

## **BEMA<sup>®</sup> BUPRENORPHINE PRODUCED EFFECTIVE ANALGESIA IN A PHASE 2 PLACEBO-CONTROLLED TRIAL IN SUBJECTS WITH SEVERE PAIN FOLLOWING DENTAL EXTRACTION (POST HOC ANALYSIS)**

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### **Purpose**

BEMA<sup>®</sup> Buprenorphine (BEMA-Bup), a small, bilayered, dissolvable polymer film formulated with the Schedule III opioid buprenorphine, employs the BioErodible MucoAdhesive (BEMA<sup>®</sup>) delivery system for transmucosal delivery of buprenorphine when the BEMA-Bup film is applied to the inside of the cheek. BEMA-Bup is being developed for the treatment of moderate to severe pain. In this double-blind Phase 2 study, BEMA-Bup produced effective analgesia versus placebo in subjects with at least moderate pain following dental extraction. In this *post hoc* analysis from that trial, analgesic efficacy of BEMA-Bup versus placebo was examined in the subset of subjects with severe baseline pain.

### **Method**

In a randomized, double-blind, double-dummy, parallel-group study, subjects with  $\geq$  moderate postsurgical (baseline) pain on a 4-point categorical scale and  $\geq 5$  on a 0- to 10-point Numeric Rating Scale (NRS) within 5 hours of completing a third molar extraction under local anesthesia received **placebo** (n=30); **BEMA-Bup 0.25 mg Formulation 2** ("low" dose; n=31); **BEMA-Bup 0.5 mg Formulation 2** ("medium" dose; n=30); **BEMA-Bup 0.5 mg Formulation 1** ("high" dose; n=31); or **oxycodone 5 mg** (overencapsulated oral tablet, active control; n=31). The bioavailability of Formulation 2 is approximately 63% that of Formulation 1, a difference that accounts for the distinction between the high dose and the medium dose. Analgesic assessments were recorded at predetermined time points through 24 hours postdose. In a *post hoc* analysis, analgesic efficacy was evaluated in subjects with severe baseline pain (NRS score  $\geq 7$ ).

### **Results**

The numbers of subjects with baseline NRS score  $\geq 7$  were 24 for placebo, 21 for BEMA-Bup 0.25 mg Formulation 2, 23 for BEMA-Bup 0.5 mg Formulation 2, and 22 for BEMA-Bup 0.5 mg Formulation 1. In the *post hoc* analysis of subjects with baseline NRS score  $\geq 7$ , values for time-weighted Sum of Pain Intensity Difference from baseline to 8 hours postdose (SPID-8) reflected significantly greater analgesia with BEMA-Bup 0.5 mg Formulation 1 versus placebo in the last observation carried forward (LOCF) primary analysis (p=0.0182) and with both groups receiving BEMA-Bup 0.5 mg versus placebo in the baseline observation carried forward (BOCF) sensitivity analysis (p<0.05 for both comparisons). Values for time-weighted Total Pain Relief over 8 hours postdose (TOPAR-8) reflected significantly greater analgesia with BEMA-Bup 0.5 mg Formulation 1 versus placebo in both the LOCF analysis (p=0.0335) and the BOCF analysis (p=0.0156). Differences between BEMA-Bup and placebo in time-weighted TOPAR-8 approached statistical significance for BEMA-Bup 0.5 mg Formulation 2 in both the LOCF analysis (p=0.0724) and the BOCF analysis (p=0.0615). Differences between BEMA-Bup 0.25 mg Formulation 2 and placebo were not statistically significant in this group of subjects with severe pain.

### **Conclusions**

This *post hoc* analysis of data from a randomized, double-blind, placebo-controlled, Phase 2 trial of subjects with at least moderate baseline pain after dental extraction demonstrated the analgesic efficacy of BEMA-Bup to be particularly robust in the subset of subjects with severe baseline pain (NRS score  $\geq 7$ ). Significant differences between BEMA-Bup and placebo in analgesic efficacy as indexed by SPID-8 and

TOPAR-8 values were observed in subjects with severe baseline pain despite the small number of subjects involved in the *post hoc* analysis. Further elucidation of the analgesic efficacy profile of BEMA-Bup in subjects with severe baseline pain is warranted.