

TARGET ALS FOUNDATION, INC.

**Financial Statements
and Supplementary Information**

Year Ended December 31, 2022

(With Independent Auditors' Report Thereon)

TARGET ALS FOUNDATION, INC.
**FINANCIAL STATEMENTS
AND SUPPLEMENTARY INFORMATION**
Year Ended December 31, 2022

	<u>Page</u>
INDEPENDENT AUDITORS' REPORT	1
FINANCIAL STATEMENTS:	
Statement of Financial Position (With Comparative Totals at December 31, 2021)	4
Statement of Activities (With Comparative Totals for the Year Ended December 31, 2021)	5
Statement of Functional Expenses (With Comparative Totals for the Year Ended December 31, 2021)	6
Statement of Cash Flows (With Comparative Totals for the Year Ended December 31, 2021)	7
Notes to the Financial Statements	8
SUPPLEMENTARY INFORMATION:	
Program Accomplishments (Unaudited)	17

INDEPENDENT AUDITORS' REPORT

To the Board of Directors of
Target ALS Foundation, Inc.:

Opinion

We have audited the accompanying financial statements of Target ALS Foundation, Inc. (a not-for-profit organization) (the Foundation), which comprise the statement of financial position as of December 31, 2022, and the related statements of activities, functional expenses, and cash flows for the year then ended, and the related notes to the financial statements.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of Target ALS Foundation, Inc. as of December 31, 2022, and the changes in its net assets and its cash flows for the year then ended in accordance with accounting principles generally accepted in the United States of America.

Basis for Opinion

We conducted our audit in accordance with auditing standards generally accepted in the United States of America. Our responsibilities under those standards are further described in the Auditors' Responsibilities for the Audit of the Financial Statements section of our report. We are required to be independent of the Foundation and to meet our other ethical responsibilities in accordance with the relevant ethical requirements relating to our audit. We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our audit opinion.

Responsibilities of Management for the Financial Statements

Management is responsible for the preparation and fair presentation of these financial statements in accordance with accounting principles generally accepted in the United States of America; and for the design, implementation, and maintenance of internal control relevant to the preparation and fair presentation of financial statements that are free from material misstatement, whether due to fraud or error.

In preparing the financial statements, management is required to evaluate whether there are conditions or events, considered in the aggregate, that raise substantial doubt about the Foundation's ability to continue as a going concern for one year after the date that the financial statements are available to be issued.

Auditors' Responsibilities for the Audit of the Financial Statements

Our objectives are to obtain reasonable assurance about whether the financial statements as a whole are free from material misstatement, whether due to fraud or error, and to issue an auditors' report that includes our opinion. Reasonable assurance is a high level of assurance but is not absolute assurance and therefore is not a guarantee that an audit conducted in accordance with generally accepted auditing standards will always detect a material misstatement when it exists. The risk of not detecting a material misstatement resulting from fraud is higher than for one resulting from error, as fraud may involve collusion, forgery, intentional omissions, misrepresentations, or the override of internal control. Misstatements, including omissions, are considered material if there is a substantial likelihood that, individually or in the aggregate, they would influence the judgment made by a reasonable user based on the financial statements.

In performing an audit in accordance with generally accepted auditing standards, we:

- Exercise professional judgment and maintain professional skepticism throughout the audit.
- Identify and assess the risks of material misstatement of the financial statements, whether due to fraud or error, and design and perform audit procedures responsive to those risks. Such procedures include examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements.
- Obtain an understanding of internal control relevant to the audit in order to design audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Foundation's internal control. Accordingly, no such opinion is expressed.
- Evaluate the appropriateness of accounting policies used and the reasonableness of significant accounting estimates made by management, as well as evaluate the overall presentation of the financial statements.
- Conclude whether, in our judgment, there are conditions or events, considered in the aggregate, that raise substantial doubt about the Foundation's ability to continue as a going concern for a reasonable period of time.

