Sponsor:	Sumitomo Pharma America, Inc. (formerly Sunovion Pharmaceuticals Inc.)
Treatment Studied:	SEP-4199 Controlled Release (CR)
Protocol Number:	SEP380-303
Title of the Study:	An extension study to evaluate the long term safety, tolerability and effectiveness of SEP-4199F CR in patients with major depressive episodes associated with Bipolar I disorder.
Original Title of the Study	A 12-Month Open-label Extension Study to Evaluate the Long-term Safety, Tolerability, and Effectiveness of SEP-4199 Controlled Release (CR) for the Treatment of Major Depressive Episode Associated with Bipolar I Disorder (Bipolar I Depression)
Study Period:	Between March 2022 and November 2023
Date of this Report	4 September 2024

General Information about the study

Researchers wanted to find out the effects of different doses of SEP-4199 CR in participants with bipolar I depression who had completed 6 weeks of study treatment (SEP-4199 CR 200 mg, SEP-4199 CR 400 mg or placebo once daily) in the SEP380-301 study (another SEP-4199 CR study).
All participants received the study drug (SEP-4199 CR 200 mg to 400 mg once daily) for up to 12 months in this study and were aware that they were receiving the study drug and at which dose.

Why was the study needed?

The study's main objective was to look at how safe treatment with SEP-4199 CR 200 mg and 400 mg once daily for 12 months was in participants with bipolar I depression.

Who took part in the study?

This study involved participants who had bipolar I depression and completed SEP380-301 study. A total of 64 participants took part in this study.
Participants were from the United States, Bulgaria, Romania and Japan.

What were the overall results of the study?

As the sponsor decided to stop the SEP380-301 study earlier than planned, this study was also stopped. This decision was not related to any safety issues or concerns.
The results did not identify any new safety concerns with SEP-4199 CR.

What side effects did participants have during the study?

Side effects are unpleasant feelings or conditions that people experience when they take a medication. Side effects that happen in a clinical study include those both related or unrelated to a study treatment. A side effect is considered

“serious”, when it leads to death, is life-threatening, requires hospital care, causes long-lasting damage, causes a health problem in the participant’s baby or is considered as an important medical problem that may put the participant in danger.

Out of 64 participants, 39 participants (60.9%) had at least one side effect. A total of 3 participants (4.7%) had serious side effects: sarcoidosis (clusters of inflammatory cells in various organs), psychotic disorder and suicide attempt in 1 participant each. There were no deaths.

Participants with side effects	Percentage (number of participants out of 64)
How many participants had side effects?	60.9% (39)
How many participants had serious side effects?	4.7% (3)

The most common side effects with frequency ≥5% were blood prolactin increased, hyperprolactinaemia (higher than normal levels of blood prolactin), nasopharyngitis (inflammation of the nose and throat), weight increased, depression, electrocardiogram QT prolonged (abnormal electrical activity of the heart that affects its rhythm), headache, and insomnia (difficulty sleeping).

Side Effect	Percentage (number of participants out of 64)
Blood prolactin increased	31.3% (20)
Hyperprolactinaemia	9.4% (6)
Nasopharyngitis	7.8% (5)
Weight increased	7.8% (5)
Depression	6.3% (4)
Electrocardiogram QT prolonged	6.3% (4)
Headache	6.3% (4)
Insomnia	6.3% (4)

What do these results tell us?

The sponsor ended the study earlier than planned. This decision was not related to any safety issues or concerns.
Results of this study tell us that treatment with SEP-4199 CR 200 mg or 400 mg once daily up to 12 months in this study was generally safe and well tolerated in participants with bipolar I depression.

Are there plans for further studies?

The sponsor has no further study of SEP-4199 CR planned.

Where can I find more information about this study?

To learn more about this study, you can find more detailed information on the

websites below, by using the corresponding study reference numbers.

・ClinicalTrials.gov: https://clinicaltrials.gov/
ClinicalTrials.gov identifier (NCT Number): NCT05227209

・European Union Clinical Trials Register: https://www.clinicaltrialsregister.eu/
EudraCT Number: 2021-002108-11

・Japan Registry of Clinical Trials (jRCT): https://jrct.niph.go.jp/
Trial ID: jRCT2031220302