

BIO WORLD[®] TODAY

THURSDAY
JULY 22, 2010

THE DAILY BIOTECHNOLOGY NEWSPAPER

VOLUME 21, No. 140
SPECIAL REPRINT

Cara Banks \$15M for Pursuit of Nonaddictive Pain Drug

By Donna Young
Washington Editor

The \$15 million Series D financing Cara Therapeutics Inc. closed this week will go a long way toward advancing the development of its peripherally restricted kappa opioid agonist CR845, said CEO Derek Chalmers.

Because of its unique mechanism of action, CR845 provides opioid-like pain relief without the gastrointestinal reactions and adverse central nervous system (CNS) effects, including addiction, plaguing narcotics currently marketed for pain, Chalmers told *BioWorld Today*.

"This is entirely a different class of molecules than classic narcotics," he explained. "This molecule doesn't interact with opioid receptors in the brain. It acts directly on kappa receptors very selectively on peripheral nerve endings and on immune cells."

Indeed, Cara's experimental drug potentially could make obsolete the pursuit by drugmakers, such as Acura Pharmaceuticals Inc., King Pharmaceuticals Inc. and Pain Therapeutics Inc., of a tamper-resistant opioid or products aimed at deterring abuse, which so far have been mostly fruitless endeavors. (See *BioWorld Today*, Sept. 11, 2008.)

Acura in April saw its shares plummet 32 percent after an FDA advisory panel refused to back approval of the firm's investigational pain drug Acurox (oxycodone HCl and niacin), voting 19 to 1 that data were insufficient to show that the niacin additive and mixture of functional excipients could effectively deter potential abuse of the oxycodone medication. (See *BioWorld Today*, April 21, 2010, and April 26, 2010.)

King and its partner Pain Therapeutics also have pursued development of an opioid aimed at deterring abuse with Remoxy, but the FDA in December 2008 rejected the drug and called for more data. King expects to resubmit the drug's application in the fourth quarter. (See *BioWorld Today*, Nov. 14, 2008, and Dec. 12, 2008.)

Only Purdue Pharma LP has been somewhat successful with achieving the tamper-resistant claim of an opioid with the approval in April of its reformulated version of OxyContin. Although Bob Rappaport, director of the FDA's Division of Anesthesia and Analgesia Products, said the medicine's tamper-resistant properties were "limited." (See

BioWorld Today, April 7, 2010.)

CR845, which has an analgesic effect and anti-inflammatory activity, also is likely to escape the FDA's mandate for a classwide risk evaluation and mitigation strategy plan for extended-release and long-acting opioid analgesics - the topic of a two-day joint meeting of the agency's Anesthetic and Life Support Drugs and Drug Safety and Risk Management Advisory Committees, starting Thursday. (See *BioWorld Today*, Feb. 17, 2009, June 1, 2009, and Dec. 7, 2009.)

Cara's chances of taking control of the market for peripherally restricted kappa opioid agonists are pretty good, considering there currently are no products sold in the U.S. in that class or with that mechanism of action - putting the Shelton, Conn.-based biotech out front of any potential competitors.

The only drug on the market that has kappa agonist activity is Remitch (nalfurafine), which was approved in January 2009 in Japan as a therapy to improve pruritus in hemodialysis patients for cases resistant to conventional treatments.

Remitch, however, is not peripherally selective, Chalmers noted.

Tioga Pharmaceuticals Inc. also has a kappa opioid receptor agonist in Phase III development: asimadoline, for diarrhea-predominant irritable bowel syndrome. But that product also is not peripherally selective, and consequently, likely comes with CNS-related adverse effects, Chalmers added.

Cara's CR845 currently is in Phase II development for the treatment of postoperative pain. Randomized, placebo-controlled Phase IIa studies have provided evidence of analgesic efficacy of CR845 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 postoperative opioids for 16 hours and showed a significant reduction in the incidence of postoperative nausea.

Cara expects to complete a Phase Ib repeat-dose safety

©2010. Reprinted With Permission From BioWorld[®] Today, Atlanta, Georgia.

study of CR845 by the fourth quarter, following up with a Phase IIb repeat-dose efficacy study in laparoscopic hysterectomy patients, Chalmers said.

He noted that more than 100 patients have been exposed to CR845, with no reports of dysphoric reactions or hallucinations.

"We don't have a euphoric effect," Chalmers said. "It doesn't produce the classic CNS side effects you'd see with a morphine or fentanyl-type drugs, so we don't see respiratory suppression, any sedation, and very importantly, we don't see any nausea and vomiting, which is important in an acute setting."

Additionally, CR845 also has not been associated with any chronic constipation-type responses, which is an

adverse effect experienced by many patients taking opioid drugs, he said.

Cara also is developing oral and subcutaneous formulations of CR 845 as treatments for chronic inflammatory and neuropathic pain conditions, such as arthritis and diabetes-associated neuropathy, Chalmers said.

To date, the small biotech has raised \$58 million. The Series D round was led by new investor, Rho Ventures, with participation from previous investors Alta Biopharma, Ascent Biomedical Ventures, CT Innovations, Devon Park BioVentures, Healthcare Private Equity, Mitsubishi International Corp. and MVM Life Science Partners. In conjunction with the financing, Martin Vogelbaum, a partner at Rho Ventures, will join Cara's board. ■