Abstract Title: Sufentanil NanoTab™ PCA System: Phase 3 Active-Comparator Data Versus IVPCA Morphine for Post-Operative Pain

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Introduction: Intravenous patient-controlled analgesia (IV PCA) is commonly used to manage postoperative pain. However, it is associated with limitations, including programming errors and reduced patient mobility. Sufentanil is an opioid approved as IV and epidural formulations. While it possesses a high therapeutic index with minimal respiratory depressive effects relative to its analgesic effect, high cardiac stability and minimal pharmacokinetic differences based on age, liver or kidney function, rapid redistribution from plasma following IV administration and short duration make it less than ideal for IV PCA. The Sufentanil NanoTab PCA System (SNPS) is a novel preprogrammed noninvasive product in Phase 3 development designed to deliver sublingual sufentanil 15 mcg microtablets with a 20-minute lockout period. This study was designed to evaluate the ability of SNPS to produce comparable patient satisfaction with post-operative pain control to IV PCA with morphine 1 mg q6 min lockout (IV PCA). Patient satisfaction with pain management as measured by the HCAHPS Survey has been identified as a key driver of patient loyalty to a hospital.

Methods: In a Phase 3 randomized, open-label, non-inferiority trial at 26 US sites, adult inpatients after major open abdominal or orthopedic surgery (knee or hip replacement) were randomized 1:1 to SNPS or IV PCA for up to 72 hours, stratified by age and type of surgery. The 48-hour Patient Global Assessment (PGA-48) using a 4-point scale (poor, fair, good, excellent), comparing the proportion of patients who responded “good” or “excellent” (collectively “success”) in each treatment arm was defined as the primary endpoint. Pain intensity scores and pain relief scores were obtained as secondary endpoints. Up to 390 patients were to be enrolled to ensure at least 176 patients per group, received treatment and had available primary efficacy data for analysis to provide 90% power to demonstrate therapeutic non-inferiority. A 95% confidence interval (CI) of the difference in success rate between two treatment groups was constructed and if the lower boundary of this CI was not less than -15%, SNPS would be considered non-inferior to IV PCA.

Results: 446 patients were screened, 359 were randomized, and 357 received study drug (ITT population: SNPS [n=177] and IV PCA [n=180]) with one patient in each group who did not receive study drug. The mean age for the SNPS group was 63.8 years (30.5% males) and IV PCA group was 64.0 yrs (40% males). Knee arthroplasty represented 32% of surgeries in both groups. The primary efficacy analysis, PGA at
48hr, included 355 patients (176 SNPS and 179 IV PCA). Overall, 78.5% vs. 66.1% of patients achieved PGA 48"success" for the SNPS group vs IV PCA group, respectively, demonstrating both non-inferiority based on the 95% CI (p <0.001 using the one-side Z-test against the -15% non-inferiority margin) as well as statistical superiority in favor of the NanoTab System (p=0.009).

**Conclusion:** The Sufentanil NanoTab PCA System provides an alternative patient-controlled analgesia modality which is easy for healthcare professionals to set-up and patients to use.