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Cara Therapeutics Announces Summary Data From Phase 1 Trial of Oral CR845 in Hemodialysis Patients with Chronic Kidney Disease

Tablet strengths exhibiting appropriate plasma levels identified for potential use in general CKD-associated pruritus patients

STAMFORD, Conn., July 12, 2017 (GLOBE NEWSWIRE) -- Cara Therapeutics, Inc. (Nasdaq:CARA), a biopharmaceutical company focused on developing and commercializing new chemical entities designed to alleviate pain and pruritus by selectively targeting peripheral kappa opioid receptors, today announced summary results from its Phase 1 safety and pharmacokinetic trial of Oral CR845 in chronic kidney disease (CKD) patients undergoing hemodialysis.

The Phase 1 results showed that all four tablet strengths of Oral CR845 (0.25, 0.5, 1.0 and 2.5 mg) were generally well-tolerated when administered either daily or after dialysis three times per week. Top-line pharmacokinetic analysis indicated that plasma levels of CR845 attained after oral administration of doses up to 2.5 mg were comparable to or exceeded those attained with clinically efficacious intravenous (I.V.) doses of CR845 for the treatment of moderate-to-severe CKD-associated pruritus (CKD-aP) in hemodialysis patients. The plasma levels of CR845 attained after oral administration of the 1.0 mg tablet strength approximated those attained with the 1.0 mcg/kg I.V. CR845 dose, which demonstrated significant clinical benefit in the recently reported Phase 2/3 trial in hemodialysis patients with CKD-aP.

"We are pleased to establish that plasma levels of CR845 attained with oral tablets equaled or exceeded plasma levels previously associated with clinically efficacious I.V. CR845 doses in hemodialysis patients with moderate-to-severe CKD-associated pruritus," said Frédérique Menzaghi, Ph.D., Vice President of Research and Development at Cara Therapeutics. "These data will inform the design of our planned Oral CR845 pruritus clinical program in the non-dialysis CKD-aP population, which we aim to initiate later this year."

Phase 1 Trial Design and Results

The Phase 1 trial was a three-part, randomized, placebo-controlled study to evaluate the safety and pharmacokinetics of Oral CR845 tablets in 90 hemodialysis patients. In Part A, ascending repeated oral doses of 0.25, 0.5, 1.0 and 2.5 mg were given to four cohorts of patients (n=47) after each dialysis (i.e., three times) over a one-week treatment period. In Part B, ascending repeated oral doses of 0.25, 0.5 and 1.0 mg were given daily to three cohorts of hemodialysis patients (n=36). In Part C, the final crossover phase of the study, patients were administered a single 1.0 mg oral dose of CR845 or a single 1.0 mcg/kg I.V. dose of CR845 (n=7) given after hemodialysis with a one-week washout period between treatments to determine the absolute bioavailability of Oral CR845. Parts A and B randomized up to 12 patients per dose group (nine active and three placebo). Part C was conducted as an open-label phase with seven patients receiving active drug.

Overall, the frequency of treatment emergent adverse events (TEAEs) in CR845-treated patients was similar to the group administered placebo. All TEAEs were generally mild and comparable to those reported in the Phase 2/3 trial after I.V. CR845 administration in CKD-aP patients undergoing hemodialysis. Absolute oral bioavailability of the 1.0 mg tablet strength was determined to be similar in hemodialysis patients to that obtained in non-CKD patients.

About CR845 for the Treatment of CKD-associated Pruritus

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.

About CKD-associated Pruritus

CKD-aP is an intractable systemic itch condition that occurs with the greatest frequency and intensity in CKD patients undergoing hemodialysis and peritoneal dialysis; however, pruritus has also been reported in CKD patients who are not yet on dialysis. Aggregate, longitudinal, multi-country studies estimate the weighted prevalence of CKD-aP to be approximately

50 percent of patients with CKD stages 3-5 with approximately 25 percent of patients reporting moderate-to-severe pruritus. This represents approximately 4-5 million patients in the United States alone. Similarly, the majority of dialysis patients (approximately 60-70 percent) report pruritus, with 30 to 40 percent reporting moderate or severe pruritus. Recent data from the ITCH National Registry Study showed that among those with pruritus, 59 percent had 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 anti-pruritic treatments, such as anti-histamines 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. CKD-aP is also an independent predictor of mortality among hemodialysis patients, mainly related to increased risk of inflammation and infections.

About CR845

CR845 is a peripherally acting kappa opioid receptor agonist currently in development for the treatment of acute and chronic pain and pruritus. In more than 1,200 subjects dosed to date either intravenously or orally, CR845 was observed to be well-tolerated, without incurring the dysphoric and psychotomimetic side effects that have been reported with centrally acting (CNS-active) kappa opioid receptor agonists, and lacking the respiratory depression and abuse liability of mu opioid receptor agonists.

About Cara Therapeutics

Cara Therapeutics is a clinical-stage biopharmaceutical company focused on developing and commercializing new chemical entities designed to alleviate pain and pruritus by selectively targeting peripheral kappa opioid receptors. Cara is developing a novel and proprietary class of product candidates, led by CR845, that target the body's peripheral nervous system and have demonstrated initial efficacy in patients with moderate-to-severe pain without inducing many of the undesirable side effects typically associated with currently available pain therapeutics.

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 CR845's potential to treat CKD-aP, the establishment of the clinical utility of Oral CR845 and the future clinical development of Oral CR845, including the expected timing and design of any additional clinical trial(s). 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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