities & Investments Commission (the “ASIC”). This document has not been lodged with ASIC and is only directed to certain categories of exempt persons. Accordingly, if you receive this document in Australia:

- (a) you confirm and warrant that you are either:
 - (i) a “sophisticated investor” under section 708(8)(a) or (b) of the Corporations Act;
 - (ii) a “sophisticated investor” under section 708(8)(c) or (d) of the Corporations Act and that you have provided an accountant’s certificate to us which complies with the requirements of section 708(8)(c)(i) or (ii) of the Corporations Act and related regulations before the offer has been made;
 - (iii) a person associated with us under section 708(12) of the Corporations Act; or
 - (iv) a “professional investor” within the meaning of section 708(11)(a) or (b) of the Corporations Act, and to the extent that you are unable to confirm or warrant that you are an exempt sophisticated investor, associated person or professional investor under the Corporations Act, any offer made to you under this document is void and incapable of acceptance; and
- (b) you warrant and agree that you will not offer any of our shares for resale in Australia within 12 months of that security being issued unless any such resale offer is exempt from the requirement to issue a disclosure document under section 708 of the Corporations Act.

Notice to Prospective Investors in Israel

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

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

CERTAIN MATERIAL U.S. FEDERAL INCOME TAX CONSIDERATIONS FOR NON-U.S. HOLDERS

The following discussion is a summary of certain material U.S. federal income tax considerations applicable to non-U.S. holders (as defined below) with respect to their ownership and disposition of shares of our common stock issued pursuant to this offering. For purposes of this discussion, a non-U.S. holder means a beneficial owner of our common stock that is for U.S. federal income tax purposes:

- a non-resident alien individual;
- a corporation or other organization taxable as a corporation for U.S. federal income tax purposes that is created or organized in or under laws other than the laws of the United States, any state thereof, or the District of Columbia;
- an estate the income of which is not subject to U.S. federal income tax on a net income basis; or
- a trust the income of which is not subject to U.S. federal income tax on a net income basis and that (1) is not subject to the primary supervision of a court within the United States or over which no U.S. persons have authority to control all substantial decisions and (2) has not made an election to be treated as a U.S. person.

This discussion does not address the tax treatment of partnerships or other entities that are pass-through entities for U.S. federal income tax purposes or persons that hold their common stock through partnerships or other pass-through entities. A partner in a partnership or other pass-through entity that will hold our common stock should consult his, her or its tax advisor regarding the tax consequences of acquiring, holding and disposing of our common stock through a partnership or other pass-through entity, as applicable.

This discussion is based on current provisions of the U.S. Internal Revenue Code of 1986, as amended, which we refer to as the Code, existing and proposed U.S. Treasury Regulations promulgated thereunder, current administrative rulings and judicial decisions, all as in effect as of the date of this prospectus supplement and, all of which are subject to change or to differing interpretation, possibly with retroactive effect. Any such change or differing interpretation could alter the tax consequences to non-U.S. holders described in this prospectus supplement. There can be no assurance that the Internal Revenue Service, which we refer to as the IRS, will not challenge one or more of the tax consequences described herein. We assume in this discussion that a non-U.S. holder holds shares of our common stock as a capital asset within the meaning of Section 1221 of the Code, which is generally property held for investment.

This discussion does not address all aspects of U.S. federal income taxation that may be relevant to a particular non-U.S. holder in light of that non-U.S. holder's individual circumstances nor does it address any U.S. state, local or non-U.S. tax considerations, the alternative minimum tax, the Medicare tax on net investment income, the rules regarding qualified small business stock within the meaning of Section 1202 of the Code, or any other aspect of any U.S. federal tax other than the income tax. This discussion also does not consider any specific facts or circumstances that may apply to a non-U.S. holder and does not address the special tax rules applicable to particular non-U.S. holders, such as:

- insurance companies;
- tax-exempt or governmental organizations;
- financial institutions;
- brokers or dealers in securities;
- regulated investment companies;
- pension plans;

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- “controlled foreign corporations,” “passive foreign investment companies,” and corporations that accumulate earnings to avoid U.S. federal income tax;
- “qualified foreign pension funds,” or entities wholly owned by a “qualified foreign pension fund”;
- persons deemed to sell our common stock under the constructive sale provisions of the Code;
- persons that hold our common stock as part of a straddle, hedge, conversion transaction, synthetic security or other integrated investment; and
- certain U.S. expatriates.

This discussion is for general information only and is not tax advice. Accordingly, all prospective non-U.S. holders of our common stock should consult their tax advisors with respect to the U.S. federal, state, local and non-U.S. tax consequences of the purchase, ownership and disposition of our common stock.

Distributions on Our Common Stock

Distributions, if any, on our common stock will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. If a distribution exceeds our current and accumulated earnings and profits, the excess will be treated as a tax-free return of the non-U.S. holder’s investment, up to such holder’s tax basis in the common stock. Any remaining excess will be treated as capital gain, subject to the tax treatment described below in “Gain on Sale, or Other Taxable Disposition of Our Common Stock.” Any such distributions will also be subject to the discussions below under the sections titled “Backup Withholding and Information Reporting” and “Withholding and Information Reporting Requirements—FATCA.”

Subject to the discussion in the following two paragraphs in this section, dividends paid to a non-U.S. holder generally will be subject to withholding of U.S. federal income tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder’s country of residence.

Dividends that are treated as effectively connected with a trade or business conducted by a non-U.S. holder within the United States and, if an applicable income tax treaty so provides, that are attributable to a permanent establishment or a fixed base maintained by the non-U.S. holder within the United States, are generally exempt from the 30% withholding tax if the non-U.S. holder satisfies applicable certification and disclosure requirements. However, such U.S. effectively connected income, net of specified deductions and credits, is taxed at the same U.S. federal income tax rates applicable to United States persons (as defined in the Code). Any U.S. effectively connected income received by a non-U.S. holder that is a corporation may also, under certain circumstances, 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 between the United States and such holder’s country of residence.

A non-U.S. holder of our common stock who claims the benefit of an applicable income tax treaty between the United States and such holder’s country of residence generally will be required to provide a properly executed IRS Form W-8BEN or W-8BEN-E (or successor form), as applicable, to the applicable withholding agent and satisfy applicable certification and other requirements. Non-U.S. holders are urged to consult their tax advisors regarding their entitlement to benefits under a relevant income tax treaty. A non-U.S. holder that is eligible for a reduced rate of U.S. withholding tax under an income tax treaty may obtain a refund or credit of any excess amounts withheld by timely filing a U.S. tax return with the IRS.

Gain on Sale or Other Taxable Disposition of Our Common Stock

Subject to the discussions below under “Backup Withholding and Information Reporting” and “Withholding and Information Reporting Requirements—FATCA,” a non-U.S. holder generally will not be subject to any U.S. federal income tax on any gain realized upon such holder’s sale or other taxable disposition of shares of our common stock unless:

- the gain is effectively connected with the non-U.S. holder’s conduct of a U.S. trade or business and, if an applicable income tax treaty so provides, is attributable to a permanent establishment or a fixed-base maintained by such non-U.S. holder in the United States, in which case the non-U.S. holder generally will be taxed on a net income basis at the U.S. federal income tax rates applicable to United States persons (as defined in the Code) and, if the non-U.S. holder is a foreign corporation, the branch profits tax described above in “Distributions on Our Common Stock” also may apply;
- the non-U.S. holder is a nonresident alien individual who is present in the United States for a period or periods aggregating 183 days or more in the taxable year of the disposition and certain other conditions are met, in which case the non-U.S. holder will be subject to a 30% tax (or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder’s country of residence) on the net gain derived from the disposition, which may be offset by certain U.S. source capital losses of the non-U.S. holder, if any (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; or
- we are, or have been, at any time during the five-year period preceding such sale or other taxable disposition (or the non-U.S. holder’s holding period, if shorter) a “U.S. real property holding corporation,” unless our common stock is regularly traded on an established securities market as defined for purposes of applicable Treasury Regulations and the non-U.S. holder holds no more than 5% of our outstanding common stock, directly or indirectly, actually or constructively, during the shorter of the 5-year period ending on the date of the disposition or the period that the non-U.S. holder held our common stock. Generally, a corporation is a U.S. real property holding corporation only 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. Although there can be no assurance, we do not believe that we are, or have been, a U.S. real property holding corporation, or that we are likely to become one in the future. No assurance can be provided that our common stock will be regularly traded on an established securities market for purposes of the rules described above.

Backup Withholding and Information Reporting

We must report annually to the IRS and to each non-U.S. holder the gross amount of the distributions on our common stock paid to such holder and the tax withheld, if any, with respect to such distributions. Non-U.S. holders may have to comply with specific certification procedures to establish that the holder is not a United States person (as defined in the Code) in order to avoid backup withholding at the applicable rate with respect to distributions on our common stock. Dividends paid to non-U.S. holders subject to withholding of U.S. federal income tax, as described above in “Distributions on Our Common Stock,” generally will be exempt from U.S. backup withholding.

Information reporting and backup withholding will generally apply to the proceeds of a disposition of our common stock by a non-U.S. holder effected by or through the U.S. office of any broker, U.S. or foreign, unless the holder certifies its status as a non-U.S. holder and satisfies certain other requirements, or otherwise establishes an exemption. Generally, information reporting and backup withholding will not apply to a payment of disposition proceeds to a non-U.S. holder where the transaction is effected outside the United States through a non-U.S. office of a broker. However, for information reporting purposes, dispositions effected through

a non-U.S. office of a broker with substantial U.S. ownership or operations generally will be treated in a manner similar to dispositions effected through a U.S. office of a broker.

