New Publication Identifies Key Proteins Involved in Amyloid Oligomer Binding and Supports Mechanism of CT1812

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NEW YORK, Feb. 06, 2024 (GLOBE NEWSWIRE) -- **Cognition Therapeutics, Inc.** (NASDAQ: CGTX), a clinical stage company developing drugs that treat neurodegenerative disorders, announced that collaborators at the University of Edinburgh, Scotland published findings in the journal, *Acta Neuropathologica*, (doi: 10.1007/s00401-023-02679-6) that provide new insight into the biology of Alzheimer's disease that is consistent with our understanding of the role the σ-2 receptor has in regulating Aβ oligomer binding.

Using a combination of two high-resolution microscopy techniques: array tomography and Förster resonance energy transfer (FRET), Professor Tara Spires-Jones and colleagues at the UK Dementia Research Institute at University of Edinburgh's Centre for Discovery Brain Sciences analyzed protein-protein interactions in over 1 million individual synapses in brain samples from people who had died with Alzheimer's disease. Results detected TMEM97, a protein component of the σ-2 receptor complex, in close proximity to cellular prion protein (PrPc) on Alzheimer's brain synapses. In addition, results found that Aβ oligomers were proximate to both PrPc, which has been shown to bind Aβ oligomers in neuronal cultures, as well as to TMEM97. These findings support the hypothesis that these receptor proteins may form a complex on the synapse surface with Aβ oligomers binding to one or both proteins.

"Losing synaptic connections in the brain contributes to Alzheimer's disease symptoms," explained Professor Spires-Jones. "Previous work indicated that Aβ oligomers damage synapses, but until now it was not possible to know which proteins bind toxic forms of Aβ in human synapses. Combining FRET and array tomography imaging overcomes the limits of traditional microscopy and lets us determine whether proteins are close enough to interact in human brain samples. In simplest terms, while we had previous evidence that certain proteins existed in the same cellular neighborhood, we couldn't precisely determine until now which houses were next to one another. Our findings help clarify the specific interactions between Aβ oligomers and synaptic receptors, which we hope will provide valuable information for drug developers."

Professor Spires-Jones' work also confirmed that in the presence of CT1812, Cognition's lead product candidate, Aβ oligomers are displaced from the oligomer receptor, a discovery echoed in the SNAP study, which was published in May 2023 in *Translational Neurodegeneration*. In Professor Spires-Jones' study using an Alzheimer's mouse model, a FRET signal was observed between TMEM97 and Aβ oligomers in synapses, which could occur if oligomers were bound to TMEM97 or to PrPc, the putative oligomer binding site. Importantly, this FRET signal is reduced in CT1812-treated mice, suggesting that CT1812 caused the release of Aβ oligomers from their binding site and prevented them from re-binding.

"Professor Spires-Jones' most recent work showing that CT1812 causes the removal of Aβ oligomers from synapses is an important confirmation of the mechanism initially proposed in the two seminal PLoS One papers authored by Cognition's founding scientists," explained Anthony Caggiano, MD, PhD, Cognition's CMO and head of R&D. "We believe these findings build on our clinical evidence that targeting the σ-2 receptor with CT1812 may offer a distinct and relevant new mechanism to fight Alzheimer's disease progression by protecting synapses from the damaging effects of Aβ oligomers."

About Cognition Therapeutics, Inc.
Cognition Therapeutics, Inc. is a clinical-stage biopharmaceutical company engaged in the discovery and development of innovative, small molecule therapeutics targeting age-related degenerative disorders of the central nervous system and retina. We are currently investigating our lead candidate CT1812 in clinical programs in Alzheimer's disease, dementia with Lewy bodies (DLB) and dry age-related macular degeneration (dry AMD). We believe CT1812 and our pipeline of σ-2 receptor modulators can regulate pathways that are impaired in these diseases. We believe that targeting the σ-2 receptor with CT1812 represents a mechanism functionally distinct from other current approaches in clinical development for the treatment of degenerative diseases. More about Cognition Therapeutics and its pipeline can be found at https://cogrx.com.

Forward Looking Statements
This press release contains forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. All statements contained in this press release, other than statements of historical facts or statements that relate to present facts or current conditions, including but not limited to, statements regarding our product candidates, including CT1812, and any expected or implied benefits or results, including that initial clinical results observed with respect to CT1812 will be replicated in later trials and our clinical development plans, including statements regarding our clinical studies of CT1812 and any analyses of the results therefrom, are forward-looking statements. These statements, including statements relating to the timing and expected results of our clinical trials, involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance, or achievements to be materially different from any future results, performance, or achievements expressed or implied by the forward-looking statements. In some cases, you can identify forward-looking statements by terms such as "may," might," "will," "should," "expect," "plan," "aim," "seek," "anticipate," "could," "intend," "target," "project," "contemplate," "believe," "estimate," "predict," "forecast," "potential" or "continue" or the negative of these terms or other similar expressions. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition, and results of operations. These forward-looking statements speak only as of the date of this press release and are subject to a number of risks, uncertainties and assumptions, some of which cannot be predicted or quantified and some of which are beyond our control. Factors that may cause actual results to differ materially from current expectations include, but are not limited to: competition; our ability to secure new (and retain existing) grant funding; our ability to grow and manage growth, maintain relationships with suppliers and retain our management and key employees; our ability to successfully advance our current and future product candidates through development activities, preclinical studies and clinical trials and costs related thereto; uncertainties inherent in the results of preliminary data, pre-clinical studies and earlier-stage clinical trials being predictive of the results of early or later-stage clinical trials; the

timing, scope and likelihood of regulatory filings and approvals, including regulatory approval of our product candidates; changes in applicable laws or regulations; the possibility that the we may be adversely affected by other economic, business or competitive factors, including ongoing economic uncertainty; our estimates of expenses and profitability; the evolution of the markets in which we compete; our ability to implement our strategic initiatives and continue to innovate our existing products; our ability to defend our intellectual property; the impact of the COVID-19 pandemic on our business, supply chain and labor force; and the risks and uncertainties described more fully in the "Risk Factors" section of our annual and quarterly reports filed with the Securities & Exchange Commission and are available at www.sec.gov. These risks are not exhaustive and we face both known and unknown risks. You should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur, and actual results could differ materially from those projected in the forward-looking statements. Moreover, we operate in a dynamic industry and economy. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties that we may face. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

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