April 3, 2012

Cara Therapeutics Successfully Completes Phase I Study With Oral Formulation of Its Novel Kappa Opioid Receptor Agonist, CR845

- robust bioavailability and pharmacologic activity seen with oral formulation of peptide-based Kappa Opioid Agonist -

SHELTON, Conn., April 3, 2012 — Cara Therapeutics, Inc. today announced the successful completion of a first-in-man Phase I clinical trial of an oral formulation of its peptide-based, peripherally-restricted kappa opioid receptor agonist, CR845. The trial was a single-center, double-blind, placebo-controlled study to evaluate the pharmacokinetics (PK), safety and pharmacodynamics of CR845 in healthy volunteers. An intravenous formulation of CR845 is currently in clinical development for the treatment of acute postoperative pain. The company recently completed enrollment of a 200-patient Phase II study with topline data expected in Q2, 2012.

In the oral Phase I study, a total of 50 male volunteers were randomized to receive either placebo or one of four single ascending doses of an enteric-coated, capsule formulation of CR845. The study demonstrated a mean oral bioavailability of 16% across all groups under fasting conditions, with peak and total exposures proportional to each dose. Peripheral kappa opioid receptor activation was seen at all doses tested as measured by a standard biomarker. Additionally, orally administered CR845 appeared to be safe and generally well tolerated across all doses tested and, as seen with the IV formulation, did not produce any of the dysphoric or psychomimetic side effects that have precluded the clinical development of centrally acting kappa opioid agonists.

"We are very impressed with the bioavailability and bioactivity exhibited by this oral formulation of CR845," said Dr. Frederique Menzaghi, V.P. of R&D at Cara Therapeutics. "The results of this Phase I trial have confirmed appropriate pharmacokinetic, pharmacodynamic and safety characteristics of this formulation and provide a basis for further clinical development."

"As we continue the development of IV CR845 for in-hospital treatment of postoperative pain, we are encouraged to confirm the potential viability of an oral formulation to provide a step-down therapy for continued pain relief following discharge," said Derek Chalmers, CEO of Cara Therapeutics. "These oral data also open up a much broader market opportunity for CR845 in the treatment of chronic pain for which there continues to be a very large unmet need for new and safer treatment modalities."

About CR845
CR845 is a highly selective, peptide-based, peripherally-restricted kappa opioid receptor agonist currently in development for the treatment of acute and chronic pain. In a previous randomized, placebo-controlled Phase II study, CR845 demonstrated evidence of analgesic efficacy when administered as a single intravenous dose to women following laparoscopic hysterectomy. In addition to decreases in reported pain levels, patients receiving CR845 required substantially lower amounts of post-operative opioids (narcotics) and showed a significant reduction in the incidence of post-operative nausea and vomiting. A multicenter, double-blind, randomized, placebo-controlled 200-patient Phase II trial to evaluate the efficacy and safety of intravenous CR845 when administered both pre and post-operatively in women undergoing laparoscopic hysterectomy has completed enrollment with topline data expected in Q2, 2012.

About Oral CR845 & Unigene
In general, clinical development of orally active peptide drugs has been limited by their physicochemical properties (i.e., high polar surface area and limited membrane permeability) and their susceptibility to enzyme breakdown. To overcome this challenge, and enhance the oral bioavailability of CR845, the compound was formulated by Unigene Laboratories using their peptide formulation technology under a Manufacturing and Clinical Supply Agreement.

About Unigene Laboratories
Unigene has designed and developed a validated, proprietary oral formulation delivery technology, Peptelligence™ with prove success in a Phase 3 clinical trial evaluating oral calcitonin and a Phase 2 proof-of-concept study with a positive outcome evaluating an oral parathyroid hormone analog. In addition, the Company currently has nine feasibility studies ongoing or completed across a broad spectrum of therapeutic areas.

About Cara Therapeutics
Cara Therapeutics is a privately held biotechnology company focused on developing novel, superior therapeutics to treat pain and inflammation associated with diverse medical conditions. Cara's pipeline includes near-term clinical drug candidates identified as mechanistically distinct, peripherally-acting analgesics.

Forward-Looking Statements
Certain statements in this press release are forward-looking statements that involve a number of risks and uncertainties. Such forward-looking statements include statements relating to the therapeutic applications of CR845 and about Cara's strategy, technologies, pre-clinical and clinical programs, and ability to identify and develop drugs, as well as other statements that are not historical facts. Actual events or results may differ materially from Cara's expectations. Factors that could cause actual results to differ materially from the forward-looking statements may include, but are not limited to, the timing, success and cost of Cara's research and clinical studies and Cara's ability to obtain additional financing. These forward-looking statements represent Cara's judgment as of the date of this release. Cara disclaims any intent or obligation to update these forward-looking statements.

Source: Cara Therapeutics, Inc.