Non-U.S. holders should consult their tax advisors regarding the application of the information reporting and backup withholding rules to them. Copies of information returns may be made available to the tax authorities of the country in which the non-U.S. holder resides or is incorporated under the provisions of a specific treaty or agreement. Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules from a payment to a non-U.S. holder can be refunded or credited against the non-U.S. holder's U.S. federal income tax liability, if any, provided that an appropriate claim is filed with the IRS in a timely manner.

Withholding and Information Reporting Requirements—FATCA

The Foreign Account Tax Compliance Act and guidance issued thereunder, or FATCA, imposes withholding taxes on certain types of payments made to “foreign financial institutions” and certain other foreign entities (including financial intermediaries). FATCA generally imposes withholding at a rate of 30% on payments to certain foreign entities of dividends on our common stock and certain other withholdable payments, unless various U.S. information reporting and due diligence requirements (generally relating to ownership by U.S. persons of interests in or accounts with those entities) have been satisfied or the entity otherwise qualifies for an exemption. An intergovernmental agreement between the United States and an applicable foreign country may modify these requirements. Such withholding may apply to gross proceeds from the sale or other disposition of our common stock, although under proposed U.S. Treasury Regulations, no withholding would apply to such gross proceeds. The preamble to the proposed regulations specifies that taxpayers (including withholding agents) are permitted to rely on the proposed regulations pending finalization. You should consult your tax advisor regarding the application of FATCA.

The preceding discussion of U.S. federal tax considerations is for general information only. It is not tax advice. Each prospective investor should consult its own tax advisor regarding the particular U.S. federal, state and local and non-U.S. tax consequences of purchasing, holding and disposing of our common stock, including the consequences of any proposed change in applicable laws.

LEGAL MATTERS

The validity of the shares of our common stock offered hereby is being passed upon for us by Goodwin Procter LLP, New York, New York. Certain legal matters in connection with this offering will be passed upon for the underwriters by Cooley LLP, New York, New York.

EXPERTS

The consolidated financial statements of Karuna Therapeutics, Inc. as of December 31, 2021 and 2020, and for each of the years in the three-year period ended December 31, 2021, and management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2021 have been incorporated by reference herein and in the registration statement in reliance upon the report of KPMG LLP, independent registered public accounting firm, incorporated by reference herein, and upon the authority of said firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We are subject to the information requirements of the Exchange Act. In accordance with the Exchange Act, we file annual, quarterly and current reports, proxy statements and other information with the SEC. Such reports, proxy statements and other information filed by us are available to the public free of charge on the SEC's website, www.sec.gov. Copies of certain information filed by us with the SEC are also available on our website at www.karunatx.com. The information available on or through our website is not part of this prospectus supplement or the accompanying prospectus.

This prospectus supplement is part of a registration statement on Form S-3 that we filed with the SEC and does not contain all the information set forth or incorporated by reference in the registration statement. You should review the information and exhibits in the registration statement for further information about us and the securities being offered hereby. Statements in this prospectus supplement concerning any document we filed as an exhibit to the registration statement or that we otherwise filed with the SEC are not intended to be comprehensive and are qualified by reference to the filings. You should review the complete document to evaluate these statements.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

SEC rules permit us to incorporate information by reference in this prospectus supplement and the accompanying prospectus. This means that we can disclose important information to you by referring you to another document filed separately with the SEC. The information incorporated by reference is considered to be part of this prospectus supplement and the accompanying prospectus, except for information superseded by information contained in this prospectus supplement or the accompanying prospectus or in any subsequently filed incorporated document. This prospectus supplement and the accompanying prospectus incorporate by reference the documents set forth below that we have previously filed with the SEC, other than information in such documents that is deemed to be furnished and not filed. These documents contain important information about us and our business and financial condition.

- Annual Report on Form 10-K for the year ended December 31, 2021, filed with the SEC on [February 24, 2022](#), including the information specifically incorporated by reference into the Annual Report on Form 10-K from our definitive proxy statement for the 2022 Annual Meeting of Stockholders, as filed with the SEC on [April 27, 2022](#);
- Quarterly Reports on Form 10-Q for the quarters ended March 31, 2022 and June 30, 2022, filed with the SEC on [May 5, 2022](#) and [August 8, 2022](#), respectively;
- Current Reports on Form 8-K filed with the SEC on [February 24, 2022](#), [June 21, 2022](#) and [August 8, 2022](#), excluding, in each case, information “furnished” pursuant to Items 2.02, 7.01, or 9.01; and
- The description of our common stock contained in our Registration Statement on Form 8-A, dated [June 26, 2019](#), including any amendments or reports filed for the purpose of updating such description.

All documents that we file (but not those that we furnish) pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act, after the date of the initial registration statement of which this prospectus supplement is a part shall be deemed to be incorporated by reference into this prospectus supplement and will automatically update and supersede the information in this prospectus supplement, the accompanying prospectus and any previously filed documents. All documents that we file (but not those that we furnish) pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act on or after the date of this prospectus supplement and prior to the termination of the offering of any of the securities covered under this prospectus supplement shall be deemed to be incorporated by reference into this prospectus supplement and the accompanying prospectus and will automatically update and supersede the information in this prospectus supplement, the accompanying prospectus and any previously filed documents.

Any statement contained herein or in a document incorporated or deemed to be incorporated by reference in this prospectus supplement or the accompanying prospectus shall be deemed to be modified or superseded for purposes of this prospectus supplement and accompanying prospectus to the extent that a statement contained in this prospectus supplement or accompanying prospectus, or in any other subsequently filed document which also is or is deemed to be incorporated by reference in this prospectus supplement and accompanying prospectus, modifies or supersedes such earlier statement. Any statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this prospectus supplement or accompanying prospectus.

Prospective investors may obtain documents incorporated by reference in this prospectus supplement and the accompanying prospectus at no cost by requesting them in writing or by telephone from us at our principal corporate office at:

Karuna Therapeutics, Inc.
99 High Street, Floor 26
Boston, MA 02110
(857) 299-2244
Attention: Corporate Secretary

PROSPECTUS



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

From time to time, we may offer and sell our Common Stock, Preferred Stock, Debt Securities, Warrants or Units, in each case in one or more issuances and at prices and on terms that we will determine at the time of the offering.

This prospectus describes the general manner in which any of these securities may be offered using this prospectus. We will specify in an accompanying prospectus supplement the terms of the securities offered and other details regarding the offering thereof.

Our common stock is listed on the Nasdaq Global Select Market under the symbol “KRTX.”

Investing in our securities involves a high degree of risk. You should review carefully the risks and uncertainties described under the heading “[Risk Factors](#)” on page 6 of this prospectus and under any similar heading in the documents that are incorporated by reference into this prospectus, as well as “Special Note Regarding Forward-Looking Statements” on page 7 of this prospectus. You should read the entire prospectus carefully before you make your investment decision.

The securities covered by this prospectus may be sold directly by us to investors, through agents designated by us from time to time or through underwriters or dealers at prices and on terms to be determined at the time of offering. We will include in an applicable prospectus supplement the names of any underwriters or agents and any applicable commissions or discounts. Additional information on the methods of sale appears under “Plan of Distribution” in this prospectus. We will also describe in an applicable prospectus supplement the way(s) in which we expect to use the net proceeds we receive from any sale.

Neither the U.S. 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.

This prospectus may not be used to offer or sell any securities unless accompanied by a prospectus supplement.

The date of this prospectus is July 2, 2020.

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You should rely only on the information contained or incorporated by reference in this prospectus and in any applicable prospectus supplement to this prospectus. We have not authorized any other person to provide you with different or additional information. If anyone provides you with different, additional or inconsistent information, you should not rely on it. We do not take responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We are not making an offer to sell these securities or soliciting any offer to buy these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus, any applicable prospectus supplement or any free writing prospectus we authorize to be delivered to you is accurate only as of the date of that document or any other date set forth in that document. Additionally, any information we have incorporated by reference in this prospectus or in any applicable prospectus supplement is accurate only as of the date of the document incorporated by reference or other date set forth in that document, regardless of the time of delivery of this prospectus, any applicable prospectus supplement or any sale of securities. Our business, financial condition, results of operations, cash flow and prospects may have changed since that date.

This prospectus, any applicable prospectus supplement and the information incorporated herein or therein by reference contains market data, industry statistics and other data that have been obtained or compiled from information made available by independent third parties. We have not independently verified the accuracy and completeness of such data. This prospectus, any applicable prospectus supplement and the information incorporated herein or therein by reference include trademarks, service marks and trade names owned by us or other companies. Solely for convenience, we may refer to our trademarks included or incorporated by reference in this prospectus, any applicable prospectus supplement or any free writing prospectus without the TM or ® symbols, but any such references are not intended to indicate that we will not assert, to the fullest extent permitted under applicable law, our rights to our trademarks or other intellectual property. All trademarks, service marks and trade names included or incorporated by reference in this prospectus, any applicable prospectus supplement or any related free writing prospectus are the property of their respective owners.

When used in this prospectus, the terms “Karuna,” “we,” “our” and “us” refer to Karuna Therapeutics, Inc., a Delaware corporation, and its consolidated subsidiaries, unless otherwise specified or the context otherwise requires.

ABOUT THIS PROSPECTUS

This prospectus is part of an automatic shelf registration statement that we have filed with the Securities and Exchange Commission, or the SEC, as a “well-known seasoned issuer” as defined in Rule 405 under the Securities Act of 1933, as amended, or the Securities Act.

