Karuna Therapeutics Reports Fourth Quarter and Year End 2020 Financial Results and Provides General Business Update

February 25, 2021

Two Phase 3 trials, EMERGENT-2 and EMERGENT-4, initiated evaluating KarXT for the treatment of psychosis in adults with schizophrenia

Results from the Phase 2 EMERGENT-1 clinical trial of KarXT in schizophrenia published in the New England Journal of Medicine

First two cohorts from Phase 1b trial in healthy elderly volunteers complete, with results from Cohort 3 expected in the second quarter of 2021

Patent exclusivity granted on co-formulation compositions of KarXT through 2039

$322.3 million in cash, cash equivalents and available-for-sale investments expected to fund multiple potential milestones, including the completion of EMERGENT program and subsequent New Drug Application (NDA) submission

BOSTON--(BUSINESS WIRE)--Feb. 25, 2021-- Karuna Therapeutics, Inc. (NASDAQ: KRTX), a clinical-stage biopharmaceutical company driven to create and deliver transformative medicines for people living with psychiatric and neurological conditions, today announced financial results for the fourth quarter and year ended 2020 and provided a general business update.

“This past year was foundational for Karuna. We realized significant milestones and achievements including the initiation of the first Phase 3 trial in our EMERGENT program evaluating our lead asset, KarXT, in schizophrenia, the expansion of our internal drug discovery efforts, as well as establishing multiple strategic collaborations. We have experienced significant growth in our organization as we’ve nearly tripled in size to support our ongoing efforts and evolution to a late-stage clinical biotech company,” said Steve Paul, M.D., chief executive officer, president and chairman. “2021 is off to a great start with the initiation of our Phase 3 EMERGENT-4 clinical trial and the recent publication in the *New England Journal of Medicine* of our positive Phase 2 EMERGENT-1 data, insights from the first two cohorts of our Phase 1b trial in healthy volunteers, and our recently issued patent extending exclusivity of KarXT through at least 2039.”

“Looking ahead, 2021 is expected to be a year of execution and expansion for Karuna, as we anticipate having comprehensive registrational EMERGENT program for schizophrenia underway within the first half of the year, initiating a Phase 2 trial evaluating KarXT in adults with schizophrenia who inadequately respond to standard of care in the second half of 2021, and exploring KarXT’s potential to treat dementia-related psychosis pending results from the third cohort of our ongoing Phase 1b dose-ranging trial in healthy elderly volunteers,” Dr. Paul commented further. “These milestones and activities represent great progress in our journey to potentially deliver a completely novel treatment for those living with schizophrenia and other serious neuropsychiatric conditions.”

“We’re encouraged by the preliminary analysis of data from the first two completed cohorts in the Phase 1b healthy elderly volunteers trial. In this trial, healthy elderly volunteers achieved mean xanomeline blood levels comparable to, or slightly higher than, the mean xanomeline blood level reported in our EMERGENT-1 trial, which demonstrated clinically meaningful reduction of symptoms of psychosis in adults with schizophrenia,” said Stephen Brannan, M.D., chief medical officer. “Data from the two completed cohorts suggest that a lower ratio of trospium to xanomeline, compared to the ratios used in trials in healthy adult volunteers and in adults with schizophrenia, was better tolerated by healthy elderly volunteers. Thus, we believe that potentially therapeutic doses of KarXT can be administered to elderly adults using titration and flexible dosing while maintaining a favorable tolerability profile, providing a path to a Phase 2 trial evaluating KarXT in dementia-related psychosis.”

Pipeline Updates

KarXT, a proprietary oral modulator of muscarinic cholinergic receptors, is Karuna’s lead product candidate combining xanomeline, a novel muscarinic agonist, with trospium, a U.S. Food & Drug Administration approved muscarinic antagonist that does not appreciably cross the blood-brain-barrier, to preferentially stimulate muscarinic receptors in the central nervous system. KarXT is currently being evaluated as a potential treatment for neuropsychiatric conditions, including schizophrenia and dementia-related psychosis.

- **KarXT in schizophrenia.** The EMERGENT program, the clinical program evaluating KarXT for the treatment of acute psychosis in adults with schizophrenia, is underway. The EMERGENT program includes the previously completed positive Phase 2 efficacy and safety trial (EMERGENT-1), two Phase 3 trials evaluating efficacy and safety (EMERGENT-2 & EMERGENT-3), and two Phase 3 trials evaluating the long-term safety of KarXT (EMERGENT-4 & EMERGENT-5).
    - **The Company initiated EMERGENT-2 and EMERGENT-4 in December 2020 and the first quarter of 2021, respectively.** EMERGENT-3 and EMERGENT-5, the remaining trials in the EMERGENT program, are on track to initiate in the first half of 2021.
    - **The Company remains on track to initiate a Phase 2 trial evaluating KarXT for the treatment of psychosis in patients with schizophrenia who have an inadequate response to current standard of care therapies in the second half of 2021.** The trial will evaluate the efficacy and safety of KarXT when dosed in conjunction with background antipsychotic treatment and its potential to improve symptoms in patients who have not achieved an adequate response on their current antipsychotic treatment.
    - **Results from EMERGENT-1 published in the *New England Journal of Medicine (NEJM)***. The published manuscript titled “Muscarinic Cholinergic Receptor Agonist and Peripheral Antagonist for Schizophrenia,” is available online, and appears in the February 25, 2021 issue of *NEJM*.

