Tetra Discovery Partners Research Supports Ability of Novel Selective PDE4D Inhibitor, BPN14770, to Improve Memory and Cognition

-- Preclinical, PET Imaging, and Phase 1 Human Clinical Trial Data Presented at 10th Clinical Trials in Alzheimer's Disease Meeting --

Grand Rapids, MI (November 6, 2017) – Preclinical, PET imaging, and Phase 1 human clinical evidence supporting the ability of Tetra Discovery Partners' drug candidate, BPN14770, to improve memory formation and provide cognitive benefit was the subject of an oral presentation on Saturday at the 10th Clinical Trials in Alzheimer's Disease Meeting held November 1-4, 2017 in Boston, MA. BPN14770 is a highly selective inhibitor of phosphodiesterase-4D (PDE4D), which regulates brain signaling pathways involved in the early and late stages of memory formation.

"Alzheimer's disease and other conditions marked by problems of cognition and memory represent a serious and growing problem for U.S. and other aging populations worldwide, and to date, there has been no effective treatment that can stem or help improve such cognitive decline," said Mark E. Gurney, Ph.D., Chairman and Chief Executive Officer of Tetra Discovery Partners. "Based on the results of our Phase 1 trial of BPN14770, and these supporting preclinical studies, we are cautiously optimistic about the potential of this drug candidate and look forward to conducting its further evaluation in a Phase 2 study in early Alzheimer's disease patients in the first half of 2018."

Tetra Discovery and the company's collaborators at the University of Buffalo and the National Institute of Mental Health demonstrated that single oral doses of BPN14770 at 0.01 or 0.03 mg/kg improved the working and long-term memory in mice with a humanized PDE4D gene, compared to wild-type mice. Moreover, after 14 days dosing at the 0.03 mg/kg level, the researchers found elevated levels of biomarkers associated with the cAMP-PKA-CREB pathway in the humanized mice. This included elevation of brain-derived neurotrophic factor (BDNF) in the hippocampus. They also demonstrated by PET imaging that PDE4D distribution was highest in specific regions of the brain in primates that were related to cognition, the hippocampus and prefrontal cortex, which are also targets of Alzheimer's pathology. The PDE4D PET tracer was displaced from the hippocampus and prefrontal cortex by pretreatment with BPN14770, indicating that the drug enters the brain and engages the desired target.

The researchers also presented data from an initial clinical assessment of BPN14770 cognitive benefit in healthy elderly volunteers that was also consistent with the mechanism of action for the drug. In a Phase 1 dose-ranging study of BPN14770 in 45 healthy elderly volunteers (age 60 or older), preliminary cognitive assessment suggested that BPN14770 oral doses of 10 and 20 mg bid improved complex attention/ working memory and 24-hour delayed recall of verbal or sight and space-related tasks. A pooled, post hoc analysis of

the elderly volunteers in the low and mid-dose groups demonstrated a significant improvement in measures of working memory. There were no adverse events related to gastrointestinal disturbance (nausea, vomiting, or diarrhea).

Working memory is a cognitive system for temporarily storing and managing the information required to carry out complex mental tasks such as learning, reasoning, and comprehension. The prefrontal cortex and hippocampus are the parts of the brain responsible for working memory. These same parts of the brain are impacted by Alzheimer's disease, and working memory is among the cognitive functions most sensitive to decline.

About BPN14770

BPN14770 is a novel therapeutic agent that selectively inhibits phosphodiesterase-4D (PDE4D) to enhance early and late stages of memory formation. 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. BPN14770 has completed three human Phase 1 clinical trials enrolling 147 subjects and has shown excellent safety, oral bioavailability, and preliminary cognitive benefit in elderly subjects. Preparations are under way to initiate a Phase 2 trial of BPN14770 in patients with Alzheimer's disease in the first half of 2018.

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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