Under this process, we may sell the securities described in this prospectus in one or more offerings. This prospectus describes the general manner in which we may offer the securities described in this prospectus. Each time we sell securities pursuant to the registration statement we will provide a prospectus supplement that will contain specific information about the offering and the securities offered, and may also add, update or change information contained in this prospectus. If there is any inconsistency between information in this prospectus and any accompanying prospectus supplement, you should rely on the information in the most recent applicable prospectus supplement and documents incorporated by reference herein and therein. This prospectus may not be used to offer to sell, solicit an offer to buy or consummate a sale of our securities unless it is accompanied by a prospectus supplement.

This prospectus, together with any accompanying prospectus supplement, contains important information you should know before investing in our securities, including important information about us and the securities being offered. You should carefully read both documents, as well as the additional information contained in the documents described under “Where You Can Find More Information” and “Incorporation of Certain Information by Reference” in both this prospectus and the applicable prospectus supplement, and in particular the annual, quarterly and current reports and other documents we file with the SEC. Neither this prospectus nor any accompanying prospectus supplement is an offer to sell these securities or is soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

SEC rules permit us to incorporate information by reference in this prospectus and the applicable prospectus supplement. This means that we can disclose important information to you by referring you to another document filed separately with the SEC. The information incorporated by reference is considered to be part of this prospectus and the applicable prospectus supplement, except for information superseded by information contained in this prospectus or the applicable prospectus supplement itself or in any subsequently filed incorporated document. This prospectus and the applicable prospectus supplement incorporate by reference the documents set forth below that we have previously filed with the SEC, other than information in such documents that is deemed to be furnished and not filed. These documents contain important information about us and our business and financial condition.

- Annual Report on Form 10-K for the year ended December 31, 2019, filed with the SEC on [March 24, 2020](#);
- Quarterly Report on Form 10-Q for the period ended March 31, 2020, filed with the SEC on [May 7, 2020](#);
- Current Reports on Form 8-K, filed with the SEC on [April 28, 2020](#) and [June 17, 2020](#) (other than information “furnished” under Items 2.02 or 7.01, or corresponding information furnished under Item 9.01 or included as an exhibit);
- The information specifically incorporated by reference into our Annual Report on [Form 10-K](#) for the year ended December 31, 2019 from our Definitive Proxy Statement on Schedule 14A, filed with the SEC on [April 29, 2020](#); and
- The description of our Common Stock contained in our Registration Statement on Form 8-A, dated [June 26, 2019](#), including any amendments or reports filed for the purpose of updating such description.

All documents that we file (but not those that we furnish) pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act, after the date of the initial registration statement of which this prospectus is a part and prior to the effectiveness of the registration statement shall be deemed to be incorporated by reference into this prospectus and will automatically update and supersede the information in this prospectus, and any previously filed documents. All documents that we file (but not those that we furnish) pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act on or after the date of this prospectus and prior to the termination of the offering of any of the securities covered under this prospectus shall be deemed to be incorporated by reference into this prospectus and will automatically update and supersede the information in this prospectus, the applicable prospectus supplement and any previously filed documents.

Any statement contained herein or in a document incorporated or deemed to be incorporated by reference in this prospectus or the applicable prospectus supplement shall be deemed to be modified or superseded for purposes of this prospectus and such applicable prospectus supplement to the extent that a statement contained in this prospectus or such applicable prospectus supplement, or in any other subsequently filed document which also is or is deemed to be incorporated by reference in this prospectus and such applicable prospectus supplement, modifies or supersedes such earlier statement. Any statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this prospectus or such applicable prospectus supplement.

Documents incorporated by reference are available from us without charge, excluding all exhibits unless specifically incorporated by reference as an exhibit to this prospectus and the applicable prospectus supplement.

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Prospective investors may obtain documents incorporated by reference in this prospectus and the applicable prospectus supplement at no cost by requesting them in writing or by telephone from us at our executive offices at:

Karuna Therapeutics, Inc.
33 Arch Street, Suite 3110
Boston, MA 02110
(857) 449-2244
Attention: Corporate Secretary

ABOUT THE COMPANY

The following highlights information about the Registrant and our business contained elsewhere or incorporated by reference in this prospectus. It is not complete and does not contain all of the information that you should consider before investing in any of our securities. You should carefully read this prospectus together with the more detailed information incorporated by reference in this prospectus.

Overview

We are an innovative clinical-stage biopharmaceutical company committed to developing novel therapies with the potential to transform the lives of people with disabling and potentially fatal neuropsychiatric disorders and pain. Our pipeline is built on the broad therapeutic potential of our lead product candidate, KarXT, an oral modulator of muscarinic receptors that are located both in the central nervous system, or CNS, and various peripheral tissues. KarXT is our proprietary product candidate that combines xanomeline, a novel muscarinic agonist, with trospium, an approved muscarinic antagonist, to preferentially stimulate muscarinic receptors in the CNS. In November 2019, we completed a Phase 2 clinical trial of KarXT for the treatment of acute psychosis in patients with schizophrenia, in which KarXT met the trial's primary endpoint and was observed to be well tolerated. We are also developing KarXT as a potential treatment for dementia-related psychosis, or DRP, and pain. In the fourth quarter of 2019, we initiated two Phase 1b clinical trials of KarXT. One trial is evaluating the safety and tolerability of KarXT in healthy elderly volunteers in order to select the most appropriate dose for future KarXT trials to assess efficacy and safety in a DRP patient population. The second trial is evaluating the effect of KarXT on experimentally induced pain in healthy volunteers.

We have assembled a team whose members have extensive expertise in the research, development and commercialization of numerous CNS agents, as well as deep familiarity with the biology of neuropsychiatric disorders, such as schizophrenia and DRP, including the role of muscarinic receptors in potential treatment of these diseases. We plan to leverage this expertise to develop a pipeline of product candidates targeting a broad range of psychiatric and neurological conditions.

Recent Developments

On June 23, 2020, we announced next steps in the clinical program evaluating KarXT for the treatment of acute psychosis in patients with schizophrenia following the completion of a successful End-of-Phase 2 meeting with the U.S. Food & Drug Administration, or the FDA. We believe that the outcome of the meeting supports the progression of KarXT into Phase 3 development. We and the FDA agreed on key elements of the Phase 3 program to support a New Drug Application, or NDA, filing, including the initiation of additional trials evaluating the efficacy and long-term safety of KarXT. The formal minutes from the meeting confirmed that the completed Phase 2 trial, along with one successful Phase 3 efficacy and safety trial, and additional safety data to meet regulatory requirements, would be acceptable to support an NDA filing.

We plan to initiate two five-week inpatient trials evaluating the efficacy and safety of KarXT for the treatment of acute psychosis in adults with schizophrenia. Both trials will share key characteristics of the completed Phase 2 trial, such as duration of treatment, patient population and primary outcome measure, among other aspects. The first Phase 3 trial is expected to commence by the end of 2020. This five-week, 1:1 randomized, flexible-dose, double-blind, placebo-controlled, inpatient trial will enroll approximately 250 adults in the U.S. and evaluate the change in Positive and Negative Syndrome Scale total score at Week 5 of KarXT versus placebo as the primary outcome measure. Details of the second efficacy trial will be finalized by the end of 2020, with initiation expected in the first half of 2021.

In conjunction with the short-term efficacy and safety trials, we will collect long-term, open-label data to assess the safety and tolerability of KarXT in patients for up to one year in an outpatient setting. Following the five-week, double-blind, inpatient phase in both efficacy trials, patients may enter a 52-week open-label safety and

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tolerability extension in which all patients will receive active treatment. We currently plan to also conduct a separate 52-week open-label trial evaluating the long-term safety of KarXT in adults with schizophrenia who have not been enrolled in the inpatient trials. This trial is expected to begin the first half of 2021. Data from these trials will be used to support regulatory safety requirements for an NDA filing.

Corporate Information

We were incorporated under the laws of the State of Delaware in July 2009 under the name Karuna Pharmaceuticals, Inc. and changed our name to Karuna Therapeutics, Inc. in March 2019. Our executive offices are located at 33 Arch Street, Suite 3110, Boston, Massachusetts 02110, and our telephone number is (857) 449-2244. Our website address is www.karunatx.com. The information contained on, or that can be accessed through, our website is not a part of this prospectus. We have included our website address in this prospectus solely as an inactive textual reference.

Our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q and Current Reports on Form 8-K and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act are available, free of charge, on or through our website as soon as reasonably practicable after such reports and amendments are electronically filed with or furnished to the SEC. The SEC maintains an Internet site that contains reports, proxy and information statements and other information regarding our filings at www.sec.gov.

For additional information about our Company, please refer to other documents we have filed with the SEC and that are incorporated by reference into this prospectus, as listed under the heading "Incorporation of Certain Information by Reference."

