Cassava Sciences Announces Phase 2a Study of PTI-125 Published in The Journal of Prevention of Alzheimer's Disease (JPAD)

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AUSTIN, Texas, Feb. 11, 2020 (GLOBE NEWSWIRE) -- Cassava Sciences, Inc. (Nasdaq: SAVA), a clinical-stage biotechnology company focused on Alzheimer's disease, today announced that *The Journal of Prevention of Alzheimer's Disease* (JPAD), a peer-reviewed journal for the research community, published results from the Company's Phase 2a study demonstrating that its lead drug candidate, PTI-125, reduced biomarkers of disease in Alzheimer's patients.

Nadav Friedmann, MD, PhD, Chief Medical Officer at Cassava Sciences commented, "We are pleased to share these study results in JPAD. This publication provides clinical insights into how our lead drug candidate, PTI-125, could make an important difference for patients living with Alzheimer's disease. In this study, PTI-125 reduced multiple biomarkers of Alzheimer's disease, including neurodegeneration and neuroinflammation. To our knowledge, no other drug has shown such effects in Alzheimer's patients."

Published results from this study demonstrate that biomarkers of Alzheimer's disease pathology (P-tau, total tau and $A\beta_{42}$), neurodegeneration (NfL and neurogranin) and neuroinflammation (YKL-40, IL-6, IL-1β and TNFα) improved significantly after 28 days of treatment with PTI-125. Biomarker reductions were at least $p< 0.001$ by paired t-test. Biomarkers effects were seen in all patients in both cerebrospinal fluid (CSF) and plasma. PTI-125 was safe and well tolerated, with no observable drug-related adverse events.

Lindsay H. Burns, PhD, VP Neuroscience at Cassava Sciences, added, "This publication supports PTI-125 as a new and potentially disease-modifying drug treatment for Alzheimer's disease. Significant improvements observed across multiple biomarkers imply a slower rate of neurodegeneration or a suppression of disease processes. These treatment effects are consistent with the drug's mechanism of action and over ten years of basic research and preclinical data."

Key results published from the Phase 2a study include:

- Total tau (T-tau) decreased 20% ($p<0.001$)
- Phosphorylated tau (P-tau) decreased 34% ($p<0.0001$)
- Neurofilament light chain (NfL), a marker for neurodegeneration, decreased 22% ($p<0.0001$)
- Neurogranin, a marker for cognitive decline, decreased 32% ($p<0.0001$)
- Neuroinflammatory marker YKL-40, an indicator of microglial activation, decreased 9% ($p<0.0001$)
- Proinflammatory Interleukin 6 (IL-6) decreased 14% ($p<0.0001$)
- Proinflammatory Interleukin 1 beta (IL-1β) decreased 11% ($p<0.0001$)
- Proinflammatory Tumor Necrosis Factor alpha (TNFα) decreased 5% ($p<0.001$)
- The ratio of CSF P-tau to $A\beta_{42}$, a widely accepted biochemical value of Alzheimer's disease, improved in all patients ($p<0.001$)

Although cognition and function were not assessed in this small Phase 2a study, independent research has shown that high levels of CSF biomarkers of P-tau and total tau/$A\beta_{42}$ ratio correlate with worse performance on a wide range of memory and attention tests. Conversely, lowering biomarkers of disease may benefit patients.

"We are now conducting a confirmatory Phase 2b study of PTI-125 in Alzheimer's disease," said Remi Barbier, President and CEO. "If positive, results of that study may be a major inflection point for us as a company and for patients, physicians and caregivers in the Alzheimer's community. We look forward to sharing results of our on-going Phase 2b study approximately mid-2020."

