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Cara Therapeutics Reports Positive Results from Phase II Trial of Novel Peripheral Kappa Agonist, CR845, in Acute Post-Operative Pain

- Statistically significant decreases in morphine use and pain intensity demonstrated in 24-hour period after surgery with pre- and post-operative administration of CR845 -

PRNewswire -- Cara Therapeutics, Inc. today announced positive results from a Phase II study for the treatment of acute post-operative pain with its novel, peptide-based, peripherally-acting kappa opioid agonist, CR845. The study successfully met its primary endpoint which measured the effect of CR845 treatment on reducing the amount of rescue opioid analgesics used in the 24 hour period post-surgery, as well as secondary endpoints which evaluated the ability of CR845 to reduce postoperative pain as assessed by a number of standard measures, including pain intensity differences (PIDs), summed pain intensity differences (SPIDs), and patient evaluation of study medication over the post-surgical 24-hour period.

The Phase II study was a double-randomized, double-blind, placebo-controlled study of intravenous CR845 (0.04mg/kg/dose) in women undergoing a laparoscopic hysterectomy. The trial was conducted at 22 sites across the U.S., and enrolled 203 patients who were randomized into four treatment arms: (1) both a pre-and a post-operative dose of CR845; (2) a single pre-operative dose of CR845; (3) a single post-operative dose of CR845; and (4) both pre- and post-operative placebo. Patients receiving both a pre- and postoperative dose of CR845 achieved the study's primary endpoint by exhibiting a statistically significant reduction (~33%, $p<0.05$) of morphine use over 24 hours compared to the placebo group. This patient group also exhibited an approximately twofold (~100%) increase in their calculated 24 hour PID0-24 ($p=0.002$) and SPID0-24 ($p=0.003$) values compared to placebo-treated subjects. Significant 24-hour analgesic effects were also seen in patients receiving a single post-operative dose of CR845 where SPID0-24 values ($p=0.014$) increased by more than 50% when compared to placebo. Global evaluation of study medication by all patients indicated a significant treatment effect of CR845 ($p=0.006$), with 80% of subjects receiving a pre- and post-operative dose of CR845 rating the drug as good-to-excellent. Pre- and/or post-surgical dosing of CR845 was safe and well tolerated, and was generally associated with a decreased incidence of the common opioid-related side effects of nausea, vomiting and pruritus. Importantly, CR845 did not produce any of the CNS-related effects seen with centrally-acting kappa opioid agonists.

“The results of this Phase II trial have further confirmed the robust analgesic efficacy of CR845 in this acute post-operative setting,” said James B. Jones, M.D., Pharm. D., Chief Medical Officer of Cara Therapeutics. “Moreover, these data have established the clear clinical advantage of dosing CR845 before and after surgery in significantly reducing the severity of patient pain and the need for opioid rescue medication in the first 24 hours post-surgery.”

Dr. Tong J. Gan, study Principal Investigator, Professor of Anesthesiology & Vice Chair for Clinical Research at Duke University commented: “Postoperative pain is still poorly managed and there is a need for novel anti-inflammatory and analgesic drugs for perioperative pain management. These results indicate that this new class of antiinflammatory/ analgesic can potentially be used in a multimodal analgesic strategy, including preoperative dosing, to improve postoperative pain and reduce the need for morphine and other opioids.”

“This trial with CR845 has clearly demonstrated that a peripherally-selective kappa opioid agonist is a fundamentally new and viable option for the treatment of acute postop pain,” said Derek Chalmers, Ph.D., President and CEO at Cara. “We have now treated over 300 patients with CR845 and have not seen any of the psychiatric side effects that have precluded the development of centrally-acting kappa opioid agonists. Additionally, we now have strong evidence of the clinical benefit of pre-operative dosing of CR845 which is a key differentiating aspect of our product as NSAIDs are no longer used in this setting due to the increased risk of bleeding.”

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 and pruritus. In addition to the development of an intravenous (IV) formulation of CR845 for hospital use, Cara has recently completed a successful Phase I study of an oral capsule formulation of CR845 suitable for clinical development for the treatment of postoperative pain following hospital discharge, as well as chronic inflammatory pain conditions. CR845 has been found to be safe and well tolerated in the more than 300 patients dosed to date, with no cases of dysphoric reactions or hallucinations that have been reported with centrally-acting, non-peptidic kappa opioid agonists.

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 forwardlooking statements.

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