Alector Presents AL001 (latozinemab) Data from the FTD-C9orf72 Cohort of the INFRONT-2 Phase 2 Clinical Trial

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Treatment with AL001 (latozinemab) demonstrated target engagement and resulted in increases in progranulin levels in all patients

FTD-C9orf72 patients treated with latozinemab demonstrated a trend toward a delay in disease progression relative to the ALLFTD matched control cohort

First clinical dataset in an indication where latozinemab elevated progranulin above physiological levels

Company to host webcast to review results today at 8:30 a.m. ET

SOUTH SAN FRANCISCO, Calif., March 15, 2022 (GLOBE NEWSWIRE) -- Alector, Inc. (Nasdaq: ALEC), a clinical-stage biotechnology company pioneering immuno-neurology, presented results from the INFRONT-2 Phase 2 clinical trial of AL001 (latozinemab) in frontotemporal dementia patients (FTD) with a *C9orf72* genetic mutation (FTD-*C9orf72*) at the AD/PD™ 2022 International Conference on Alzheimer's and Parkinson's Diseases and related neurological disorders taking place virtually and in person in Barcelona, Spain. Latozinemab is a potential first-in-class monoclonal antibody designed to elevate progranulin, a key regulator of immune activity and lysosomal health in the brain. FTD is a rare and rapidly progressing neurodegenerative disease that is the most common form of dementia for people under the age of 60.

In 2021, Alector presented results showing that latozinemab elevated progranulin levels in a cohort of symptomatic carriers of the progranulin mutation causative of FTD (FTD-*GRN*) patients for the duration of treatment, and as compared to matched controls, showed associated changes in exploratory biomarkers and a trend toward a delay in annual disease progression. Today's data from the FTD- *C9orf72* cohort build upon the results observed in the Company's studies to date in FTD- *GRN* patients.

The results presented include 12-month data from up to 10 symptomatic FTD-*C9orf72* patients treated with 60 mg/kg of latozinemab every four weeks in an open-label study designed to primarily assess the safety and tolerability of chronic dosing. The study also includes exploratory clinical outcomes assessments and biomarkers. Highlights from the presentation included the following observations:

- Latozinemab was generally well tolerated when administered monthly for a year or more, consistent with other study cohorts.
- Latozinemab elevated progranulin in both plasma and cerebrospinal fluid (CSF) in FTD-*C9orf72* patients for the duration of treatment.
- Clinical outcome assessments using the CDR® plus NACC FTLD-SB scale, a standard FTD clinical rating instrument that assesses cognitive, functional, behavioral and language impairments over time, found that when compared to a matched control cohort from the ALLFTD consortium, treatment with latozinemab in FTD-*C9orf72* patients resulted in a trend toward a delay of approximately 54 percent in annualized disease progression.
- Mean levels of neurofilament light chain (NfL), a marker of axonal damage, remained stable over the course of treatment in both plasma and CSF in latozinemab-treated FTD-*C9orf72* patients.
- Mean levels of glial fibrillary acidic protein (GFAP), a biomarker of astrogliosis that is an indicator of disease and/or injury to the central nervous system, decreased over 12 months in both plasma and CSF in latozinemab-treated FTD-*C9orf72* patients.

In published preclinical studies from the literature, using multiple models of acute and chronic neurodegeneration, increased progranulin levels have been shown to be protective against TDP-43 pathology. TDP-43 pathology has been shown to be associated with the *C9orf72* repeat expansion.

"Mutations in the *C9orf72* gene are the most common genetic cause of frontotemporal dementia, a devastating disease with no approved treatments. These mutations are also an important cause of ALS," said Sam Jackson, M.D., interim Chief Medical Officer of Alector. "Building upon the results we presented last year on the potential benefit associated with using latozinemab to elevate progranulin levels in the symptomatic FTD-*GRN* cohort of our INFRONT-2 Phase 2 clinical study, these data further validate Alector's approach of elevating progranulin levels to address a range of neurodegenerative diseases. We are encouraged by these findings and look forward to evaluating latozinemab in additional indications as part of our progranulin franchise in partnership with GlaxoSmithKline (GSK)."

Alector is actively enrolling the Phase 3 INFRONT-3 pivotal clinical study of latozinemab in at-risk and symptomatic FTD-*GRN* patients. The global randomized, double-blind, placebo-controlled study is designed to assess the efficacy and safety of latozinemab in inhibiting disease progression as measured through the primary endpoint, CDR® plus NACC FTLD-SB scale. Latozinemab 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 latozinemab, as well as to gather data related to pharmacokinetics and pharmacodynamics, exploratory biomarkers of pharmacologic activity and efficacy. INFRONT-2 included three cohorts of patients with FTD: asymptomatic FTD-*GRN* mutation carriers, symptomatic FTD-*GRN* patients, and symptomatic FTD-*C9orf72* patients. Data presented today focused on the FTD-*C9orf72* cohort and included 12-month data for up to 10 patients with at least one post-baseline clinical outcomes assessment, who received 60 mg/kg of latozinemab every four weeks. As of the data cut, six FTD-*C9orf72* patients had completed 12 months of

treatment and all biomarker and clinical outcomes assessments.

