



August 3, 2011

## **Cara Therapeutics Initiates Phase II Trial of Novel Analgesic In Acute Post-Operative Pain**

### **Peripherally-Acting Kappa Opioid Agonist, CR845, to Be Studied in Both Pre- and Post-Operative Drug Regimens**

Cara Therapeutics, Inc. today announced the dosing of the first patient in a Phase II clinical trial of its peripherally-selective, kappa opioid agonist, CR845, for the treatment of acute post-operative pain. The double-blind, placebo-controlled trial is expected to enroll a minimum of 200 patients at multiple clinical sites in the United States, and will evaluate the efficacy and safety of intravenous CR845 administered both pre- and post-operatively in women undergoing laparoscopic hysterectomy. This trial follows the successful completion of a 46 patient, multi-center, double-blind Phase II study of CR845, in the same surgical population, where both analgesic and opioid-sparing effects of CR845 were demonstrated and the drug was found to be safe and well tolerated after a single post-operative dose.

"Initiation of this Phase II trial represents an important advancement in the clinical development of CR845 and will further our understanding of the optimal dosing regimen for the drug in the treatment of acute post-operative pain," said James B. Jones, M.D. Pharm. D., Chief Medical Officer of Cara Therapeutics. "There remains a significant unmet need among surgical patients for an effective analgesic which greatly reduces the need for centrally-acting opioids and their associated adverse effects, such as nausea and vomiting. We believe that CR845 has the potential to become a new standard in the treatment of post-operative pain."

"This trial is of particular importance as it will reinforce previous positive Phase II results for CR845 in a single-dose postoperative pain study," said Timothy Melson, M.D., study Principal Investigator, Anesthesiologist and pain management specialist, at Helen Keller Memorial Hospital in Sheffield, AL. "As a clinical investigator who has assessed the effects of many different analgesics in women undergoing hysterectomy, I am excited at the prospect of deploying this new class of drug that has been previously shown to substantially decrease the need for postoperative opioids, as well as greatly reduce the incidence of postoperative nausea & vomiting; two of the most troubling side effects experienced by patients using currently available analgesics. The goal of this study is to now find the most effective way to use CR845 in this patient population"

#### **About CR845**

CR845 is a highly selective, peripherally-restricted kappa opioid receptor agonist currently in development for the treatment of post-operative pain. In a 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. Cara recently completed a Phase 1b repeat dose safety study of intravenous CR845 and plans to complete a Phase 1 safety and pharmacokinetic study of an oral capsule formulation of CR845 later this year. More than 140 human subjects have been exposed to CR845 to date, with no cases of dysphoric reactions or hallucinations that are seen with centrally-acting kappa opioids.

#### **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 current 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.

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