Concert Pharmaceuticals Initiates Phase 1 Clinical Program of CTP-692 for the Treatment of Schizophrenia

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LEXINGTON, Mass.--(BUSINESS WIRE)--Dec. 17, 2018-- Concert Pharmaceuticals, Inc. (NASDAQ: CNCE) today announced that it has initiated its Phase 1 clinical program for CTP-692, which is being developed as a novel adjunctive treatment for schizophrenia, a devastating, chronic illness with significant unmet need. CTP-692 is a deuterated form of D-serine, an endogenous co-agonist of the N-methyl-D-aspartate (NMDA) receptor, which has been demonstrated to be important to mood, memory, and cognition. Concert's Phase 1 program will include a crossover pharmacokinetic comparison of CTP-692 to D-serine and single- and multiple-ascending dose studies to assess the safety, tolerability and pharmacokinetic profile of CTP-692 in healthy volunteers. Initial Phase 1 data are expected in the first quarter of 2019.

"Significant unmet need still exists to improve upon the existing standard-of-care in schizophrenia and we believe CTP-692 has the potential to act on a key mechanism not addressed today with currently available agents. By enhancing NMDA receptor activity, CTP-692 offers the promise of improved clinical outcomes for patients with schizophrenia," said James Cassella, Ph.D., Chief Development Officer of Concert Pharmaceuticals. "We plan to advance CTP-692 through Phase 1 and then into a single Phase 2 efficacy trial in patients with inadequately controlled symptoms of schizophrenia in 2019."

The Phase 1 program is expected to enroll approximately 80 healthy volunteers. Dosing has been initiated to assess the safety, tolerability, and pharmacokinetics of a single oral dose pharmacokinetic comparison of CTP-692 versus D-serine. Following successful completion of the crossover trial, Concert will assess the safety, tolerability, and pharmacokinetics of single-ascending oral doses of CTP-692 in a double-blind, placebo-controlled trial. The Phase 1 program will also assess multiple doses of CTP-692 dosed orally over several days in a double-blind, placebo-controlled, multiple-ascending dose trial.

The CTP-692 clinical program is supported by Concert's preclinical studies which have shown the potential for 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 resulted in no changes in serum creatinine and blood urea nitrogen at doses where D-serine caused substantial nephrotoxicity assessed by these kidney 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 and Schizophrenia

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 is expected to have similar pharmacology 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 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 CSF levels of endogenous D-serine are reduced in patients with 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 exhibit efficacy for positive symptoms, but are limited in their capacity to treat negative symptoms and cognitive dysfunction which are related to poor functional outcomes for these patients.

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 has a broad pipeline of innovative medicines targeting autoimmune and inflammatory 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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