PRESSRELEASE

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Shionogi Submits New Drug Application in Japan for Zuranolone as a Treatment for Major Depressive Disorder

OSAKA, Japan, September 27, 2024 - Shionogi & Co., Ltd. (Head Office: Osaka, Japan; Chief Executive Officer: Isao Teshirogi, Ph.D.; hereafter "Shionogi") announced that Shionogi submitted today a New Drug Application (NDA) in Japan for zuranolone, a treatment in development for major depressive disorder (MDD). Through a strategic collaboration with Sage Therapeutics, Inc. (Head Office: Massachusetts, USA; Chief Executive Officer: Barry Greene; hereafter "Sage"), Shionogi has been granted exclusive development and commercialization rights in Japan, Taiwan, and South Korea[1]. The NDA submission is based on data from the Phase 3 program conducted by Shionogi in Japan[2].

A Phase 3 validation trial in Japan was conducted to evaluate the efficacy, safety, and tolerability of zuranolone in 412 patients with moderate to severe MDD who were not on other anti-depressant medications. In that study, a statistically-significant improvement in the change from baseline in the HAM-D total score, a measure of MDD severity, was observed in the zuranolone group compared to the placebo group at day 15, achieving the primary endpoint. Additionally, zuranolone showed a statistically significant improvement in MDD symptoms as early as day 3 as measured by the HAM-D total score, demonstrating its rapid onset of action.

It is estimated that there are approximately 5 million patients with depression in Japan[3], making it the most prevalent non-fatal health condition. Existing treatments often take several weeks to become effective[4], highlighting the need for fast-acting therapies. Zuranolone, which has demonstrated rapid efficacy in previous clinical trials, has the potential to be a novel and much-needed treatment option for MDD, if approved.

About zuranolone

Zuranolone is neuroactive steroid (NAS) GABA-A receptor positive allosteric modulator (PAM). The GABA system is the major inhibitory signaling pathway of the brain and central nervous system and contributes to regulating brain function. Based on clinical trial results conducted by Shionogi, oral administration once a day for 14 days is expected to rapidly improve MDD symptoms without the need for dose adjustment. Zuranolone has been approved by the U.S. Food and Drug Administration (FDA) as the first and only oral treatment specifically indicated in the U.S. for postpartum depression (PPD) in adults (product name in the U.S.: ZURZUVAE™).

About Shionogi

Shionogi & Co., Ltd. is a leading global 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 well-being of the patients we serve." Shionogi has discovered and developed novel antibiotics, medicines for HIV and influenza and currently markets medicines for infectious diseases and central nervous

system disorders. Shionogi's global pipeline includes research programs in infectious disease, pain/CNS, metabolic disorders, rare disease, oncology and stroke. For more information, please visit https://www.shionogi.com/global/en/.

References:

1. Press release on June 14, 2018
2. SHIONOGI R&D Day 2024 presentation on page 98
3. WHO, Depression and Other Common Mental Disorders Global Health Estimates
4. Japanese Society of Mood Disorders Treatment Guidelines

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, lack of availability 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:

SHIONOGI Website Inquiry Form: https://www.shionogi.com/global/en/contact.html