RISK FACTORS

Investing in our securities involves certain risks. Before you invest in any of our debt securities, common stock, preferred stock, warrants or units, in addition to the other information included in, or incorporated by reference into, this prospectus, you should carefully consider the risk factors contained in Item 1A under the caption “Risk Factors” and elsewhere in our annual report on Form 10-K for the fiscal year ended December 31, 2019, which is incorporated into this prospectus by reference, as updated by our annual or quarterly reports for subsequent fiscal years or fiscal quarters that we file with the SEC and that are so incorporated. See “Where You Can Find More Information” for information about how to obtain a copy of these documents. You should also carefully consider the risks and other information that may be contained in, or incorporated by reference into, any prospectus supplement relating to specific offerings of securities.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and any accompanying prospectus supplement, and the information incorporated by reference into this prospectus and any accompanying prospectus supplement, contain express or implied forward-looking statements that are based on our management's belief and assumptions and on information currently available to our management. Although we believe that the expectations reflected in these forward-looking statements are reasonable, these statements relate to future events or our future operational or financial performance, and involve known and unknown risks, uncertainties, and other factors that may cause our actual results, performance, or achievements to be materially different from any future results, performance, or achievements expressed or implied by these forward-looking statements. Forward-looking statements in this prospectus include, but are not limited to, those described under "Risk Factors" and include, among other things:

- the timing, progress and results of preclinical studies and clinical trials for KarXT in our current indications and other product candidates we may develop, including statements regarding the timing of initiation and completion of studies or trials and related preparatory work and the period during which the results of the trials will become available;
- our research and development plans, including our plans to explore the therapeutic potential of KarXT in additional indications;
- our plans to develop and commercialize KarXT and other product candidates;
- the impact of COVID-19 on our business operations and that of our third-party manufacturers and suppliers;
- the timing of and our ability to obtain and maintain marketing approvals for our product candidates;
- the rate and degree of market acceptance and clinical utility of any product candidates for which we receive marketing approval;
- our commercialization, marketing and manufacturing capabilities and strategy;
- our intellectual property position and strategy;
- our ability to identify additional product candidates with significant commercial potential;
- our plans to enter into collaborations for the development and commercialization of product candidates;
- the potential benefits of any future collaboration;
- our expectations related to the use of proceeds from this offering;
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- our ability to raise additional capital in sufficient amounts or on terms acceptable to us;
- our ability to retain the continued service of our key professionals and to identify, hire and retain additional qualified professionals;
- developments relating to our competitors and our industry; and
- the impact of government laws and regulations.

In some cases, forward-looking statements can be identified by terminology such as "may," "should," "expects," "intends," "plans," "anticipates," "believes," "estimates," "predicts," "potential," "continue," or the negative of these terms or other comparable terminology. These statements are only predictions. You should not place undue reliance on forward-looking statements because they involve known and unknown risks, uncertainties, and other factors, which are, in some cases, beyond our control and which could materially affect results. Factors that may

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cause actual results to differ materially from current expectations include, among other things, those listed under the section entitled “Risk Factors” and elsewhere in this prospectus and any related free writing prospectus, and in any other documents incorporated herein or therein (including in our most recent annual report on Form 10-K, subsequent quarterly reports on Form 10-Q and other filings we make with the SEC pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act). Any forward-looking statement in this prospectus reflects our current view with respect to future events and is subject to these and other risks, uncertainties and assumptions relating to our operations, results of operations, industry and future growth. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future. If one or more of these risks or uncertainties occur, or if our underlying assumptions prove to be incorrect, actual events or results may vary significantly from those expressed or implied by the forward-looking statements. No forward-looking statement is a guarantee of future performance.

The forward-looking statements in this prospectus represent our views as of the date of this prospectus. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we have no current intention of doing so except to the extent required by applicable law. You should therefore not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this prospectus.

This prospectus includes statistical and other industry and market data that we obtained from industry publications and research, surveys, and studies conducted by third parties. Industry publications and third-party research, surveys, and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. We have not independently verified the information contained in such sources.

USE OF PROCEEDS

We intend to use the net proceeds from the sale of any securities offered under this prospectus for general corporate purposes unless otherwise indicated in the applicable prospectus supplement. General corporate purposes may include research and development costs, potential strategic acquisitions or licensing of complementary businesses, services or technologies, working capital and capital expenditures. We may temporarily invest the net proceeds in a variety of capital preservation instruments, including investment grade, interest bearing instruments and U.S. government securities, until they are used for their stated purpose. We have not determined the amount of net proceeds to be used specifically for such purposes. As a result, management will retain broad discretion over the allocation of net proceeds.

DIVIDEND POLICY

We currently intend to retain all available funds and any future earnings to fund the growth and development of our business. We do not intend to pay cash dividends to our stockholders in the foreseeable future. Any future determination to declare dividends will be made at the discretion of our board of directors and will depend on our financial condition, operating results, capital requirements, general business conditions, and other factors that our board of directors may deem relevant.

GENERAL DESCRIPTION OF SECURITIES

We may offer shares of common or preferred stock, various series of senior or subordinated debt securities, warrants, or units consisting of combinations of the foregoing, in each case from time to time under this prospectus, together with the applicable prospectus supplement, at prices and on terms to be determined by market conditions at the time of offering. This prospectus provides you with a general description of the securities we may offer. At the time we offer a particular type or series of securities, we will provide an applicable prospectus supplement describing 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;
- voting or other rights;
- rates and times of payment of interest, dividends or other payments;
- liquidation preference;
- original issue discount;
- maturity;
- ranking;
- restrictive covenants;
- redemption, conversion, exercise, exchange, settlement or sinking fund terms, including prices or rates, and any provisions for changes to or adjustments in such prices or rates and in the securities or other property receivable upon conversion, exercise, exchange or settlement;
- any securities exchange or market listing arrangements; and
- important U.S. federal income tax considerations.

This prospectus may not be used to offer or sell securities unless accompanied by an applicable prospectus supplement. The applicable prospectus supplement may add, update or change information contained in this prospectus or in documents incorporated by reference in this prospectus. You should read the prospectus supplement related to any securities being offered.

We may sell the securities directly to or through underwriters, dealers or agents. We and our underwriters, dealers 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 (i) the names of the underwriters or agents and applicable fees, discounts and commissions to be paid to them; (ii) details regarding over-allotment options, if any; and (iii) net proceeds to us.

The following descriptions are not complete and may not contain all the information you should consider before investing in any securities we may offer hereunder; they are summarized from, and qualified by reference to, our amended and restated certificate of incorporation, amended and restated bylaws and the other documents referred to in the descriptions, all of which are or will be publicly filed with the SEC, as applicable. See “Where You Can Find More Information.”

DESCRIPTION OF CAPITAL STOCK

The following descriptions are summaries of the material terms of our amended and restated certificate of incorporation and amended and restated bylaws and are qualified by reference to our amended and restated certificate of incorporation and amended and restated bylaws, copies of which have been filed with the SEC and are incorporated by reference as exhibits to the registration statement of which this prospectus is a part. We refer in this section to our amended and restated certificate of incorporation as our certificate of incorporation, and we refer to our amended and restated bylaws as our bylaws. The terms of our common stock and preferred stock may also be affected by Delaware law.

Authorized capital stock

Our authorized capital stock consists of 150,000,000 shares of common stock, par value \$0.0001 per share, and 10,000,000 shares of preferred stock, par value \$0.0001 per share, all of which shares of preferred stock are undesignated.

As of June 30, 2020, 26,580,533 shares of our common stock were outstanding and held by 8 stockholders of record. The actual number of stockholders is greater than this number of record holders and includes stockholders who are beneficial owners but whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Common stock

The holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of the stockholders. The holders of our common stock do not have any cumulative voting rights. Holders of our common stock are entitled to receive ratably any dividends declared by our board of directors out of funds legally available for that purpose, subject to any preferential dividend rights of any outstanding preferred stock. Our common stock has no preemptive rights, conversion rights or other subscription rights or redemption or sinking fund provisions.

In the event of our liquidation, dissolution or winding up, holders of our common stock will be entitled to share ratably in all assets remaining after payment of all debts and other liabilities and any liquidation preference of any outstanding preferred stock. The shares to be issued by us in this offering will be, when issued and paid for, validly issued, fully paid and non-assessable.

Preferred stock

Our board of directors has the authority, without further action by our stockholders, to issue up to 10,000,000 shares of preferred stock in one or more series and to fix the rights, preferences, privileges and restrictions thereof. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting, or the designation of, such series, any or all of which may be greater than the rights of common stock. The issuance of our preferred stock could adversely affect the voting power of holders of common stock and the likelihood that such holders will receive dividend payments and payments upon our liquidation. In addition, the issuance of preferred stock could have the effect of delaying, deferring or preventing a change in control of our Company or other corporate action. We have no shares of preferred stock outstanding, and we have no present plan to issue any shares of preferred stock.

Registration rights

The holders of up to 17,453,036 shares of our common stock are entitled to rights with respect to the registration of such securities under the Securities Act pursuant to the terms of an amended and restated investors', or the

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investors' rights agreement, between us and holders of our preferred stock. The investors' rights agreement includes demand registration rights, short-form registration rights and piggyback registration rights. All fees, costs and expenses of underwritten registrations under this agreement will be borne by us and all selling expenses, including underwriting discounts and selling commissions, will be borne by the holders of the shares being registered.

Demand registration rights

The holders of 16,468,403 shares of our common stock are entitled to demand registration rights. Under the terms of the investors' rights agreement, we will be required, upon the written request of the holders of at least 40% of our outstanding registrable securities, as defined in the investors' rights agreement, or a lesser percent if the total amount of registrable shares requested to be registered has an anticipated aggregate offering price to the public, net of selling expenses, of least \$10.0 million, to file a registration statement and use commercially reasonable efforts to effect the registration of all or a portion of their registrable securities for public resale. We are required to effect only two registrations pursuant to this provision of the investors' rights agreement.

Short-form registration rights

Pursuant to the investor rights agreement, if we are eligible to file a registration statement on Form S-3, upon the written request of the holders of our outstanding registrable securities, as defined in the investors' rights agreement, may demand in writing that we register their registrable securities under the Securities Act so long as the total amount of registrable shares requested to be registered has an anticipated aggregate offering price to the public, net of selling expenses, of least \$5.0 million. We are required to effect only two registrations in any twelve month period pursuant to this provision of the investors' rights agreement. The right to have such shares registered on Form S-3 is further subject to other specified conditions and limitations.