Latozinemab was well tolerated in the INFRONT-2 study. Twenty-eight study participants from all three cohorts were assessed for safety, with twenty-one patients treated for 12 months or more. Within the FTD-C*9orf72* cohort there were a total of seven treatment related AEs, all of which were mild or moderate.

Treatment with latozinemab in the FTD-*C9orf72* cohort resulted in elevated levels of progranulin when measured in both the plasma and CSF.

Table 1: Progranulin Levels from Baseline to 12 months with Latozinemab Treatment (ng/mL)					
Plasma			**CSF[1]**		
Baseline (N=10)	**25 weeks (N=7)**	**49 weeks (N=6)**	**Baseline (N=8)**	**25 weeks (N=7)**	**49 weeks (N=6)**
123.6 (13.49)	324.4 (37.41)	315.7 (21.12)	4.4 (0.42)	9.3 (1.31)	8.7 (0.90)

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

The CDR® plus NACC FTLD-SB scores in the ALLFTD matched control cohort had a projected annual increase of 3.4 points from baseline over one year. By comparison, the projected annual increase in the latozinemab treated FTD-*C9orf72* cohort (N=10) from baseline was estimated at 1.6 points over one year. This suggested a trend toward an approximately 54 percent decrease in the annualized rate of clinical progression for patients treated with latozinemab. The CDR® plus NACC FTLD-SB scale is the primary endpoint being used to measure latozinemab's efficacy in Alector's ongoing INFRONT-3 Phase 3 clinical study.

Table 2: Clinical Outcomes Assessment as Measured by the CDR® plus NACC FTLD-SB		
Parameter	**Estimate**	**95% CI**
Annual Change in ALLFTD matched control (n=10)[1]	3.4	[1.30,5.60]
Annual Change in latozinemab-treated group (n=10)[2]	1.6	[-0.63,3.78]
Difference in Annual Change (ALLFTD – latozinemab)[3]	**1.9**	**[-1.21,4.95]**
Percentage Decrease in Rate of Disease Progression	**~54%**	**n/a**

1. ALLFTD matched control – one post-baseline timepoint at ~12 months.
2. Latozinemab-treated group – all available post-baseline assessments (range from 3 to 12 months).
3. Model – Random coefficient model with repeated measurements.

In order to provide context for the clinical outcomes assessed in the FTD-*C9orf72* patients enrolled in the open-label INFRONT-2 study, a matched control cohort of FTD-*C9orf72* patients from the ALLFTD database was created using propensity score matching and blinded clinical adjudication. ALLFTD is a comprehensive natural history study of FTD collecting cognitive and behavior assessment data, as well as imaging, blood and CSF biomarkers co-directed by Dr. Brad Boeve at the Mayo Clinic in Rochester, Minnesota, and Drs. Adam Boxer and Howard Rosen, at University of California, San Francisco (UCSF). A total of 10 ALLFTD patients were identified whose baseline cognitive assessment scores and characteristics, including age, sex, NfL level at baseline and diagnosis or variant of FTD-*C9orf72*, were comparable to those of the FTD-*C9orf72* patient cohort in the INFRONT-2 Phase 2 study. Propensity score matching and clinical adjudication was performed by researchers blinded to the one-year follow-up data from the ALLFTD 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.

Changes in exploratory biomarkers from baseline to 12-months were also assessed. NfL, a marker of axonal damage, was measured in plasma and CSF. During the 12-month period of treatment, NfL levels in plasma and CSF remained stable in the latozinemab-treated FTD-*C9orf72* cohort.

GFAP, a biomarker of astrogliosis that is an indicator of disease and/or injury to the central nervous system and is associated with faster rates of brain atrophy in FTD, was also measured. Treatment with latozinemab resulted in a decline of GFAP in both plasma and CSF in the latozinemab-treated FTD-*C9orf72* cohort.

Conference Call Information
Alector management will host a conference call to review and discuss data presented at AD/PD™ today at 8:30 a.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 6957317. The live webcast can be accessed on the investor page of Alector's website at investors.alector.com. 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 FTD-*C9orf72*
C9orf72 repeat expansions are the most common genetic cause of the neurodegenerative diseases frontotemporal dementia (FTD) and amyotrophic lateral sclerosis (ALS). 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.

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, including FTD-*GRN* and FTD-*C9orf72*. 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, Alzheimer's disease, and amyloid lateral sclerosis. 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.

Cautionary Note Regarding Forward-Looking Statements
This press release contains forward-looking statements as that term is defined in 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 preclinical studies, clinical trials, expected milestones, expectations of our collaborations, and financial guidance. 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 Annual Report on Form 10-K filed with the Securities and Exchange Commission (the "SEC") on February 24, 2022, 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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