Erratum to the FDA Briefing Document
Anesthetic and Analgesic Drug Products Advisory Committee Meeting
October 11, 2018

This erratum contains corrections to FDA's briefing information for the October 11, 2018, Anesthetic and Analgesic Drug Products Advisory Committee Meeting. At this meeting, the committee will discuss oliceridine 1 milligram/milliliter injection, submitted by Trevena, Inc., for the management of moderate-to-severe acute pain in adult patients for whom an intravenous opioid is warranted.

1) On page 107, first paragraph, the last sentence:

   "As shown in Table 1 (below), oliceridine has a potency that is slightly greater than that of fentanyl, 2 times that of hydromorphone and 6 times that of morphine (EC_{50} of ~8 nM vs. ~6 nM, ~16 nM and ~50 nM, respectively)."

Should be revised to read (change bolded and underlined)

   "As shown in Table 1 (below), oliceridine has a potency that is **similar to that** of fentanyl, but 2 times **greater than** that of hydromorphone and 6 times **greater than** that of morphine (EC_{50} of ~8 nM vs. ~6 nM, ~16 nM and ~50 nM, respectively)."

2) On page 111, Table 2, the last row ("Any Effects"), sixth column "Oliceridine [1 mg] vs. Morphine 10 mg" should be revised so that the arrow pointing up (increase) are **pointing down (decrease).**

3) On page 111, Table 2, in the legend:

   The second arrow should be **pointing down** representing 'statistically significant decrease'.

4) On pages 114-115, the text and Table 6 should be replaced with the following table and text (change bolded and underlined):

Phase 2/3 Clinical Efficacy Studies (Study # CP130-3001, CP130-3002, CP130-3003).

In Phase 2/3 clinical efficacy studies conducted with **0.5**-4 mg intravenous oliceridine for the treatment of pain, there was **a rate** of abuse-related adverse events **that was similar to that from placebo**, as shown in Table 6 below. Somnolence was the most frequently reported adverse event **for oliceridine and saline** (~**5**% **vs. 4%, respectively**), followed by sedation (~3% **both**), anxiety (~2% **vs. 1%, respectively**), restlessness (~1% **vs. 2%, respectively**), and paraesthesia (~1% **both**). **Morphine produced similar rates of anxiety, restlessness and paresthesia (2%, 2% and 1%, respectively), but a higher rate of somnolence (13%) and sedation (8%) compared to oliceridine and placebo.** Notably, euphoric effects were low for **oliceridine and morphine**, but this is common when abuse-related adverse events are assessed in a subject population being treated for pain conditions.

Table 6: Abuse-Related Adverse Events in Phase 2/3 Studies

Preferred Term	Placebo (N=252)	Morphine (N=305)	Oliceridine (N=1185)
Euphoria	**0**	**2 (0.7%)**	**20 (1.3%)**
Somnolence	10 (4.0%)	41 (13.4%)	79 (**5.1**%)
Sedation	8 (3.2%)	24 (7.9%)	**41 (2.7%)**
Anxiety	3 (1.2%)	6 (2.0%)	**36 (2.3%)**
Restlessness	5 (2.0%)	5 (1.6%)	14 (1.2%)
Paraesthesia	3 (1.2%)	4 (1.3%)	15 (1.3%)

Overall, oliceridine produced abuse-related adverse events in Phase 2/3 clinical studies that were similar to those produced by placebo.