Alector Presents Encouraging New AL001 Data from the Symptomatic FTD-GRN Cohort of INFRONT-2 Phase 2 Open-label Clinical Study

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Progranulin Levels Increase to Normal Ranges

Multiple Biomarkers of Disease Showed Improvement from Baseline with AL001 Treatment, Including GFAP, a Prognostic Marker for FTD Associated with Brain Atrophy

FTD-GRN Patients Showed a Slowing of Clinical Progression with AL001 Treatment Relative to GENFI2 Matched Control Cohort

Data from Phase 2 Study Presented at Clinical Trials of Alzheimer Disease Conference; Management to Host Webcast to Review Results Today at 4:00 p.m. ET

BOSTON, Nov. 12, 2021 (GLOBE NEWSWIRE) -- Alector, Inc. (Nasdaq: ALEC), a clinical-stage biotechnology company pioneering immuno-neurology, presented encouraging results from the company's INFRONT-2 Phase 2 clinical trial of AL001 at the 14th Clinical Trials on Alzheimer's Disease (CTAD) conference taking place virtually and in Boston. AL001 is a potential first-in-class monoclonal antibody designed to elevate progranulin, a key regulator of immune activity in the brain. Decreased progranulin levels due to genetic mutations are a known cause of frontotemporal dementia (FTD), a rare and rapidly progressing neurodegenerative disease that is the most common form of dementia for people under the age of 60. AL001 is initially being developed for the treatment of adults at risk for or with symptomatic FTD due to a progranulin gene mutation (FTD-*GRN*).

The INFRONT-2 Phase 2 clinical trial was designed to assess the safety and tolerability of chronic dosing of AL001 in symptomatic FTD-*GRN* patients treated for up to 96 weeks. Highlights from the presentation included observations that:

- AL001 restored progranulin to normal levels (based on age-matched controls) in both plasma and cerebrospinal fluid (CSF) for the duration of treatment.
- Multiple biomarkers of lysosomal dysfunction and complement activation, known to be elevated in FTD-*GRN,* decreased toward normal levels (based on age-matched controls) following treatment with AL001.
- Glial fibrillary acidic protein (GFAP), a biomarker of astrogliosis that is an indicator of disease and/or injury to the central nervous system, was elevated at baseline and decreased towards normal levels (vs. asymptomatic FTD-*GRN* mutation carriers following AL001 treatment.
- AL001 treatment was estimated to slow disease progression at twelve months by 48% based on 12 patients as compared to a matched control cohort of participants from the Genetic FTD Initiative (GENFI2 [(1)])
- AL001 was generally well tolerated when administered monthly for a year or more.

"The consistency of the activity observed with AL001 in patients with frontotemporal dementia with a progranulin gene mutation across multiple measurements of disease is very encouraging. As we look across the physiological changes in the FTD-*GRN* brain that we know occur once symptoms are present, we see signs of AL001 having an impact by elevating progranulin, improving biomarkers of lysosomal and immune system function, reducing soluble and imaging biomarkers of brain injury and disease, and appearing to slow the cognitive decline typical of this population," said Sam Jackson, M.D., interim Chief Medical Officer of Alector. "We look forward to reproducing these data in our placebo-controlled INFRONT-3 Phase 3 clinical trial of AL001 in FTD-*GRN*, and to exploring the potential of AL001 to improve outcomes in other neurodegenerative conditions in which progranulin is known to play a role."

Alector is actively enrolling the INFRONT-3 Phase 3 pivotal clinical study of AL001 in at-risk and symptomatic carriers of the progranulin mutation causative of FTD. The global randomized, double-blind, placebo-controlled study is designed to assess the efficacy and safety of AL001 in inhibiting disease progression with the primary endpoint, CDR® plus NACC FTLD-SB scale. AL001 is also being studied in FTD patients with a *C9orf72* mutation, and in a randomized Phase 2 trial of patients with amyotrophic lateral sclerosis (ALS) with a *C9orf72* mutation. AL001 is being developed in collaboration with GSK.

INFRONT-2 Phase 2 Clinical Trial Results

The open-label study was designed to assess safety and tolerability of chronic dosing of AL001, as well as gathering data related to pharmacokinetics and pharmacodynamics, exploratory biomarkers of pharmacologic activity and efficacy. INFRONT-2 included three cohorts of FTD patients: asymptomatic FTD-*GRN* mutation carriers, symptomatic FTD-*GRN* patients, and FTD-*C9orf72* patients. Data presented today during the Oral Communications session at CTAD focused on the symptomatic FTD-*GRN* cohort and included 12-month data for up to twelve patients who received 60 mg/kg of AL001 every four weeks. As of the data cut, ten FTD-*GRN* patients had completed twelve months of treatment, and data presented today include those study participants (at least 9) who were able to complete all assessments.

