Cassava Sciences Announces Top-line Results of 12-month Interim Analysis from Open-label Study Evaluating Simufilam in Alzheimer's Disease

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- **Cognition Scores Improved 3.2 Points on ADAS-Cog, Baseline to Month 12 (p<0.001)**
- **Two Independent Biostatisticians Analyzed Changes in ADAS-Cog Scores, Baseline to Month 12**
- **No Behavior Disorders on NPI in Over 50% Of Study Subjects at Month 12**
- **Initiation of Pivotal Phase 3 Clinical Program Remains On-track for Q4 2021, with Special Protocol Assessments from FDA**

AUSTIN, Texas, Sept. 22, 2021 (GLOBE NEWSWIRE) -- Cassava Sciences, Inc. (Nasdaq: SAVA) announced top-line clinical data today from a pre-planned interim analysis of an on-going open-label study with its drug candidate simufilam in patients with mild-to-moderate Alzheimer's disease.

In a study funded by the National Institutes of Health (NIH), ADAS-Cog11 scores improved an average of 3.2 points from baseline (p<0.001) in the first 50 study subjects who completed 12 months of open-label treatment with simufilam. To emphasize impartiality, changes in ADAS-Cog scores baseline to month 12 were independently analyzed by two consulting biostatisticians.

"I feel energized and encouraged by the clinical data," said Remi Barbier, President & CEO. "We look forward to the initiation of a randomized, double-blind, placebo-controlled pivotal Phase 3 clinical program with simufilam in people with Alzheimer's disease."

Response Analysis

In the first 50 study subjects who completed 12 months of open-label treatment with simufilam:

- ADAS-Cog11 scores improved an average of 3.2 points from baseline (S.D. ± 6.3; p<0.001)
- 68% of study subjects improved on ADAS-Cog at 12 months; these study subjects improved an average of 6.8 points (S.D. ± 3.8)
- An additional 20% of study subjects declined less than 5 points on ADAS-Cog at 12 months; these study subjects declined an average of 2.5 points (S.D. ± 1.3)

An independent, published meta-analysis of patients with mild-to-moderate Alzheimer's disease reports an average decline of 5.5 points over 12 months[1] amongst study subjects who were administered placebo in randomized, controlled trials.

Study subjects entered the open-label study with a clinical diagnosis of mild-to-moderate Alzheimer's, Mini-Mental State Examination (MMSE) range 16-26.

Safety Analysis

Drug is well-tolerated. There are no drug-related serious adverse events through the 12-month interim analysis.

Chain of Custody for Clinical Data

Investigator sites collect clinical data from study subjects. Sites enter their clinical data directly into an electronic data capture (EDC) system managed by an outside data management vendor. The data management vendor also maintains the clinical database. At Cassava Sciences' request, the data management vendor transmitted baseline and month-12 ADAS-Cog scores directly to two independent consulting biostatisticians for analysis. Both consultants hold PhD's in statistics and provide consulting expertise in support of medical research. One consultant is based in Texas, the other in Arizona. Both statisticians independently reached the same statistical conclusions on changes in ADAS-Cog scores, baseline to month 12.

Neuropsychiatric Inventory (NPI) at the 12 Month Interim Analysis

Alzheimer's is often accompanied by behaviors disorders, such as anxiety, agitation or delusions. These may become more frequent as disease progresses. The Neuropsychiatric Inventory (NPI) is a clinical tool widely used to measure changes in dementia-related behavior. At baseline, 34% of these study subjects had no neuropsychiatric symptoms on the NPI. At 12 months, over 50% had no neuropsychiatric symptoms on the NPI.

Clinical Strategy Around Open-label Study

Long-term safety data is a regulatory requirement. To collect these data, some drug development companies conduct an open-label study at the conclusion of a Phase 3 clinical testing program. Cassava Sciences believes it is prudent to conduct an open-label study *before* undertaking a large, complex and expensive Phase 3 clinical program in Alzheimer's disease: if an experimental drug for Alzheimer's fails to show long-term safety or any treatment benefit in a large, well-designed, open-label study, such drug is unlikely to succeed under the more rigorous conditions of a randomized, controlled trial. However, treatment effects observed in an open-label study are not proof of drug safety or efficacy, nor can open-label data predict clinical success in a Phase 3 program. Proof of safety and efficacy will always rest on results of a randomized, double-blind, placebo-controlled pivotal Phase 3 clinical program, which has not yet been conducted with simufilam.

About the Open-label Study

In March 2020, Cassava Sciences initiated a long-term, open-label study to evaluate simufilam in patients with Alzheimer's disease. This study is funded by a research grant award from the National Institutes of Health (NIH). The open-label study is intended to monitor the long-term safety and tolerability of simufilam 100 mg twice-daily for 12 or more months. Another study objective is to measure changes in cognition using ADAS-Cog and to assess the presence and severity of dementia-related behavior using the Neuropsychiatric Inventory (NPI). Approximately 200 study subjects are now enrolled in the open-label study from 16 investigator sites in the U.S and Canada. The study's dropout rate is currently under 10%.

Next Step: Phase 3 Clinical Program under FDA Special Protocol Assessments

Cassava Sciences is advancing simufilam into a Phase 3 clinical program in Alzheimer's disease. Study initiation is on-track for Q4 2021. On August 24, 2021, Cassava Sciences announced it had reached agreement with the U.S. Food and Drug Administration (FDA) under a Special Protocol Assessment (SPA) for both of its Phase 3 studies.

About Simufilam

Simufilam (sim-uh-FILL-am) 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.* Simufilam is substantially supported by peer-reviewed 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.

For More Information Contact:

Eric Schoen, Chief Financial Officer
eschoen@CassavaSciences.com
(512) 501-2450

Cautionary Note Regarding Forward-Looking Statements: *This press release includes forward looking statements including but not limited to those regarding the timing of the initiation of our pivotal Phase 3 program with simufilam in Alzheimer's disease and its likelihood of success, the interpretation of clinical data generated in a 12-month interim analysis of an open-label study, the clinical safety profile of simufilam, the occurrence of neuropsychiatric symptoms in people with Alzheimer's disease, the publication of an analysis regarding the expected rate of cognitive decline in people with Alzheimer's disease and oral or written comments made by our employees regarding simufilam and its clinical development.*

Drug development involves a high degree of risk, and historically only a small number of research and development programs result in commercialization of a product. Clinical results from our 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 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 initiation, conduct or completion of our 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, 2020 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.

The content of this press release is solely our responsibility and does not represent the official views of the National Institutes of Health (NIH).

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.

[1] *Disease Progression Meta-analysis Model in Alzheimer's disease* (Ito, et al., Pfizer Global Research), Alzheimer's & Dementia 6 (2010) 39-53

Source: Cassava Sciences, Inc.