# Cara Therapeutics Announces No Modifications in Trial Size for Phase 2 Trial of Oral KORSUVA™ in Chronic Kidney Disease Patients with Pruritus after Completion of Interim Statistical Assessment

July 22, 2019

***- Study now fully enrolled; topline data expected in 4Q 2019 -***

STAMFORD, Conn., July 22, 2019 (GLOBE NEWSWIRE) -- Cara Therapeutics, Inc. (Nasdaq:CARA), a biopharmaceutical company focused on developing and commercializing new chemical entities designed to alleviate pruritus by selectively targeting peripheral kappa opioid receptors, today announced the completion of an interim statistical assessment of its Phase 2 trial of Oral KORSUVA ™ (CR845/difelikefalin) for the treatment of pruritus in patients with stage III-V (moderate-to-severe) chronic kidney disease (CKD). In addition, the Company announced that the trial is now fully enrolled at 240 patients.

Based on the recommendation of the Independent Data Monitoring Committee (IDMC), the trial does not require any modifications to the original enrollment target of 240 patients. The IDMC's recommendation was based on the results of a prespecified interim conditional power assessment conducted after approximately 50% of the 240 patients had completed the designated 12-week treatment period.

"CKD-associated pruritus remains a significant unmet need for approximately one-third of diagnosed CKD patients in the United States," said Derek Chalmers, Ph.D., D.Sc., President and Chief Executive Officer of Cara Therapeutics. "We are very pleased with the IDMC's recommendation that the Phase 2 trial proceed as planned with no modifications. As with our KALM-1 Phase 3 trial, we commend our clinical team for designing a well-powered study that enrolled on schedule, and we look forward to reporting topline data from the trial in the fourth quarter."

**Phase 2 Trial Design**

The Phase 2, multicenter, randomized, double-blind, placebo-controlled, 12-week trial is designed to evaluate the safety and efficacy of three dose levels (0.25 mg, 0.5 mg and 1 mg, once daily) of Oral KORSUVA versus placebo in approximately 240 stage III-V CKD patients with moderate-to-severe pruritus.

The primary efficacy endpoint is the change from baseline in the weekly mean of the daily 24-hour Worst Itch Numeric Rating Scale (NRS) score at Week 12 of the treatment period. Secondary endpoints include change from baseline in itch-related quality of life scores at the end of Week 12, as assessed by the total Skindex-10 and 5-D itch scales, as well as the proportion of patients achieving an improvement from baseline ≥3 points with respect to the weekly mean of the daily 24-hour Worst Itch NRS score at Week 12.

**About CKD-Associated Pruritus (CKD-aP)**

CKD-aP is an intractable systemic itch condition that occurs with high frequency and intensity in patients with CKD undergoing hemodialysis and peritoneal dialysis. Pruritus has also been reported in patients with stage III-V CKD who are not on dialysis. According to estimates from the Centers for Disease Control and Prevention, approximately 15% of the adult population in the United States, or 30 million people, suffer from CKD, with an estimated 50% in stages III-V. Of the patients diagnosed with stage III-V CKD, approximately 25% suffer from moderate-to-severe pruritus. Recent data from the ITCH National Registry Study showed that among those with pruritus, approximately 59% experienced symptoms daily or nearly daily for more than a year. Given its association with CKD/end-stage renal disease, most afflicted patients will continue to have symptoms for months or years with currently employed antipruritic treatments, such as antihistamines and corticosteroids, which are unable to provide consistent adequate relief. Moderate-to-severe chronic pruritus has repeatedly been shown to directly decrease quality of life, contribute to symptoms that impair quality of life (such as poor sleep quality), and is associated with depression.

**References:**


1. Centers for Disease Control and Prevention: Chronic Kidney Disease (CKD) Surveillance Project. National Health and Nutrition Examination Survey. 2014.
2. Sukul N, et al. Pruritus in Chronic Kidney Disease Patients: Early Results from CKDopps. ERA-EDTA Abstract. December 2016.
3. IMS Pruritus Market Landscape Analysis. September 2014.
4. Mathur VS, et al. A longitudinal study of uremic pruritus in hemodialysis patients. Clin J Am Soc Nephrol. 2010; 5(8):1410-1419.


**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 reporting of topline data from the Phase 2 trial of Oral KORSUVA. 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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