TARGET ALS FOUNDATION, INC.

Financial Statements
and Supplementary Information

Year Ended December 31, 2023

(With Independent Auditors' Report Thereon)

TARGET ALS FOUNDATION, INC.
PROGRAM ACCOMPLISHMENTS (UNAUDITED)
Year Ended December 31, 2023

- *Collaboration with FBRI:* A collaboration is being forged with FBRI to analyze longitudinal biofluid samples to generate unbiased proteomics, lipidomics and metabolomics datasets. These datasets will be integrated with the detailed demographic and clinical information from these cases along with the whole genome sequencing data.

- *Collaboration with Broad Institute/Bloomberg L.P.:* A critical aspect of this effort is to ensure that this data can be accessed and analyzed by any investigator worldwide to further ALS research. We are working with the Broad Institute and a team of software engineers from Bloomberg L.P. to build a unique data platform that will allow integration, access, and the ability to analyze these datasets.

- *Genomic datasets core:* Whole genome sequencing (WGS) and bulk RNAseq datasets are now being generated from all PM cases.

- *In vivo Target Validation Core:* We have now initiated all five projects that were identified for support by the independent review Committee.

- *C9orf72 BAC-based transgenic mouse model:* The BAC transgenic model characterization is being completed at Jackson labs. This mouse model presents abundant C9Orf72 RNA foci pathology, affecting major brain regions.

- *TDP43 models: Knock- in of a single base change, K181E in RRM1 domain:* Several cohorts of mice were evaluated for TDP43-related pathology at 3-, 6- and 9- months of age, while data from the 12-month time point is pending. Key hallmarks of ALS including pTDP43 accumulation and neurodegeneration have not been detected.

- *Knock-in of mutant NLS domain:* Original technical approaches taken to develop this mouse line in 2021 were unsuccessful due to lethality of the mutation. A different technical approach to develop a conditional knock-in line targeting the ES cells is being evaluated. To-date, this approach has not been successful due to incorrect targeting in ES cells or to poor transmission of targeted allele. The remaining ES cell clones are all being injected and in vitro fertilizations on existing low chimeric founder animals will replace traditional breeding. Alternative methods to create ES clones and to perform blastocyst injections are being evaluated.