Cara Therapeutics Doses First Patient in Second Pivotal Phase 3 Efficacy Trial of KORSUVA ™ (CR845/difelikefalin) Injection in Hemodialysis Patients with Chronic Kidney Disease-Associated Pruritus

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KALM™-2 trial to evaluate the efficacy of KORSUVA™ injection at 12 weeks

STAMFORD, Conn., Aug. 07, 2018 (GLOBE NEWSWIRE) -- Cara Therapeutics, Inc. (Nasdaq:CARA), a biopharmaceutical company focused on developing and commercializing new chemical entities designed to alleviate pruritus and pain by selectively targeting peripheral kappa opioid receptors, today announced the dosing of the first patient in its second pivotal Phase 3 efficacy trial (KALM™-2) of KORSUVA™ (CR845/difelikefalin) injection in hemodialysis patients suffering from moderate-to-severe chronic kidney disease-associated pruritus (CKD-aP). The global trial is expected to enroll hemodialysis patients in the U.S., Europe and some countries in the Pacific Rim region. The U.S. Food and Drug Administration (FDA) has granted Breakthrough Therapy designation to KORSUVA™ injection for this indication, for which there are currently no approved therapies in the U.S. or European Union (EU).

"The initiation of our second Phase 3 efficacy trial in dialysis patients with CKD-aP is an important step toward our goal of developing and commercializing KORSUVA injection as a potential novel treatment option for a patient population with significant unmet medical need," said Derek Chalmers, Ph.D., D.Sc., President and Chief Executive Officer of Cara Therapeutics. "We will continue to focus on patient enrollment in the coming quarters and expect data readouts from both our U.S. and global Phase 3 trials in 2019."

KALM-2 Phase 3 Trial Design

The Phase 3 international, multicenter, randomized, double-blind, placebo-controlled 12-week treatment trial (with a 52-week open label extension phase) is designed to evaluate the safety and efficacy of 0.5 mcg/kg 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 with respect to the weekly mean of the daily 24-hour worst itching intensity numeric rating scale (NRS) score at week 12. In a completed Phase 2 trial, the proportion of patients with an improvement from baseline in the weekly mean worst itching intensity NRS score of ≥3 points at week 8 was statistically significantly higher in the CR845/difelikefalin 0.5 mcg/kg group compared to the placebo group (64% vs. 29%; $p<0.01$)[1].

Secondary endpoints of the Phase 3 trial include assessment of itch-related quality of life changes measured using validated self-assessment 5-D Itch and Skindex-10 scales as well as the proportion of patients achieving > 4-point improvement from baseline in weekly mean of the daily 24-hour worst itching intensity NRS score at week 12.

About CKD-aP

CKD-aP is an intractable systemic itch condition that occurs with high frequency and intensity in patients with chronic kidney disease undergoing hemodialysis and peritoneal dialysis. Pruritus has also been reported in patients with stage III-V CKD who are not on dialysis. Aggregate, longitudinal, multi-country studies estimate the weighted prevalence of CKD-aP to be approximately 40 percent in patients with end-stage renal disease (ESRD), with approximately 25 percent of patients reporting severe pruritus. The majority of dialysis patients (approximately 60-70 percent) report pruritus, with 30 to 40 percent reporting moderate or severe pruritus.[2,3] Recent data from the ITCH National Registry Study showed that among those with pruritus, approximately 59 percent experienced symptoms daily or nearly daily for more than a year. Given its association with CKD/ESRD, most afflicted patients will continue to have symptoms for months or years, with currently employed antipruritic treatments, such as antihistamines and corticosteroids, 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] CKD-aP is also an independent predictor of mortality among hemodialysis patients, mainly related to increased risk of inflammation and infections.

References:

1. Data presentation at 2017 American Society of Nephrology's Annual Meeting (Kidney Week 2017).
2. Pisoni RL, et al. Pruritus in haemodialysis patients: international results from the Dialysis Outcomes and Practice Patterns Study (DOPPS). Nephrol Dial Transplant. 2006; 21:3495-3505.
3. Ramakrishnan K, et al. Clinical characteristics and outcomes of end-stage renal disease patients with self-reported pruritus symptoms. International Journal of Nephrology and Renovascular Disease. 2014; 7: 1-12.
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 and pain 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 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), and is currently being investigated in Phase 3 trials in hemodialysis patients with CKD-aP. Additionally, in a recently completed Phase 2/3 trial in post-operative patients, I.V. CR845/difelikefalin has demonstrated reduction in moderate-to-severe pain, while also reducing the incidence and intensity of nausea and vomiting throughout the post-operative period.

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 expected enrollment of the CR845/difelikefalin injection Phase 3 pivotal efficacy trials; the timing of data readouts for CR845/difelikefalin injection clinical trials; the ability of the clinical trials to demonstrate an extended patient benefit; and the potential for CR845/difelikefalin injection to be a therapeutic option for CKD-aP. 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 Therapeutics' filings with the Securities and Exchange Commission, including the "Risk Factors" section of the Company's Annual Report on Form 10-K for the year ended December 31, 2016 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. Cara Therapeutics 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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