Results of On-going Phase 2b Study Expected mid-2020
Sixty-four (64) patients with mild-to-moderate Alzheimer's disease are enrolled in a randomized, placebo-controlled, confirmatory Phase 2b study to assess the safety, tolerability and biomarkers effects of PTI-125. More information for this study is available on-line at ClinicalTrials.gov: https://clinicaltrials.gov/ct2/show/NCT04079803

About the Published Phase 2a Study
Phase 2a was a first-in-patient, open-label, multi-center, safety, pharmacokinetic and biomarker study of PTI-125 in the U.S. Thirteen patients with mild-to-moderate Alzheimer's disease, age 50-85, received 100 mg oral PTI-125 twice daily for 28 days. A diagnosis of Alzheimer's disease was confirmed with Mini-Mental State Examination (MMSE) ≥ 16 and ≤ 24 and a CSF T-tau/$A\beta_{42}$ ratio ≥ 0.30. Safety was assessed by ECGs, clinical labs, adverse event monitoring and physical examinations. CSF was drawn from patients before dosing started and again after 28 continuous days of dosing with PTI-125. CSF samples were then analyzed for biomarkers of Alzheimer's pathology (T-tau, P-tau, $A\beta_{42}$); neurodegeneration (NfL, neurogranin); and neuroinflammation (YKL-40, IL-6, IL-1β and TNFα). A consulting *biostatistician* conducted an independent analysis of the data set.

Reference
"PTI-125 Reduces Biomarkers of Alzheimer's Disease In Patients" , *The Journal of Prevention of Alzheimer's Disease (2020)* (**DOI: 10.14283);**

H.-Y. Wang[1,2], Z. Pei[1], K.-C. Lee[1], E. Lopez-Brignoni[3], B. Nikolov[3], C.A. Crowley[4], M.R. Marsman[4], R. Barbier[4], N. Friedmann[4], L.H. Burns[4]
The publication is available on-line: http://link.springer.com/article/10.14283/jpad.2020.6

About PTI-125

The target of PTI-125 is an altered form of filamin A (FLNA), a scaffolding protein. Altered FLNA in the brain disrupts the normal function of neurons, leading to Alzheimer's pathology, neurodegeneration and neuroinflammation. Lead drug candidate PTI-125 is a proprietary small molecule that restores the normal shape and function of FLNA in the brain. This action improves the function of certain receptors in the brain, slows neurodegeneration and exerts powerful anti-neuroinflammatory effects. The underlying science for PTI-125 is published in peer-reviewed scientific journals, including *Journal of Neuroscience*, *Neurobiology of Aging*, and *Journal of Biological Chemistry*.

Cassava Sciences is also developing an investigational diagnostic, called PTI-125Dx, to detect Alzheimer's disease with a simple blood test.

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. [5] The number of people living with Alzheimer's disease is expected to grow dramatically in the years ahead, which may also result in a growing social and economic burden.[6]

About Cassava Sciences, Inc.

The mission of Cassava Sciences is to detect and treat neurodegenerative diseases, such as Alzheimer's disease. 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. Cassava Sciences owns worldwide development and commercial rights to its research programs in Alzheimer's disease, and related technology, without royalty obligations to any third-party.

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Cautionary Note Regarding Forward-Looking Statements: *This press release contains "forward-looking statements" for purposes of the Private Securities Litigation Reform Act of 1995 (the Act). Cassava Sciences claims the protection of the Safe Harbor for forward-looking statements contained in the Act. All statements other than statements of historical fact contained in this press release including, but not limited to, statements regarding the status of clinical studies with PTI-125; the interpretation of results of clinical studies, including target engagement and potential health benefits, if any, of changes in levels of biomarkers; verbal commentaries made by Cassava Sciences' employees; and other potential benefits, if any, of the Company's product candidates for Alzheimer's disease, are forward-looking statements. Such statements are based largely on the Company's current expectations and projections about future events. Such statements speak only as of the date of this press 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 trials on expected timelines, to demonstrate the specificity, safety, efficacy or potential health benefits of our product candidates and including those described in the section entitled "Risk Factors" in Cassava Sciences' Annual Report on Form 10-K for the year ended December 31, 2018 and future reports to be filed with the SEC. In light of these risks, uncertainties and assumptions, the forward-looking statements and events discussed in this press 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, the Company disclaims any intention or responsibility for updating or revising any forward-looking statements contained in this press 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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[5, 6] Source: Alzheimer's Association. *2019 Alzheimer's Disease Facts and Figures* . Available online at: https://www.alz.org/media/documents/alzheimers-facts-and-figures-2019-r.pdf

Source: Cassava Sciences, Inc.