Alector Announces Achievement of Target Enrollment in the Pivotal INFRONT-3 Phase 3 Clinical Trial of Latozinemab in Individuals with Frontotemporal Dementia Due to a Progranulin Gene Mutation (FTD-GRN)

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--101 symptomatic FTD-GRN participants enrolled in INFRONT-3 --

SOUTH SAN FRANCISCO, Calif., Oct. 27, 2023 (GLOBE NEWSWIRE) -- Alector, Inc. (Nasdaq: ALEC), a clinical-stage biotechnology company pioneering immuno-neurology, today announced that it has achieved target enrollment in INFRONT-3, the pivotal Phase 3 clinical trial of latozinemab (AL001). INFRONT-3 is evaluating the safety and efficacy of latozinemab in slowing disease progression in individuals with frontotemporal dementia due to a progranulin gene mutation (FTD-*GRN*). Latozinemab is an investigational human monoclonal antibody designed to block sortilin, a degradation receptor for progranulin (PGRN). It is intended to elevate PGRN levels and enhance the activity of microglia, the primary cells of the brain's innate immune system. Latozinemab is the most advanced PGRN modulating product candidate in clinical trials and the most advanced potential treatment for FTD-*GRN*. Latozinemab is being developed in collaboration with GSK.

Earlier this year, Alector and GSK held a Type C meeting with the U.S. Food and Drug Administration (FDA) and received scientific advice from the European Medicines Agency (EMA) regarding INFRONT-3. The companies aligned with the FDA and EMA to conduct the primary analysis on symptomatic FTD-*GRN* participants, supporting an enrollment target of approximately 90-100 symptomatic participants in INFRONT-3. Alector and GSK achieved target enrollment in INFRONT-3 with 101 symptomatic participants.

"Decreased progranulin levels due to genetic mutations in the progranulin gene are a known cause of FTD, a rare and rapidly progressing neurodegenerative disease, which is the most common form of dementia for people under the age of 60," said Arnon Rosenthal, Ph.D., Chief Executive Officer of Alector. "By achieving target enrollment in INFRONT-3, we are an important step closer to generating data from this pivotal trial of latozinemab, which could pave the way for registration. Currently, there are no approved treatment options available for any form of FTD, and we are eager to learn more about the potential of latozinemab."

INFRONT-3 is a pivotal, randomized, double-blind, placebo-controlled Phase 3 clinical trial, which is enrolling symptomatic and at-risk FTD-*GRN* participants at multiple sites across North America, Europe, Argentina and the Asia-Pacific region. Participants are randomized to receive latozinemab or placebo intravenously every four weeks for the duration of the 96-week trial and are being given the option to continue receiving treatment in the open-label extension (OLE) study after the 96-week treatment period. Following the 96-week OLE, if completed, participants will have another opportunity to roll over into a continuation study. The primary endpoint in INFRONT-3 is disease progression as measured by the Clinical Dementia Rating scale plus National Alzheimer's Disease Coordinating Center Frontotemporal Lobar Degeneration Sum of Boxes (CDR® plus NACC FTLD-SB). The CDR® plus NACC FTLD-SB, which is used to assess (score) the severity of FTD, is a validated instrument that assesses both cognitive and functional domains and has been accepted as the efficacy endpoint for FTD-*GRN* by the FDA and EMA. The trial also employs other clinical and functional outcome assessments. Additionally, the trial includes cerebrospinal fluid (CSF) and plasma biomarkers assessing PGRN levels, along with multiple disease-relevant biomarkers of lysosomal function, complement activation, astrocyte function, neurodegeneration, and brain atrophy.

About Latozinemab
Latozinemab (AL001) is an investigational human monoclonal antibody designed to modulate progranulin (PGRN), a key regulator of immune activity in the brain with genetic links to multiple neurodegenerative disorders, including frontotemporal dementia (FTD), Alzheimer's disease, and Parkinson's disease. Latozinemab aims to increase the level of PGRN in humans by inhibiting sortilin, a degradation receptor for PGRN. Latozinemab has received Orphan Drug designation for the treatment of FTD and Fast Track designation for the treatment of FTD due to a progranulin gene mutation (FTD-*GRN)* from the U.S. Food and Drug Administration.

About Frontotemporal Dementia (FTD)
Frontotemporal dementia (FTD) is a rare neurodegenerative disease, but it is the most common form of dementia for people under the age of 60.[1] It affects an estimated 50,000 to 60,000 people in the United States and roughly 110,000 in the European Union, with potentially higher prevalence in Asia and Latin America.[2,3] There are multiple heritable forms of FTD, and FTD patients with a progranulin gene mutation (FTD-*GRN)* represent 5% to 10% of all people with FTD.[4] Patients with FTD frequently develop symptoms such as behavioral changes, lapses in judgment, and diminished language skills when they are in their 40's and 50's with the disease running its course in 7-10 years. [5] There are no U.S. Food and Drug Administration-approved treatment options available for any form of FTD.[1]

Collaboration with GSK
In July 2021, Alector entered into a collaboration and license agreement with GSK (NYSE: GSK) to collaborate on the global development and commercialization of progranulin-elevating monoclonal antibodies, including latozinemab and AL101. Under the terms of the GSK agreement, Alector received $700 million in upfront payments. In addition, Alector may be eligible to receive up to an additional $1.5 billion in clinical development, regulatory, and commercial launch-related milestone payments. In the United States, the companies will equally share profits and losses from commercialization of latozinemab and AL101. Outside of the United States, Alector will be eligible for double-digit tiered royalties.

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 rejuvenated immune cells to counteract emerging brain pathologies. Alector's immuno-neurology product candidates are supported by biomarkers and seek to treat indications, including Alzheimer's disease and genetically defined frontotemporal dementia patient populations. Alector is headquartered in South San Francisco, California. For additional information, please visit www.alector.com.

About GSK
GSK is a global biopharma company with a purpose to unite science, technology, and talent to get ahead of disease together. Find out more at gsk.com.

Forward-Looking Statements
This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Forward-looking statements in this press release include, but are not limited to, statements regarding our product candidates, planned and ongoing preclinical studies and clinical trials, expected milestones, including the timing of data from our INFRONT-3 trial, and expectations of our collaborations. Such statements are subject to numerous risks and uncertainties, including but not limited to risks and uncertainties as set forth in Alector's Quarterly Report on Form 10-Q filed on August 3, 2023, 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.

REFERENCES

1. The Association for Frontotemporal Degeneration (AFTD).
2. Patient estimates based on internal forecasting analysis using published literature sources.
3. E.U. estimates include EU5 countries only (Spain, Italy, France, U.K. and Germany).
4. FTD Disorders Registry.
5. Moore KM, Nicholas J, Grossman M, et al. *Lancet Neurol.* 2020 Feb;19(2).

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