Piggyback registration rights

The holders of 17,453,036 shares of our common stock are entitled to piggyback registration rights. Pursuant to the investors' rights agreement, if we register any of our securities either for our own account or for the account of other security holders, the holders of these shares are entitled to include their shares in the registration. Subject to certain exceptions contained in the investors' rights agreement, we and the underwriters may limit the number of shares included in the underwritten offering to the number of shares which we and the underwriters determine in our sole discretion will not jeopardize the success of the offering.

Indemnification

Our investor rights agreement contains customary cross-indemnification provisions, under which we are obligated to indemnify holders of registrable securities in the event of material misstatements or omissions in the registration statement attributable to us, and they are obligated to indemnify us for material misstatements or omissions attributable to them.

Expiration of registration rights

The demand registration rights and short form registration rights granted under the investor rights agreement will terminate on June 27, 2024.

Anti-takeover effects of our certificate of incorporation and bylaws and Delaware Law

Our certificate of incorporation and bylaws include a number of provisions that may have the effect of delaying, deferring or preventing another party from acquiring control of us and encouraging persons considering unsolicited tender offers or other unilateral takeover proposals to negotiate with our board of directors rather than pursue non-negotiated takeover attempts. These provisions include the items described below.

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Board composition and filling vacancies

Our certificate of incorporation provides for the division of our board of directors into three classes serving staggered three-year terms, with one class being elected each year. Our certificate of incorporation also provides that directors may be removed only for cause and then only by the affirmative vote of the holders of 75% or more of the shares then entitled to vote at an election of directors. Further, any vacancy on our board of directors, however occurring, including a vacancy resulting from an increase in the size of our board, may only be filled by the affirmative vote of a majority of our directors then in office even if less than a quorum. The classification of directors, together with the limitations on removal of directors and treatment of vacancies, has the effect of making it more difficult for stockholders to change the composition of our board of directors.

No written consent of stockholders

Our certificate of incorporation provides that all stockholder actions are required to be taken by a vote of the stockholders at an annual or special meeting, and that stockholders may not take any action by written consent in lieu of a meeting. This limit may lengthen the amount of time required to take stockholder actions and would prevent the amendment of our bylaws or removal of directors by our stockholders without holding a meeting of stockholders.

Meetings of stockholders

Our certificate of incorporation and bylaws provide that only a majority of the members of our board of directors then in office may call special meetings of stockholders and only those matters set forth in the notice of the special meeting may be considered or acted upon at a special meeting of stockholders. Our bylaws limit the business that may be conducted at an annual meeting of stockholders to those matters properly brought before the meeting.

Advance notice requirements

Our bylaws establish advance notice procedures with regard to stockholder proposals relating to the nomination of candidates for election as directors or new business to be brought before meetings of our stockholders. These procedures provide that notice of stockholder proposals must be timely given in writing to our corporate secretary prior to the meeting at which the action is to be taken. Generally, to be timely, notice must be received at our principal executive offices not less than 90 days nor more than 120 days prior to the first anniversary date of the annual meeting for the preceding year. Our bylaws specify the requirements as to form and content of all stockholders' notices. These requirements may preclude stockholders from bringing matters before the stockholders at an annual or special meeting.

Amendment to certificate of incorporation and bylaws

Any amendment of our certificate of incorporation must first be approved by a majority of our board of directors, and if required by law or our certificate of incorporation, must thereafter be approved by a majority of the outstanding shares entitled to vote on the amendment and a majority of the outstanding shares of each class entitled to vote thereon as a class, except that the amendment of the provisions relating to stockholder action, board composition, limitation of liability and the amendment of our bylaws and certificate of incorporation must be approved by not less than 75% of the outstanding shares entitled to vote on the amendment, and not less than 75% of the outstanding shares of each class entitled to vote thereon as a class. Our bylaws may be amended by the affirmative vote of a majority of the directors then in office, subject to any limitations set forth in the bylaws; and may also be amended by the affirmative vote of at least 75% of the outstanding shares entitled to vote on the amendment, or, if our board of directors recommends that the stockholders approve the amendment, by the affirmative vote of the majority of the outstanding shares entitled to vote on the amendment, in each case voting together as a single class.

Undesignated preferred stock

Our certificate of incorporation provides for 10,000,000 authorized shares of preferred stock. The existence of authorized but unissued shares of preferred stock may enable our board of directors to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise. For example, if in the due exercise of its fiduciary obligations, our board of directors were to determine that a takeover proposal is not in the best interests of our stockholders, our board of directors could cause shares of preferred stock to be issued without stockholder approval in one or more private offerings or other transactions that might dilute the voting or other rights of the proposed acquirer or insurgent stockholder or stockholder group. In this regard, our certificate of incorporation grants our board of directors broad power to establish the rights and preferences of authorized and unissued shares of preferred stock. The issuance of shares of preferred stock could decrease the amount of earnings and assets available for distribution to holders of shares of common stock. The issuance may also adversely affect the rights and powers, including voting rights, of these holders and may have the effect of delaying, deterring or preventing a change in control of us.

Exclusive Jurisdiction for Certain Actions

Our bylaws provide that, unless we consent in writing to an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for state law claims for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers and employees to us or our stockholders, (iii) any action asserting a claim arising pursuant to any provision of the Delaware General Corporation Law, our certificate of incorporation or our bylaws, or (iv) any action asserting a claim that is governed by the internal affairs doctrine, in each case subject to the Court of Chancery having personal jurisdiction over the indispensable parties named as defendants therein. This provision will not apply to actions arising under the Securities Act or the Exchange Act. Although we believe this provision benefits us by providing increased consistency in the application of Delaware law in the types of lawsuits to which it applies, the provision may have the effect of discouraging lawsuits against our directors and officers. The enforceability of similar exclusive forum provisions in other companies' bylaws has been challenged in legal proceedings, and it is possible that a court could rule that this provision in our bylaws is inapplicable or unenforceable.

Section 203 of the Delaware General Corporation Law

We are subject to the provisions of Section 203 of the Delaware General Corporation Law. In general, Section 203 prohibits a publicly held Delaware corporation from engaging in a "business combination" with an "interested stockholder" for a three-year period following the time that this stockholder becomes an interested stockholder, unless the business combination is approved in a prescribed manner. Under Section 203, a business combination between a corporation and an interested stockholder is prohibited unless it satisfies one of the following conditions:

- before the stockholder became interested, our board of directors approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;
- upon consummation of the transaction which resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, shares owned by persons who are directors and also officers, and employee stock plans, in some instances, but not the outstanding voting stock owned by the interested stockholder; or
- at or after the time the stockholder became interested, the business combination was approved by our board of directors and authorized at an annual or special meeting of the stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder.

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Section 203 defines a business combination to include:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, transfer, lease, pledge or other disposition involving the interested stockholder of 10% or more of the assets of the corporation;
- subject to exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;
- subject to exceptions, any transaction involving the corporation that has the effect of increasing the proportionate share of the stock of any class or series of the corporation beneficially owned by the interested stockholder; and
- the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges, or other financial benefits provided by or through the corporation.

In general, Section 203 defines an interested stockholder as any entity or person beneficially owning 15% or more of the outstanding voting stock of the corporation and any entity or person affiliated with or controlling or controlled by the entity or person.

Nasdaq Global Select Market listing

Our common stock is listed on the Nasdaq Global Select Market under the trading symbol “KRTX.”

Transfer agent and registrar

The transfer agent and registrar for our common stock is American Stock Transfer & Trust Company, LLC.

DESCRIPTION OF DEBT SECURITIES

This section describes the general terms and provisions of our debt securities that we may issue from time to time. We may issue debt securities, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. While the terms we have summarized below will apply generally to any future debt securities we may offer under this prospectus, the applicable prospectus supplement or free writing prospectus will describe the specific terms of any debt securities offered through that prospectus supplement or free writing prospectus. The terms of any debt securities we offer under a prospectus supplement or free writing prospectus may differ from the terms we describe below. Unless the context requires otherwise, whenever we refer to the “indentures,” we also are referring to any supplemental indentures that specify the terms of a particular series of debt securities.

We will issue any senior debt securities under the senior indenture that we will enter into with the trustee named in the senior indenture. We will issue any subordinated debt securities under the subordinated indenture that we will enter into with the trustee named in the subordinated indenture. We have filed forms of these documents 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.

The indentures will be qualified under the Trust Indenture Act of 1939, as amended, or the Trust Indenture Act. We use the term “trustee” to refer to either the trustee under the senior indenture or the trustee under the subordinated indenture, as applicable.

The following summaries of material provisions of the senior debt securities, the subordinated debt securities and the indentures are subject to, and qualified in their entirety by reference to, all of the provisions of the indenture applicable to a particular series of debt securities. We urge you to read the applicable prospectus supplement or free writing prospectus and any related free writing prospectuses related to the debt securities that we may offer under this prospectus, as well as the complete applicable indenture that contains the terms of the debt securities. Except as we may otherwise indicate, the terms of the senior indenture and the subordinated indenture are identical.

