Cassava Sciences Topline Phase 3 Data Did Not Meet Co-Primary Endpoints

Nov 25, 2024

Simufilam did not show a significant reduction in cognitive or functional decline versus placebo in patients with mild-to-moderate Alzheimer's disease in the ReThink-ALZ Phase 3 study

Simufilam continued to demonstrate an overall favorable safety profile

Cassava intends to present the data at an upcoming medical meeting

The Company will hold a webcast today, November 25, 2024, at 8:00 AM ET

AUSTIN, Texas, Nov. 25, 2024 (GLOBE NEWSWIRE) -- Cassava Sciences, Inc. (NASDAQ: SAVA, "Cassava", the "Company"), a clinical-stage biotechnology company focused on developing a novel, investigational treatment for Alzheimer's disease (AD) dementia, today announced that the topline results from the Phase 3 ReThink-ALZ study of simufilam in mild-to-moderate AD did not meet each of the pre-specified co-primary, secondary and exploratory biomarker endpoints. The co-primary endpoints were the change in cognition and function from baseline to the end of the double-blind treatment period at week 52, assessed by the ADAS-COG12 and ADCS-ADL scales, comparing simufilam to placebo. Simufilam continued to demonstrate an overall favorable safety profile. The Company will hold a webcast today at 8 AM ET.

"The results are disappointing for patients and their families who are living with this disease and physicians who have been looking for novel treatment options. We took careful measures to enroll patients with mild-to-moderate AD. Despite that, the loss of cognition in the placebo group was less pronounced than was previously reported in other placebo-controlled studies in AD. We are working to understand this better," said **Rick Barry, President and Chief Executive Officer**. "A result like this has implications on our second Phase 3 trial, ReFocus-ALZ. We have made the difficult decision to discontinue ReFocus-ALZ, given the nature of today's reported results. The complete 52-week dataset will be available from the study along with a large portion of 76-week data. We intend to report detailed analyses of both studies in the future. We will also be discontinuing the Open Label Extension study."

Mr. Barry continued, "We have a special gratitude for the patients and their families and caregivers who participated in our clinical program for AD. We are also immensely grateful to our employees, study investigators and site coordinators, as well as our other partners, for their commitment to this program. We hope the information we have gathered can ultimately be used to benefit ongoing research in AD."

The table below provides a high-level summary of the co-primary endpoints data. Topline analysis of the mild and moderate sub-groups, likewise, did not demonstrate statistical significance at week 52.

Co-Primary Endpoint Data*	**Simufilam 100 mg BID N= 403**	**Placebo BID N=401**	**Delta**	**P-value**
Co-Primary Endpoints LS means change from baseline to the end of the double-blind treatment period				
ADAS-COG12 (SE)	2.8 (0.36)	3.2 (0.36)	-0.39 (0.50)	P=0.43
ADCS-ADL (SE)	-3.3 (0.44)	-3.8 (0.44)	0.51 (0.61)	P=0.40
*Based on the intent-to-treat population BID = twice daily ADAS-COG12 = The Alzheimer's Disease Assessment Scale – Cognitive Subscale (a lower number represents less cognitive impairment) ADCS-ADL = Alzheimer's Disease Cooperative Study – Activities of Daily Living (a higher number represents less functional impairment)				

The table below provides a high-level summary of the patient demographic and safety data. Simufilam continued to demonstrate an overall favorable safety profile.

Metrics for Simufilam and Placebo	**Simufilam 100 mg BID**	**Placebo BID**
Baseline*		
Age, mean (SD), in years	73.7 7.9	74.3 7.6
Sex, n (%) female	225 (55.8%)	222 (55.4%)
MMSE Score (No.%,)		
21-27	244 (60.5%)	250 (62.3%)
16-20	155 (38.5%)	146 (36.4%)
Race/Ethnicity		
White	366 (90.8%)	376 (93.8%)
Black	20 (5.0%)	18 (4.5%)
Asian	8 (2.0%)	2 (0.5%)
Other	9 (2.2%)	5 (1.0%)

Safety**		
Any Adverse Event (AE)	284 (71.2%)	269 (67.6%)
Serious AEs	52 (13.0%)	36 (9.0%)
Death	1 (0.3%)	3 (0.8%)
AEs leading to discontinuation from the study	26 (6.5%)	17 (4.3%)
Most Frequent AEs		
1: COVID-19	32 (8.0%)	36 (9.0%)
2: Urinary Tract Infection	31 (7.8%)	29 (7.3%)
3: Fall	30 (7.5%)	30 (7.5%)
4: Dizziness	21 (5.3%)	1 (0.3%)
5: Headache	18 (4.5%)	11 (2.8%)

*Based on the intent-to-treat population
**Based on the safety population
BID = twice daily
AD = Alzheimer's disease
MMSE = Mini-Mental State Examination

Cassava will continue to review all of the data and evaluate next steps. We plan to share the detailed results at a future medical meeting.

