Alector Presents 12-Month Results from the INFRONT-2 Phase 2 Open-label Clinical Study of AL001 for the Treatment of Symptomatic Frontotemporal Dementia Patients with a Progranulin Mutation

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AL001 Successfully Restored Progranulin to Normal Levels in FTD-GRN Patients

Treatment with AL001 Slowed Clinical Progression by 47% Based on the CDR® plus NACC FTLD-SB Scale Relative to GENFI2 Matched Control Cohort

Consistent Trends toward Normalization or Stabilization in Multiple Disease Biomarkers Observed with AL001 Treatment

Data from Phase 2 Study Presented at Alzheimer's Association International Conference; Management to Host Webcast to Review Results Today at 1:00 p.m. ET

DENVER, July 29, 2021 (GLOBE NEWSWIRE) -- Alector, Inc. (Nasdaq: ALEC), a clinical-stage biotechnology company pioneering immuno-neurology, presented promising results from the company's INFRONT-2 Phase 2 clinical trial of AL001 at the Alzheimer's Association International Conference (AAIC 2021). AL001 is initially being developed for the treatment of adults at risk for or with symptomatic frontotemporal dementia due to a progranulin gene mutation (FTD-*GRN*). 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, rapidly progressing neurodegenerative disease that is the most common form of dementia for people under the age of 60.

Data presented today focused on up to twelve symptomatic FTD-*GRN* patients treated over twelve months in an open-label study designed to assess safety, pharmacokinetics and pharmacodynamics, exploratory biomarkers and efficacy. AL001 showed a favorable safety profile and rapidly restored progranulin levels to normal ranges in both plasma and cerebrospinal fluid (CSF) for the duration of treatment. While the INFRONT-2 Phase 2 study was not designed to demonstrate clinical benefit, clinical outcome assessments using the CDR® plus NACC FTLD-SB scale found that AL001 treatment slowed clinical progression by 47% compared to a matched control cohort of participants from the Genetic FTD Initiative (GENFI2)[(1)]. Additionally, multiple disease-relevant biomarkers of lysosomal function, complement activation and neuronal health trended toward normalization or remained stable.

"Though this is a small open-label study, the totality of the data presented from the INFRONT-2 Phase 2 study paint an encouraging picture of AL001's potential to slow disease progression in patients with FTD, a devastating disease for which there are currently no approved treatment options," said Robert Paul, M.D., Ph.D., Alector's Chief Medical Officer. "Chronic treatment with AL001 demonstrated durable, on-target activity with a complete reversal of the progranulin deficiency that is causing disease. The effect of AL001 treatment on clinical disease progression, and consistent improvements observed across diverse biomarkers, strengthen our confidence that AL001 is working as designed. We look forward to building upon these data in our Phase 3 study of AL001 in FTD-*GRN* mutation carriers and other planned studies in patient populations in which progranulin deficiencies are a known risk factor."

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, with plans to begin testing AL001 in *C9orf72* amyotrophic lateral sclerosis (ALS) in the second half of 2021.

INFRONT-2 Phase 2 Clinical Trial Results

The open-label INFRONT-2 Phase 2 study was designed primarily to assess the safety and tolerability of chronic dosing of AL001 over 96 weeks. INFRONT-2 included three cohorts of FTD patients: asymptomatic FTD-*GRN* patients, symptomatic FTD-*GRN* patients and FTD-*C9orf72* patients. Biomarker and clinical results presented today focused on the symptomatic FTD-*GRN* cohort and included 12-month data for up to twelve patients who received 60mg/kg of AL001 every four weeks. As of the data cut, nine FTD-*GRN* patients had completed twelve months of treatment, and between seven and nine patients were able to complete all assessments.

Safety data was reported across all three cohorts (N=27) who received a median of 15 doses of AL001. AL001 showed a favorable safety profile in the Phase 2 study. Six of the 27 patients reported mild treatment-related adverse events (AEs). The most common AEs observed on study in more than two patients were falls (5/27, 18.5%) and rash (3/27, 11.1%). Three patients in the FTD-*GRN* cohort experienced serious AEs, but none of these were attributed to treatment with AL001.

Among the symptomatic FTD-*GRN* cohort, AL001 treatment resulted in rapid and sustained 2-2.5-fold elevations of progranulin comparable to normal levels from an age-matched procured control group of healthy volunteers.

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)**
Baseline (N=12)	40.3 (2.64)	64.6 – 196.0	**Baseline (N=10)**	2.3 (0.22)	3.48 – 7.06
25 weeks (N=9)	99.0 (4.94)		**25 weeks (N=9)**	4.4 (0.43)	
49 weeks (N=7)	86.8 (3.72)		**49 weeks (N=7)**	4.2 (0.54)	

CSF: cerebrospinal fluid, (): standard error of the mean.