General

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

- the title;
- the principal amount being offered, and if a series, the total amount authorized and the total amount outstanding;
- any limit on the amount that may be issued;
- whether or not we will issue the series of debt securities in global form, and, if so, the terms and who the depository will be;
- the maturity date;
- whether and under what circumstances, if any, we will pay additional amounts on any debt securities held by a person who is not a United States person for tax purposes, and whether we can redeem the debt securities if we have to pay such additional amounts;
- the annual interest rate, which may be fixed or variable, or the method for determining the rate and the date interest will begin to accrue, the dates interest will be payable and the regular record dates for interest payment dates or the method for determining such dates;
- whether or not the debt securities will be secured or unsecured, and the terms of any secured debt;

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- the terms of the subordination of any series of subordinated debt;
- the place where payments will be payable;
- restrictions on transfer, sale or other assignment, if any;
- our right, if any, to defer payment of interest and the maximum length of any such deferral period;
- the date, if any, after which, the conditions upon which, and the price at which, we may, at our option, redeem the series of debt securities pursuant to any optional or provisional redemption provisions and the terms of those redemption provisions;
- the date, if any, on which, and the price at which we are obligated, pursuant to any mandatory sinking fund or analogous fund provisions or otherwise, to redeem, or at the holder's option, to purchase, the series of debt securities and the currency or currency unit in which the debt securities are payable;
- whether the indenture will restrict our ability or the ability of our subsidiaries to:
 - incur additional indebtedness;
 - issue additional securities;
 - create liens;
 - pay dividends or make distributions in respect of our capital stock or the capital stock of our subsidiaries;
 - redeem capital stock;
 - place restrictions on our subsidiaries' ability to pay dividends, make distributions or transfer assets;
 - make investments or other restricted payments;
 - sell or otherwise dispose of assets;
 - enter into sale-leaseback transactions;
 - engage in transactions with stockholders or affiliates;
 - issue or sell stock of our subsidiaries;
 - effect a consolidation or merger;
 - whether the indenture will require us to maintain any interest coverage, fixed charge, cash flow-based, asset-based or other financial ratios;
 - a discussion of certain material or special United States federal income tax considerations applicable to the debt securities;
 - information describing any book-entry features;
 - provisions for a sinking fund purchase or other analogous fund, if any;
 - the applicability of the provisions in the indenture on discharge;
 - whether the debt securities are to be offered at a price such that they will be deemed to be offered at an "original issue discount" as defined in paragraph (a) of Section 1273 of the Internal Revenue Code of 1986, as amended;
 - the denominations in which we will issue the series of debt securities, if other than denominations of \$1,000 and any integral multiple thereof;
 - the currency of payment of debt securities if other than U.S. dollars and the manner of determining the equivalent amount in U.S. dollars; and

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- any other specific terms, preferences, rights or limitations of, or restrictions on, the debt securities, including any additional events of default or covenants provided with respect to the debt securities, and any terms that may be required by us or advisable under applicable laws or regulations or advisable in connection with the marketing of the debt securities.

Conversion or exchange rights

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

Consolidation, merger or sale

Unless we provide otherwise in the prospectus supplement or free writing prospectus applicable to a particular series of debt securities, the indentures will not contain any covenant that restricts our ability to merge or consolidate, or sell, convey, transfer or otherwise dispose of all or substantially all of our assets. However, any successor to or acquirer of such assets must assume all of our obligations under the indentures or the debt securities, as appropriate. If the debt securities are convertible into or exchangeable for other securities of ours or securities of other entities, the person with whom we consolidate or merge or to whom we sell all of our property must make provisions for the conversion of the debt securities into securities that the holders of the debt securities would have received if they had converted the debt securities before the consolidation, merger or sale.

Events of default under the indenture

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

- if we fail to pay interest when due and payable and our failure continues for 90 days and the time for payment has not been extended;
- if we fail to pay the principal, premium or sinking fund payment, if any, when due and payable at maturity, upon redemption or repurchase or otherwise, and the time for payment has not been extended;
- if we fail to observe or perform any other covenant contained in the debt securities or the indentures, other than a covenant specifically relating to another series of debt securities, and our failure continues for 90 days after we receive notice from the trustee or holders of at least 25% in aggregate principal amount of the outstanding debt securities of the applicable series; and
- if specified events of bankruptcy, insolvency or reorganization occur.

We will describe in each applicable prospectus supplement or free writing prospectus any additional events of default relating to the relevant series of debt securities.

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

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

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

- the direction so given by the holder is not in conflict with any law or the applicable indenture; and
- subject to its duties under the Trust Indenture Act, the trustee need not take any action that might involve it in personal liability or might be unduly prejudicial to the holders not involved in the proceeding.

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

- the holder has given written notice to the trustee of a continuing event of default with respect to that series;
- the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series have made written request, and such holders have offered reasonable indemnity to the trustee or security satisfactory to it against any loss, liability or expense or to be incurred in compliance with instituting the proceeding as trustee; and
- the trustee does not institute the proceeding, and does not receive from the holders of a majority in aggregate principal amount of the outstanding debt securities of that series other conflicting directions within 90 days after the notice, request and offer.

These limitations do not apply to a suit instituted by a holder of debt securities if we default in the payment of the principal, premium, if any, or interest on, the debt securities, or other defaults that may be specified in the applicable prospectus supplement or free writing prospectus.

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

Modification of indenture; waiver

Subject to the terms of the indenture for any series of debt securities that we may issue, we and the trustee may change an indenture without the consent of any holders with respect to the following specific matters:

- to fix any ambiguity, defect or inconsistency in the indenture;
- to comply with the provisions described above under “Description of Debt Securities-Consolidation, Merger or Sale”;
- to comply with any requirements of the SEC in connection with the qualification of any indenture under the Trust Indenture Act;
- to add to, delete from or revise the conditions, limitations, and restrictions on the authorized amount, terms, or purposes of issue, authentication and delivery of debt securities, as set forth in the indenture;

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- to provide for the issuance of and establish the form and terms and conditions of the debt securities of any series as provided under “Description of Debt Securities—General,” to establish the form of any certifications required to be furnished pursuant to the terms of the indenture or any series of debt securities, or to add to the rights of the holders of any series of debt securities;
- to evidence and provide for the acceptance of appointment hereunder by a successor trustee;
- to provide for uncertificated debt securities and to make all appropriate changes for such purpose;
- to add to our covenants such new covenants, restrictions, conditions or provisions for the benefit of the holders, to make the occurrence, or the occurrence and the continuance, of a default in any such additional covenants, restrictions, conditions or provisions an event of default or to surrender any right or power conferred to us in the indenture; or
- to change anything that does not materially adversely affect the interests of any holder of debt securities of any series.

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

- extending the stated maturity of the series of debt securities;
- reducing the principal amount, reducing the rate of or extending the time of payment of interest, or reducing any premium payable upon the redemption or repurchase of any debt securities; or
- reducing the percentage of debt securities, the holders of which are required to consent to any amendment, supplement, modification or waiver.

Discharge

Each indenture provides that, subject to the terms of the indenture and any limitation otherwise provided in the prospectus supplement or free writing prospectus applicable to a particular series of debt securities, we can elect to be discharged from our obligations with respect to one or more series of debt securities, except for specified obligations, including obligations to:

- register the transfer or exchange of debt securities of the series;
- replace stolen, lost or mutilated debt securities of the series;
- maintain paying agencies;
- hold monies for payment in trust;
- recover excess money held by the trustee;
- compensate and indemnify the trustee; and
- appoint any successor trustee.

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

Form, exchange and transfer

We will issue the debt securities of each series only in fully registered form without coupons and, unless we otherwise specify in the applicable prospectus supplement or free writing prospectus, in denominations of \$1,000 and any integral multiple thereof. The indentures provide that we may issue debt securities of a series in temporary or permanent global form and as book-entry securities that will be deposited with, or on behalf of, The Depository Trust Company or another depository named by us and identified in a prospectus supplement or free writing prospectus with respect to that series.

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

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

We will name in the applicable prospectus supplement or free writing prospectus the security registrar, and any transfer agent in addition to the security registrar, that we initially designate for any debt securities. We may at any time designate additional transfer agents or rescind the designation of any transfer agent or approve a change in the office through which any transfer agent acts, except that we will be required to maintain a transfer agent in each place of payment for the debt securities of each series. If we elect to redeem the debt securities of any series, we will not be required to:

- issue, register the transfer of, or exchange any debt securities of that series during a period beginning at the opening of business 15 days before the day of mailing of a notice of redemption of any debt securities that may be selected for redemption and ending at the close of business on the day of the mailing; or
- register the transfer of or exchange any debt securities so selected for redemption, in whole or in part, except the unredeemed portion of any debt securities we are redeeming in part.

Information concerning the trustee

The trustee, other than during the occurrence and continuance of an event of default under an indenture, undertakes to perform only those duties as are specifically set forth in the applicable indenture. Upon an event of default under an indenture, the trustee must use the same degree of care as a prudent person would exercise or use in the conduct of his or her own affairs.

Subject to this provision, the trustee is under no obligation to exercise any of the powers given it by the indentures at the request of any holder of debt securities unless it is offered reasonable security and indemnity against the costs, expenses and liabilities that it might incur.

Payment and paying agents

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

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

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

Governing law

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

Ranking of debt securities

The subordinated debt securities will be subordinate and junior in priority of payment to certain of our other indebtedness to the extent described in a prospectus supplement or free writing prospectus. The subordinated indenture does not limit the amount of subordinated debt securities that we may issue. It also does not limit us from issuing any other secured or unsecured debt.

The senior debt securities will rank equally in right of payment to all our other senior unsecured debt. The senior indenture does not limit the amount of senior debt securities that we may issue. It also does not limit us from issuing any other secured or unsecured debt.

