



Cassava Sciences' Simufilam Improves Cognition and Behavior in Alzheimer's Disease in Interim Analysis of Open-label Study

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- Patients' Cognition Improved 1.6 Points on ADAS-Cog11 -

- Patients' Behavior Improved 1.3 Points on NPI -

- Improvements Maintained at 6 Months -

- Results Support Advancing Simufilam into Phase 3 Clinical Program -

AUSTIN, Texas, Feb. 02, 2021 (GLOBE NEWSWIRE) -- Cassava Sciences, Inc. (Nasdaq: SAVA) today announced results of an interim analysis from an open-label study of simufilam, its lead drug candidate for the treatment of Alzheimer's disease. Patients' cognition and behavior scores both improved following six months of simufilam treatment, with no safety issues.

In a clinical study funded by the National Institutes of Health and conducted by Cassava Sciences, six months of simufilam treatment improved cognition scores by 1.6 points on ADAS-Cog11, a 10% mean improvement from baseline to month 6. In these same patients, simufilam also improved dementia-related behavior, such as anxiety, delusions and agitation, by 1.3 points on the Neuropsychiatric Inventory, a 29% mean improvement from baseline to month 6.

Alzheimer's is a progressive disease. Over time, a patient's cognition will always worsen. *"Experience based on longitudinal studies of ambulatory patients with mild to moderate Alzheimer's disease suggest that scores on ADAS-cog decline by 6 - 12 points per year"*, according to FDA's Prescription Information sheet for ARICEPT® (donepezil), a drug approved for the treatment of dementia of the Alzheimer's type ¹.

"We could not be more pleased with these interim results," said Remi Barbier, President & CEO. "We would have been satisfied to show simufilam stabilizes cognition in patients over 6 months. An improvement in cognition and behavior tells us this drug candidate has potential to provide lasting treatment effects for people living with Alzheimer's disease. It's an exciting development."

The safety profile of simufilam in the interim analysis was consistent with prior human studies. There were no drug-related serious adverse events. Adverse events were mild and transient.

"Today's data once again suggests simufilam could be a transformative, novel therapeutic," added Nadav Friedmann, PhD, MD, Chief Medical Officer. "It appears the drug's unique mechanism of action has potential to provide a treatment benefit following 6 months of dosing."

About the Interim Analysis

Cassava Sciences' on-going, one-year, open-label, multi-center study is evaluating the long-term safety and tolerability of simufilam 100 mg twice daily in 100 patients with mild-to-moderate Alzheimer's disease. This study was initiated March 2020 and is now approximately 80% enrolled. Today's pre-planned interim analysis summarizes clinical data at the midway point of enrollment, i.e., the first 50 patients who have completed at least 6 months of drug treatment.

ADAS-Cog (Alzheimer's Disease Assessment Scale-Cognitive Subscale) is a standard test for assessing changes in cognition in Alzheimer's disease trials. NPI (Neuropsychiatric Inventory) is a widely used tool for measuring changes in dementia-related behavior. The Mini-Mental State Exam (MMSE) is a widely used test of cognitive function among the elderly. The interim analysis shows mean baseline scores of 15.5 on ADAS-Cog11, 4.5 on NPI and 22.1 on MMSE.

Much of the value of the open-label study is to gain data to support simufilam's long-term safety profile in patients. Interim efficacy data from an open-label study has limitations compared to efficacy data from a fully completed, large, randomized controlled clinical trial, or from a fully enrolled open-label study. However, prior clinical research in Alzheimer's disease conducted by other sponsors can serve as a contextual reference for estimates of an expected rate of decline in cognition in placebo patients:

- In 2019, a randomized controlled trial of aducanumab (Biogen) was conducted in >1,000 patients with early Alzheimer's disease.² In this Phase 3 study (EMERGE), patients on placebo showed a mean decline in cognition of approximately 1.4 points on ADAS-Cog13, a 6.3% decline, from baseline to month 6. Mean baseline ADAS-Cog13 score was 22.2. Mean baseline MMSE was 26.4.
- A randomized controlled study of ARICPET® (donepezil, Eisai) was conducted in >400 patients with mild-to-moderate Alzheimer's disease.³ In this Phase 3 study, patients on placebo showed a mean decline in cognition of approximately 1.9 points on ADAS-Cog, a 7.3% decline, from baseline to week 24. Mean baseline ADAS-Cog score was 26. MMSE range was 10-26.

Next Steps

Cassava Sciences believes today's data and prior clinical results support advancing simufilam into a Phase 3 clinical program in Alzheimer's disease. Initiation of a Phase 3 trial remains on schedule for 2nd half 2021.

Cassava Sciences and the U.S. Food and Drug Administration (FDA) recently concluded a successful end-of-phase 2 (EOP2) meeting for the simufilam drug development program. Details of the EOP2 meeting will be announced Q1 2021 after official FDA meeting minutes are finalized.

Based on today's results and inbound demand from Alzheimer's patients and their caregivers, the enrollment target for the open-label study will be increased by up to 50 additional patients, to a total target of approximately 150 patients. The Company is also in discussions with its scientific and clinical advisors about other potential enhancements to the open-label program.