We are required to communicate with those charged with governance regarding, among other matters, the planned scope and timing of the audit, significant audit findings, and certain internal control related matters that we identified during the audit.

Report on Summarized Comparative Information

We have previously audited the Foundation's 2021 financial statements, and we expressed an unmodified audit opinion on those audited financial statements in our report dated March 29, 2022. In our opinion, the summarized comparative information presented herein as of and for the year ended December 31, 2021, is consistent, in all material respects, with the audited financial statements from which it has been derived.

Supplementary Information

Our audit was conducted for the purpose of forming an opinion on the financial statements as a whole. The information on Supplemental Schedule I is presented for purposes of additional analysis and is not a required part of the financial statements. Such information is the responsibility of management and is of a non-accounting nature. The information has not been subjected to the auditing procedures applied in the audit of the financial statements and, accordingly, we express no opinion on it.

Kahn, Litwin, Renya & Co., Ltd.

June 7, 2023

TARGET ALS FOUNDATION, INC.
STATEMENT OF FINANCIAL POSITION
December 31, 2022
(With Comparative Totals at December 31, 2021)



Assets	2022	2021
	<hr/>	<hr/>
Cash	\$ 38,202,262	\$ 11,363,138
Investments	3,099,063	2,015,656
Receivables:		
Grants, net	52,487,810	9,678,336
Pledges, net	21,728,583	3,066,743
Prepaid expenses	44,750	81,727
	<hr/>	<hr/>
Total Assets	\$ 115,562,468	\$ 26,205,600
	<hr/> <hr/>	<hr/> <hr/>
Liabilities and Net Assets		
Liabilities:		
Grants payable	\$ 1,735,469	\$ 1,476,927
Accounts payable and accrued expenses	13,921	24,675
Total liabilities	1,749,390	1,501,602
	<hr/>	<hr/>
Net Assets:		
Without donor restrictions	34,358,955	4,579,135
With donor restrictions	79,454,123	20,124,863
Total net assets	113,813,078	24,703,998
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Total Liabilities and Net Assets	\$ 115,562,468	\$ 26,205,600
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See accompanying notes to the financial statements and independent auditors' report.

TARGET ALS FOUNDATION, INC.
STATEMENT OF ACTIVITIES
Year Ended December 31, 2022
(With Comparative Totals for the Year Ended December 31, 2021)



	<u>2022</u>	<u>2021</u>
Change in Net Assets Without Donor Restrictions:		
Revenue and Support:		
Contributions and grants	\$ 31,335,271	\$ 690,721
Investment earnings, net	22,235	21,918
Other income	861	67,923
Net assets released from restrictions	7,693,442	8,625,954
Total revenue and support	<u>39,051,809</u>	<u>9,406,516</u>
Expenses:		
Research grants	7,275,438	6,197,522
Management and general	1,281,655	975,528
Development	714,896	616,547
Total expenses	<u>9,271,989</u>	<u>7,789,597</u>
Change in net assets without donor restrictions	<u>29,779,820</u>	<u>1,616,919</u>
Change in Net Assets With Donor Restrictions:		
Contributions and grants	67,021,314	5,872,441
Interest income	1,388	2,998
Net assets released from restrictions	(7,693,442)	(8,625,954)
Change in net assets with donor restrictions	<u>59,329,260</u>	<u>(2,750,515)</u>
Change in Net Assets	89,109,080	(1,133,596)
Net Assets, beginning of year	<u>24,703,998</u>	<u>25,837,594</u>
Net Assets, end of year	<u>\$ 113,813,078</u>	<u>\$ 24,703,998</u>

TARGET ALS FOUNDATION, INC.
STATEMENT OF FUNCTIONAL EXPENSES
Year Ended December 31, 2022
(With Comparative Totals for the Year Ended December 31, 2021)