DESCRIPTION OF WARRANTS

The following description, together with the additional information we may include in any applicable prospectus supplements, summarizes the material terms and provisions of the warrants that we may offer under this prospectus and the related warrant agreements and warrant certificates. While the terms summarized below will apply generally to any warrants that we may offer, we will describe the particular terms of any series of warrants in more detail in the applicable prospectus supplement. If we indicate in the prospectus supplement, the terms of any warrants offered under that prospectus supplement may differ from the terms described below. Specific warrant agreements will contain additional important terms and provisions and will be incorporated by reference as an exhibit to the registration statement, which includes this prospectus.

General

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.

We will evidence each series of warrants by warrant certificates that we will issue under a separate warrant agreement. We will enter into the warrant agreement with a warrant agent. We will indicate the name and address of the warrant agent in the applicable prospectus supplement relating to a particular series of warrants.

We will describe in the applicable prospectus supplement the terms of the series of warrants, including:

- the offering price and aggregate number of warrants offered;
- the currency for which the warrants may be purchased;
- if applicable, the designation and terms of the securities with which the warrants are issued and the number of warrants issued with each such security or each principal amount of such security;
- if applicable, the date on and after which the warrants and the related securities will be separately transferable;
- in the case of warrants to purchase debt securities, the principal amount of debt securities purchasable upon exercise of one warrant and the price at which, and currency in which, this principal amount of debt securities may be purchased upon such exercise;
- in the case of warrants to purchase common stock or preferred stock, the number of shares of common stock or preferred stock, as the case may be, purchasable upon the exercise of one warrant and the price at which these shares may be purchased upon such exercise;
- the effect of any merger, consolidation, sale or other disposition of our business on the warrant agreement and the warrants;
- the terms of any rights to redeem or call the warrants;
- any provisions for changes to or adjustments in the exercise price or number of securities issuable upon exercise of the warrants;
- the periods during which, and places at which, the warrants are exercisable;
- the manner of exercise;
- the dates on which the right to exercise the warrants will commence and expire;
- the manner in which the warrant agreement and warrants may be modified;
- federal income tax consequences of holding or exercising the warrants;
- the terms of the securities issuable upon exercise of the warrants; and
- any other specific terms, preferences, rights or limitations of or restrictions on the warrants.

DESCRIPTION OF UNITS

We may issue units comprised of shares of common stock, shares of preferred stock, debt securities and warrants in any combination. We may issue units in such amounts and in as many distinct series as we wish. This section outlines certain provisions of the units that we may issue. If we issue units, they will be issued under one or more unit agreements to be entered into between us and a bank or other financial institution, as unit agent. The information described in this section may not be complete in all respects and is qualified entirely by reference to the unit agreement with respect to the units of any particular series. The specific terms of any series of units offered will be described in the applicable prospectus supplement. If so described in a particular supplement, the specific terms of any series of units may differ from the general description of terms presented below. We urge you to read any prospectus supplement related to any series of units we may offer, as well as the complete unit agreement and unit certificate that contain the terms of the units. If we issue units, forms of unit agreements and unit certificates relating to such units will be incorporated by reference as exhibits to the registration statement, which includes this prospectus.

Each unit that we may issue will be issued so that the holder of the unit is also the holder of each security included in the unit. Thus, the holder of a unit will have the rights and obligations of a holder of each included security. The unit agreement under which a unit is issued may provide that the securities included in the unit may not be held or transferred separately, at any time or at any time before a specified date. The applicable prospectus supplement may describe:

- the designation and terms of the units and of the securities comprising the units, including whether and under what circumstances those securities may be held or transferred separately;
- any provisions of the governing unit agreement;
- the price or prices at which such units will be issued;
- the applicable United States federal income tax considerations relating to the units;
- any provisions for the issuance, payment, settlement, transfer or exchange of the units or of the securities comprising the units; and
- any other terms of the units and of the securities comprising the units.

The provisions described in this section, as well as those described under “Description of Capital Stock,” “Description of Debt Securities” and “Description of Warrants” will apply to the securities included in each unit, to the extent relevant and as may be updated in any prospectus supplements.

Issuance in series

We may issue units in such amounts and in as many distinct series as we wish. This section summarizes terms of the units that apply generally to all series. Most of the financial and other specific terms of a particular series of units will be described in the applicable prospectus supplement.

Unit agreements

We will issue the units under one or more unit agreements to be entered into between us and a bank or other financial institution, as unit agent. We may add, replace or terminate unit agents from time to time. We will identify the unit agreement under which each series of units will be issued and the unit agent under that agreement in the applicable prospectus supplement.

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The following provisions will generally apply to all unit agreements unless otherwise stated in the applicable prospectus supplement:

Modification without consent

We and the applicable unit agent may amend any unit or unit agreement without the consent of any holder:

- to cure any ambiguity, or any provisions of the governing unit agreement that differ from those described below;
- to correct or supplement any defective or inconsistent provision; or
- to make any other change that we believe is necessary or desirable and will not adversely affect the interests of the affected holders in any material respect.

We do not need any approval to make changes that affect only units to be issued after the changes take effect. We may also make changes that do not adversely affect a particular unit in any material respect, even if they adversely affect other units in a material respect. In those cases, we do not need to obtain the approval of the holder of the unaffected unit; we need only obtain any required approvals from the holders of the affected units.

Modification with consent

We may not amend any particular unit or a unit agreement with respect to any particular unit unless we obtain the consent of the holder of that unit, if the amendment would:

- impair any right of the holder to exercise or enforce any right under a security included in the unit if the terms of that security require the consent of the holder to any changes that would impair the exercise or enforcement of that right; or
- reduce the percentage of outstanding units or any series or class the consent of whose holders is required to amend that series or class, or the applicable unit agreement with respect to that series or class, as described below.

Any other change to a particular unit agreement and the units issued under that agreement would require the following approval:

- If the change affects only the units of a particular series issued under that agreement, the change must be approved by the holders of a majority of the outstanding units of that series; or
- If the change affects the units of more than one series issued under that agreement, it must be approved by the holders of a majority of all outstanding units of all series affected by the change, with the units of all the affected series voting together as one class for this purpose.

These provisions regarding changes with majority approval also apply to changes affecting any securities issued under a unit agreement, as the governing document.

In each case, the required approval must be given by written consent.

Unit agreements will not be qualified under Trust Indenture Act

No unit agreement will be qualified as an indenture, and no unit agent will be required to qualify as a trustee, under the Trust Indenture Act. Therefore, holders of units issued under unit agreements will not have the protections of the Trust Indenture Act with respect to their units.

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Mergers and similar transactions permitted; no restrictive covenants or events of default

The unit agreements will not restrict our ability to merge or consolidate with, or sell our assets to, another corporation or other entity or to engage in any other transactions. If at any time we merge or consolidate with, or sell our assets substantially as an entirety to, another corporation or other entity, the successor entity will succeed to and assume our obligations under the unit agreements. We will then be relieved of any further obligation under these agreements.

The unit agreements will not include any restrictions on our ability to put liens on our assets, nor will they restrict our ability to sell our assets. The unit agreements also will not provide for any events of default or remedies upon the occurrence of any events of default.

Governing law

The unit agreements and the units will be governed by the laws of the State of New York.

Form, exchange and transfer

We will issue each unit in global, i.e., book-entry-form only. Units in book-entry form will be represented by a global security registered in the name of a depositary, which will be the holder of all the units represented by the global security. Those who own beneficial interests in a unit will do so through participants in the depositary's system, and the rights of these indirect owners will be governed solely by the applicable procedures of the depositary and its participants. We will describe book-entry securities, and other terms regarding the issuance and registration of the units, in the applicable prospectus supplement.

Each unit and all securities comprising the unit will be issued in the same form.

If we issue any units in registered, non-global form, the following will apply to them.

The units will be issued in the denominations stated in the applicable prospectus supplement. Holders may exchange their units for units of smaller denominations or combined into fewer units of larger denominations, as long as the total amount is not changed.

- Holders may exchange or transfer their units at the office of the unit agent. Holders may also replace lost, stolen, destroyed or mutilated units at that office. We may appoint another entity to perform these functions or perform them ourselves.
- Holders will not be required to pay a service charge to transfer or exchange their units, but they may be required to pay for any tax or other governmental charge associated with the transfer or exchange. The transfer or exchange, and any replacement, will be made only if our transfer agent is satisfied with the holder's proof of legal ownership. The transfer agent may also require an indemnity before replacing any units.
- If we have the right to redeem, accelerate or settle any units before their maturity, and we exercise our right as to less than all those units or other securities, we may block the exchange or transfer of those units during the period beginning 15 days before the day we mail the notice of exercise and ending on the day of that mailing, in order to freeze the list of holders to prepare the mailing. We may also refuse to register transfers of or exchange any unit selected for early settlement, except that we will continue to permit transfers and exchanges of the unsettled portion of any unit being partially settled. We may also block the transfer or exchange of any unit in this manner if the unit includes securities that are or may be selected for early settlement.

Only the depositary will be entitled to transfer or exchange a unit in global form, since it will be the sole holder of the unit.

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Payments and notices

In making payments and giving notices with respect to our units, we will follow the procedures as described in the applicable prospectus supplement.

PLAN OF DISTRIBUTION

We may sell the offered securities in and outside the United States (1) through underwriters or dealers, (2) directly to one or more purchasers, including to a limited number of institutional purchasers, to a single purchaser or to our affiliates and stockholders, (3) through agents or (4) through a combination of any of these methods.