- **KarXT in dementia-related psychosis.** The multi-cohort, placebo-controlled, inpatient Phase 1b dose-ranging trial evaluating the safety and tolerability of KarXT in healthy elderly volunteers is ongoing. The Company completed the first two cohorts in this trial, Cohorts 1 and 2, and expects data from the final cohort, Cohort 3, in the second quarter of 2021.
    - **The Company has completed data collection from Cohorts 1 and 2.** The two completed cohorts in the ongoing Phase 1b trial consisted of 16 healthy elderly volunteers each, randomized 3:1 to receive KarXT or placebo. As part of the flexible dosing protocol, a volunteer's dose was increased if they were tolerating KarXT well at the time of the potential dose increase, as determined by the clinician.
    - **In both cohorts, healthy elderly volunteers achieved mean xanomeline blood levels comparable to, or slightly higher than, the mean xanomeline blood levels reported in the EMERGENT-1 trial, which demonstrated a statistically significant reduction in total PANSS score in adults with schizophrenia.** The majority of healthy elderly volunteers in both cohorts were titrated to xanomeline doses of 150 to 200 mg when dosed with KarXT three times per day. Data from the two completed cohorts suggest that a lower dose ratio of trospium to xanomeline, compared to the ratios used in trials in healthy adult volunteers and in adults with schizophrenia, was better tolerated by healthy elderly volunteers.
    - **The cholinergic and anticholinergic adverse events (or AEs) seen in Cohorts 1 and 2 were similar to those observed in prior trials of KarXT.** The vast majority of AEs (>80%) were rated as mild. No syncopal events were observed. In Cohort 1, one serious adverse event (SAE) of urinary retention was reported related to the higher dose of trospium used in this cohort. In Cohort 2, which utilized a lower trospium dose, all AEs were rated mild or moderate in severity and there were no SAEs.
    - **Based on data from Cohorts 1 and 2, the Company believes that potentially therapeutic doses of KarXT can be administered to elderly adults while maintaining a favorable tolerability profile, providing a path to a Phase 2 trial evaluating KarXT in dementia-related psychosis.** Cohort 3 will serve to further refine the dose range of xanomeline and trospium and titration protocol. Planning for this Phase 2 trial in dementia-related psychosis has commenced and the Company expects to provide further guidance following the completion of Cohort 3 later this year.

Business Updates

- **The United States Patent and Trademark Office (USPTO) granted a new patent, extending exclusivity through 2039 with potential for patent term extension.** USPTO granted US Patent No. 10,925,832 related to compositions and methods for treating disorders ameliorated by muscarinic receptor activation, with an expiration date of September 27, 2039. This patent is directed to co-formulation compositions, dose levels of xanomeline and trospium, and pharmacokinetics.
- **Strengthened Board of Directors and management team through key appointments.** In December 2020, the Company announced the appointments of David Wheadon, M.D., former Senior Vice President, Global Regulatory Affairs, Patient Safety and Quality Assurance at AstraZeneca Pharmaceuticals, and Denice Torres, J.D., former Chief Strategy and Business Transformation Officer for the Medical Device division of Johnson & Johnson, to the Board of Directors. In January 2021, the Company appointed Ron Marcus, M.D., as Senior Vice President of Medical. In this role, Dr. Marcus will provide strategic and operational leadership of Karuna's clinical stage pipeline of novel neuropsychiatric medicines, including KarXT.
- **COVID-19 update.** The Company continues to monitor the impact of COVID-19 on operations and will provide relevant updates on its impact on activities as deemed appropriate.

Fourth Quarter and Full Year 2020 Financial Results

The Company reported a net loss of $24.0 million for the fourth quarter 2020, and a net loss of $68.6 million for the year ended 2020, as compared to $7.8 million and $44.0 million for the prior year periods, respectively. The increase in net loss for the year was due to higher research and development expenses related to the Company's preparation and initiation of the Phase 3 clinical trials within its EMERGENT program, increased employee headcount across the organization, and increased general and administrative expenses due to the impact of operating as a public company for the full year in 2020 relative to a partial year in 2019.

