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MCRI Updates

Trevena's (TRVN) TRV130 for Acute Pain

November 3, 2014

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Summary

We recently hosted a conference call to discuss Trevena's (TRVN) TRV130, an infusible opioid for acute pain. The product is in phase II testing in patients undergoing bunionectomy. The phase I data indicates the product has some benefit to morphine in regards to respiratory depression but otherwise has a comparable adverse event profile at similar analgesic doses. We believe the current phase IIb trial will show that higher doses of TRV130 have comparable analgesia to 4 mg of morphine but also comparable adverse events. At the 1 mg dose of TRV130 analgesia and adverse events may be less than at 4 mg of morphine. Based on the phase I trial we see a decline in respiratory depression as possibly the main benefit of TRV130. This feature may be desired in certain patients at high anesthesia risk because of their age, preexisting condition, or anesthesia history. We believe if this feature is substantiated TRV130 could be a niche product, but it is unlikely to be a general replacement for morphine.

Stocks Impacted

- **Trevena (TRVN-$5.81-NR)**

Background

- ***TRV130 is in a phase II trial.*** Results are expected in 2H14.

Reasons for Research

- ***Investors are waiting to learn the results of the phase II trial.***

The Impact

- ***Data from the phase I single-dose trial in healthy volunteers was less than stellar.*** The phase I study showed that at the lowest dose of TRV130, 1.5 mg, the analgesic effect was not as good as 10 mg of morphine but there were much fewer side effects. However, at higher doses of TRV130 (3 mg, 4.5 mg) where the analgesic effect was similar to 10 mg morphine, the side effect profile was similar. There does seem to be a substantial advantage of TRV130 over morphine regarding respiratory depression.
- ***Phase IIb trial is likely to show results similar to phase I data.*** The phase II trial administers doses (1, 2, 3, 4 mg) of TRV130 every four hours for 48 hours and compares analgesia to 4 mg of morphine. The basic parameters of the trial are similar enough to the phase I trial to expect similar results.
- ***Phase IIb trial likely to be labeled a success by the company.*** At higher doses of TRV130 (3, 4 mg) analgesia is likely to be equivalent to 4 mg of morphine. At lower doses of TRV130 (1 mg) adverse events are likely less common than with 4 mg of morphine.

MCRI Insights

- ***We believe the current phase IIb trial will show that higher doses of TRV130 will have comparable analgesia to 4 mg of morphine but also comparable adverse events.*** At the 1 mg dose of TRV130 analgesia and adverse events may be less than at 4 mg of morphine. Based on the phase I trial we see a benefit in respiratory depression as the main benefit of TRV130. This feature may be desired in certain patients at high anesthesia risk because of their age, preexisting condition, or anesthesia history. We believe if this feature is substantiated TRV130 could be a niche product, but it is unlikely to be a general replacement for morphine.

Tech Assessment: Trevena's (TRVN) TRV130 for Acute Pain

I. TRV130
- Intravenous
- Infusion
- Small molecule
- Short half-life
- μ-opioid receptor agonist

II. Mechanism of TRV130
- μ-opioid receptor agonist
- Acts to bias the receptor to specific secondary messenger pathways
- Acts to increase affinity of μ-opioid receptor to G protein
- Acts to decrease affinity of μ-opioid receptor to β-arrestin
- β-arrestin pathway is associated with adverse events of opioids

III. Current Treatment of Acute Pain at Hospitals
- Pain related to surgery and other procedures
- Injectable narcotics: Morphine, fentanyl, buprenorphine
- Patients may not be able to eat, need injectable medicines
- Medicine fast acting, quickly reversible, and titratable

IV. Pathophysiology of Adverse Events to Opioids
- Nausea and vomiting
- Constipation
- Respiratory depression

V. Market for Infused Pain Medicine
- 30 million reimbursed for IV opioids by US hospitals
- 14 million were inpatient and 16 million were outpatient claims
- 75% of inpatient claims and 50% of outpatient claims were surgery related
- Competition: Generics, CBST, PGNX, SLXP, CARA

VI. Phase I Data
- Randomized, double blind, cross over
- n= 30 healthy men
- Five separate treatments for each patient: placebo, 1.5, 3.0, 4.5 mg of TRV130, 10 mg morphine
- 11 days sequestration
- Single-dose treatments days: 1, 3, 5, 7, 9
- Primary endpoint: Safety and tolerability
- Results: Only 1.5 mg dose had clearer reduction in adverse events than 10 mg morphine
- 1.5 mg dose had substantial reduction in respiratory depression compared to 10 mg morphine
- 1.5 mg dose showed substantially less analgesia than 10 mg of morphine
- Doses of TRV130 that have similar analgesia have similar side effects; slight difference

VII. Ongoing Phase II Clinical Trial
- Randomized, double blind
- n=333 patients under going bunionectomy
- Six treatment groups: Placebo, 4 mg morphine, 1 mg, 2 mg, 3 mg, 4 mg TRV130
- TRV130 administered intravenously every four hours for 48 hours
- Treatment while in-patient
- Primary endpoint: Reduction of pain intensity for up to 48 hours
- Secondary endpoints: Safety and tolerability

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BUY	25	89%	16%
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Companies under coverage at 9/30/14	**28**	**100%**	**14%**