Concert Pharmaceuticals Presents Preclinical Data on CTP-692, a Novel Drug Candidate for Schizophrenia, Supporting Potential to Improve Safety Profile of D-Serine

November 5, 2018

Findings Presented at American College of Toxicology 2018 Annual Meeting

LEXINGTON, Mass.--(BUSINESS WIRE)--Nov. 5, 2018-- Concert Pharmaceuticals, Inc. (NASDAQ: CNCE) today presented preclinical results that support the potential of CTP-692, the Company's novel drug candidate for schizophrenia, to improve the safety profile of D-serine. CTP-692 is a deuterated form of D-serine, an endogenous co-agonist of the N-methyl-D-aspartate (NMDA) receptor. In preclinical evaluation, Concert demonstrated that selective deuterium modification resulted in increased exposure of CTP-692 compared to a similar dose of D-serine. Unlike D-serine, CTP-692 did not cause undesirable changes in important markers of kidney function. These findings will be presented as a poster at the American College of Toxicology 2018 Annual Meeting being held November 4-7, 2018 in West Palm Beach, FL.

"Despite its therapeutic potential as an adjunctive medication for schizophrenia, D-serine's therapeutic potential has likely been limited by renal safety concerns. As a result of the preclinical profile we have observed with CTP-692 showing a potentially lower risk of renal toxicity compared to non-deuterated D-serine, we believe it's possible for us to explore a wider exposure range to achieve optimal therapeutic dosing levels of CTP-692," said Roger Tung, Ph.D., President and Chief Executive Officer of Concert Pharmaceuticals. "These results support the further advancement of CTP-692, which we are preparing to move into Phase 1 clinical evaluation."

In preclinical evaluation, CTP-692 and D-serine were shown to have similar functional activation of the NMDA receptor in the presence of glutamate. Relative to D-serine, CTP-692 showed increased metabolic stability in the preclinical study. CTP-692 provided greater exposure, based on area under the curve (AUC) analysis, and a longer half-life than corresponding doses of D-serine *in vivo*. Notably, in animal models, serum creatinine and blood urea nitrogen, important markers of kidney function, were highly elevated upon acute dosing with D-serine but stayed within the normal range with CTP-692.

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 is pursuing the development of CTP-692 as a treatment of schizophrenia by potentially restoring NMDA receptor activity in key disease-related areas of the brain. 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. Concert is developing CTP-692 as an adjunctive therapy administered in addition to standard antipsychotic medicines with the potential to improve both positive and negative symptoms as well as cognitive function in patients with schizophrenia.

There is an extensive body of evidence supporting 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 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 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 our expectations for 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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