Tetra Discovery Partners Announces Positive Results from Phase 1 Studies of Cognition Drug Candidate, BPN14770

- **BPN14770 shown safe and orally bioavailable in single and multiple dose studies**
- **Cognitive benefit on working memory seen at lower doses in healthy elderly subjects in multiple dose trial**
- **Results support planned initiation of Phase 2 study in Alzheimer's disease in mid- 2017**

Grand Rapids, MI (December 19, 2016) – Tetra Discovery Partners today announced positive results from two Phase 1 studies of its selective PDE4D allosteric inhibitor drug candidate, BPN14770. The double blind, placebo-controlled, dose-ranging studies were designed primarily to study the safety and pharmacokinetics of single ascending doses and multiple ascending doses of BPN14770 in healthy young and elderly volunteers. In addition, cognitive benefit was explored in the 45 elderly volunteers (age 60 and older) enrolled in the multiple ascending dose study. A pooled, post hoc analysis of elderly subjects in the low and mid-dose groups demonstrated a significant improvement measures of working memory. Based on the overall results of these two studies, Tetra Discovery Partners plans to initiate a Phase 2 trial of BPN14770 in patients with Alzheimer's disease in mid-2017.

"While we designed these first clinical studies of BPN14770 primarily to look at the safety and dosing of our drug candidate, we were very pleased to see a cognitive benefit in a number of the elderly participants in the dose-ranging study, as measured by two different tests of working (immediate) memory," said Mark Gurney, Ph.D., Chairman and Chief Executive Officer of Tetra Discovery Partners. "Thus we are cautiously optimistic and look forward to expanding our study of BPN14770 to a larger trial in Alzheimer's disease patients in the coming months, where we hope to show its ability to reverse memory dysfunction as well as slow the progression of Alzheimer's disease." Patients in the Alzheimer's trial will be dosed for a longer duration than those in the Phase 1 multiple dose trial, allowing for better detection of drug effects.

A total of 109 volunteers participated in the two studies. In both studies, BPN14770 was shown to be orally bioavailable, safe, and well-tolerated. In the elderly, high dose group, headaches were the most frequently reported adverse event (5 of 10 subjects) and were observed in the one subject who withdrew by choice midway in the trial. In the cognitive portion of the multiple dose study, analysis of the low, mid and high dose cohorts revealed impaired reaction times in the high dose group with no change in the low and mid dose groups. Therefore the high dose group was excluded from a pooled exploratory analysis of elderly volunteers receiving drug in comparison to placebo. This post hoc analysis of the elderly subjects in the low and mid dose groups (20 subjects received drug and 15 subjects received placebo) demonstrated significant improvements ($p<0.05$, effect size >0.70) in two measures of working memory at doses of 10 and 20 mg bid. No detectable effect was observed on other cognitive domains, however, inference is limited by the small sample size.

Working memory is a system for temporarily storing and managing the information required to carry out complex cognitive tasks such as learning, reasoning, and comprehension. The part of the brain responsible for working memory is also responsible for focus and concentration. Working memory is a domain of cognition that is impacted by Alzheimer's disease.

The Phase 1 single-ascending and multiple-ascending dose studies of BPN14770 were conducted with the support of the National Institute of Health through a grant from the National Institute on Aging (AG054243) and funding from the Alzheimer's Drug Discovery Foundation. BPN14770 was developed through a cooperative research agreement with the Blueprint Neurotherapeutics Program (NS078034). The company plans full disclosure of the clinical trial data at future medical conference presentations and through peer-reviewed journal publication.

About BPN14770

BPN14770 is a novel therapeutic agent that selectively inhibits phosphodiesterase-4D (PDE4D). PDE4D works through the PKA-CREB pathway to enhance synaptic action of the brain neurons involved in memory and cognition. This unique mechanism of action has the potential to improve cognitive and memory function in devastating disorders including Alzheimer's disease, schizophrenia, and learning/developmental disabilities such as Fragile X syndrome.

About Tetra Discovery Partners

Tetra Discovery Partners is a clinical stage biotechnology company developing a portfolio of therapeutic products that will bring clarity of thought to people suffering from Alzheimer's disease and other brain disorders. Tetra uses structure-guided drug design to discover mechanistically novel, allosteric inhibitors of phosphodiesterase 4 (PDE4), an enzyme family that plays key roles in memory formation, learning, neuroinflammation, and traumatic brain injury. Tetra was a recipient of an NIH Blueprint Neurotherapeutics Program cooperative research agreement, and also receives major funding from the National Institute on Aging and the National Institute of Mental Health through the Small Business Innovation Research (SBIR) program. Tetra Discovery Partners is headquartered in Grand Rapids, Michigan. For more information, please visit the company's website at http://www.tetradiscovery.com.

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