Alector Presents Baseline Characteristics for Pivotal INFRONT-3 Phase 3 Clinical Trial at the 14th International Conference on Frontotemporal Dementias (ISFTD 2024)

September 19, 2024

--Participant baseline characteristics in INFRONT-3 suggest a representative study population that enables testing of the effects of latozinemab in frontotemporal dementia with a progranulin gene mutation (FTD-GRN)--

--Latozinemab, a novel investigational human monoclonal antibody, is the most advanced PGRN-elevating candidate in development for the treatment of FTD-GRN--

SOUTH SAN FRANCISCO, Calif., Sept. 19, 2024 (GLOBE NEWSWIRE) -- Alector, Inc. (Nasdaq: ALEC), a clinical-stage biotechnology company pioneering immuno-neurology, today announced the presentation of a poster on participant baseline characteristics for the pivotal INFRONT-3 Phase 3 clinical trial evaluating the safety and efficacy of latozinemab in potentially slowing disease progression in individuals with frontotemporal dementia due to a progranulin gene mutation (FTD-*GRN*). The conference is being held in Amsterdam from September 19 – 22, 2024.

Heterozygous loss-of-function mutations in the *GRN* gene cause FTD due to progranulin (PGRN) haploinsufficiency.[1,2] Latozinemab is a novel investigational human monoclonal antibody that aims to increase PGRN levels by inhibiting sortilin, a degradation receptor for PGRN. The candidate is being developed in collaboration with GSK.

"The baseline characteristics of the participants in INFRONT-3 are important for assessing the representativeness of the population enrolled in our pivotal, double-blind, placebo-controlled Phase 3 clinical trial evaluating the safety and efficacy of latozinemab, the most advanced progranulin-elevating candidate in development for the treatment of FTD-*GRN*," said Gary Romano, M.D., Ph.D., Chief Medical Officer of Alector. “We are pleased that the baseline clinical assessments show that the INFRONT-3 trial enrolled the intended population of participants with FTD-*GRN*, allowing us to test our hypothesis that treatment with this first-in-class PGRN-elevating candidate may slow disease progression.”

Baseline characteristics are important in Phase 3 trials because they influence the reliability, interpretability and generalizability of trial results. A total of 119 participants were randomized in INFRONT-3, including 103 symptomatic individuals with FTD-*GRN* and 16 at-risk carriers for FTD-*GRN*. The mean age of participants at baseline was 62.1 years (range: 37-85 years). Overall, 51.3% of participants are female and 84.9% are Caucasian. The symptomatic cohort had a mean Clinical Dementia Rating scale plus National Alzheimer’s Disease Coordinating Center Frontotemporal Lobar Degeneration Sum of Boxes (CDR® plus NACC FTLD-SB) score of 6.9 and a mean serum neurofilament light chain (NfL) of 73.0 pg/mL at baseline. In the symptomatic cohort, the mean approximate age at diagnosis was 61.7 years, with a standard deviation of 6.7 years.

Compared against available registry data[3], the baseline characteristics of symptomatic INFRONT-3 participants, including age, CDR plus NACC FTLD-SB score and NfL levels, were representative of the broader FTD-*GRN* registry population. In a combined cohort of registry participants from GENFI and ALLFTD, symptomatic FTD-*GRN* carriers (n=84) had a mean age of 63.7 years, mean CDR plus NACC FTLD-SB score of 9.19, with a standard deviation of 6.53, and mean plasma NfL of 56.8 pg/mL at baseline.

Additional details will be presented during the poster presentation, “Baseline Characteristics for INFRONT-3: A Phase 3, Double-Blind, Placebo-Controlled, 96-Week Study Evaluating Latozinemab in FTD-*GRN*” on Friday, September 20, 2024, at 9:30 am CEST at ISFTD 2024.

INFRONT-3 enrollment was completed in October 2023. The trial is ongoing, with a treatment duration of 96 weeks.

About INFRONT-3
INFRONT-3 is a pivotal, randomized, double-blind, placebo-controlled Phase 3 clinical trial, that enrolled symptomatic and at-risk FTD-*GRN* participants at multiple sites across North America, Europe, Argentina and the Asia-Pacific region. Participants were 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 PGRN levels by inhibiting sortilin, a degradation receptor for PGRN. Latozinemab has received Orphan Drug Designation for the treatment of FTD from the U.S. Food and Drug Administration (FDA) and the European Commission as well as both Breakthrough Therapy and Fast Track designations for the treatment of FTD due to a progranulin gene mutation (FTD-*GRN)* from the FDA.

About Frontotemporal Dementia (FTD)
Frontotemporal dementia (FTD) is a rare neurodegenerative disease, but it is one of the most common causes of early onset dementia.[4] 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.[5,6] 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.[7] 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. [8] There are no approved treatment options available for any form of FTD.[4]

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 (GSK4527226). 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 business plans, business strategy, product candidates, planned and ongoing preclinical studies and clinical trials, anticipated timing and detail or release of data for INFRONT-3, expected milestones, expectations of our collaborations, and expectations of our interactions with regulatory authorities. 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 7, 2024, 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.

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3. Staffaroni AM, et al; Frontotemporal Dementia Prevention Initiative (FPI) Investigators. Temporal order of clinical and biomarker changes in familial frontotemporal dementia. *Nat Med.* 2022 Oct;28(10):2194-2206.
4. The Association for Frontotemporal Degeneration (AFTD).
5. Patient estimates based on internal forecasting analysis using published literature sources.
6. E.U. estimates include EU5 countries only (Spain, Italy, France, U.K. and Germany).
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