

March 20, 2014

CNCE-NASDAQ--Outperform (1) / V

Biotechnology

## NCE: Publication Of Potential Mechanism For Dextromethorphan In Depression Lends More Support For One Of CNCE's Partnered Programs

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### Sector Rating: Biotechnology, Market Weight

**\*\*Today, a publication was announced by Avanir Pharmaceuticals on the potential mechanism for dextromethorphan in treating depression. The preclinical work was published in PLOS ONE, a peer-reviewed medical journal.**

**\*\*Recall that Concert is partnered with Avanir on AVP-786, a deuterated form of dextromethorphan with lower-dose quinidine, for treating major depression, expected to enter phase II later this year.**

**\*\*While there was some evidence from prior studies in pseudobulbar affect that dextromethorphan-based agents could improve depressive symptoms in certain patients, the article provides some corroboration on the underlying mechanism. While dextromethorphan had been previously hypothesized to hold rapid-acting antidepressant activity given its pharmacodynamic resemblance to ketamine, an NMDA receptor antagonist, the study found some antidepressant action through sigma-1 ( $\sigma_1$ ) receptors in vivo.**

**\*\*BOTTOM LINE: The program does not account for a significant proportion of our current CNCE valuation -- we currently model U.S. commercial launch of AVP-786 by 2021, with net royalties to CNCE of 10% and AVP-786 only representing 3.3% and 6.5% of our 2022 probability-weighted and unweighted EPS projections, respectively. Still, we note that this additional information on the mechanism of dextromethorphan may differentiate it from other antidepressants without action at the  $\sigma_1$  receptor, and could increase the likelihood of ultimate success. We continue to like CNCE based on the versatile deuteration platform, potential of their pipeline programs, and optionality on higher-risk/high-reward partnership programs such as AVP-786.**

### Concert Pharmaceuticals, Inc. (CNCE-NASDAQ)

**Price as of 3/20/2014: \$14.00**

**FY 14 EPS: \$2.05**

**FY 15 EPS: \$-2.05**

**Shares Out.: 0.0 MM**

**Market Cap.: \$0.0 MM**

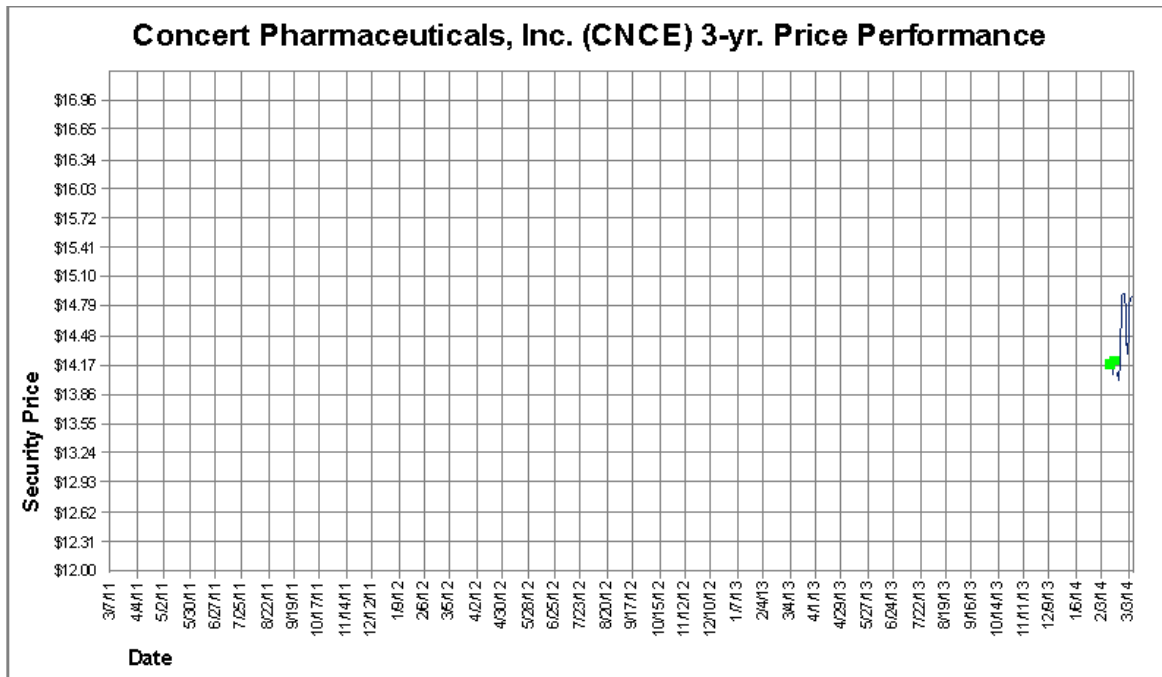
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### Required Disclosures



	Date	Publication Price (\$)	Rating Code	Val. Rng. Low	Val. Rng. High	Close Price (\$)
□	2/13/2014		IPO at \$14.00			

Source: Wells Fargo Securities, LLC estimates and Reuters data

#### Symbol Key

- ▼ Rating Downgrade
- ▲ Rating Upgrade
- Valuation Range Change
- ◆ Initiation, Resumption, Drop or Suspend
- Analyst Change
- Split Adjustment

#### Rating Code Key

- 1 Outperform/Buy
- 2 Market Perform/Hold
- 3 Underperform/Sell
- SR Suspended
- NR Not Rated
- NE No Estimate

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**CNCE:** Key risks, in our view, are failure of '354 and/or '499 to show efficacy in subsequent studies and regulatory hurdles in spasticity or CKD.

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**2 = Market Perform:** The stock appears appropriately valued, and we believe the stock's total return will be in line with the market over the next 12 months. HOLD

**3 = Underperform:** The stock appears overvalued, and we believe the stock's total return will be below the market over the next 12 months. SELL

#### SECTOR RATING

**O = Overweight:** Industry expected to outperform the relevant broad market benchmark over the next 12 months.

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#### As of: March 20, 2014

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