Research and development expenses were $15.6 million for the fourth quarter 2020, and $43.4 million for the year ended 2020, as compared to $5.0 million and $24.5 million for the prior year periods, respectively. The increase in research and development expenses for the year was primarily driven by expenses related to the Company's initiation of EMERGENT-2, and preparation for the initiation of the remaining Phase 3 trials within the EMRGENT program. The Company had additional expenses related to its Phase 1b trial in healthy elderly volunteers, increased personnel-related costs due to the increase in employee headcount, as well as expenses associated with the Company's discovery programs.

General and administrative expenses were $8.8 million for the fourth quarter 2020, and $28.4 million for the year ended 2020, as compared to $3.9 million and $20.9 million for the prior year periods, respectively. The increase in general and administrative expenses was primarily due to the impact of operating as a public company for the full year in 2020 relative to a partial year in 2019, as well as an increase in employee headcount.

The Company ended the year 2020 with $322.3 million in cash, cash equivalents and available-for-sale investment securities compared to $389.4 million as of December 31, 2019. The Company expects that current cash, cash equivalents, and available-for-sale investment securities as of December 31, 2020, will enable the Company to fund its operating expenses and capital expenditure requirements into 2023. This includes multiple potential clinical and development milestones, including an NDA submission of KarXT for the treatment of acute psychosis in patients with

schizophrenia pending the outcomes of the Company's planned EMERGENT clinical trials. Additional activities which may be funded include the initiation of the potential Phase 2 trial for the treatment of dementia-related psychosis and continued investment into pipeline expansion, including evaluating KarXT in patients with schizophrenia who have an inadequate response to standard of care therapies.

About Karuna Therapeutics

Karuna Therapeutics is a clinical-stage biopharmaceutical company driven to create and deliver transformative medicines for people living with psychiatric and neurological conditions. At Karuna, we understand there is a need for differentiated and more effective treatments that can help patients navigate the challenges presented by these severe and disabling disorders. Utilizing our extensive knowledge of neuroscience, we are harnessing the untapped potential of the brain in pursuit of novel pathways to develop medicines that make meaningful differences in peoples' lives. For more information, please visit www.karunatx.com.

Forward Looking Statements

This press release contains forward looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, including statements regarding our expectations about the timing of advancing of our planned clinical trials and regulatory filings, our goals to develop and commercialize our product candidates, our identification of additional product candidates, our liquidity and capital resources and other statements identified by words such as "could," "expects," "intends," "may," "plans," "potential," "should," "will," "would," or similar expressions and the negatives of those terms. Forward-looking statements are not promises or guarantees of future performance, and are subject to a variety of risks and uncertainties, many of which are beyond our control, and which could cause actual results to differ materially from those contemplated in such forward-looking statements. These factors include risks related to our limited operating history, our ability to obtain necessary funding, our ability to generate positive clinical trial results for our product candidates and other risks inherent in clinical development, the timing and scope of regulatory approvals, changes in laws and regulations to which we are subject, competitive pressures, our ability to identify additional product candidates, risks relating to business interruptions resulting from the coronavirus (COVID-19) pandemic, and other risks set forth under the heading "Risk Factors" of our Annual Report on Form 10-K for the year ended December 31, 2020. Our actual results could differ materially from the results described in or implied by such forward-looking statements. Forward-looking statements speak only as of the date hereof, and, except as required by law, we undertake no obligation to update or revise these forward-looking statements.

Karuna Therapeutics, Inc.
Unaudited Consolidated Statements of Operations
(in thousands, except share and per share data)

	Three Months Ended December 31,		Twelve Months Ended December 31,	
	2020	**2019**	**2020**	**2019**
Revenue	—	—	—	—
Operating expenses:				
Research and development	$ 15,584	$ 4,992	$ 43,408	$ 24,536
General and administrative	8,823	3,874	28,408	20,869
Total operating expenses	24,407	8,866	71,816	45,405
Loss from operations	(24,407)	(8,866)	(71,816)	(45,405)
Other income, net:				
Interest income	441	1,092	3,305	2,517
Interest income, net	—	—	—	11
Accretion of debt discount	—	—	—	(945)
Change in fair value of derivative	—	—	—	(135)
Total other income, net	441	1,092	3,305	1,448
Net loss before income taxes	(23,966)	(7,774)	(68,511)	(43,957)
Income tax provision	(43)	—	(43)	—
Net loss attributable to common stockholders	$ (24,009)	$ (7,774)	$ (68,554)	$ (43,957)
Net loss per share, basic and diluted	$ (0.89)	$ (0.32)	$ (2.59)	$ (3.68)
Weighted average common shares outstanding used in computing net loss per share, basic and diluted	26,883,923	24,430,145	26,446,006	11,958,152

Karuna Therapeutics, Inc.
Unaudited Consolidated Balance Sheet Data
(in thousands)

	December 31, 2020	December 31, 2019
Cash, cash equivalents and available-for-sale investments	$ 322,330	$ 389,397
Working capital	337,746	389,748
Total assets	347,625	393,024
Total stockholders' equity	$ 338,931	$ 389,916

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