	Research Grants	Management and General	Development	2022 Total	2021 Total
Research awards	\$ 6,463,758	\$ -	\$ -	\$ 6,463,758	\$ 6,070,896
Personnel and related:					
Salaries	-	792,677	187,348	980,025	888,547
Payroll taxes and employee benefits	-	209,746	36,170	245,916	216,717
Total personnel and related	-	1,002,423	223,518	1,225,941	1,105,264
Other expenses:					
Advertising and promotion	-	17,565	167,274	184,839	154,475
Conferences, conventions and meetings	512,994	-	-	512,994	126,626
Office expenses	-	35,924	-	35,924	13,323
Professional services	-	186,125	324,104	510,229	287,002
Travel	-	1,376	-	1,376	231
Meals	-	418	-	418	378
Telephone and internet	-	37,824	-	37,824	31,402
Business loss	298,686	-	-	298,686	-
Total other expenses	811,680	279,232	491,378	1,582,290	613,437
Total Expenses	\$ 7,275,438	\$ 1,281,655	\$ 714,896	\$ 9,271,989	\$ 7,789,597

TARGET ALS FOUNDATION, INC.
STATEMENT OF CASH FLOWS
Year Ended December 31, 2022
(With Comparative Totals for the Year Ended December 31, 2021)



	<u>2022</u>	<u>2021</u>
Cash Flows from Operating Activities:		
Change in net assets	\$ 89,109,080	\$ (1,133,596)
Adjustments to reconcile change in net assets to net cash provided by operating activities:		
Investment return	(22,235)	(21,918)
Contributions of stock received	(1,061,172)	(1,913,678)
Discount on pledges and grants receivable	18,708,686	377,559
Changes in operating assets and liabilities:		
Grants receivable	(55,750,000)	10,050,000
Pledges receivable	(24,430,000)	(1,932,300)
Prepaid expenses	36,977	(3,788)
Grants payable	258,542	306,060
Accounts payable and accrued expenses	(10,754)	6,495
Net cash provided by operating activities	<u>26,839,124</u>	<u>5,734,834</u>
Cash Flows from Investing Activities:		
Proceeds from sale of investments	-	500,000
Net cash provided by investing activities	<u>-</u>	<u>500,000</u>
Net Increase in Cash	26,839,124	6,234,834
Cash, beginning of year	<u>11,363,138</u>	<u>5,128,304</u>
Cash, end of year	<u><u>\$ 38,202,262</u></u>	<u><u>\$ 11,363,138</u></u>
Supplemental Cash Flow Information, noncash investing activities:		
Noncash contributions of investments	<u><u>\$ 1,061,172</u></u>	<u><u>\$ 1,913,678</u></u>

TARGET ALS FOUNDATION, INC.
NOTES TO THE FINANCIAL STATEMENTS
Year Ended December 31, 2022

1. Nature of Operations

Target ALS Foundation, Inc. (the Foundation), a not-for-profit Delaware corporation operating in New York, New York, was incorporated on December 3, 2015 to promote, support, and further the funding of medical and scientific research to accelerate drug discovery and development for Amyotrophic Lateral Sclerosis (ALS). The Foundation pursues its mission by awarding grants to fund ALS - related research.

2. Summary of Significant Accounting Policies

This summary of significant accounting policies of the Foundation is presented to assist the reader in understanding the Foundation's financial statements. The financial statements and notes are representations of the Foundation's management, who is responsible for their integrity and objectivity. These accounting policies conform to accounting principles generally accepted in the United States of America and have been consistently applied in the preparation of the financial statements.

Comparative Financial Information

The accompanying financial statements include certain prior year summarized comparative information without accompanying note disclosures and certain functional expense information. Such information does not include sufficient detail to constitute a presentation in conformity with accounting principles generally accepted in the United States of America. Accordingly, such information should be read in conjunction with the Foundation's financial statements and related notes to the financial statements for the year ended December 31, 2021, from which the summarized information was derived.

Financial Statement Presentation

The Foundation prepares its financial statements on the accrual basis of accounting and, in accordance with authoritative guidance, reports information regarding its financial position and activities according to two classes of net assets: net assets without donor restrictions, and net assets with donor restrictions.