Overall, AL001 was well tolerated in the Phase 2 study. Twenty-seven study participants from all three cohorts of the INFRONT-2 trial were assessed for safety. Fifteen of the 27 reported mild adverse events (AEs), and three participants experienced serious AEs but none of the serious AEs reported were attributed to treatment.

AL001 treatment of symptomatic FTD-*GRN* patients resulted in rapid and sustained increases in progranulin whether measured in the plasma or CSF.

Mean progranulin levels doubled from baseline and achieved normal levels comparable to those of an age-matched procured control group.

Table 1: Progranulin Levels from Baseline to 12 months with AL001 Treatment (ng/mL)					
Plasma			**CSF**		
	AL001	**Age-matched procured control (N=46)**		**AL001**	**Age-matched procured control (N=44)**
	Mean (standard error of the mean)			Mean (standard error of the mean)	
Baseline (N=12)	40.3 (2.64)	64.6 – 196.0	**Baseline (N=10)**	2.3 (0.22)	3.48 – 7.06
49 weeks (N=9)	91.2 (4.90)		**49 weeks (N=7)**	4.2 (0.42)	

CSF: cerebrospinal fluid

Changes in biomarkers from baseline to 12-months suggest that AL001 restores normal lysosome and complement function in FTD-*GRN* patients. Over the course of treatment with AL001, biomarkers of lysosomal function (CTSD and LAMP1) and complement activation (C1QB), which were elevated in FTD-*GRN* patients at baseline decreased to levels comparable to an age-matched control group. Mean levels of neurofilament light chain (NfL) remained stable over the course of AL001 treatment in both plasma and CSF.

Table 2: CSF Lysosomal and Complement System Biomarkers of Disease Activity from Baseline to 12 months with AL001 Treatment (fmol/L)			
Biomarker	**AL001 Baseline (N=11)**	**AL001 12 months (N=10)**	**Age-matched procured control (N=44)**
	Mean (standard error of the mean)		
CTSD	4.6 (1.03)	3.2 (0.20)	3.4 (0.08)
LAMP1	0.5 (0.10)	0.4 (0.04)	0.4 (0.01)
C1QB	0.7 (0.12)	0.5 (0.07)	0.5 (0.02)

CTSD: cathepsin D, LAMP1: lysosomal-associated membrane protein 1, C1QB: complement C1q B chain,
CSF: cerebrospinal fluid

Astrocytes are the most abundant cells in the adult central nervous system. When injury or disease are present, astrocytes become reactive (known as astrogliosis) and glial fibrillary acidic protein (GFAP) levels increase. GFAP has been identified as a prognostic marker in FTD patients[(2)], and elevated levels have been associated with disease severity. In the INFRONT-2 Phase 2 study, symptomatic FTD-*GRN* patients showed elevated levels of GFAP at baseline, and over the course of treatment with AL001, GFAP levels decreased to be within the range of an asymptomatic FTD-*GRN* cohort.

Table 3: GFAP Levels from Baseline to 12 months with AL001 Treatment					
Plasma (pg/mL)			**CSF (ng/mL)**		
Mean (standard error of the mean)			Mean (standard error of the mean)		
	AL001	**Asymptomatic FTD-*GRN* (N=5)**		**AL001**	**Asymptomatic FTD-*GRN* (N=5)**
Baseline (N=12)	330.9 (49.02)	101.17-228.63	**Baseline (N=11)**	14.1 (2.12)	2.61-10.7
49 weeks (N=9)	183.4 (29.43)		**49 weeks (N=10)**	9.9 (1.35)	

GFAP: glial fibrillary acidic protein, CSF: cerebrospinal fluid

In order to provide context for the clinical outcome observed in the open-label INFRONT-2 study, a matched control cohort of FTD-*GRN* participants from the Genetic FTD Initiative (GENFI2) was created using propensity score matching. A total of ten GENFI2 patients were identified whose baseline cognitive assessment scores and characteristics were comparable to those of participants in the symptomatic cohort of the AL001 Phase 2. Researchers were blinded to the one-year follow-up data from the GENFI matched control cohort. Cognitive assessment was measured using the CDR® plus NACC FTLD-SB scale, a standard FTD clinical rating instrument that assesses cognitive, functional, behavioral and language impairments over time. The CDR® plus NACC FTLD-SB scores in the GENFI2 matched control group had a projected annual increase of 6.4 points from baseline over one year. By comparison, the projected annual increase in the AL001 cohort (N=12) was estimated at 3.3 points over one year, representing a 48 percent decrease in the rate of clinical progression for patients treated with AL001. The CDR® plus NACC FTLD-SB scale is the primary endpoint being used to measure AL001's efficacy in Alector's ongoing INFRONT-3 Phase 3 clinical study.

