Cassava Sciences Announces Science Publication That Confirms Mechanism of Action of Simufilam, a Novel Drug Candidate for People with Alzheimer's Disease

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- **New cell biology data from Europe shows simufilam interrupts a pathogenic signaling pathway in Alzheimer's disease.**
- **Results corroborate prior research from other academic researchers.**
- **These data once again confirm the biological activity of simufilam.**

AUSTIN, Texas, Sept. 11, 2023 (GLOBE NEWSWIRE) -- Cassava Sciences, Inc. (Nasdaq: SAVA), a biotechnology company focused on Alzheimer's disease, today announced the publication of new research that confirms the biological activity of simufilam. Simufilam is Cassava Sciences' novel drug candidate for people with Alzheimer's disease dementia and is currently under evaluation in a pair of global Phase 3 clinical trials.

Researchers at the Cochin Institute (Paris, France) used a highly precise cell-based assay to show that simufilam interrupts amyloid binding to the α7 nicotinic acetylcholine receptor (α7nAChR). Cassava Sciences believes this protein interaction underlies simufilam's mechanism of action in Alzheimer's disease. The research appears in a special issue of *International Journal of Molecular Sciences,* a peer-reviewed scientific publication.

"Four academic institutions have now generated data in support of the biological activity of simufilam," said Remi Barbier, President & CEO. "They can't all be wrong."

"Today's data are an elegant confirmation of simufilam's mechanism of action," said Lindsay Burns, PhD, VP of Neuroscience at Cassava Sciences and co-author on the publication. "They show that simufilam potently disrupts a known pathological action of amyloid β using a robust and highly sensitive assay based on a technique called TR-FRET."

Journal:	*International Journal of Molecular Sciences,* special issue: *Neurodegenerative Disease: From Molecular Basis to Therapy*
Title:	Simufilam Reverses Aberrant Receptor Interactions of Filamin A in Alzheimer's Disease
Access:	Available on-line, and expected to be posted shortly in the publication section of www.CassavaSciences.com

Summary of New Research
A team of researchers led by Dr. Ralf Jockers at the Cochin Institute (Paris, France) used an amyloid binding assay to measure the ability of simufilam to prevent amyloid β from binding to the α7 nicotinic acetylcholine receptor (α7nAChR). Their study showed that simufilam potently reduced amyloid β binding to α7nAChR. This new data is consistent with prior research showing that simufilam prevents amyloid β from binding to α7nAChR. The Cochin Institute is a biomedical research center affiliated with public research organizations (Inserm and CNRS) and the University of Paris, France.

Dr. Jockers and his team developed their amyloid binding assay as a means of determining whether '*a novel generation of [Alzheimer's disease] drug candidates could effectively interrupt the high-affinity binding of amyloid β to α7nAChR.*'[1] The cell-based assay uses time-resolved fluorescence resonance energy transfer (TR-FRET) to accurately measure the degree to which a drug candidate such as simufilam can inhibit amyloid β binding to α7nAChR. Testing several concentrations of a drug in this assay allows calculation of its potency. TR-FRET is different from any prior technique used by other academic collaborators to show the biological activity of simufilam.

The Cochin Institute is the fourth academic institution to produce data supporting the biological activity of simufilam on FLNA. Simufilam was developed by Cassava Sciences in collaboration with researchers at CUNY School of Medicine who first showed the effects of simufilam on FLNA and on the signaling pathways of amyloid β in Alzheimer's disease. In 2020, Dr. Angelique Bordey of Yale University published data showing that simufilam reduced seizure frequency and alleviated neuronal abnormalities in mice with a form of epilepsy associated with FLNA overexpression. In 2023, Dr. Erika Peverelli of the University of Milan showed that simufilam reduced FLNA phosphorylation and enhanced the effects of a pituitary cancer treatment in experiments using both patient tumor biopsies and rat cell lines.

On-going Phase 3 Studies with Simufilam
Cassava Sciences is evaluating simufilam oral tablets for Alzheimer's disease dementia in two global Phase 3 clinical studies. These are randomized, double-blind, placebo-controlled trials. The Phase 3 program aims to enroll a total of approximately 1,750 patients with mild-to-moderate Alzheimer's disease who also meet other study eligibility criteria. Patient enrollment is expected to be completed for both Phase 3 studies by yearend 2023. Both Phase 3 studies have received a Special Protocol Assessment (SPA) from the U.S. Food and Drug Administration.

About Simufilam

Simufilam is Cassava Sciences' proprietary, small molecule (oral) drug candidate for the treatment of Alzheimer's disease dementia. Unlike monoclonal antibody treatments for Alzheimer's disease, simufilam does not purport to directly remove amyloid β from the brain. Instead, simufilam binds to altered filamin A (FLNA), a receptor-associated protein that amyloid β requires to bind to α7nAChR. By preventing amyloid β from signaling via α7nAChR and other receptors, simufilam reduces the neurodegeneration and neuroinflammation characteristic of Alzheimer's disease.

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 is a clinical-stage biotechnology company based in Austin, Texas. Our mission is to detect and treat neurodegenerative diseases, such as Alzheimer's disease. For more information, please visit: https://www.CassavaSciences.com

Disclosures
Cassava Sciences' product candidates have not been approved by any regulatory authority or health agency, and their safety or efficacy have not been established in humans. The TR-FRET research was conducted by the Cochin Institute and funded by Cassava Sciences. The Cochin Institute has no financial benefit tied to the outcome of the research. The contents of this press release are solely the responsibility of Cassava Sciences and do not represent the views of the National Institutes of Health, the Cochin Institute or any other research or governmental agency.

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Cautionary Note Regarding Forward-Looking Statements:
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 current expectations regarding the target patient enrollment numbers for our Phase 3 studies; comments made by our employees regarding the evaluation of simufilam in Phase 3 trials of Alzheimer's disease; the mechanism of action of simufilam, or any lab methods used to demonstrate such effects; and potential benefits, if any, of our product candidates. These statements may be identified by words such as "may," "anticipate," "believe," "could," "expect," "would", "forecast," "intend," "plan," "possible," "potential," and other words and terms of similar meaning.

Drug development involves a high degree of risk, and only a small number of research and development programs result in regulatory approval and commercialization of a product. Our interim data and analyses should not be relied upon as predictive of full study results for any of our studies. Our clinical results from earlier-stage clinical trials may not be indicative of full study 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, 2021, 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.

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[1] Cecon E, Dam J, Luka M, Gautier C, Chollet AM, Delagrange P, Danober L, Jockers R. Quantitative assessment of oligomeric amyloid β peptide binding to α7 nicotinic receptor. *Br J Pharmacol*. 2019 Sep;176(18):3475-3488.

Source: Cassava Sciences, Inc.