Sumitomo Pharma

Press Release

July 31, 2023

Sumitomo Pharma Co., Ltd.

Sumitomo Pharma and Otsuka Announce Topline Results from Phase 3 DIAMOND 1 and DIAMOND 2 Clinical Studies Evaluating Ulotaront in Schizophrenia

Sumitomo Pharma Co., Ltd. (Head Office: Osaka, Japan; Representative Director, President, and CEO: Hiroshi Nomura; Securities Code: 4506, Prime Market of TSE) and Otsuka Pharmaceutical Co., Ltd. (Head Office: Tokyo, Japan; president and representative director: Makoto Inoue), a subsidiary of Otsuka Holdings Co., Ltd. (Head Office: Tokyo, Japan; president and representative director, CEO: Tatsuo Higuchi) announced today the topline results from the DIAMOND (**D**eveloping **I**nnovative **A**pproaches for **M**ental **D**isorders) 1 clinical study and the DIAMOND 2 clinical study evaluating the efficacy, safety, and tolerability of ulotaront (generic name; development code: SEP-363856), a trace amine-associated receptor 1 (TAAR1) agonist with 5-HT_{1A} agonist activity, dosed once-daily in acutely psychotic adults living with schizophrenia as per the attachment.

The impact of this matter on its consolidated financial results for the fiscal year ending March 31, 2024 will be minimal.

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Sumitomo Pharma Co., Ltd. (Head Office: Osaka, Japan; Representative Director, President, and CEO: Hiroshi Nomura; Securities Code: 4506, First Section of TSE) and Otsuka Pharmaceutical Co., Ltd. (Head Office: Tokyo, Japan; president and representative director: Makoto Inoue) announced today that the DIAMOND (**D**eveloping **I**nnovative **A**pproaches for **M**ental **D**isorders) 1 clinical study and the DIAMOND 2 clinical study of ulotaront (generic name; development code: SEP-363856), a trace amine-associated receptor 1 (TAAR1) agonist with 5-HT_{1A} agonist activity, dosed once-daily in acutely psychotic adults living with schizophrenia did not meet their primary endpoint.

The multicenter, randomized, double-blind, parallel-group, fixed-dosed DIAMOND 1 study, evaluated the efficacy, safety, and tolerability of ulotaront (50 mg/day and 75 mg/day) versus placebo over six weeks in 435 acutely psychotic adults with schizophrenia.

In the DIAMOND 1 study all three groups showed a reduction in the Positive and Negative Syndrome Scale (PANSS) total score over time, however neither ulotaront treatment group was superior to placebo on the primary endpoint of change from baseline in PANSS total score at Week 6 (least squares [LS] mean: -16.9 and -19.6 in ulotaront 50 mg/day and 75 mg/day-treated patients, respectively, compared to -19.3 in placebo-treated patients).

The multicenter, randomized, double-blind, parallel-group, fixed-dosed DIAMOND 2 study, evaluated the efficacy, safety, and tolerability of ulotaront (75 mg/day and 100 mg/day) versus placebo over six weeks in 464 acutely psychotic adults with schizophrenia.

In the DIAMOND 2 study, ulotaront 75 mg/day and 100 mg/day treatment groups did not demonstrate statistically significant improvement compared to placebo on the primary endpoint. At Week 6 both ulotaront treatment groups showed numerically larger mean reductions in PANSS total score from baseline compared to placebo (LS mean: -16.4 and -18.1 in ulotaront 75 mg/day and 100 mg/day-treated patients, respectively, compared to -14.3 in placebo-treated patients).

In both the DIAMOND 1 study and the DIAMOND 2 study, a large placebo effect was observed which may have masked the molecule's therapeutic effect.

Ulotaront was generally safe and well-tolerated in both studies.