Net Assets without Donor Restrictions

Net assets without donor restrictions are available for use at the discretion of the Board of Directors (the Board) and/or management for general operating purposes. From time to time, the Board may designate a portion of these net assets for specific purposes which make them unavailable for use at management's discretion.

Net Assets with Donor Restrictions

Net assets with donor restrictions consist of assets whose use is limited by donor-imposed time and/or purpose restrictions. Other donor-imposed restrictions are perpetual in nature, where the donor stipulates that resources be maintained in perpetuity. The Foundation had no net assets to be maintained in perpetuity as of December 31, 2022.

TARGET ALS FOUNDATION, INC.
NOTES TO THE FINANCIAL STATEMENTS
Year Ended December 31, 2022

Donor-restricted contributions are reported as increases in net assets with donor restrictions. When a restriction is satisfied, net assets are reclassified from net assets with donor restrictions to net assets without donor restrictions in the statement of activities.

Investments and Fair Value Measurement

The Foundation measures its investments at fair value. Fair value is the price that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. A fair value measurement assumes that the transaction to sell the asset or transfer the liability occurs in the principal market for the asset or liability or, in the absence of a principal market, the most advantageous market. Valuation techniques that are consistent with the market, income or cost approach, as specified by authoritative guidance, are used to measure fair value.

The fair value hierarchy prioritizes the inputs to valuation techniques used to measure fair value into three broad levels:

Level 1 inputs are quoted prices (unadjusted) in active markets for identical assets or liabilities the Foundation has the ability to access.

Level 2 inputs (other than quoted prices included within level 1) are observable for the asset or liability, either directly or indirectly.

Level 3 inputs are unobservable inputs for the asset or liability and rely on management's own assumptions about the assumptions that market participants would use in pricing the asset or liability. The unobservable inputs are developed based on the best information available in the circumstances and may include the Foundation's own data.

The Foundation reports investments at fair value on a recurring basis. The investments are classified as level 1 within the fair value hierarchy.

Level 1 investments owned by the Foundation and listed on a National Securities Exchange are valued at the last recorded sales price as of the financial statement reporting date, or in the absence of recorded sales, at the last quoted bid price reported as of the financial statement reporting date.

Realized and unrealized gains and losses on investments are reported as changes in net assets without donor restrictions, unless gains and losses on investments are restricted by a donor's explicit stipulation or by a law that extends a donor's restriction.

Dividends and interest are recorded as received, which does not differ materially from the accrual basis. Purchases and sales of securities are recorded on the trade date.

TARGET ALS FOUNDATION, INC.
NOTES TO THE FINANCIAL STATEMENTS
Year Ended December 31, 2022

Grants and Pledges Receivable

The Foundation carries its receivables at net realizable value. Pledges receivable consist of unconditional promises to give. Amounts that are expected to be collected within one year are recorded at net realizable value. Receivables expected to be collected after more than one year are recorded at the present value of the estimated future cash flows to be received. On a periodic basis, the Foundation evaluates its receivables and establishes an allowance for doubtful accounts, based on a history of past bad debt expense and collections and current credit conditions.

The Foundation does not accrue interest on receivables. A receivable is considered past due if payment has not been received within stated terms. The Foundation will then exhaust all methods in-house to collect the receivable. Once all practical resources to collect the receivable have been utilized without success, the receivable is deemed uncollectible and charged against the allowance for doubtful accounts. At December 31, 2022, management determined that no allowance for doubtful accounts was necessary.

Grants Payable

Unconditional research grants are recognized in the financial statements when they are recommended and approved by the Independent Review Committee (IRC) and the Chief Advisor of the Foundation. Conditional research grants are expensed by the Foundation as the researchers substantially meet the terms and conditions of the grant during the grant period.

