CR845 is a peripherally-acting kappa opioid receptor agonist that is associated with pain relief and has potential for abuse.

**Results:**

Drug liking VAS (VAS) was the primary measurement and was assessed periodically between 5 minutes to 8 hours after dosing.

**Main Outcome Measures:**

- Drug liking VAS scores (MITT)
- Demographics (MITT)
- Other assessments

**Objectives:**

The results of this clinical study suggest that CR845, a novel and selective peripherally restricted kappa opioid receptor agonist, may present a low risk for abuse in humans.

**Methods:**

**Patients:**

- 18 to 50 years old
- Opioid user (not currently physically dependent based on naloxone challenge tests)

**Interventions:**

- Single-center, randomized, double-blind, active- and placebo-controlled, 4-way crossover study
- Subjects received a single bolus IV dose of the following treatments in random order: Placebo, CR845 5 mcg/kg, CR845 15 mcg/kg, Pentazocine 0.5 mg/kg

**Analysis:**

- Each outcome variable was analyzed by analysis of variance using a modified intent-to-treat (MITT) population and was based on guidance from the Food and Drug Administration (FDA) regarding the evaluation of this type of study.

**Conclusions:**

- Overall Drug Liking and Take Drug Again VAS scores were significantly greater than for the other 3 treatments (CR845 5 mcg/kg, CR845 15 mcg/kg, and Placebo)

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**Conflict of Interest:**

Facial pain, masticatory muscle pain, trigeminal neuralgia, and tempomandibular joint pain were statistically significantly greater than placebo. All comparisons are p ≤ 0.0005. No significant difference was found for comparisons between placebo, CR845 5 mcg/kg, and CR845 15 mcg/kg periods compared with each of the other 3 treatments.

**Figure 1. Study Schedule of Events**

- Drug liking VAS scores were statistically significantly greater than the other 3 treatments (Placebo, CR845 5 mcg/kg, CR845 15 mcg/kg) and were significantly lower than Emax values with Placebo and CR845 5 mcg/kg periods compared with each of the other 3 treatments (CR845 15 mcg/kg, Placebo).

**Figure 2. Drug Liking VAS Scores (MITT)**

- The primary analysis population was the Modified-Intent-to-Treat (MITT) population.

**Figure 3. Drug Liking Visual Analog Scale (VAS) Primary Endpoint**

- The primary endpoint variable was the maximum Drug Liking score during the 8 hours after dosing (Emax).

**Figure 4. Maximum Drug Liking VAS Scores (primary endpoint; MITT)**

- Each outcome variable was analyzed by analysis of variance using a modified intent-to-treat (MITT) population and was based on guidance from the Food and Drug Administration (FDA) regarding the evaluation of this type of study.

**Figure 5. Overall Drug Liking VAS Scores (MITT)**

- Overall Drug Liking and Take Drug Again VAS scores were significantly greater than for the other 3 treatments (CR845 5 mcg/kg, CR845 15 mcg/kg, and Placebo).

**Figure 6. Take Drug Again VAS Scores (MITT)**

- The study was statistically significantly greater than Placebo and CR845 5 mcg/kg periods compared with each of the other 3 treatments (CR845 15 mcg/kg, Placebo) and was significantly lower than Emax values with Placebo and CR845 5 mcg/kg periods compared with each of the other 3 treatments (CR845 15 mcg/kg, Placebo).

**Figure 7. Overall Drug Liking VAS Scores (primary endpoint; MITT)**

- Overall Drug Liking and Take Drug Again VAS scores were significantly greater than for the other 3 treatments (CR845 5 mcg/kg, CR845 15 mcg/kg, and Placebo).

**Table 1. Patients With Treatment-Related Adverse Events Reporting in 2 or More Patients That Occurred During the Double-Blind Treatment Period**

- The study was statistically significantly greater than Placebo and CR845 5 mcg/kg periods compared with each of the other 3 treatments (CR845 15 mcg/kg, Placebo) and was significantly lower than Emax values with Placebo and CR845 5 mcg/kg periods compared with each of the other 3 treatments (CR845 15 mcg/kg, Placebo).

**Table 2. Patients With Treatment-Related Adverse Events Reporting in 2 or More Patients That Occurred During the Double-Blind Treatment Period**

- The study was statistically significantly greater than Placebo and CR845 5 mcg/kg periods compared with each of the other 3 treatments (CR845 15 mcg/kg, Placebo) and was significantly lower than Emax values with Placebo and CR845 5 mcg/kg periods compared with each of the other 3 treatments (CR845 15 mcg/kg, Placebo).

**Table 3. Safety Results**

- The study was statistically significantly greater than Placebo and CR845 5 mcg/kg periods compared with each of the other 3 treatments (CR845 15 mcg/kg, Placebo) and was significantly lower than Emax values with Placebo and CR845 5 mcg/kg periods compared with each of the other 3 treatments (CR845 15 mcg/kg, Placebo).

**Figure 8. Overall Drug Liking VAS Scores (primary endpoint; MITT)**

- Overall Drug Liking and Take Drug Again VAS scores were significantly greater than for the other 3 treatments (CR845 5 mcg/kg, CR845 15 mcg/kg, and Placebo).

**Figure 9. Take Drug Again VAS Scores (MITT)**

- The study was statistically significantly greater than Placebo and CR845 5 mcg/kg periods compared with each of the other 3 treatments (CR845 15 mcg/kg, Placebo) and was significantly lower than Emax values with Placebo and CR845 5 mcg/kg periods compared with each of the other 3 treatments (CR845 15 mcg/kg, Placebo).