Hiroshi Nomura, representative director, president and CEO of Sumitomo Pharma commented, "Sumitomo Pharma and our collaborator Otsuka Pharmaceutical have done preliminary analyses of the data and we believe that a high placebo response may have masked the therapeutic effect of this innovative molecule. High placebo responses, like those seen in DIAMOND 1 and DIAMOND 2, are well documented in psychiatric clinical studies. The placebo response in DIAMOND 1 was particularly high. These studies were conducted throughout the COVID-19 pandemic and initial analyses of these data suggest an impact of COVID-19 on the placebo responses that were seen. We continue to work closely with Otsuka and analyze the data to determine our next steps and plan to discuss with the U.S. FDA how to proceed based on these results."

Makoto Inoue, president and representative director of Otsuka Pharmaceutical Co., Ltd. noted, "The two companies believe that ulotaront, as a new, potential treatment option in the future, can contribute to patients and healthcare professionals by addressing unmet needs in the treatment of schizophrenia. Based on these study results, Otsuka and Sumitomo Pharma will continue to collaborate to explore the full range of possibilities for ulotaront, as well to develop other drug candidates in the neuropsychiatric area, in order to contribute to patients suffering from psychiatric disorders worldwide."

* Positive and Negative Symptom Scale (PANSS): An evaluation scale mainly intended to capture the overall mental status of individuals living with schizophrenia. It consists of a total of 30 symptom items including seven positive items, seven negative and 16 general psychopathology items. For each item the mental status is rated in a scale of 7 from 1 (no symptoms) to 7 (most serious).

Reference

About Ulotaront

Ulotaront, a TAAR1 agonist with 5-HT_{1A} agonist activity, is currently under investigation for the treatment of schizophrenia (the DIAMOND 5 clinical study in Japan and China), generalized anxiety disorder (GAD) and the adjunctive treatment of major depressive disorder (MDD), with additional indications under consideration.

Ulotaront was granted Breakthrough Therapy Designation by the U.S. Food and Drug Administration (FDA) for the treatment of schizophrenia in May 2019. Ulotaront is the first and only TAAR1 agonist to enter into Phase 3 clinical studies in people living with schizophrenia. It's also the first TAAR1 agonist to enter into Phase 2/3 clinical studies in GAD, and as an adjunctive therapy in MDD.

Ulotaront is being jointly developed and commercialized as part of a collaboration between Sumitomo Pharma, its U.S. subsidiary Sumitomo Pharma America, Inc. (SMPA), and Otsuka.

SMPA discovered ulotaront in collaboration with PsychoGenics based in part on a mechanism-independent approach using the in vivo phenotypic SmartCube® platform and associated artificial intelligence algorithms.

About Trace Amine-Associated Receptor 1 (TAAR1)

Trace amine-associated receptor 1 (TAAR1) is a G-protein coupled receptor located in the central nervous system and periphery. TAAR1 – the first discovered in the TAAR family of receptors – is prominently expressed in areas of the brain involved in psychiatric disorders as well as in areas of the body that regulate energy metabolism. TAAR1 has shown the ability to affect dopamine, serotonin, and glutamate signaling, supporting its potential to modulate aspects of reward processing, cognition, and mood relevant to schizophrenia as well as other psychiatric disorders.

About Schizophrenia

Schizophrenia is a chronic, serious and often severely disabling brain disorder that affects more than 24 million people worldwide and over 2 million people in the United States.[1,2] It is characterized by positive symptoms, such as hallucinations, delusions and disorganized thinking as well as negative symptoms, such as lack of emotion, social withdrawal, lack of spontaneity and cognitive impairment that includes problems with memory, attention and the ability to plan, organize and make decisions.[3]

Source:

1. Schizophrenia and Psychosis Action Alliance. Societal Costs of Schizophrenia & Related Disorders. Schizophrenia & Psychosis Action Alliance; 2021. Accessed June 10, 2022. https://sczaction.org/insight-initiative/societal-costs/
2. GBD 2019 Mental Disorders Collaborators. Global, regional, and national burden of 12 mental disorders in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet Psychiatry. 2022;9(2):137-150. doi:10.1016/S2215-0366(21)00395-3
3. Rutigliano G, Accorroni A, Zucchi R. The case for TAAR1 as a modulator of central nervous system function. Front Pharmacol. 2018;8. Accessed October 4, 2022. https://www.frontiersin.org/articles/10.3389/fphar.2017.00987

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