Cara Therapeutics Announces Completion of Interim Statistical Assessment and Small Increase in Target Enrollment for KALM-2 Phase 3 Global Trial of KORSUVA™ Injection in Hemodialysis Patients with Pruritus

October 14, 2019

- Patient enrollment increased approximately 20% to maintain >90% statistical power -

- Full trial enrollment expected in fourth quarter of 2019 -

STAMFORD, Conn., Oct. 14, 2019 (GLOBE NEWSWIRE) -- Cara Therapeutics, Inc. (Nasdaq:CARA), a biopharmaceutical company focused on developing and commercializing new chemical entities with a primary focus on the treatment of pruritus by selectively targeting peripheral kappa opioid receptors, today announced the completion of an interim statistical assessment of its pivotal KALM-2 Phase 3 global clinical trial of KORSUVA ™ (CR845/difelikefalin) Injection in hemodialysis patients with moderate-to-severe chronic kidney disease-associated pruritus (CKD-aP).

Based on the Independent Data Monitoring Committee's (IDMC) recommendation, the size of the trial will be increased by approximately 20 percent, from an original enrollment target of 350 patients to 430 patients, to maintain the pre-specified statistical power of 90 percent or greater on the trial's primary endpoint. The IDMC charter allowed for the trial size to be increased up to a maximum of 500 patients. The IDMC's recommendation was based on the results of a prespecified interim conditional power assessment conducted after approximately 50 percent of the targeted patient number completed the designated 12-week treatment period.

"The IDMC recommendation to increase the target enrollment of KALM-2 aligns with our objective to maintain similar statistical power in this global trial to that of our positive KALM-1 US trial," said Derek Chalmers, Ph.D., D.Sc., President and Chief Executive Officer of Cara Therapeutics. "As we have already randomized a significant number of patients in KALM-2, beyond the initial target enrollment of 350, we expect the trial to be fully enrolled by the end of this quarter and remain on track to file our New Drug Application (NDA) for KORSUVA Injection for the treatment of moderate-to-severe CKD-aP in hemodialysis patients in the second half of 2020."

KALM-2 Phase 3 Trial Design

The Phase 3, global, multicenter, randomized, double-blind, placebo-controlled, 12-week trial (with a 52-week open label extension phase) is designed to evaluate the safety and efficacy of 0.5 mcg/kg KORSUVA (CR845/difelikefalin) Injection in 350 hemodialysis patients with moderate-to-severe pruritus.

The primary efficacy endpoint is the proportion of patients achieving at least a 3-point improvement from baseline in the weekly mean of the daily 24-hour Worst Itching Intensity Numeric Rating Scale (WI-NRS) score at week 12. Secondary endpoints include assessment of the proportion of patients achieving >4-point improvement from baseline in weekly mean of the daily 24-hour WI-NRS score at week 12 as well as itch-related quality of life changes measured using the validated self-assessment 5-D itch and Skindex-10 scales.

The pivotal KALM-1 Phase 3 US trial is complete and topline data were reported in May 2019. The trial met the primary endpoint, with a statistically significant improvement in the proportion of patients on KORSUVA Injection achieving a 3-point or greater improvement in the mean WI-NRS score versus placebo (p=0.000019). The trial also met all secondary endpoints and KORSUVA Injection was generally well-tolerated through 12 weeks of treatment with a safety profile consistent with prior clinical trials.

About Cara Therapeutics

Cara Therapeutics is a clinical-stage biopharmaceutical company focused on developing and commercializing new chemical entities designed to alleviate pruritus by selectively targeting peripheral kappa opioid receptors (KORs). Cara is developing a novel and proprietary class of product candidates, led by KORSUVA™ (CR845/difelikefalin), a first-in-class KOR agonist that targets the body's peripheral nervous system, as well as certain immune cells. In both Phase 3 and Phase 2 trials, KORSUVA Injection has demonstrated statistically significant reductions in itch intensity and concomitant improvement in quality of life measures in hemodialysis patients with moderate-to-severe chronic kidney disease-associated pruritus (CKD-aP). KORSUVA Injection is currently being investigated in pivotal Phase 3 trials in hemodialysis patients with CKD-aP. Oral KORSUVA is in Phase 2 trials for the treatment of pruritus in patients with CKD, atopic dermatitis and primary biliary cholangitis (PBC).

The FDA has conditionally accepted KORSUVA™ as the trade name for difelikefalin injection. CR845/difelikefalin is an investigational drug product and its safety and efficacy have not been fully evaluated by any regulatory authority.

Forward-looking Statements

Statements contained in this press release regarding matters that are not historical facts are "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Examples of these forward-looking statements include statements concerning the ongoing trials and future development of the Company's product candidates, including the timing for completion and reporting of topline results of Cara's KALM-2 Phase 3 clinical trial, the timing for filing an NDA, and the potential for KORSUVA to be a therapeutic option for pruritus. Because such statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements. Risks are described more fully in Cara's filings with the Securities and Exchange Commission, including the "Risk Factors" section of Cara's Annual Report on

Form 10-K for the year ended December 31, 2018 and its other documents subsequently filed with or furnished to the Securities and Exchange Commission. All forward-looking statements contained in this press release speak only as of the date on which they were made. Except to the extent required by law, Cara undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made.

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