



Alector Announces First Participant Dosed in Phase 2 Study Evaluating AL001 in Amyotrophic Lateral Sclerosis (ALS)

September 9, 2021

Randomized, placebo-controlled Phase 2 trial will enroll patients with C9orf72-associated ALS

SOUTH SAN FRANCISCO, Calif., Sept. 09, 2021 (GLOBE NEWSWIRE) -- Alector, Inc. (Nasdaq: ALEC), a clinical-stage biotechnology company pioneering immuno-neurology, today announced that the first participant has been dosed in a Phase 2 clinical study evaluating the safety, tolerability, pharmacokinetics and pharmacodynamics of AL001 in people with amyotrophic lateral sclerosis (ALS) who carry a *C9orf72* mutation. AL001 is being developed in collaboration with GlaxoSmithKline (GSK).

AL001 is a potential first-in-class monoclonal antibody designed to elevate progranulin, a key regulator of immune activity in the brain. Alector is also actively enrolling the Phase 3 INFRONT-3 pivotal clinical study of AL001 in individuals at-risk for and symptomatic patients with frontotemporal dementia (FTD) who carry a progranulin mutation (FTD-*GRN*), as well as currently enrolling the Phase 2 INFRONT-2 study in symptomatic patients with FTD who carry a *C9orf72* mutation (FTD-*C9orf72*).

"AL001 has shown encouraging results in patients with FTD-*GRN*, rapidly increasing progranulin levels and normalizing inflammatory biomarkers along the disease cascade that contribute to neurodegeneration," said Sam Jackson, M.D., Alector's interim Chief Medical Officer. "Frontotemporal dementia and amyotrophic lateral sclerosis share common clinical, pathological and genetic features and it is now recognized that FTD and ALS are two diseases that form a broad neurodegenerative continuum. ALS is the first of several potential indications beyond frontotemporal dementia where we believe AL001 may have a positive impact on brain health by elevating progranulin levels."

Both decreased progranulin levels and mutations in the chromosome 9 open reading frame 72 (*C9orf72*) gene are associated with abnormal accumulation of the TAR DNA-binding protein 43 (TDP-43). Excess aggregation of TDP-43 in brain cells is thought to lead to neuronal cell death and is associated with multiple neurodegenerative diseases, including ALS, where 95% of patients with ALS have TDP-43 pathology. In preclinical studies using multiple models of acute and chronic neurodegeneration, increasing progranulin levels has been shown in the literature to reverse and be protective against TDP-43 pathology.

Dr. Jackson continued, "We have seen consistent clinical and preclinical evidence of AL001's ability to increase progranulin levels in the brain, and we are optimistic that in doing so, we may be able to mitigate or halt the downstream damage caused to motor neurons by excess TDP-43, and thereby slow the progression of ALS. We look forward to exploring the potential of AL001 to improve outcomes for ALS patients."

"ALS, also known as Lou Gehrig's disease, is a progressive and ultimately fatal neurodegenerative condition, with few FDA-approved treatment options. As we learn more about the genetic and biologic underpinnings of ALS, there is an opportunity to develop targeted treatments that address the mechanism of disease," said Katharine Nicholson, M.D., neurologist and ALS clinical trialist at the Sean M. Healey & AMG Center for ALS at Massachusetts General Hospital, and the principal investigator for the Phase 2 study of AL001. "TDP-43 accumulation is found in the majority of patients with ALS, and by elevating progranulin levels, it is hoped that AL001 may have a neuroprotective effect. I look forward to working with Alector to study AL001's disease-modifying potential in ALS."

The Phase 2 trial of AL001 is a randomized, double-blind, placebo-controlled, multicenter study that is expected to enroll approximately 45 adult participants with *C9orf72*-associated ALS. Participants will receive AL001 or placebo intravenously every four weeks for 24 weeks added to their current treatment regimen. The primary endpoint of the study is safety, tolerability, pharmacokinetics and pharmacodynamics of AL001, including plasma and cerebrospinal fluid (CSF) progranulin levels. The Phase 2 will also gather data on changes to multiple liquid biomarkers. Taken together, these data are intended to inform trial design and dosing for future efficacy studies of AL001 in ALS.

About Amyotrophic Lateral Sclerosis

Amyotrophic lateral sclerosis (ALS) is a devastating, fatal, progressive neurodegenerative disorder. In ALS, the motor neurons in the brain and spinal cord die, resulting in weakness, muscle atrophy, paralysis and frequently, cognitive impairment, before resulting in death from respiratory failure. Each year, more than 5,000 people in the U.S. are diagnosed with ALS and an estimated 20,000 are living with the disease. Mutations within multiple genes, including the *C9orf72* gene, are believed to cause the disease. Such mutations can lead to an accumulation of TDP-43 in the cells resulting in neuronal death and an estimated 95% of ALS cases are linked to TDP-43 pathology. Approximately 40-50% of all familial ALS and up to 10% of sporadic ALS cases are attributed to the *C9orf72* mutation. Currently approved medications for ALS confer only a modest survival benefit and new treatment options are urgently needed.

About AL001

Decreased levels of PGRN, a key regulator of immune response, lysosomal function, and neuronal survival in the brain, are genetically linked to many neurodegenerative disorders. AL001 is a novel human monoclonal antibody that elevates levels of progranulin by blocking the sortilin receptor responsible for progranulin degradation. AL001 is currently in a pivotal Phase 3 clinical study in people at risk for or with frontotemporal dementia due to a progranulin gene mutation (FTD-*GRN*). AL001 is also being evaluated in a Phase 2 study in symptomatic patients with FTD who carry a *C9orf72* mutation, and a Phase 2 study in patients with amyotrophic lateral sclerosis (ALS) who carry a *C9orf72* mutation. In July 2021, Alector and GSK announced a global collaboration to co-develop AL001 for a range of neurodegenerative diseases, including FTD, ALS, Parkinson's disease and Alzheimer's disease.

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 has discovered and is developing a broad portfolio of innate immune system 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. Alector's immuno-neurology product candidates are supported by biomarkers and target genetically defined patient populations in frontotemporal dementia and Alzheimer's disease. This scientific approach is also the basis for the company's immuno-oncology programs. Alector is headquartered in South San Francisco, California. For additional information, please visit www.alector.com.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Such statements are subject to numerous important factors, risks and uncertainties that may cause actual events or results to differ materially from current expectations and beliefs, including but not limited to risks and uncertainties related to market conditions, Alector and its business as set forth in our Quarterly Report on Form 10-Q, as filed on August 3, 2021 with the Securities and Exchange Commission ("SEC"), as well as the other documents Alector files from time to time with the SEC. These documents contain and identify important factors that could cause the actual results for Alector to differ materially from those contained in Alector's forward-looking statements. Any forward-looking statements contained in this press release speak only as of the date hereof, and Alector specifically disclaims any obligation to update any forward-looking statement, except as required by law.

Alector Contacts

Michelle Corral
VP, Communications and Investor Relations
650-808-7016
michelle.corral@alector.com

1AB (media)
Dan Budwick
973-271-6085
dan@1abmedia.com

Argot Partners (investors)
Laura Perry/Eric Kasper
Argot Partners
212.600.1902
alector@argotpartners.com



Source: Alector, Inc.