Cara Therapeutics Announces Dosing of Patients in Phase 2 Trial of Oral KORSUVA ™ (CR845/difelikefalin) for Pruritus in Stage III-V Chronic Kidney Disease (CKD) Patients

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Completed Phase 1 trial establishes Oral KORSUVA tablet strengths for treatment of CKD-associated pruritus

STAMFORD, Conn., July 11, 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 that the first patients have been dosed in a Phase 2 trial of Oral KORSUVA (CR845/difelikefalin) for the treatment of pruritus in stage III-V (moderate-to-severe) CKD patients. CKD-associated pruritus (CKD-aP) is a condition that affects approximately 25% of pre-dialysis CKD patients, for which there are currently no approved therapies in the U.S.

Systemic Exposure in Patients with Moderate CKD With Once-Daily Dosing of Oral CR845

Data for oral dosing (tablet strengths of 0.25 mg 0.5 mg and 1.0 mg) represent the arithmetic mean +- SEM. Mean exposure (AUC) in hemodialysis patients (HD) is normalized to an equivalent 24-hour interval.

“The initiation of this Phase 2 trial in pre-dialysis CKD patients is an important milestone in the development of Oral KORSUVA as a potential novel treatment option for moderate-to-severe pruritus in this patient population,” said Derek Chalmers, Ph.D., D.Sc., President and Chief Executive Officer of Cara Therapeutics. “Throughout the remainder of this year, we plan to expand our clinical activities with Oral KORSUVA beyond CKD into additional patient populations, such as those with chronic hepatic and dermatologic conditions, in which treatment-resistant pruritus also remains a significant unmet medical need.”

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 sample size may be increased up to 480 patients (120 per treatment group) based on the results of an interim analysis that will be conducted when approximately 50% of the planned 240 patients have completed the 12-week treatment period.

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.

Top-Line Results from Phase 1 Pharmacokinetic Trial of Oral KORSUVA in Moderate-to-Severe CKD Patients

The Phase 1, open-label trial was designed to evaluate the safety and pharmacokinetic (PK) profile of once-daily doses of Oral KORSUVA administered over a period of one week to CKD patients with moderate or severe renal impairment. Once-daily dosing with Oral KORSUVA tablets of 0.25 mg, 0.5 mg or 1.0 mg was evaluated sequentially in three groups of patients with moderate renal impairment and three groups of patients with severe renal impairment (six groups total). PK blood samples were collected at prespecified time points during the treatment period after the study drug was administered. The graph below is representative of Day 1 exposure of Oral KORSUVA as represented by area under the curve (AUC).

The exposure levels demonstrated with Oral KORSUVA tablets were approximately equivalent to the exposure level achieved with 0.5 mcg/kg dose of I.V. KORSUVA that exhibited statistically significant and clinically meaningful reduction in itch intensity in hemodialysis patients with moderate to severe CKD-aP. The efficacy and safety data from the previous Phase 2 trial of I.V. KORSUVA in dialysis patients with CKD-aP were presented at the

2017 American Society of Nephrology's Annual Meeting.

A photo accompanying this announcement is available at http://www.globenewswire.com/NewsRoom/AttachmentNg/d02918dc-ebcf-4856-9197-5e53bf036a5f

About KORSUVA for the Treatment of CKD-Associated Pruritus (CKD-aP)

The U.S. Food and Drug Administration (FDA) has granted Breakthrough Therapy designation to I.V. CR845 for the treatment of moderate-to-severe pruritus in CKD patients undergoing hemodialysis. Breakthrough Therapy designation is granted to expedite the development and review process for new therapies addressing serious or life-threatening conditions where preliminary clinical evidence indicates that the drug candidate may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. There are currently no FDA-approved drugs for the treatment of CKD-aP.

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.

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:

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3. IMS Pruritus Market Landscape Analysis. September 2014.
4. 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.
5. Ramakrishnan, 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.
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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.

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 potential of Oral KORSUVA (CR845/difelikefalin) as a treatment for moderate-to-severe pruritus in stage III-V CKD patients, the planned expansion of clinical activities with Oral KORSUVA (CR845/difelikefalin) beyond CKD patients into additional populations, or the potential of Oral KORSUVA (CR845/difelikefalin) to be a treatment option for such patients. 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, 2017, 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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