Alector Announces Publication of Preclinical and Phase 1 Data Validating Potential of AL002, a TREM2 Activating Antibody for the Treatment of Alzheimer's Disease, in The Journal of Experimental Medicine

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- Antibody-mediated engagement of TREM2 expanded unique subpopulations of metabolically active and proliferating microglia in a human TREM2 expressing mouse model of Alzheimer's disease

- Chronic treatment enhanced neuroprotective microglia, reduced neuronal damage, tempered microglial inflammatory response and contained toxic beta amyloid plaques in a mouse model of Alzheimer's disease. The treated mice also demonstrated improved cognitive and behavioral outcomes compared to placebo control

- AL002 was shown to be well-tolerated in a first-in-human Phase 1 SAD study in healthy volunteers and modulated cerebrospinal fluid biomarkers indicative of brain target engagement

SOUTH SAN FRANCISCO, Calif., June 25, 2020 (GLOBE NEWSWIRE) -- Alector, Inc. (Nasdaq: ALEC), a clinical-stage biotechnology company pioneering immuno-neurology, announced the publication of preclinical and preliminary Phase 1 clinical data of AL002, a TREM2 activating antibody, in *The Journal of Experimental Medicine*. The paper elucidates how a variant of AL002 reduces pathology in an Alzheimer's disease mouse model and induces a novel transcriptional signature in microglia associated with proliferation, and it includes data from the AL002 Phase 1 clinical trial that demonstrates target engagement in healthy volunteers and AL002's overall safety profile. The paper, "Anti-human TREM2 antibody induces microglia proliferation and reduces pathology in an Alzheimer's Disease model," was carried out in collaboration with Marco Colonna, M.D. at Washington University in St. Louis and can be accessed here.

"This publication is a culmination of years of research by the Alector team and our academic collaborators," said Robert Paul, M.D., Ph.D., Chief Medical Officer of Alector. "Specifically, the data show that antibody-mediated engagement of TREM2 enhances neuroprotective microglia and restrains neurotoxic plaques and neuronal damage in an Alzheimer's disease mouse model. Together with the safety and target engagement data from our Phase 1 trial of AL002, these results provide strong support for continued development of AL002 as a potential treatment for Alzheimer's disease. We look forward to the expected initiation of a Phase 2 trial of AL002 later this year."

Highlights of the findings from the Preclinical Study:

- TREM2 is a receptor for lipids expressed in microglia. The R47H variant of human TREM2 impairs ligand binding and increases Alzheimer's disease risk. In mouse models of amyloid beta accumulation, defective TREM2 function affects microglial response to neuronal damage, inflammation, and toxic amyloid beta plaques, whereas TREM2 overexpression attenuates these pathologies.

- The study examined the impact of an anti-human TREM2 agonistic monoclonal antibody, AL002c, a variant of AL002, in a mouse model of Alzheimer's disease expressing either the common variant or the R47H variant of human TREM2 to determine potential benefit from TREM2 activation on Alzheimer's disease.

- The study found that a single injection of AL002c expanded unique subpopulations of metabolically active and proliferating microglia. Prolonged treatment with AL002c tempered the microglial inflammatory response and reduced the formation of toxic filamentous plaques, which curtailed neurite dystrophy.

- The study further showed that AL002c treatment was beneficial after plaque formation, suggesting that anti-TREM2 antibodies may be helpful even if introduced at relatively late stages of disease.

Highlights of Findings from Phase 1 Clinical Study:

- The Phase 1a clinical study was a first-in-human study in healthy adults, designed to assess the safety (including immunogenicity), tolerability, pharmacokinetics (PK) and pharmacodynamics (PD) of AL002.

- In the single ascending dose portion of the Phase 1 study, 56 healthy volunteers were sequentially enrolled into 10 cohorts and received a single intravenous dose of AL002. In addition to safety, the study assessed the effect of AL002 on cerebrospinal fluid biomarkers, sTREM2 and sCSF-1R.

- Preliminary data from the completed Phase 1 study of AL002 indicates that AL002 was generally well-tolerated with no drug-related serious adverse events or dose-limiting toxicities up to the highest dose. The data also indicated target engagement of AL002 in the brain, as measured by the cerebrospinal fluid biomarkers sTREM2 and sCSF-1R.

About AL002
AL002 is a monoclonal antibody that targets a triggering receptor expressed on myeloid cells 2 (TREM2) with the strongest genetic links after APOE4 to sporadic Alzheimer's disease. TREM2 is a transmembrane receptor expressed on a subset of innate immune cells and selectively on microglia, which constitute the brain's immune system. TREM2 is thought to promote improved cell migration to the site of injury, improved cell survival, increased phagocytosis, and increased cell proliferation. Loss of TREM2 function leads to Alzheimer's disease and other forms of dementia and research suggests that boosting TREM2 levels in the brain may prevent or reduce the severity of neurodegenerative disorders.

About Collaboration with AbbVie
In October 2017, Alector entered into a global strategic collaboration with AbbVie (NYSE: ABBV), a leader in neuroscience drug development, to co-develop and commercialize therapeutics to treat Alzheimer's disease and other neurodegenerative diseases.

Under the terms of the agreement, Alector granted AbbVie an exclusive option to global development and commercialization for two programs, including TREM2. For each program, Alector is responsible for the design and execution of Phase 1 and Phase 2 studies, leveraging the Company's in-house expertise in running clinical trials in Alzheimer's disease. Following its exercise of an option for a program, AbbVie will be responsible for certain development activities and global commercialization. The terms of the agreement included an initial upfront payment of $205M in cash and $20M in equity and if AbbVie exercises its option for either program (or both programs), Alector is eligible for additional option exercise and milestone payments totaling up to $986M. Following AbbVie's exercise of its option, Alector and AbbVie will share the development costs and will split global profits equally after marketing approval.

About Alzheimer's Disease
Alzheimer's disease is a degenerative brain disease and the most common form of dementia. It is an irreversible, progressive brain disorder that slowly destroys memory and thinking skills, and eventually the ability of patients to care for themselves. In most people with Alzheimer's disease, symptoms first appear in their mid-60s. The Alzheimer's Association estimates that as of 2018, there are 5.7 million Americans suffering from Alzheimer's disease, and projects that number will rise to nearly 14 million by 2050.

About Alector
Alector is a clinical stage biotechnology company pioneering immuno-neurology, a novel therapeutic approach for the treatment of neurodegenerative diseases. Immuno-neurology targets immune dysfunction as a root cause of multiple pathologies that are drivers of degenerative brain disorders. Alector is developing a broad portfolio of programs designed to functionally repair genetic mutations that cause dysfunction of the brain's immune system and enable the rejuvenated immune cells to counteract emerging brain pathologies. The Company's product candidates are supported by biomarkers and target genetically defined patient populations in frontotemporal dementia and Alzheimer's disease. Alector is headquartered in South San Francisco, California. For additional information, please visit www.alector.com.

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