Cassava Sciences Announces Positive End-of-Phase 2 Meeting with FDA and Outlines Pivotal Phase 3 Program for Simufilam in Alzheimer's Disease

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- Two Upcoming Phase 3 Studies and a Previously Completed Phase 2 Program Support a New Drug Application Filing for Simufilam in Alzheimer's disease -

- Agreement Reached to Use ADAS-Cog as Co-Primary Efficacy Endpoint -

- Pivotal Phase 3 Program Remains On-track to be Initiated 2nd Half 2021 -

AUSTIN, Texas, Feb. 22, 2021 (GLOBE NEWSWIRE) -- Cassava Sciences, Inc. (Nasdaq: SAVA), a biotechnology company developing product candidates for Alzheimer's disease, today announced the successful completion of an End-of-Phase 2 (EOP2) meeting with the U.S. Food and Drug Administration (FDA) for simufilam, its lead drug candidate for the treatment of Alzheimer's disease. Official EOP2 meeting minutes indicate FDA and Cassava Sciences agree on key elements of a pivotal Phase 3 clinical program in support of a New Drug Application (NDA) filing for simufilam in Alzheimer's disease. Agreements reached during the EOP2 meeting show a clear path forward for advancing simufilam into Phase 3 studies in the second half of 2021.

"For over 10 years we've been doing basic research and early drug development with simufilam," said Remi Barbier, President & CEO. "We are excited to finally advance simufilam into pivotal Phase 3 clinical studies in people with Alzheimer's disease. We believe the underlying science is solid, the drug appears safe and the clinical roadmap makes sense. We've crossed the Rubicon."

"We appreciate the valuable guidance and flexibility FDA has provided," added Jim Kupiec, MD, Cassava Sciences' Chief Clinical Development Officer. "We look forward to continuing a collaborative dialogue throughout the pivotal Phase 3 clinical development program."

Simufilam is a novel drug, discovered at Cassava Sciences, that targets both neuroinflammation and neurodegeneration. The EOP2 meeting discussion was supported by years of scientific and clinical data, including positive results from a previously completed Phase 2 clinical program with simufilam in Alzheimer's disease. In a double-blind, randomized, placebo-controlled Phase 2b study, simufilam demonstrated robust effects on primary and secondary outcome measures, with no safety issues. Recently, the Company announced that simufilam improved cognition in subjects with Alzheimer's disease in a 6-month interim analysis of an open-label study, with no safety issues.

The EOP2 meeting took place mid-January. FDA attendees included Robert Temple, MD, Deputy Center Director for Clinical Science and Senior Advisor in the Office of New Drugs; Billy Dunn, MD, Director, Office of Neuroscience; Eric Bastings, MD, Director, Division of Neurology, and others.

Official meeting minutes confirm that Cassava Sciences and FDA are aligned on key elements of a Phase 3 clinical program for simufilam. FDA has agreed that the completed Phase 2 program, together with an upcoming and well-defined Phase 3 clinical program, are sufficient to show evidence of clinical efficacy for simufilam in Alzheimer's disease. There is also agreement that the use of separate clinical scales to assess cognition (ADAS-cog [1]) and function (ADCS-ADL[2]) are appropriate co-primary endpoints of efficacy. A clinical scale that combines cognition and function, such as iADRS[3], is a secondary efficacy endpoint.

Cassava Sciences' pivotal Phase 3 clinical program consists of two double-blind, randomized, placebo-controlled studies, each described below.

Cassava Sciences' first Phase 3 study is designed to evaluate *disease-modifying* effects of simufilam in Alzheimer's disease. The goal is to demonstrate a slower rate of decline in cognition and health function in subjects treated with simufilam compared to placebo.

Details of the first Phase 3 study include:

- Approximately 1,000 subjects with mild-to-moderate Alzheimer's disease to be enrolled.
- Subjects to be randomized (1:1:1) to simufilam 100 mg, 50 mg, or placebo BID.
- Subjects to be treated for 18 months.
- The co-primary efficacy endpoints are ADAS-Cog, a cognitive scale, and ADCS-ADL, a functional scale; both are widely used clinical tools in trials of Alzheimer's disease.
- A secondary efficacy endpoint is iADRS, a widely used clinical tool in trials of Alzheimer's disease that combines cognitive and functional scores from ADAS-Cog & ADCS-ADL.
- Other secondary endpoints include biomarkers of disease and NPI[4], a clinical tool that assesses the presence and severity of dementia-related behavior.
- The Company plans to initiate the first pivotal Phase 3 study Q3 2021.

