Cara Therapeutics Announces Positive Topline Data From Phase 2 Trial of Oral KORSUVA™ in Chronic Kidney Disease Patients with Moderate-to-Severe Pruritus

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– Met primary endpoint with statistically significant reduction in mean worst itching intensity NRS scores with 1 mg tablet strength vs. placebo after 12-week treatment period (p=0.018) –
– Oral KORSUVA™ well-tolerated after 12 weeks of treatment –
– Conference call today at 8:30 a.m. ET –

STAMFORD, Conn., Dec. 03, 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 positive topline results from its Phase 2 dose-ranging trial of Oral KORSUVA™ (CR845/difelikefalin) for the treatment of pruritus in patients with stage III-V (moderate-to-severe) chronic kidney disease (CKD).

"CKD-associated pruritus remains a significant unmet need for approximately one-third of diagnosed CKD patients in the U.S.," said Derek Chalmers, Ph.D., D.Sc., President and Chief Executive Officer of Cara Therapeutics. "We are pleased that this Phase 2 study has successfully identified an appropriate tablet strength of Oral KORSUVA to carry forward into a pivotal Phase 3 registration program which we expect to initiate next year."

"These exciting results underscore Oral KORSUVA's potential to be the first approved therapy in the U.S. for CKD patients suffering from moderate-to-severe pruritus," said Gil Yosipovitch, M.D., Professor, Dr. Phillip Frost Department of Dermatology and Cutaneous Surgery and Director of the Miami Itch Center. "There is an unmet medical need for an effective long-term therapy for treating intractable pruritus and the results from this trial suggest Oral KORSUVA holds great promise for CKD patients."

Phase 2 Trial

The Phase 2, multicenter, randomized, double-blind, placebo-controlled 12-week trial was 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 vs. placebo (randomized 1:1:1:1) in approximately 240 stage III-V CKD patients with moderate-to-severe pruritus.

The primary efficacy endpoint was the change from baseline in the weekly mean of the daily 24-hour Worst Itching Intensity Numeric Rating Scale (WI-NRS) score at Week 12 of the treatment period for any of the three tablet strengths vs. placebo. Secondary endpoints included 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 of ≥3 points with respect to the weekly mean of the daily 24-hour Worst Itch NRS score at Week 12.

Primary Endpoint: Patients treated with the 1 mg tablet strength of Oral KORSUVA™ achieved the primary endpoint of statistically significant reduction in weekly mean of the daily WI-NRS scores vs. placebo after the 12-week treatment period (-4.4 KORSUVA vs. -3.3 placebo, p=0.018). The treatment effect was statistically significant after two weeks of treatment and sustained through the 12-week treatment period.

Secondary Endpoints: The proportion of patients on 1 mg tablet strength achieving a 3 point or greater improvement from baseline in the weekly mean of the daily WI-NRS score at week 12 was 72% vs. 58% for placebo but did not achieve statistical significance.

Patients on 1 mg tablet strength showed positive improvements vs. placebo in itch- related quality of life endpoints as measured using self-assessment Skindex-10 and 5-D Itch scales but did not achieve statistical significance.

Safety and Tolerability: Oral KORSUVA was generally well-tolerated with a safety profile consistent with that seen in earlier KORSUVA clinical trials. Overall, the incidence of treatment emergent adverse events (AEs) were similar across KORSUVA and placebo groups. The most common treatment emergent AEs reported in >5% of patients in the 1 mg KORSUVA group vs. placebo were dizziness (7.5% KORSUVA vs. 0% placebo), fall (6% KORSUVA vs. 0% placebo), diarrhea (6% KORSUVA vs. 1.5% placebo) and constipation (KORSUVA 6% vs. 3% placebo).

Conference Call

Cara management will host a conference call today at 8:30 a.m. ET to discuss the topline results of the trial.

To participate in the conference call, please dial (855) 445-2816 (domestic) or (484) 756-4300 (international) and refer to conference ID 8695654. A live webcast of the call can be accessed under "Events & Presentations" in the News & Investors section of the Company's website at www.CaraTherapeutics.com.

An archived webcast recording will be available on the Cara website beginning approximately two hours after the call.

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.[1] 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.[4]

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 planned Phase 3 registration trials of Oral KORSUVA, as well as the potential for Oral KORSUVA to be approved for treatment of CKD-associated 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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