

## **Concert Pharmaceuticals Presents Clinical Results Demonstrating Reduced Drug-Drug Interactions with a Deuterium-Modified Compound; Phase I Results Presented at American College of Clinical Pharmacology**

San Antonio, TX -- Concert Pharmaceuticals, Inc. announced today the presentation of Phase 1 data on CTP-347, a deuterium modified analog of paroxetine for the treatment of hot flashes. Concert presented the results during a poster session at the American College of Clinical Pharmacology's 38th Annual Meeting. This presentation highlighted that subjects treated with CTP-347 substantially retained cytochrome P450 2D6 (CYP2D6) enzyme activity. This enzyme is necessary for the metabolism of many common drugs, but is irreversibly inactivated by a metabolite of paroxetine, causing significant drug-drug interactions. Concert believes these findings represent the first reported clinical data demonstrating that deuterium substitution can alter a drug's metabolism to reduce the potential for drug-drug interactions in humans.

"This proof-of-concept study, combined with our preclinical findings, demonstrates how we can apply deuterium chemistry to a proven drug to suppress formation of an undesirable metabolite, while retaining the drug's beneficial pharmacologic activity," said Roger Tung, Ph.D., President and Chief Executive Officer. "These are exciting results and provide one example of how our deuterium chemistry platform can leverage proven drugs to create highly differentiated yet risk-reduced new medicines."

The Phase 1 clinical trial was a randomized, single-blind, placebo-controlled, ascending single- and multiple-dose study in 94 healthy volunteers. The primary objective of the study was to evaluate the safety, tolerability and pharmacokinetics of CTP-347. In this trial, CTP-347 was well-tolerated at all doses evaluated and there were no clinically significant adverse events reported. The most common adverse events were typical of selective serotonin reuptake inhibitors (SSRIs) including headache, nausea and dizziness. *In vitro* studies have previously shown that CTP-347, unlike paroxetine, does not exhibit mechanism-based inactivation of CYP2D6 in human liver microsomes. The pharmacokinetics of CTP-347 were consistent with those observed in preclinical studies.

CTP-347 is a new chemical entity developed from Concert's deuterium chemistry platform by replacing key hydrogen atoms of paroxetine with deuterium as a non-hormonal treatment for vasomotor symptoms (VMS) or hot flashes. Paroxetine has been shown to be an effective treatment for VMS. However, it is a potent and irreversible inactivator of CYP2D6 (cytochrome P450 2D6), a key liver enzyme responsible for the metabolism of many commonly-prescribed drugs. Currently, there is no FDA-approved non-hormonal treatment for VMS, a serious and sometimes long-term condition associated with a range of undesirable effects including depression, insomnia and lost productivity. Hormone replacement therapy can effectively treat VMS. However, patients who currently or previously have been treated for cancers of the breast or ovary, or who have a familial history of these cancers, are often advised to avoid hormonal treatment. A non-hormonal therapy may also be preferred by women who experience VMS following menopause in whom hormone therapy is contraindicated or who have concerns about long-term health risks posed by hormone replacement therapy.

### **About Deuterium**

Deuterium is a safe, non-radioactive relative of hydrogen that can be isolated from sea water and has been used extensively in human metabolic and clinical studies. Since deuterium resembles hydrogen, deuterium-containing compounds are expected to preserve the pharmacological activity of their hydrogen analogs. An important difference is that deuterium is heavier than hydrogen and therefore forms a stronger chemical bond to a carbon atom of a drug. The stronger chemical bond obtained by selective deuterium modification in select instances may substantially improve the drug's metabolic properties, potentially resulting in better safety, tolerability and/or efficacy.

### **About Concert**

Concert Pharmaceuticals is a clinical stage biotechnology company focused on the application of deuterium chemistry to create novel small molecule drugs. Concert's approach leverages known activity and safety of existing drugs to reduce time, risk and expense of drug research and development. The Company has a broad research pipeline encompassing many therapeutic areas including infectious disease and renal disease, among others. Its lead development candidate is the HIV protease inhibitor CTP-518. In 2009, Concert entered into a potential \$1 billion collaboration with GlaxoSmithKline to develop certain deuterium-containing medicines. Founded in 2006, Concert has raised more than \$110 million of venture and institutional capital. For more information on Concert Pharmaceuticals, please visit [www.concertpharma.com](http://www.concertpharma.com).