Eric Schoen, Chief Financial Officer at Cassava commented, "We remain focused on the interests of Cassava shareholders and are committed to enhancing shareholder value. Cassava is well-capitalized with approximately $149.0 million in cash and cash equivalents as of the end of the third quarter of 2024."

Webcast Info

Date: Monday, November 25th
Time: 8:00 a.m. Eastern Time
Webcast: https://lifescievents.com/event/cassava/

A webcast of the live call will be available in the investor relations section of the Cassava website. Access to the webcast replay will be available on the Company's website approximately two hours after completion of the call for approximately 90 days.

About Re-THINK-ALZ

ReThink-ALZ (NCT04994483) is a Phase 3 trial designed to evaluate the safety and efficacy of simufilam compared to a placebo in a multi-center, double-blinded, placebo-controlled, randomized parallel group study involving over 75 clinical trial sites in the U.S., Canada and Australia. The trial randomized 804 people with confirmed mild or moderate AD, defined by several well validated parameters including a mini-mental state examination (MMSE) of >16 and <27, stratified as mild or moderate. Subjects were randomized 1:1 to receive simufilam 100 mg (n=403) or a matched placebo (n=401), dosed orally twice daily (BID) for 52 weeks.

The co-primary endpoints were the change in cognition and function from baseline to the end of the double-blind treatment period at week 52, assessed by the ADAS-COG12 and ADCS-ADL scales, comparing simufilam to placebo. Secondary endpoints also included several well validated measures of neuropsychiatric symptoms and caregiver burden. Safety was evaluated through multiple measures, including adverse event monitoring. The study also included a pharmacokinetic and plasma biomarker sub-study comprised of approximately 100 subjects, evaluated at three timepoints. ReThink-ALZ was conducted under a Special Protocol Assessment (SPA) with the U.S. Food and Drug Administration (FDA).

About Simufilam

Simufilam is a proprietary, investigational oral small molecule that targets the filamin A protein.

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.

Simufilam, an investigational oral, small molecule drug candidate that targets the filamin A protein, is under evaluation for the potential treatment of Alzheimer's disease. Cassava Sciences owns exclusive, worldwide rights to its investigational product candidates and related technologies, without royalty obligations to any third party.

For more information, please visit: https://www.CassavaSciences.com

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Cautionary Note Regarding Forward-Looking Statements:
This news release contains forward-looking statements that include but are not limited to statements regarding: the completion and future results of our Phase 3 clinical studies of simufilam in patients with Alzheimer's disease; the planned discontinuation of the ReFocus-ALZ and open-label extension studies; our intent to share detailed study results at a future medical meeting; the timing of anticipated milestones; and the potential for simufilam to be approved as a treatment for Alzheimer's disease. These statements may be identified by words such as "anticipate", "before," "believe", "could", "expect", "forecast", "intend", "may", "pending," "plan", "possible", "potential", "prepares for," "will", and other words and terms of similar meaning.

Such statements are based 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; the ability to demonstrate the specificity, safety, efficacy or potential health benefits of simufilam; our current expectations regarding timing of clinical data for our Phase 3 studies; and other risks inherent in drug discovery and development or specific to Cassava Sciences, Inc., as described in the section entitled "Risk Factors" in our Annual Report on Form 10-K for the year ended December 31, 2023 and Quarterly Report on Form 10-Q for the period ended September 30, 2024, 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. 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.

All of our pharmaceutical assets under development are investigational product candidates. These have not been approved for use in any medical indication by any regulatory authority in any jurisdiction and their safety, efficacy or other desirable attributes, if any, have not been established in any patient population. Consequently, none of our product candidates is approved or available for sale anywhere in the world.

Source: Cassava Sciences, Inc.