If underwriters or dealers are used in the sale, the securities will be acquired by the underwriters or dealers for their own account and may be resold from time to time in one or more transactions, including:

- in one or more transactions at a fixed price or prices, which may be changed from time to time;
- in “at-the-market offerings,” within the meaning of Rule 415(a)(4) of the Securities Act into an existing trading market, on an exchange or otherwise;
- through a market maker or into an existing trading market on an exchange or otherwise;
- at prices related to those prevailing market prices; or
- at negotiated prices.

The applicable prospectus supplement will set forth the following information to the extent applicable:

- the terms of the offering;
- the names of any underwriters, dealers or agents;
- the name or names of any managing underwriter or underwriters;
- the purchase price of the securities;
- the net proceeds from the sale of the securities;
- any delayed delivery arrangements;
- any underwriting discounts, commissions and other items constituting underwriters’ compensation;
- any initial public offering price;
- any discounts or concessions allowed or reallocated or paid to dealers; and
- any commissions paid to agents.

Sale through underwriters or dealers

If any securities are offered through underwriters, the underwriters will acquire the securities for their own account and may resell them from time to time in one or more transactions, including negotiated transactions, at a fixed public offering price or at varying prices determined at the time of sale. Underwriters may offer and sell securities to the public either through underwriting syndicates represented by one or more managing underwriters or directly by one or more firms acting as underwriters. Unless otherwise provided in the applicable prospectus supplement, the obligations of the underwriters to purchase the securities will be subject to certain conditions, and the underwriters will be obligated to purchase all of the offered securities if they purchase any of them. In connection with the sale of securities, underwriters may be deemed to have received compensation from us in the form of underwriting discounts or commissions and dealers may receive compensation from the underwriters in the form of discounts or concessions. The underwriters may change from time to time any initial public offering price and any discounts or concessions allowed or reallocated or paid to dealers.

In order to facilitate the offering of securities, the underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of the securities. Specifically, the underwriters may over allot in connection

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with the offering, creating a short position in the securities for their account. In addition, to cover overallocments or to stabilize the price of the shares, the underwriters may bid for, and purchase, shares in the open market.

Finally, an underwriting syndicate may reclaim selling concessions allowed to an underwriter or a dealer for distributing the securities in the offering if the syndicate repurchases previously distributed shares in transactions to cover syndicate short positions, in stabilization transactions, or otherwise. Any of these activities may stabilize or maintain the market price of the offered securities above independent market levels. The underwriters are not required to engage in these activities, and may discontinue any of these activities at any time.

Some or all of the securities that we offer through this prospectus may be new issues of securities with no established trading market. Any underwriters to whom we sell securities for public offering and sale may make a market in those securities, but they will not be obligated to do so and they may discontinue any market making at any time without notice. Accordingly, we cannot assure you of the liquidity of, or continued trading markets for, any securities offered pursuant to this prospectus.

If any securities are offered through dealers, we will sell the securities to them as principals. They may then resell those securities to the public at varying prices determined by the dealers at the time of resale.

Direct sales and sales through agents

We may sell the securities directly to purchasers. If the securities are sold directly to institutional investors or others who may be deemed to be underwriters within the meaning of the Securities Act with respect to any sale of those securities, we will describe the terms of any such sales in the applicable prospectus supplement. We may also sell the securities through agents designated from time to time. Sales may be made by means of ordinary brokers' transactions on the Nasdaq Global Select Market at market prices, in block transactions and such other transactions as agreed by us and any agent. In the applicable prospectus supplement, we will name any agent involved in the offer or sale of the offered securities, and we will describe any commissions payable to the agent. Unless otherwise provided in the applicable prospectus supplement, any agent will agree to use its reasonable best efforts to solicit purchases for the period of its appointment.

At-the-market offerings

To the extent that we make sales through one or more underwriters or agents in at-the-market offerings, we will do so pursuant to the terms of a sales agency financing agreement or other at-the-market offering arrangement between us, on one hand, and the underwriters or agents, on the other. If we engage in at-the-market sales pursuant to any such agreement, we will issue and sell our securities through one or more underwriters or agents, which may act on an agency basis or a principal basis. During the term of any such agreement, we may sell securities on a daily basis in exchange transactions or otherwise as we agree with the underwriters or agents. Any such agreement will provide that any securities sold will be sold at prices related to the then prevailing market prices for our securities. Therefore, exact figures regarding proceeds that will be raised or commissions to be paid cannot be determined at this time. Pursuant to the terms of the agreement, we may agree to sell, and the relevant underwriters or agents may agree to solicit offers to purchase blocks of our common stock or other securities. The terms of any such agreement will be set forth in more detail in the applicable prospectus supplement.

Remarketing arrangements

Offered securities may also be offered and sold, if we so indicate in the applicable prospectus supplement, in connection with a remarketing upon their purchase, in accordance with a redemption or repayment pursuant to their terms, or otherwise, by one or more remarketing firms, acting as principals for their own accounts or as our agents. Any remarketing firm will be identified and the terms of its agreements, if any, with us and its compensation will be described in the applicable prospectus supplement. Remarketing firms may be deemed to be underwriters of the offered securities under the Securities Act.

Delayed delivery contracts

If we so indicate in the applicable prospectus supplement, we may authorize agents, underwriters or dealers to solicit offers by certain institutions to purchase securities from us pursuant to contracts providing for payment and delivery on a specified future date. The applicable prospectus supplement will describe the conditions to those contracts and the commission payable for solicitation of those contracts.

General information

We may have agreements with the agents, dealers, underwriters and remarketing firms to indemnify them against certain civil liabilities, including liabilities under the Securities Act, or to contribute with respect to payments that the agents, dealers or underwriters may be required to make. Agents, dealers, underwriters and remarketing firms may be customers of, engage in transactions with or perform services for us in the ordinary course of their businesses.

Each underwriter, dealer and agent participating in the distribution of any of the securities that are issuable in bearer form will agree that it will not offer, sell or deliver, directly or indirectly, securities in bearer form in the United States or to United States persons, other than qualifying financial institutions, during the restricted period, as defined in United States Treasury Regulations Section 1.163-5(c)(2)(i)(D)(7).

LEGAL MATTERS

Certain legal matters in connection with this offering will be passed upon for us by Goodwin Procter LLP, New York, New York. Any underwriters will also be advised about the validity of the securities and other legal matters by their own counsel, which will be named in the prospectus supplement.

EXPERTS

The consolidated financial statements of Karuna Therapeutics, Inc. as of December 31, 2019 and 2018, and for each of the years then ended, have been incorporated by reference herein and in the registration statement in reliance upon the report of KPMG LLP, independent registered public accounting firm, incorporated by reference herein, and upon the authority of said firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-3 under the Securities Act with respect to the securities offered by this prospectus and the applicable prospectus supplement. This prospectus and the applicable prospectus supplement do not contain all of the information set forth in the registration statement and its exhibits and schedules in accordance with SEC rules and regulations. For further information with respect to us and the securities being offered by this prospectus and the applicable prospectus supplement, you should read the registration statement of which this prospectus is a part, including its exhibits and schedules. Statements contained in this prospectus and the applicable prospectus supplement, including documents that we have incorporated by reference, as to the contents of any contract or other document referred to are not necessarily complete, and, with respect to any contract or other document filed as an exhibit to the registration statement or any other such document, each such statement is qualified in all respects by reference to the corresponding exhibit. You should review the complete contract or other document to evaluate these statements. You may obtain copies of the registration statement and its exhibits via the SEC's EDGAR database or our website.

We file annual, quarterly and current reports, proxy statements and other documents with the SEC under the U.S. Securities Exchange Act of 1934, as amended, or the Exchange Act. The SEC maintains a website that contains reports, proxy and information statements and other information regarding issuers, including us, that file electronically with the SEC. You may obtain documents that we file with the SEC at www.sec.gov.

We also make these documents available on our website at karunatx.com. Our website and the information contained or connected to our website is not incorporated by reference in this prospectus or any prospectus supplement, and you should not consider it part of this prospectus or any prospectus supplement.

3,488,373 Shares



Common Stock

PROSPECTUS SUPPLEMENT

Goldman Sachs & Co. LLC

J.P. Morgan

Jefferies

Stifel

Guggenheim Securities

RBC Capital Markets

JMP Securities, a Citizens Company

Wedbush PacGrow

August 9, 2022

Calculation of Filing Fee Tables

424(b)(5)
(Form Type)

Karuna Therapeutics, Inc.
(Exact Name of Registrant as Specified in its Charter)

Table 1: Newly Registered and Carry Forward Securities

	Security Type	Security Class Title	Fee Calculation or Fee Carry Forward Rule	Amount Registered	Proposed Maximum Offering Price	Maximum Aggregate Offering Price	Fee Rate	Amount of Registration Fee ⁽¹⁾	Filing Fee Previously Paid In Connection with Unsold Securities to be Carried Forward	
Newly Registered Securities										
Fees to Be Paid	Equity	Common Stock, \$0.0001 per share	457(r)	4,011,628	–	\$862,500,020	0.0000927	\$79,953.75		
Fees Previously Paid	–	–	–	–	–	–	–	–		
Carry Forward Securities										
Carry Forward Securities	–	–	–	–	–	–	–	–	–	
	Total Offering Amounts							\$862,500,020	\$79,953.75	
	Total Fees Previously Paid								–	
	Total Fee Offsets								–	
	Net Fee Due								\$79,953.75	

- (1) Calculated in accordance with Rule 457(r) under the Securities Act of 1933, as amended (the “Securities Act”). The fee payable in connection with the offering pursuant to this prospectus supplement has been paid in accordance with Rule 456(b) under the Securities Act, and represents deferred payment of the registration fees in connection with the registrant’s Registration Statement on Form S-3ASR (Registration No. 333-239657).