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Equity Research

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JAZZ/CNCE: JZP-386 Not Quite There Yet, But Still Some Hope

Health Care Team

- **Summary:** This morning (12/9), JAZZ/CNCE provided an update on their ongoing phase 1 study of JZP-386, a deuterated version of JAZZ's Xyrem. We believe the program is important to JAZZ in that it could enable a lifecycle extension strategy by being longer-acting and eliminating middle of the night dosing, and for CNCE in that it could provide meaningful future milestone and royalty revenue. Following our analysis and discussions with both companies, we see both positives and negatives from today's update, but overall believe it does add incrementally more risk to the program overall. Still, for JAZZ we continue to remain comfortable with Xyrem's durability to at least the 2020 patents and with the amount of time remaining to execute life cycle management strategies and we believe CNCE's valuation continues to reflect overly low probabilities of success for the multiple partnered deuterated programs.
- **What happened:** This morning before the open, JAZZ and CNCE announced that their Phase 1 trial for JZP-386 supports completing evaluation at the originally planned highest dose, which was not administered in the first Phase 1 due to a "technical dosing issue," and the companies will run a second Phase 1 at this dose in Q1 2015, with data available to the companies in Q2 2015.
- **What we learned from JAZZ and CNCE:** The recently-completed Phase 1 study included multiple dose strengths and placebo, and the data (not disclosed) includes safety, PK/PD, sleepiness, and cognitive measures. The highest planned dose was not given, due to a "technical dosing issue" that JAZZ/CNCE will not disclose. According to JAZZ/CNCE, the data showed no safety issues and supports dosing at the highest planned level. JAZZ/CNCE are to administer this dose in a second Phase 1 trial starting in Q1 2015, and expect to have data in Q2 2015. At that time or later, JAZZ would provide an update, which would include next steps, and may or may not include the study data. The second Phase 1 is to include about 30 patients (approximately the same as the first Phase 1).
- **Potential positives:** The fact that the originally planned high dose can be explored suggests safety was likely benign and PK/PD may have shown a dose-dependent response in sodium oxybate exposure. Though the program now gets pushed out, if the higher dose works, the delay would be relatively minor (2 quarters).
- **Potential negatives:** Suggests magnitude of drug's exposure was inadequate at administered doses. Only one dose will initially be given in the second Phase 1, raising risk of more studies being needed; while it could be amended to explore higher doses if necessary, it is not clear why the companies are not using this as an opportunity to explore a broader range of higher doses, to maximize likelihood of success (especially given that the data on exposures to date had clearly "missed" enough such that it enabled them to recognize the dosing error, so they may not be that close to the desired range yet).

Michael Faerm, Senior Analyst
(212) 214-8026
michael.faerm@wellsfargo.com
Brian Abrahams, M.D., Senior Analyst
(212) 214-8060
brian.abrahams@wellsfargo.com

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