Conference Call Information
Alector management will host a conference call to review and discuss data presented this week for four of its pipeline candidates at CTAD and at the Society for Immunotherapy of Cancer (SITC) today at 4:00 p.m. ET. Analysts and investors are invited to participate in the conference call by dialing (888) 705-0365 from the U.S. and Canada or (415) 817-9241 internationally and using the conference ID 2065957. The live webcast can be accessed on the investor page of Alector's website at investors.alector.com where a copy of this week's CTAD and SITC data presentations have been posted. A replay of the webcast will be available on Alector's website approximately two hours after the completion of the event and will be archived for up to 30 days.

About the Phase 3 INFRONT-3 Clinical Trial
The pivotal Phase 3 INFRONT-3 study is a randomized, double-blind, placebo-controlled trial designed to evaluate the efficacy and safety of AL001 in treating symptomatic patients with FTD and people at-risk with FTD due to a progranulin gene mutation (FTD-*GRN*). The study aims to enroll up to 180 progranulin gene mutation carriers across approximately 50 sites in the United States, Europe, and the Asia Pacific Region. Participants will be

randomized to receive AL001 or placebo intravenously every four weeks for the duration of the 96-week study and will be given the option to continue receiving treatment in an optional open-label extension study after the 96-week treatment period. The primary endpoint of the pivotal Phase 3 trial is the effect of AL001 on clinical decline by utilizing the CDR® plus NACC FTLD-SB scale, which evaluates clinical impairments in behavior, language, orientation, memory, judgment, and functional activities in trial participants. In addition, the trial will assess secondary clinical endpoints of clinical status, cognition and function, multiple biomarkers, and safety.

About Frontotemporal Dementia
FTD is a rare neurodegenerative disease, but it is the most common form of dementia for people under the age of 60. 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. There are multiple heritable forms of FTD, and FTD-*GRN* patients represent 5% to 10% of all people with FTD. 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. There are no FDA-approved treatment options available for any form of frontotemporal dementia.

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.

(1) The GENFI2 historic matched control group was selected on a blinded basis without access to clinical longitudinal data based on a propensity score matching technique combined with clinical adjudication of select baseline characteristics (NfL plasma levels, age, diagnosis, and gender).
(2) Heller, et al. 2020. "Plasma glial fibrillary acidic protein is raised in progranulin-associated frontotemporal dementia". *J. Neurol Neurosurg Psychiatry*

Cautionary Note Regarding Forward-Looking Statements
This press release contains forward-looking statements as that term is defined in Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. Statements in this press release that are not purely historical are forward-looking statements. Such forward-looking statements include, among other things, statements regarding the continued clinical development of AL001; the expected timing of reporting future data from the AL001 clinical trial; the potential benefits of AL001 or Alector's (the Company) other product candidates; and statements by the Company's chief medical officer. Words such as "believes," "anticipates," "plans," "expects," "intends," "will," "goal," "potential" and similar expressions are intended to identify forward-looking statements. The forward-looking statements contained herein are based upon Alector's current expectations and involve assumptions that may never materialize or may prove to be incorrect. Actual results could differ materially from those projected in any forward-looking statements due to numerous risks and uncertainties, including but not limited to: the Company's plans relating to the development and manufacturing of its product candidates and research programs; the ability of the Company's clinical trials to demonstrate safety and efficacy of its product candidates, and other positive results; the timing and focus of the Company's future clinical trials, and the reporting of data from those trials; the Company's plans relating to commercializing its product candidates, if approved, including the geographic areas of focus and sales strategy; the expected potential benefits of strategic collaborations with third parties and the Company's ability to attract collaborators with development, regulatory and commercialization expertise; the Company's estimates of the number of patients in the United States who suffer from the diseases it is targeting and the number of patients that will enroll in its clinical trials; the size of the market opportunity for the Company's product candidates in each of the diseases it is targeting; the Company's ability to expand its product candidates into additional indications and patient populations; the success of competing therapies that are or may become available; the beneficial characteristics, safety, efficacy, and therapeutic effects of the Company's product candidates; the timing or likelihood of regulatory filings and approvals, including the Company's expectation to seek special designations, such as orphan drug designation, for its product candidates for various diseases; the Company's ability to obtain and maintain regulatory approval of its product candidates; the Company's plans relating to the further development and manufacturing of its product candidates, including additional indications that it may pursue; existing regulations and regulatory developments in the United States and other jurisdictions; the Company's continued reliance on third parties to conduct additional clinical trials of its product candidates, and for the manufacture of its product candidates for preclinical studies and clinical trials; and other risks. Information regarding the foregoing and additional risks may be found in the section entitled "Risk Factors" in Alector's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (the "SEC") on November 4, 2021, and Alector's future reports to be filed with the SEC. These forward-looking statements are made as of the date of this press release, and Alector assumes no obligation to update the forward-looking statements, or to update the reasons why actual results could differ from those projected in the forward-looking statements, except as required by law.

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