

Notice Regarding Tetra becoming a wholly owned subsidiary of Shionogi

OSAKA, Japan, May 26, 2020 - Shionogi & Co., Ltd. (Head Office: Osaka, Japan; President and CEO: Isao Teshirogi, Ph.D.; hereafter "Shionogi") today announced that Shionogi resolved at a meeting of the Board of Directors held on May 25, 2020 to acquire all the shares of Tetra Therapeutics Inc. (hereafter "Tetra") and make it a subsidiary.

1. Purpose of This Acquisition

Shionogi is dedicated to the challenge of "Creating a more vigorous society" in the mid-term business plan SGS2020 and, as part of that effort, is progressing a range of programs in the field of psychological and central nervous system (CNS) disorders. Tetra is a clinical stage biotechnology company developing a portfolio of therapeutic products seeking to address the impact on cognitive function of disorders such as Fragile X syndrome (FXS), Alzheimer's disease (AD), traumatic brain injury, and other brain disorders. Shionogi and Tetra entered into a collaboration agreement, granting Shionogi rights to BPN14770 in Japan, Taiwan, and Korea, and an investment agreement in December 2018 to pursue the research and clinical development of BPN14770, a drug candidate for the treatment of brain disorders associated with cognitive and memory deficits¹. Currently, Tetra is conducting a Phase II study in FXS, and recently completed a Phase II study in AD, in the US. To further strengthen of the strategic alliance, Shionogi and Tetra entered into a new investment agreement in March 2020³, 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.

This randomized, placebo-controlled, double-blind Phase II AD study was designed to assess the efficacy and safety of BPN14770 in early AD patients. In this study, BPN14770 10mg or 25mg was orally administered twice-daily for 13 weeks. The primary endpoint was the change from baseline to 13 weeks of treatment in the Repeatable Battery for the Assessment of Neurological Status- Delayed Memory Index (RBANS- DMI) scores.

The results of this study didn't show statistically significant change in RBANS-DMI scores, which was the primary endpoint, in BPN14770 10mg and 25mg groups compared with the placebo-treated group. On the other hand, in a subgroup analysis of this study, the 25mg group showed a significant improvement on the Clinical Dementia Rating Sum of Boxes (CDR-SB) scores at week 13 in patients with an above median CDR-SB score at baseline ($p = 0.0295$). It is therefore Shionogi believes that further development of BPN14770 in AD and other indications (such as FXS, which is ongoing) is warranted. There were no clinically significant issues observed in the safety of BPN14770. In addition, Shionogi anticipates that Tetra's deep level of drug discovery know-how in the CNS area will strengthen Shionogi's research and development efforts in this field. Consequently, we decided to acquire all the shares of Tetra and to make the company a wholly owned subsidiary of Shionogi. As a result of this acquisition, Shionogi will have all global rights to BPN14770 and all Tetra compounds.

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2. Overview of Tetra

1. Name	Tetra Therapeutics Inc.
2. Location	State of Michigan, US
3. Representative	CEO : Mark Gurney
4. Business	Research and development of pharmaceuticals
5. Date of establishment	2011

3. Schedule of the Conversion into a Wholly Owned Subsidiary

May 26, 2020

4. Future Outlook

The impact of this matter on the consolidated earnings forecast for the fiscal year ending March 31, 2021 will be limited at this time, but we will promptly announce any future impact on our financial results when recognized.

About BPN14770

BPN14770 is a novel therapeutic agent that selectively inhibits phosphodiesterase-4D 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 FXS, 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 FXS, and to protect connections between neurons which otherwise are lost in patients with AD. Tetra currently is conducting an investigational Phase 2 study of BPN14770 in adults with FXS, an indication for which BPN14770 has received Orphan Drug Designation from the U.S. Food and Drug Administration (FDA).

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 FXS, AD, traumatic brain injury, and

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other brain disorders. Tetra uses structure-guided drug design to discover mechanistically novel, allosteric inhibitors of phosphodiesterase 4, 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 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.

For Further Information, Contact:

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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. [Press release on March 6, 2020](#)
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