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Cara Therapeutics Announces Successful End-of-Phase 2 Meeting with FDA for I.V. CR845 in Chronic Kidney Disease-Associated Pruritus

Phase 3 pivotal program in hemodialysis patients expected to commence in Q4 2017

STAMFORD, Conn., Oct. 16, 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 the successful completion of its End-of-Phase 2 Meeting with the U.S. Food and Drug Administration (FDA). The Company, in consultation with the FDA, has established the key elements of the Phase 3 program to support a New Drug Application (NDA) for I.V. CR845 for the treatment of moderate-to-severe chronic kidney disease-associated pruritus (CKD-aP) in hemodialysis patients. The FDA previously granted Breakthrough Therapy designation to I.V CR845 for moderate-to-severe CKD-aP, for which there are currently no approved therapies in the United States (U.S.).

"We are very pleased with the productive guidance we have received from the FDA during our recent End-of-Phase 2 meeting," said Derek Chalmers, Ph.D., D.Sc., President and Chief Executive Officer of Cara Therapeutics. "We expect to initiate our pivotal Phase 3 program of I.V. CR845 for the treatment of CKD-aP in hemodialysis patients in the U.S. by the end of 2017, and will continue working closely with the agency to develop CR845 as a potential new therapeutic option for this highly debilitating aspect of CKD as quickly as possible."

The End-of-Phase 2 discussion was supported by positive top-line results from an eight-week clinical trial of I.V. CR845 in 174 hemodialysis patients with moderate-to-severe pruritus. The trial met both its primary endpoint, with a 68 percent reduction in worst itching scores versus placebo after an eight-week treatment period ($p < 0.0019$), and its secondary endpoint, with a 100 percent improvement in quality of life domains versus placebo ($p < 0.0007$). I.V. CR845 was well-tolerated in the trial.

About the Ongoing Safety Trial of I.V. CR845 in Hemodialysis Patients

The 52-week Phase 3 safety study, which was initiated in the second quarter of 2017, is enrolling hemodialysis patients with CKD-associated pruritus (CKD-aP) who previously completed one of the Company's prior studies (CR845-CLIN2101 Part A or CR845-CLIN2005 Part B). This open-label trial is evaluating the long-term safety of I.V. CR845 at the 0.5 mcg/kg dose, which met both primary and secondary efficacy endpoints (reduction of itch and improved quality of life, respectively) in the completed Phase 2 trial in hemodialysis patients with moderate-to-severe CKD-aP, and is the selected dose for the planned Phase 3 pivotal trial.

About CKD-aP

CKD-aP is an intractable systemic itch condition that occurs with the greatest frequency and intensity in chronic kidney disease 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 40 percent in patients with end-stage renal disease (ESRD), with approximately 24 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, 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 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 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 (KORs). Cara is developing a novel and proprietary class of product candidates, led by CR845, a first-in-class KOR agonist that targets the

body's peripheral nervous system. In Phase 2 trials, CR845 has demonstrated statistically significant reductions in itch intensity and concomitant improvement in quality of life measures in patients with moderate-to-severe chronic kidney disease-associated pruritus. Additionally, CR845 has demonstrated initial signs of efficacy in patients with moderate-to-severe pain, without inducing many of the undesirable side effects typically associated with currently available opioid pain therapeutics.

References

1. Pisoni RL, Wikstrom B, Elder SJ, 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 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

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 timing of the initiation of the company's planned pivotal Phase 3 efficacy trial for the treatment of CKD-aP in hemodialysis 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. Such risks include the risk that the planned clinical trial may not be initiated as expected based on delays, for example in onboarding the clinical trial sites and screening and enrolling candidates. Additional factors that could cause actual results to differ from those expressed or implied by forward-looking statements are described 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, 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. 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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