Cassava Sciences' second Phase 3 study is designed to evaluate *symptomatic improvement* in Alzheimer's disease. The goal is to demonstrate improved cognition and health function in subjects treated with simufilam compared to placebo.

Details of the second Phase 3 study include:

- Approximately 600 subjects with mild-to-moderate Alzheimer's disease to be enrolled.
- Subjects to be randomized (1:1) to simufilam 100 mg or placebo BID.
- Subjects to be treated for 9 to 12 months.
- The co-primary efficacy endpoints are ADAS-Cog, a cognitive scale, and ADCS-ADL, a functional scale; both are widely used clinical tools in trials of Alzheimer's disease.
- A secondary efficacy endpoint is iADRS, a widely used clinical tool in trials of Alzheimer's disease that combines cognitive and functional scores from ADAS-Cog & ADCS-ADL.
- Other secondary endpoints include biomarkers of disease and NPI, a clinical tool that assesses the presence and severity of dementia-related behavior.
- The Company plans to initiate the second pivotal Phase 3 study Q4 2021.

FDA has provided further flexibility to Cassava Sciences by agreeing to review the final version of each protocol for the two Phase 3 studies, and to conduct a Special Protocol Assessment (SPA) for each Phase 3 study. An SPA is a formal regulatory procedure that confirms certain critical details of a Phase 3 study protocol, such as the statistical analyses, meet FDA's standards of approvability.

In addition to the planned pivotal Phase 3 clinical program, other clinical studies in support of simufilam's safety and efficacy in Alzheimer's disease are briefly described below.

Open-label Study
Cassava Sciences recently expanded the size of an ongoing open-label study of simufilam. The study's target enrollment was increased by up to 50 additional subjects with mild-to-moderate Alzheimer's disease, for a total target enrollment of up to 150 subjects. To accommodate increased enrollment, the Company is opening new clinical sites in the U.S. and Canada.

The Company plans to conduct a second interim analysis of the open-label study mid-year 2021, when approximately 50 subjects complete 12 months of drug treatment. Much like the first pre-planned interim analysis (6 months), the second pre-planned interim analysis (12 months) is expected to generate clinical data around long-term safety, cognition and dementia-related behavior.

Cognition Maintenance Study (CMS)
In Q2 2021, Cassava Sciences plans to initiate a double-blind, randomized, placebo-controlled study in subjects with Alzheimer's disease who have completed at least one year of open-label treatment with simufilam. In this *Cognition Maintenance Study* (CMS), subjects who complete one year of open-label treatment will be randomized (1:1) to simufilam or placebo for 6 months. The CMS is designed to compare simufilam's effects on cognition and dementia-related in subjects who continue with drug treatment versus those who discontinue drug treatment. For ethical and other reasons, subjects who successfully complete the 6-month CMS will be given the option to return to open-label simufilam again.

Slide Deck
Cassava Sciences' latest corporate presentation is available on its website under the Investors/Presentations page: https://www.CassavaSciences.com

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. As of 2020, there were approximately 50 million people worldwide living with dementia, a figure expected to increase to 150 million by 2050.[5] The annual global cost of dementia is now above $1 trillion, according to *Alzheimer's Disease International*, a charitable organization.

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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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 an open-label study and Phase 2 program results; plans to conduct a second interim analysis of an open-label study and the timing thereof; planned enrollment and other changes to said open-label program; results of our EOP2 meeting with FDA including agreement on elements to support a New Drug Application filing for simufilam in Alzheimer's disease; our intention to initiate a Phase 3 clinical program with simufilam and the timing, enrollment, duration and other details thereof; 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 press release also contains information based on independent industry publications. We have not independently verified the accuracy or completeness of the information contained in these publicly available sources. Accordingly, we make no representations as to the accuracy or completeness of such information. You are cautioned not to give undue weight to such information.

[1] *ADAS-Cog = The Alzheimer's Disease Assessment Scale – Cognitive Subscale, a measure of cognition*

[2] *ADCS-ADL = Alzheimer's Disease Cooperative Study – Activities of Daily Living, a measure of health function*

[3] *iADRS = integrated Alzheimer's Disease Rating Scale, a composite measure of cognition and health function*

[4] *Neuropsychiatric Inventory (NPI)*

[5] *Alzheimer's Disease International, Dementia Statistics, available on-line and accessed February 20, 2021: https://www.alzint.org/about/dementia-facts-figures/dementia-statistics/*

Source: Cassava Sciences, Inc.