Concert Pharmaceuticals Reports Positive Results from Phase 1 Studies Evaluating CTP-692 in Healthy Volunteers

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The Company Expects to Initiate a Phase 2 Trial in Patients with Schizophrenia in the Fourth Quarter of 2019

LEXINGTON, Mass.--(BUSINESS WIRE)--Jun. 12, 2019-- Concert Pharmaceuticals, Inc. (NASDAQ: CNCE) today reported positive results from two studies in its Phase 1 program evaluating CTP-692, a novel deuterium-modified form of D-serine being developed as an adjunctive treatment for schizophrenia. The safety assessments in the single- and multiple-ascending dose trials in healthy volunteers showed that the drug was well tolerated over the dose ranges tested, which include the doses expected to be evaluated in Phase 2 testing. Importantly, key blood and urine markers of kidney function did not indicate any signs of renal impairment. These data are consistent with preclinical findings with CTP-692 indicating an improved renal safety profile compared to non-deuterated D-serine which is known to produce renal toxicity in rats. Despite evidence of benefit in multiple published clinical studies of non-deuterated D-serine in the treatment of schizophrenia, its use has been limited due to renal safety concerns. Furthermore, in contrast to non-deuterated D-serine, which has been reported to display highly variable pharmacokinetic behavior in humans, CTP-692 was found to have low inter-individual pharmacokinetic variability. The Company expects data from the single-and multiple-ascending dose Phase 1 trials to be presented at a future scientific meeting.

“We are pleased that CTP-692 demonstrated favorable clinical properties including an excellent safety profile in its Phase 1 studies, and we look forward to advancing it into Phase 2 evaluation later this year,” said Roger Tung, Ph.D., President and Chief Executive Officer of Concert Pharmaceuticals.

The Phase 1 program was designed to assess CTP-692’s safety, tolerability and pharmacokinetic profile in healthy volunteers. The Phase 1 program includes three studies: a crossover comparison of CTP-692 versus D-serine, a single-ascending dose study that also assessed the effect of food on the pharmacokinetics of CTP-692, and a multiple-ascending dose trial assessing CTP-692 dosed orally over seven days. In the single- and multiple-ascending dose trials, CTP-692 was evaluated across doses ranging from 0.5 to 4 grams compared to placebo in a total of 72 volunteers. CTP-692 demonstrated a favorable safety, tolerability and pharmacokinetic profile with no serious adverse events reported. In a separate study in 11 healthy volunteers treated in a crossover design with both CTP-692 and D-serine, CTP-692 was found to have increased plasma exposure compared to D-serine. These results were presented as a poster at the 2019 American Society of Clinical Psychopharmacology Annual Meeting in Scottsdale, AZ.

About CTP-692
CTP-692 is a deuterium-modified analog of the endogenous NMDA receptor co-agonist, 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 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 renal safety profile and improved clinical outcomes in the treatment of schizophrenia. Preclinical studies have demonstrated that CTP-692 provides preferentially higher concentrations in the forebrain, compared to plasma and brainstem regions, as well as overall higher exposure in the brain relative to non-deuterated D-serine. CTP-692 will be initially developed as an adjunctive therapy administered in addition to standard antipsychotic medicines with the potential to improve 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 receptor co-agonist. It has been postulated for some time that administration of NMDA co-agonists could benefit patients with schizophrenia across multiple symptom domains since there is evidence that plasma 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 are frequently associated with neurologic and metabolic adverse effects. 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.comor 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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Source: Concert Pharmaceuticals, Inc.

Justine Koenigsberg (investors)
Concert Pharmaceuticals, Inc.
(781) 674-5284
ir@concertpharma.com

Kathryn Morris (media)
The Yates Network
(914) 204-6412
kathryn@theyatesnetwork.com