Revenue Recognition

The Foundation recognizes contributions and grant income in the year in which the contribution or grant is made. Conditional promises to give are recognized in the period in which the condition is met. Contributions and grants are recorded either as without donor restrictions or with donor restrictions depending on the existence and/or nature of any donor-imposed restrictions. However, it is the policy of the Foundation to recognize restricted contributions and grants that are both received and fully expended during the current fiscal year as net assets without donor restrictions.

Donated assets are recorded as contributions at their fair value on the date of donation.

Allocation of Expenses

The Foundation's operating costs have been allocated between research grants, management and general and development based on direct identification when possible, and allocation if a single expenditure benefits more than one program or function. Expenditures that require allocation are allocated based on personnel cost. Development expenses consist of fundraising expenses.

TARGET ALS FOUNDATION, INC.
NOTES TO THE FINANCIAL STATEMENTS
Year Ended December 31, 2022

Business Loss

During September 2022, one of the Foundation's foreign grant recipients had their email account compromised. As a result of the compromise, the fraudster was able to redirect three instances of grant funding that were intended for a lab site, for a total loss of \$298,686. The Foundation's financial institution was unable to recover the funding and the Foundation did not attempt to send more funding to the foreign lab.

Income Taxes

The Foundation is exempt from income taxes as a public charity under Section 501(c)(3) of the Internal Revenue Code. The Foundation is considered a Private Foundation under Section 170(b); therefore, it pays an excise tax on its net investment income at either 1% or 2%, depending on the ratio of qualifying disbursements to the fair value of Foundation assets. The qualifying disbursements include amounts paid to qualifying charities. Management believes that the Foundation operates in a manner consistent with its tax-exempt status. The Foundation has notified the Internal Revenue Service (IRS) of its intention to convert to a public charity, and the IRS has ruled that grantors and contributors may consider Target ALS Foundation, Inc. a public charity for the purpose of making contributions to the Foundation.

The Foundation annually files IRS Form 990-PF, *Return of Private Foundation*, reporting various information that the IRS uses to monitor the activities of private foundations. The Foundation currently has no tax examinations in progress.

Estimates and Assumptions

The preparation of financial statements in conformity with accounting principles generally accepted in the United States of America requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. Accordingly, actual results could differ from those estimates.

Reclassifications

Certain amounts in the 2021 comparative financial information have been reclassified to conform to the 2022 financial statement presentation.

Subsequent Events

The Foundation has evaluated subsequent events through June 7, 2023, which is the date these financial statements were available to be issued.

TARGET ALS FOUNDATION, INC.
NOTES TO THE FINANCIAL STATEMENTS
Year Ended December 31, 2022

3. Liquidity and Availability

Financial assets available for general expenditure, that is, without donor or other restrictions limiting their use, within one year of the statement of financial position date, comprise the following at December 31, 2022:

Financial assets:	
Cash	\$ 38,202,262
Investments	3,099,063
Grants receivable	52,487,810
Pledges receivable	<u>21,728,583</u>
Total financial assets	<u>115,517,718</u>
Less: financial assets unavailable for general expenditure:	
Receivables scheduled to be collected in more than one year	69,304,093
Required to satisfy donor purpose restrictions within one year	<u>5,237,730</u>
Total financial assets unavailable for general expenditure	<u>74,541,823</u>
Financial assets available to meet cash needs for general expenditures within one year	<u><u>\$ 40,975,895</u></u>

The Foundation has a policy to structure its financial assets to be available as its general expenditures, liabilities and other obligations come due. In addition, as part of its liquidity management, the Foundation manages its liquidity by developing and adopting annual operating budgets that provide sufficient funds for general expenditures in meeting its liabilities and other obligations as they come due. Actual performance is reported and monitored monthly in comparison to budgets. Adjustments are made to the policy as needed to ensure adequate liquidity.

Included within the cash balance above is \$21,606,554 of grant funding maintained within a separately designated account at the Foundation’s financial institution. These funds can be utilized to support the Foundation’s mission, as defined in the grant agreement.

