Research Use Statement for Application for Genomic Data from NIAGADS
Please limit to 2,200 characters max. The statement should include the following components:

- Objectives of the proposed research;

Alector is a biotech company that is developing antibody-based therapies for cancer and neurodegenerative disorder such as Alzheimer's disease. Our therapeutic targets are immune-related genes for which common genetic variants were identified to be associated with diseases in large GWAS.
For the gene targets we have already identified we wish to first study whether they are also associated with Alzheimer's Disease risk (AD) or with AD related phenotypes (age of onset, cognitive decline, CSF biomarkers). In a second time we will look for modifiers of those associations.

- Study design;

SA1 Effect of genetic variants of interest on AD phenotypes
We will query the effect of the genetic variants of interest –found to be associated with a specific neurodegenerative disorder by GWAS – on AD risk, age of onset or AD-associated phenotypes (such as CSF Tau or Ab). Candidate association studies will be conducted for all the neurodegenerative diseases associated variant in the context of each phenotype.
SA2 Identification of population subgroups modifying association for variants of interest
We query whether the effect of the genetic variants of interest associated with one of the AD phenotypes defined in SA1 is stronger or weaker in specific subpopulations, based either on genotype or clinical phenotypes. This will be conducted as an interaction analysis (with genotypes or clinical trait) for the candidate genetic variants.
SA3 Biomarkers associated with genetic variants of interest
For the gene targets we have already identified - such as TREM2 in Alzheimer's - we wish to study the impact of the risk-associated allele on gene expression or protein levels 1) in –cis to evaluate their effect on the target gene 2) in –trans to gain better understanding of the pathways affected and to identify biomarkers for treatment efficiency.

- Analysis plan, including the phenotypic characteristics that will be evaluated in association with genetic variants

In SA1, association will be queried for the candidate genetic variants using plink software, correcting for covariates such as gender, age and population structure defined by Principal Component Analysis, with either AD status, age of onset or cognition as a phenotype.

In SA2, we will conduct interaction analysis (of genotypes or clinical traits) with the candidate genetic variants using plink software, correcting for covariates such as gender, age and population structure defined by Principal Component Analysis, with either AD status, age of onset or cognition as a phenotype.
In SA3 association will be queried for the candidate genetic variants using plink software, correcting for covariates such as gender, age and population structure defined by Principal Component Analysis, with gene levels as quantitative traits.

Non-Technical Summary for Application for Genomic Data from NIAGADS

Prevail Therapeutics is an emerging biotech company based in New York City that is developing gene-therapy for brain disorders such as Parkinson's or Alzheimer's disease. Our therapeutic targets are genes that are genetically associated with neurodegenerative diseases - such as GBA in Parkinson's Disease. We plan to use NIAGADS datasets to query whether the genes we target are associated with Alzheimer's Disease and to identify specific subpopulation in which the genetic association is stronger.