December 2, 2014

Cara Therapeutics Announces Positive Top-Line Results From Phase 1a / 1b Trial of Tablet Formulation of Oral CR845 for the Treatment of Acute and Chronic Pain

- *All tested tablet strengths pharmacologically active, safe and well tolerated after single and multiple dose administration*
- *Establishes dosing range and regimen for Phase 2 trial design*

SHELTON, Conn., Dec. 2, 2014 (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 kappa opioid receptors, today announced the successful completion of a Phase 1a / 1b clinical trial of an oral tablet formulation of its peripherally-selective kappa opioid agonist, CR845, for the treatment of acute and chronic pain.

The double-blind, randomized, placebo-controlled trial evaluated the pharmacokinetic and safety profile of single and multiple escalating doses of Oral CR845 in 150 healthy volunteers at a single U.S. site. The single ascending dose study, which included six tablet strengths ranging from 0.1 mg to 10 mg, demonstrated a mean oral bioavailability of 10% across all dose groups under fasting conditions, with a range of maximum plasma concentrations of CR845 bracketing the concentrations seen in previously successful Phase 2 trials with I.V. CR845. All tested dose strengths were also shown to be active at the kappa opioid receptor, as assessed by statistically significant ($p < 0.0001$) acute changes in blood measurements of an established neuroendocrine biomarker.

The multiple ascending dose study, which used repeat dose studies of the 0.1 mg, 1 mg and 5 mg tablets, administered twice a day (b.i.d.) for one week, demonstrated that all tablet doses were well tolerated with no serious adverse events (SAEs) reported and all adverse events (AEs) were mild and generally similar to those reported with I.V. CR845. Additionally, clinical safety laboratory measurements were normal across all tablet strengths after single or repeat dosing.

"Successful completion of this Phase 1 trial of the tablet formulation of Oral CR845 represents a key milestone for Cara as we look to expand the clinical development of CR845 beyond the treatment of acute pain in a hospital setting," said Derek Chalmers, Ph.D., D.Sc., President and Chief Executive Officer of Cara Therapeutics. "We are very encouraged that the plasma levels of CR845 attained within this tablet strength range equaled or exceeded those previously associated with clinical analgesic effects seen in acute post-operative pain models with I.V. CR845."

Dr. Chalmers also noted, "These findings complement our recently successful human abuse liability study of I.V. CR845, as well as our recently completed quantitative primary research study indicating that Oral CR845 has the potential to meet a significant physician demand for a safer, non-abusable alternative to narcotic opioids and NSAIDs for the treatment of moderate-to-severe acute and chronic pain."

About CR845

CR845 is a peripherally acting kappa opioid receptor agonist currently in development for the treatment of acute and chronic pain. In multiple randomized, double blind, placebo-controlled Phase 2 trials in patients undergoing laparoscopic hysterectomy or bunionectomy procedures, I.V. CR845 treatment resulted in statistically significant reductions in pain intensity and opioid-related side effects. In over 400 subjects dosed to date, I.V. CR845 was found to be safe and well tolerated, without incurring the dysphoric and psychotomimetic side effects that have been reported with centrally acting (CNS-active) kappa opioid receptor agonists. In a human abuse liability trial, I.V. CR845 met the primary endpoint showing highly statistically significant reductions ($p < 0.0001$) in scores for "drug liking," as well as "feeling high," "overall liking," and "take drug again" when compared to I.V. pentazocine, a Schedule IV opioid analgesic.

About Tablet Formulation of Oral CR845

The oral tablet formulation of CR845 was synthesized utilizing the peptide formulation technology developed by Enteris Biopharma under a Manufacturing and Clinical Supply Agreement.

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 kappa opioid receptors. Cara is developing a novel and

proprietary class of product candidates that target the body's peripheral nervous system and have demonstrated 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 the Company's planned Phase 2 clinical trial of the tablet formulation of oral CR845, potential ability of oral CR845 to meet significant physician demand, the likelihood of physicians prescribing oral CR845 if regulatory approval is received, and the potential future regulatory and development milestones for the Company's product candidates. 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, 2013 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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