4. Investments

Investments consisted of the following:

Level 1:	
Money market funds	\$ 25,805
Mutual funds	<u>3,073,258</u>
Total investments	<u><u>\$ 3,099,063</u></u>

TARGET ALS FOUNDATION, INC.
NOTES TO THE FINANCIAL STATEMENTS
Year Ended December 31, 2022



5. Pledges and Grants Receivable

Pledges receivable consist of unconditional promises to give from contributors to support the Foundation's mission.

The present value of pledges and grants receivable has been calculated using interest rates of 4.41% to 3.88%, which approximates the Federal Reserve five-to-ten year Treasury bill rates.

Grants receivable are due as follows:

<u>Year Ending</u>	
December 31, 2023	\$ 250,000
December 31, 2024	15,250,000
December 31, 2025	10,250,000
December 31, 2026	10,000,000
December 31, 2027	10,000,000
Thereafter	20,000,000
	<hr/>
	65,750,000
Less present value component	<hr/> 13,262,190
	<hr/>
Grants receivable, net	<u>\$ 52,487,810</u>

Pledges receivable are due as follows:

<u>Year Ending</u>	
December 31, 2023	\$ 4,662,300
December 31, 2024	4,200,000
December 31, 2025	2,750,000
December 31, 2026	2,700,000
December 31, 2027	2,650,000
Thereafter	10,600,000
	<hr/>
	27,562,300
Less present value component	<hr/> 5,833,717
	<hr/>
Pledges receivable, net	<u>\$ 21,728,583</u>

TARGET ALS FOUNDATION, INC.
NOTES TO THE FINANCIAL STATEMENTS
Year Ended December 31, 2022

6. Net Assets

A summary of net assets is as follows:

Net Assets without Donor Restrictions	
Undesignated – available for operations	\$ 34,358,955
Total net assets without donor restrictions	34,358,955
Net Assets with Donor Restrictions	
Subject to expenditure for specified purposes:	
ALS research development	4,052,611
Gates Ventures grant	602,556
TDP-43 biomarker initiative	282,150
Biorepository initiative	200,000
Biogen collection project	100,413
	5,237,730
Subject to time restriction	74,216,393
Total net assets with donor restrictions	79,454,123
Total net assets	\$113,813,078

ALS Research Development

Funds have been restricted to support programmatic efforts to accelerate discovery, validation and development of new ALS therapeutic targets and biomarkers, and foster interactions between academia and industry.

Gates Ventures Grant

Funds have been restricted to accelerating the development of Biofluid-based Biomarkers that are applicable to ALS, Alzheimer’s disease and frontotemporal lobar degeneration. Gates Ventures will provide \$1,000,000 to the Foundation to support this initiative; however, the Foundation will also be required to contribute \$1,400,000 to investigators that are part of the approved collaborative consortia.

TDP-43 Biomarker Initiative

Funds have been restricted with the goal of developing improved immunoassays that can accurately measure and quantify TDP-43 in human biofluids, which would have tremendous impact on clinical research and therapeutic development for ALS and other neurodegenerative diseases.

TARGET ALS FOUNDATION, INC.
NOTES TO THE FINANCIAL STATEMENTS
Year Ended December 31, 2022

Biorepository Initiative

Funds have been restricted to support the acquisition of and the data migration to the BioLims biorepository database. The database will centralize samples and associated clinical data available for use by the neurodegenerative research community to further clinical research.

Biogen Collection Project

Funds have been restricted to support the biofluid core sites that collect patient specimens for clinical research.

7. Commitments and Subsequent Event

The Foundation enters into conditional commitments annually to award scientific research grants. All research distribution-making decisions are made by the IRC and are reviewed by the Conflict-of-Interest Committee to ensure the IRC has no stake in the projects selected. Subject to annual review and reapproval process, these distributions generally cover a period of one to two years. Research commitments at December 31, 2022 are reported as grants payable in the accompanying statement of financial position. Subsequent to year-end, the Foundation committed to future research distributions in the amount of approximately \$969,200 for the year ending December 31, 2023.

