

Shionogi and Tetra Therapeutics Entered into New Strategic Collaboration for BPN14770, the Drug Candidates for the Treatment of Brain Disorders Marked by Cognitive and Memory Deficits

OSAKA, Japan, March 6, 2020 - Shionogi & Co., Ltd. (Head Office: Osaka, Japan; President and CEO: Isao Teshirogi, Ph.D.; hereafter "Shionogi") today announced that Shionogi and Tetra Therapeutics (hereafter "Tetra") have entered into a new investment agreement and merger agreement for further strengthening of the strategic alliance which Shionogi and Tetra had entered into in December 2018 to promote the research and clinical development of BPN14770 ¹.

As a negative allosteric modulator targeting phosphodiesterase 4D (PDE4D), an enzyme that is associated with memory formation, BPN14770, a compound discovered and developed by Tetra, is expected to improve cognitive function without concern of adverse reactions such as nausea which is often seen with existing PDE4 enzyme inhibitors. In non-clinical animal models, BPN14770 has demonstrated an effect on cognitive impairment, including in models of Alzheimer's disease (AD) and Fragile X syndrome, and is expected to show a beneficial clinical effect on various diseases accompanied by cognitive decline.

Currently, Tetra is conducting Phase 2 clinical studies in AD and Fragile X syndrome. In the Phase 2 study in AD patients (PICASSO AD trial²), Tetra completed enrollment earlier than originally planned, and topline results will be available in March 2020.

Based on the results of non-clinical and clinical studies obtained thus far, Shionogi has high expectations for this drug. Shionogi anticipates that the know-how of Tetra in drug discovery for the central nervous system area will accelerate our research and development. Therefore, at this time, Shionogi has signed a new investment agreement with Tetra to increase its investment level in Tetra to up to 50%, as well as a merger agreement including the option right to make Tetra a wholly owned subsidiary of Shionogi if certain closing conditions are met.

"We are pleased to strengthen our strategic alliance with Tetra. With the aging of our society, cognitive disorders are becoming a serious social issue. We believe BPN14770 has the potential to become an innovative new treatment to help solve for this issue. This new collaboration with Tetra reinforces our steadfast commitment to advancing cutting-edge science in central nervous system (CNS) disorders including Alzheimer's disease," said Dr. Isao Teshirogi, President and Chief Executive Officer, Shionogi & Co., Ltd.

"This expanded alliance with Shionogi further validates our platform and the potential for BPN14770 to provide a new treatment option for patients suffering from Alzheimer's disease," said Mark Gurney, Ph.D., Chairman and Chief Executive Officer of Tetra Therapeutics. "We are delighted to be expanding our collaboration with Shionogi and thank them for their continued conviction in our mission. We look

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forward to announcing topline results from our Phase 2 PICASSO AD trial in Alzheimer’s disease later this month.”

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 CNS disorders, including Fragile X syndrome, AD and other dementias, learning/developmental disabilities and schizophrenia. Preclinical animal models show that BPN14770 has the potential to promote the maturation of connections between neurons, which is impaired in patients with Fragile X Syndrome, and to protect connections between neurons which otherwise are lost in patients with AD. Tetra has completed Phase 1 double blind, placebo-controlled, dose-ranging studies of the safety and pharmacokinetics of BPN14770 in healthy volunteers. Evidence of cognitive benefit was found in elderly subjects. Tetra currently is conducting an investigational Phase 2 study of BPN14770 in adults with Fragile X syndrome, an indication for which BPN14770 has received Orphan Drug Designation from the U.S. Food and Drug Administration (FDA) and a second Phase 2 study of BPN14770 in patients with AD.

About Shionogi & Co., Ltd.

Shionogi & Co., Ltd. is a major research-driven pharmaceutical company dedicated to bringing benefits to patients based on its corporate philosophy of “supplying the best possible medicine to protect the health and wellbeing of the patients we serve.” Shionogi’s research and development currently targets two therapeutic areas: infectious diseases, and pain/CNS disorders. For over 50 years, Shionogi has developed and commercialized innovative oral and parenteral anti-infectives. In addition, Shionogi is engaged in new research areas, such as obesity/geriatric metabolic diseases and oncology/immunology. Contributing to the health and QOL of patients around the world through development in these therapeutic areas is Shionogi’s primary goal. For more details, please visit www.shionogi.co.jp/en/.

About Tetra Therapeutics

Tetra Therapeutics is a clinical stage biotechnology company developing a portfolio of therapeutic products that will bring clarity of thought to people suffering from Fragile X syndrome, AD, traumatic brain injury, 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 Therapeutics is headquartered in Grand Rapids, Michigan. For more information, please visit the company’s website at <http://www.tetratherapeutics.com>.

Forward-Looking Statements

This announcement contains forward-looking statements. These statements are based on expectations in light of the information currently available, assumptions that are subject to risks and uncertainties

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which could cause actual results to differ materially from these statements. Risks and uncertainties include general domestic and international economic conditions such as general industry and market conditions, and changes of interest rate and currency exchange rate. These risks and uncertainties particularly apply with respect to product-related forward-looking statements. Product risks and uncertainties include, but are not limited to, completion and discontinuation of clinical trials; obtaining regulatory approvals; claims and concerns about product safety and efficacy; technological advances; adverse outcome of important litigation; domestic and foreign healthcare reforms and changes of laws and regulations. Also for existing products, there are manufacturing and marketing risks, which include, but are not limited to, inability to build production capacity to meet demand, unavailability of raw materials and entry of competitive products. The company disclaims any intention or obligation to update or revise any forward-looking statements whether as a result of new information, future events or otherwise.

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References

1. [Press release on December 19, 2018](#)
Tetra Discovery Partners and Shionogi & Co., Ltd. Collaborate on BPN14770 Development and Commercialization
2. <https://clinicaltrials.gov/ct2/show/NCT03817684>
3. Hunter J. Am J Med Genet 2014 Jul;164A(7):1648-58.