Representative biomarkers associated with progranulin deficiencies measuring lysosomal function (CTSD and LAMP1) and complement activation (C1QB) were elevated in FTD-*GRN* patients at baseline compared to an age-matched procured control group, indicative of a disease state. AL001 treatment resulted in a time-dependent and durable decreases over twelve months to levels seen in age-matched controls, suggesting that AL001 restores normal lysosome and complement function in these patients.

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=9)	AL001 6 months (N=8)	AL001 12 months (N=8)	Age-matched procured control (N=44)
CTSD	5.2 (1.16)	3.8 (0.57)	3.1 (0.21)	3.4 (0.08)
LAMP1	0.6 (0.12)	0.4 (0.06)	0.4 (0.043)	0.4 (0.01)
C1QB	0.7 (0.12)	0.6 (0.07)	0.5 (0.02)	0.5 (0.02)

CTSD: cathepsin D, LAMP1: lysosomal-associated membrane protein 1, C1QB: complement C1q B chain, CSF: cerebrospinal fluid, (): standard error of the mean.

Neuronal degeneration was assessed by measuring neurofilament light chain (NfL) in the plasma and CSF, and by measuring brain atrophy via volumetric magnetic resonance imaging (vMRI). NfL showed within-patient variability in patients and over time, with mean levels stable at 49 weeks compared to baseline.

Table 3: NfL Levels from Baseline to 12 months with AL001 Treatment

Plasma (pg/mL)			CSF (ng/mL)		
Baseline (N=12)	**25 weeks (N=9)**	**49 weeks (N=7)**	**Baseline (N=11)**	**25 weeks (N=9)**	**49 weeks (N=9)**
62.8 (13.57)	67.5 (24.51)	46.3 (12.93)	7.3 (1.51)	7.7 (1.63)	6.5 (1.29)

NfL: neurofilament light chain protein, CSF: cerebrospinal fluid, (): standard error of the mean.

Volume changes of the whole brain, the frontotemporal cortex and the ventricles were measured over one year and compared to a matched control cohort (N=7) developed from participants in the GENFI2 patient registry. Treatment with AL001 resulted in a greater than 10% difference in the atrophy rates in favor of AL001 for the whole brain and frontotemporal cortex measures, and an approximately 50% reduction in ventricular enlargement.

Table 4: Percent Volume Changes Observed in the Brain over 12 Months Using Volumetric MRI with AL001 Treatment vs. GENFI2 Matched Control

	GENFI2 control cohort (N=7*)	AL001 (N=8*)	Difference in relative atrophy rates
Whole brain	-4.6 (0.93)	-4.1 (0.93)	10.9%
Frontotemporal cortex	-1.8 (0.51)	-1.5 (0.54)	16.7%
Ventricles	25.6 (14.6)	12.9 (4.99)	49.6%

(): standard error of the mean. *N=8 for whole brain; N=7 for frontotemporal (FT) cortex and ventricles.
One GENFI2 control cohort patient with a 2.58% annual volume increase in the frontotemporal cortex is excluded as an image processing outlier.

The potential clinical benefit of AL001 in FTD-*GRN* patients 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, and which is also the primary endpoint of Alector's ongoing Phase 3 study of AL001 for the treatment of FTD-*GRN*.

Treatment with AL001 showed a 47% slowing of clinical progression among the INFRONT-2 patients relative to matched GENFI2 controls. The CDR® plus NACC FTLD-SB scores in the GENFI2 matched control group (N=10), showed an annual increase of 6.4 points from baseline over one year, indicating rapid disease progression. In contrast, the annual increase in the AL001 cohort (N=12) was only 3.4 points over one year, a 3.0-point difference in annual change.

Conference Call Information
Alector management will host a conference call to review and discuss data presented at AAIC 2021 today at 1:00 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 5267479. The live webcast can be accessed on the investor page of Alector's website at investors.alector.com where a copy of the AAIC 2021 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 and at-risk people with FTD due to a progranulin gene mutation (FTD-*GRN*). The study aims to enroll up to 180 FTD-*GRN* 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 frontotemporal dementia, 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 currently 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. The company 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. Immuno-neurology targets immune dysfunction as a root cause of multiple pathologies that are drivers of degenerative brain disorders. 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).

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 May 5, 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.

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)
Joseph Rayne
Argot Partners
212.600.1902
joseph@argotpartners.com

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