U.S. FOOD & DRUG ADMINISTRATION

Allain A. Roy
(b) (6)

February 28, 2023

Re: Docket No. FDA-2022-P-3321

Dear Allain Roy:

This letter responds to your citizen petition received on December 20, 2022 (Petition). In the Petition, you request that the Food and Drug Administration (FDA or the Agency) immediately grant breakthrough therapy designation for Simufilam (Petition at 1). To support your request, you cite certain data and information regarding Simufilam (Petition at 1).[1] Your Petition states that the Simufilam is "sponsored by Cassava Sciences," which we understand to be a party other than you (Petition at 1).

We have carefully reviewed your Petition. For the reasons set forth below, your Petition is denied.

Alzheimer's disease is a devastating disease that can have a profound impact on the lives of a patient and their family. FDA recognizes the need for new therapies and for science-based approaches to drug development. In your Petition, you request that FDA "[i]mmediately grant Breakthrough Therapy Designation (BTD) for Simufilam (formerly PTI-125) sponsored by Cassava Sciences," and you cite certain data and information in support of that request (see Petition at 1).

The breakthrough therapy designation framework was designed to expedite the development and review of drugs that are intended to treat a serious condition when preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over available therapy on a clinically significant endpoint(s).[2] For purposes of breakthrough therapy designation, FDA considers clinically significant endpoint generally to refer to an endpoint that measures an effect on irreversible morbidity or mortality (IMM) or on symptoms that represent serious consequences of the disease. It can also refer to findings that suggest an effect on IMM or serious symptoms.[3]

[1] We note that the seventh numbered item in your statement of grounds refers to "[c]harts showing an improvement in cerebral spinal fluid biomarkers and cognition testing [that] are included below," but no such charts are included in your Petition. As discussed in this response, FDA is denying your Petition for a reason that is independent of your reference to these charts.

[2] See section 506(a)(1) of the FD&C Act (21 U.S.C. 356(a)(1)).

[3] Guidance for industry, *Expedited Programs for Serious Conditions – Drugs and Biologics* (May 2014) at 12.

The Federal Food, Drug, and Cosmetic Act (FD&C Act) provides a mechanism for "the sponsor of the drug" to request breakthrough therapy designation.[4] Accordingly, FDA does not make breakthrough therapy designation determinations in response to requests from parties other than the drug sponsor. A request for breakthrough therapy designation may be made by a drug sponsor concurrently with, or at any time after, the submission of an application for an investigational new drug (IND).[5] A drug sponsor who wishes to request breakthrough therapy designation should submit the IND or amendment to the IND administrative file to the attention of the appropriate FDA review division or office.[6] FDA's Guidance for Industry, *Expedited Programs for Serious Conditions—Drugs and Biologics*, provides additional information on FDA's policies and procedures concerning breakthrough therapy designation.

FDA denies your request for breakthrough therapy designation of Simufilam because you are not the drug sponsor.[7] As discussed above, the FD&C Act specifies that requests for breakthrough therapy designation are submitted to the Agency by the sponsor of the drug.[8]

Based on the reasons above, we are denying the Petition. However, as mentioned, we recognize the need for new therapies for Alzheimer's disease. We will continue to do everything we can within the boundaries of our regulatory authority to encourage the development of safe and effective medicines to treat this disease.

Sincerely,

Douglas C. Throckmorton -S

Digitally signed by Douglas C. Throckmorton -S
Date: 2023.02.28 10:58:57 -05'00'

Patrizia Cavazzoni, M.D.
Director
Center for Drug Evaluation and Research

[4] Sections 506(a)(1), (2) of the FD&C Act (21 U.S.C. 356(a)(1), (2)).

[5] See section 506(a)(2) of the FD&C Act.

[6] Guidance for industry, *Expedited Programs for Serious Conditions – Drugs and Biologics* (May 2014) at 31.

[7] Petition at 1; see also Cassava Sciences Press Release, *Cassava Sciences Announces Agreement with FDA on Special Protocol Assessments (SPA) for its Phase 3 Studies of Simufilam for the Treatment of Alzheimer's Disease* (Aug. 24, 2021), available at https://www.cassavasciences.com/node/15526/pdf.

[8] See section 506(a) of the FD&C Act.