Sponsor:	Sumitomo Pharma America, Inc. (formerly Sunovion Pharmaceuticals Inc.)
Treatment Studied:	SEP-4199 Controlled Release (CR)
Protocol Number:	SEP380-301
Title of the Study:	Research study to evaluate the effectiveness of SEP-4199 CR in patients with major depressive episodes associated with Bipolar I Disorder
Original Title of the Study	A Multi-region, Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study Evaluating SEP-4199 Controlled Release (CR) for the Treatment of Major Depressive Episode Associated With Bipolar I Disorder (Bipolar I Depression)
Study Period:	Between December 2021 and October 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 compared with placebo in participants with bipolar I depression.
Researchers measured the participants' depression symptoms with a questionnaire called Montgomery-Åsberg Depression Rating Scale (MADRS). Lower scores mean fewer or less severe depression symptoms.
Participants were divided into 3 groups in a manner they were unaware of which group they belonged to, and they received study treatment that was assigned to their respective group.

- Group 1: placebo, once daily 6 weeks
- Group 2: SEP-4199 CR 200 mg, once daily 6 weeks
- Group 3: SEP-4199 CR 400 mg, once daily 6 weeks

A placebo looks like SEP-4199 CR but contains no medicine in it.
A total of 522 participants, 174 participants per group, were planned to take part in the study.

Why was the study needed?

The study's main objective was to look at how effective and safe SEP-4199 CR was in treating participants with bipolar I depression over 6 weeks of treatment compared with placebo.

Who took part in the study?

The study involved participants aged 18 to 65 years who had bipolar I depression.

A total of 83 participants took part in the study and 82 participants received study drug: 27 received placebo (Group 1), 27 received SEP-4199 CR 200 mg (Group 2), and 28 received SEP-4199 CR 400 mg (Group 3).
Participants were from the United States of America, Bulgaria, Romania and Japan.

What were the overall results of the study?

The sponsor decided to stop the study earlier than planned, as it was difficult to enroll enough participants due to limitations imposed by the coronavirus disease

(COVID-19) pandemic and competition with other studies for bipolar I depression. This decision was not related to any safety issues or concerns.

Because of the small number of participants, results for Group 2 and Group 3 were combined to compare with Group 1. On average, Group 2 and Group 3 combined showed a decrease in number of MADRS total score at Week 6 from start of treatment compared with Group 1.

What side effects did participants have in 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.

The percentage of participants having at least one side effect was similar between Group 1 (40.7%) and Group 2 and Group 3 combined (38.2%). No participants had serious side effects.

Percentage (Number of participants)	Group 1 (Out of 27 participants)	Group 2 (Out of 27 participants)	Group 3 (Out of 28 participants)	Group 2 and Group 3 (Out of 55 participants)
How many participants had side effects?	40.7% (11)	37.0% (10)	39.3% (11)	38.2% (21)
How many participants had serious side effects?	0% (0)	0% (0)	0% (0)	0% (0)

Group 1: placebo, once daily for 6 weeks
Group 2: SEP-4199 CR 200 mg, once daily for 6 weeks
Group 3: SEP-4199 CR 400 mg, once daily for 6 weeks

Side effects reported in ≥ 2% of participants in Group 2 and Group 3 combined and at least twice the rate of participants in Group 1 were electrocardiogram QT prolonged (abnormal electrical activity of the heart that affects its rhythm), increased appetite, diarrhoea, and weight increased.

Percentage (Number of participants)	Group 1 (Out of 27 participants)	Group 2 (Out of 27 participants)	Group 3 (Out of 28 participants)	Group 2 and Group 3 (Out of 55 participants)
Electrocardiogram QT prolonged	0% (0)	3.7% (1)	7.1% (2)	5.5% (3)
Increased appetite	0% (0)	3.7% (1)	3.6% (1)	3.6% (2)
Diarrhoea	0% (0)	3.7% (1)	3.6% (1)	3.6% (2)
Weight increased	0% (0)	3.7% (1)	3.6% (1)	3.6% (2)

Group 1: placebo, once daily for 6 weeks
Group 2: SEP-4199 CR 200 mg, once daily for 6 weeks
Group 3: SEP-4199 CR 400 mg, once daily for 6 weeks

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 and 400 mg once daily for 6 weeks 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): NCT05169710
- European Union Clinical Trials Register : https://www.clinicaltrialsregister.eu/
  EudraCT Number: 2021-002126-24
- Japan Registry of Clinical Trials (jRCT) : https://jrct.niph.go.jp/
  Trial ID: jRCT2031210559