Cara Therapeutics Announces Publication of Difelikefalin (KORSUVA™ Injection) KALM™-1 Phase 3 Trial Results in the New England Journal of Medicine

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- Treatment with KORSUVA Injection resulted in statistically significant reduction in pruritus intensity and improvement in itch-related quality of life measures vs placebo for both primary and secondary endpoints -

STAMFORD, Conn., Nov. 11, 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 that the *New England Journal of Medicine* (NEJM) published full results from the randomized, double-blind pivotal Phase 3 (KALM-1) trial of difelikefalin (KORSUVA ™ Injection) in patients undergoing hemodialysis with moderate-to-severe chronic kidney disease-associated pruritus (CKD-aP).

The paper, titled "A Phase 3 Trial of Difelikefalin in Hemodialysis Patients with Pruritus," summarizes data from 378 patients, randomized to receive intravenous bolus difelikefalin at a dose of 0.5 mcg/kg or placebo at the end of each dialysis session, administered over a 12-week treatment period. Overall, 51.9% of patients in the difelikefalin group achieved the pre-specified primary outcome of a three point or greater improvement in the weekly mean of the daily worst itch intensity numeric rating scale (WI-NRS) versus 30.9% in the placebo group at week 12. In an additional analysis conducted for NEJM, the imputed proportion of patients achieving the primary outcome was 49.1% in the difelikefalin group, as compared to 27.9% in the placebo group ($p<0.001$) at week 12. Difelikefalin treatment also resulted in statistically significant improvements in the proportion of patients achieving a four point or greater improvement in WI-NRS, as well as in itch-related quality of life measures, as assessed by the 5-D itch and Skindex-10 scales, from baseline to week 12. Diarrhea, dizziness, and vomiting were more common in the difelikefalin group than the placebo group, consistent with earlier clinical trials of difelikefalin in hemodialysis patients with CKD-aP.

"I am impressed by the clinically meaningful efficacy demonstrated in this Phase 3 trial of difelikefalin in hemodialysis patients with chronic pruritus," said Steven Fishbane, M.D., Chief, Division of Kidney Disease and Hypertension, Northwell Health, Professor of Medicine at Hofstra/Northwell, a KALM-1 clinical investigator and lead author of the NEJM paper. "Pruritus is a significant problem for many of our CKD patients undergoing hemodialysis and the present efficacy and safety data exhibited in this trial suggest that difelikefalin, if approved, has the potential to be an important drug to address this unmet need."

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.[1,2] 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.[3] CKD-aP is also an independent predictor of mortality among hemodialysis patients, mainly related to increased risk of inflammation and infections.

References:

1. 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.
2. 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.
3. 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, or 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 KORs located in the peripheral nervous system, and on immune cells. In a Phase 3 and two Phase 2 trials, KORSUVA (CR845/difelikefalin) Injection has demonstrated statistically significant reductions in itch intensity and concomitant improvement in pruritus-related quality of life measures in hemodialysis patients with moderate-to-severe CKD-aP and is currently being investigated in 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.

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 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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