About Alzheimer's Disease

Alzheimer's disease is a progressive brain disorder that destroys memory and thinking skills. Currently, there are no drug therapies to halt Alzheimer's disease, much less reverse its course. In the U.S. alone, approximately 5.8 million people are currently living with Alzheimer's disease, and approximately 487,000 people age 65 or older developed Alzheimer's in 2019. ⁴ The number of people living with Alzheimer's disease is expected to grow dramatically in the years ahead, resulting in a growing social and economic burden. ⁵

About Simufilam

Simufilam is a proprietary, small molecule (oral) drug that restores the normal shape and function of altered filamin A (FLNA), a scaffolding protein, in the brain. Altered FLNA in the brain disrupts the normal function of neurons, leading to Alzheimer's pathology, neurodegeneration and neuroinflammation. The underlying science for simufilam is published in peer-reviewed journals, including *Journal of Neuroscience*, *Neurobiology of Aging*, *Journal of Biological Chemistry*, *Neuroimmunology and Neuroinflammation* and *Journal of Prevention of Alzheimer's Disease*.

Cassava Sciences is also developing an investigational diagnostic, called SavaDx, to detect Alzheimer's disease with a simple blood test.

Simufilam and SavaDx were both developed in-house. Both product candidates are substantially funded by peer-review research grant awards from the National Institutes of Health (NIH). Cassava Sciences owns worldwide development and commercial rights to its research programs in Alzheimer's disease, and related technologies, without royalty obligations to any third party.

About Cassava Sciences, Inc.

Cassava Sciences' mission is to discover and develop innovations for chronic, neurodegenerative conditions. Over the past 10 years, Cassava Sciences has combined state-of-the-art technology with new insights in neurobiology to develop novel solutions for Alzheimer's disease. For more information, please visit: <https://www.CassavaSciences.com>

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The content of this press release is solely the responsibility of Cassava Sciences and does not necessarily represent the official views of the NIH/NIA.

Cassava Sciences Safe Harbor

This news release contains forward-looking statements, including statements made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995, relating to: our strategy and plans; the treatment of Alzheimer's disease; the status of current and future clinical studies with simufilam, including the interpretation of an interim analysis of open-label study results; inherent limitations of the ADAS-Cog and NPI testing batteries; planned enrollment and other changes to the open-label program; our intention to initiate a Phase 3 clinical program with simufilam in 2nd half 2021; results of our EOP2 meeting with FDA and the timing of further announcements; verbal commentaries made by our employees; and potential benefits, if any, of the our product candidates. These statements may be identified by words such as "may," "anticipate," "believe," "could," "expect," "forecast," "intend," "plan," "possible," "potential," and other words and terms of similar meaning. Drug development and commercialization involve a high degree of risk, and only a small number of research and development programs result in commercialization of a product. Our clinical results from earlier-stage clinical trials may not be indicative of full results or results from later-stage or larger scale clinical trials and do not ensure regulatory approval. You should not place undue reliance on these statements or any scientific data we present or publish.

Such statements are based largely on our current expectations and projections about future events. Such statements speak only as of the date of this news release and are subject to a number of risks, uncertainties and assumptions, including, but not limited to, those risks relating to the ability to conduct or complete clinical studies on expected timelines, to demonstrate the specificity, safety, efficacy or potential health benefits of our product candidates, the severity and duration of health care precautions given the COVID-19 pandemic, any unanticipated impacts of the pandemic on our business operations, and including those described in the section entitled "Risk Factors" in our Annual Report on Form 10-K for the year ended December 31, 2019 and future reports to be filed with the SEC. The foregoing sets forth many, but not all, of the factors that could cause actual results to differ from expectations in any forward-looking statement. In light of these risks, uncertainties and assumptions, the forward-looking statements and events discussed in this news release are inherently uncertain and may not occur, and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements. Accordingly, you should not rely upon forward-looking statements as predictions of future events. Except as required by law, we disclaim any intention or responsibility for updating or revising any forward-looking statements contained in this news release. For further information regarding these and other risks related to our business, investors should consult our filings with the SEC, which are available on the SEC's website at www.sec.gov.

This news release may also contain statistical data and drug information based on independent industry publications or other publicly available information. We have not independently verified the accuracy or completeness of the data contained in these publicly available sources of data and information. Accordingly, we make no representations as to the accuracy or completeness of such data or information. You are cautioned not to give undue weight to such data.

¹ Source: https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/020690s042.021720s014.022568s011lbl.pdf (2018)

² Source: Biogen, EMERGE Phase III study, slide 24, <https://investors.biogen.com/static-files/8e58afa4-ba37-4250-9a78-2ecfb63b1dcb> (2020)

³ Source: https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/020690s042.021720s014.022568s011lbl.pdf (2018)

^{4, 5} Source: Alzheimer's Association. Disease Facts and Figures. <https://www.alz.org/media/documents/alzheimers-facts-and-figures-2019-r.pdf>



Source: Cassava Sciences, Inc.