Except as previously provided for by restricted gifts, the Foundation's ability to meet these distribution commitments may be dependent on future contributions to be received.

8. Retirement Plan

The Foundation sponsors a defined contribution plan under Internal Revenue Code Section 403(b). The plan covers all employees over 21 years old, excluding temporary employees. In addition, the Foundation elects to make a noncontributory match equal to 4% of total wages. Employer contributions of approximately \$38,700 were made to the plan during the year ended December 31, 2022.

TARGET ALS FOUNDATION, INC.
NOTES TO THE FINANCIAL STATEMENTS
Year Ended December 31, 2022

9. Concentrations of Risks

Financial instruments that potentially subject the Foundation to concentrations of credit risk consist principally of cash, grants and pledges receivable and investments.

The Foundation maintains its bank accounts in one financial institution. The balance is insured by the Federal Deposit Insurance Corporation up to \$250,000. At year-end, the uninsured portion of these balances was approximately \$37,943,400. The Foundation monitors its exposure with regard to cash and cash equivalents and has not experienced losses on such accounts.

At December 31, 2022, the Foundation's grants receivable were due from three contributors, one of which represents approximately 99% of grants receivable. At December 31, 2022, the Foundation's outstanding pledges receivable were due from sixteen contributors, three of which represent approximately 65% of pledges receivable. Management has performed an analysis of these receivables at year end and does not believe that there is a significant credit risk related to those receivables.

Investment securities are exposed to various risks, such as interest rate, market and credit risks. Due to the level of risk associated with certain investment securities, it is possible that changes in values of investment securities could occur in the near term and that such changes could materially affect investment balances and activity included in the financial statements. At year end, management does not believe that significant credit risk exists relative to the investments.

TARGET ALS FOUNDATION, INC.
PROGRAM ACCOMPLISHMENTS (UNAUDITED)
Year Ended December 31, 2022

The Foundation continues to make strides toward its mission to promote, support and further the funding of medical and scientific research to accelerate drug discovery and development for ALS. Select accomplishments during 2022 include the following:

- Our precompetitive biomarker initiative that involves experts from 15 pharma/biotech companies, a panel of academics and 6 not-for-profit organizations is continuing to move two active projects forward.
- Continued to expand the Foundation's core facilities, which are comprised of a network of academic centers and contract research organizations that, for the first time in the history of the disease, provide access to critical ALS research tools and resources to scientists.
 - *Postmortem tissue (PMT) core*: The PMT core has integrated a new BioLims data platform that enables efficient inventory management and expedites fulfillment of tissue requests.
 - *TDP-43 Immunoassay development*: Mass spectrometry to determine TDP-43 Species in biofluids.
 - *Treatment of Ultra-rare Forms of ALS: Partnership with n-Lorem Foundation*: The Foundation's goal is to expand this program to enable more ALS patients with ultra-rare forms of ALS to benefit from ASO-based treatments.
 - *Grant from Chan Zuckerberg Initiative (CZI)*: Based on the work and impact of the PM core, the Foundation was invited to submit a proposal to CZI to help modernize neuropathology. We received a grant from CZI to generate and digitize stained neuropathology slides from brain and spinal cord tissue of all PM core cases (ALS and ALS/FTD). The digitized dataset will be made accessible through platforms that will also offer support for analysis. We have received an additional grant from CZI to enable participation of underrepresented communities and minorities. Two initiatives will be launched under this grant at the Barrow Neurological Institute.
 - *Longitudinal biofluid repository*: This core was launched in November 2020. There are currently six sites participating in this effort with at least four additional sites to be added in 2023 (2 within USA and 2 outside USA).

TARGET ALS FOUNDATION, INC.
PROGRAM ACCOMPLISHMENTS (UNAUDITED)
Year Ended December 31, 2022

- *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. Results anticipated by Q2 2023.