



Concert Pharmaceuticals Initiates Phase 1 Single-Ascending Dose Trial of CTP-692 as an Adjunctive Treatment for Schizophrenia

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LEXINGTON, Mass.--(BUSINESS WIRE)--Jan. 24, 2019-- [Concert Pharmaceuticals, Inc.](#) (NASDAQ: CNCE) today announced that it has initiated the second Phase 1 clinical trial with CTP-692, a novel deuterium-modified form of D-serine being developed as an adjunctive treatment for schizophrenia. The Phase 1 single-ascending dose trial will evaluate the safety, tolerability, and pharmacokinetic profile of CTP-692 in healthy volunteers.

"For decades all approved schizophrenia drugs have acted predominantly by modulation of dopamine, or dopamine and serotonin receptors. By activating glutamatergic pathways as an NMDA co-agonist, CTP-692 has the potential to be a safe and effective new adjunctive treatment for schizophrenia, and treat positive and negative symptoms and cognitive dysfunction," stated Roger Tung, Ph.D., President and Chief Executive Officer of Concert Pharmaceuticals, Inc. "We are excited about continuing our Phase 1 program and in the fourth quarter of 2019 are preparing to advance CTP-692 into a Phase 2 trial that is intended to support advancement into pivotal evaluation."

The initial Phase 1 trial evaluated the safety, tolerability, and pharmacokinetics of a single oral dose of CTP-692 versus D-serine in a crossover study conducted in Australia. In individuals treated with both compounds, CTP-692 was found to have increased plasma exposure compared to D-serine. In addition, CTP-692 was found to be well tolerated in healthy volunteers and no serious adverse events were reported. Under its Investigational New Drug application in the United States, Concert will conduct this second study in the Phase 1 program to assess the safety, tolerability, and pharmacokinetics of single-ascending oral doses of CTP-692 in a double-blind, placebo-controlled trial. The Phase 1 single-ascending dose trial will also evaluate the effect of food on the pharmacokinetics of the compound. In addition, the Phase 1 program will include a double-blind, placebo-controlled, multiple-ascending dose trial assessing CTP-692 dosed orally over seven days. Topline data from the Phase 1 program is expected in the first half of 2019.

The CTP-692 clinical program is supported by Concert's preclinical studies which have shown the potential of CTP-692 to improve upon the safety profile of D-serine. D-Serine has been shown to cause nephrotoxicity in published preclinical studies. Concert's preclinical studies have demonstrated that selective deuterium modification resulted in increased exposure of CTP-692 relative to a similar dose of D-serine, and administration of CTP-692 did not cause changes in serum creatinine and blood urea nitrogen at doses where D-serine caused substantial nephrotoxicity as assessed by these kidney function markers. These preclinical results were presented by Concert at the American College of Toxicology 2018 Annual Meeting in November 2018. A copy of the poster may be accessed in the Scientific Presentations section of the Company's website at www.concertpharma.com.

About CTP-692

CTP-692 is a deuterium-modified analog of endogenous D-serine. Based on documented effects of D-serine, the Company believes that CTP-692 has the potential to restore NMDA receptor activity in key areas of the brain and improve clinical outcomes in patients with schizophrenia. CTP-692 has been shown to have similar ability to bind to and activate human NMDA receptors relative to D-serine, with the potential for an improved safety profile and improved clinical outcomes in the treatment of schizophrenia. CTP-692 will be developed as an adjunctive therapy administered in addition to standard antipsychotic medicines to improve both positive and negative symptoms as well as cognitive function in patients with schizophrenia.

An extensive body of evidence supports NMDA receptor hypofunction as a key underlying mechanism of schizophrenia. The NMDA receptor comprises two binding domains and, in addition to requiring glutamate binding, activation with a co-agonist such as D-serine or glycine is necessary for NMDA receptor activation. D-Serine is believed to be the most important human NMDA synaptic co-agonist. It has been postulated for some time that administration of NMDA co-agonists could benefit patients with schizophrenia since there is evidence that plasma and cerebrospinal fluid (CSF) levels of endogenous D-serine are reduced in patients with schizophrenia.

About Schizophrenia

Schizophrenia is a chronic and devastating neuropsychiatric disorder that is ranked as a leading cause of disability worldwide. The disease afflicts nearly 1% of the world's population, affecting both men and women equally, and striking all ethnic and socioeconomic groups with a similar level of prevalence. The illness is characterized by multiple symptoms that are categorized into three main clusters known as positive symptoms (hallucinations, delusional behaviors and thought disorder), negative symptoms (social withdrawal, flattened affect and poverty of speech), and cognitive dysfunction (diminished capacity for attention, working memory and executive function). The underlying basis of the current antipsychotic therapy is that excessive dopaminergic neurotransmission and dysfunctional D2 receptor signaling play key pathophysiological roles in the disease, and consequently all typical and atypical antipsychotics in clinical practice possess some level of D2 antagonist activity. Currently available antipsychotic drugs offer some benefit for positive symptoms but many patients are not adequately treated since currently available treatments are limited in their capacity to treat negative symptoms and cognitive dysfunction which are related to poor functional outcomes.

About Concert

[Concert Pharmaceuticals](#) is a clinical stage biopharmaceutical company focused on applying its [DCE Platform®](#) (deuterated chemical entity platform) to create novel medicines designed to treat serious diseases and address unmet patient needs. The Company's approach starts with previously studied compounds, including approved drugs, in which deuterium substitution has the potential to enhance clinical safety, tolerability or efficacy. Concert's [pipeline](#) of innovative medicines currently targets autoimmune diseases and central nervous systems (CNS) disorders. For more information please visit www.concertpharma.com or follow us on Twitter at [@ConcertPharma](#) or on [LinkedIn](#).

Cautionary Note on Forward Looking Statements

Any statements in this press release about our future expectations, plans and prospects, including statements about the clinical development of CTP-692 and other statements containing the words "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "should," "target," "would," and similar expressions, constitute forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Actual results may differ materially from those indicated by such forward-looking statements as a result of

various important factors, including: the uncertainties inherent in the initiation of future clinical trials, availability and timing of data from ongoing and future clinical trials and the results of such trials, whether preliminary results from a clinical trial will be predictive of the final results of that trial or whether results of early clinical trials will be indicative of the results of later clinical trials, expectations for regulatory approvals and other factors discussed in the "Risk Factors" section of our most recent Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission and in other filings that we make with the Securities and Exchange Commission. In addition, any forward-looking statements included in this press release represent our views only as of the date of this release and should not be relied upon as representing our views as of any subsequent date. We specifically disclaim any obligation to update any forward-looking statements included in this press release.

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