

The background of the entire page is a vibrant, abstract image of a neuron. The cell body is a complex, multi-colored mass of purple, blue, and orange, with numerous small, glowing yellow and white dots scattered around it. The neuron's processes extend outwards, with one prominent branch reaching towards the top right. The overall color palette is dominated by deep blues and teals, with bright, glowing light effects that create a sense of energy and movement.

TARGET
ALS

Creating a World Where Everyone with ALS Lives

Annual Report **2021**

FOUNDER

From the

Dear Friends and Colleagues,

We all hoped we would finally return to normal in 2021. But despite the ongoing challenges caused by the COVID-19 pandemic, I am amazed at what Target ALS has continued to accomplish. We have forged ahead with our funding for breakthrough research; established a one-of-a-kind scientific core; nurtured important new alliances, including across related neurodegenerative diseases; and helped bring more attention to the fight against ALS.

All these encouraging signs came in a year in which I was given a likely ALS diagnosis. As a result, I've pulled back from many of my responsibilities so that I can focus on two life-affirming activities: spending more time with friends and family and helping advance ALS research.

We are all working together to create a world in which everyone with an ALS diagnosis lives a long, high-quality life. Thank you for bringing us to a place where the achievement of these goals may be possible.

Yours in this fight against ALS,



Daniel L. Doctoroff
Founder



From the CEO

Dear Target ALS Community,

It has been a privilege to work this past year with extraordinary scientists from academia and the pharma/biotech industry, executives from for-profit and nonprofit organizations, and especially all the supporters who have helped Target ALS change the landscape of ALS research.

As you review our Annual Report 2021, please pay special attention to these milestone accomplishments:

- *We forged a partnership with Gates Ventures/Alzheimer's Drug Discovery Foundation (ADDF), which will fund collaborative projects focused on biomarkers applicable to ALS, Alzheimer's disease (AD), and frontotemporal dementia (FTD). Recipient grantees were announced recently.*
- *We continued our partnership with The Association for Frontotemporal Degeneration (AFTD). One of the co-funded projects has already led to a clinical trial.*
- *We funded five projects to test novel drug targets in animal models of ALS through our in vivo target validation core.*
- *Our Longitudinal Biofluid Core began active case recruitment to collect biosamples from ALS and control cases.*

As we move closer to 2023 and beyond, Dan, the Target ALS team, and I have redoubled our efforts and focused on our short- and long-term ambitions. We plan to build on our successes and accelerate the work of Target ALS, introducing seven areas of new and increased funding to catalyze our collaborative teams even more efficiently and broadly. To those of you who have helped in the past or are just being introduced to Target ALS, we can't express our appreciation enough and hope you will be further inspired to participate as you read on.

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By the Numbers

Forging New Partnerships

As we advance our efforts toward developing therapies for ALS, one thing is clear: we must continue to engage new talents and technologies working on ALS.

That is why we are collaborating with partners working on related neurodegenerative disorders like AD and FTD. We aim to expand the breadth of talent and technologies applied to finding potential treatments and biomarkers for these diseases that often share genetic causes or biological mechanisms. Partnerships we have forged with Gates Ventures, ADDF and AFTD, among others are helping us achieve this goal.



Key Statistics

▶ In partnership with Gates Ventures and the ADDF, we dedicated \$2.4 million in funding to researchers investigating biomarkers useful for ALS and related neurodegenerative diseases like AD and FTD.

▶ We established a one-of-a-kind Longitudinal Biofluid Core that will, for the first time, allow access to biofluid samples collected over the course of ALS, complete with associated de-identified clinical and demographic information as well as genomic data sets. These critically needed samples will be available to researchers in 2023.

▶ Our partnership with AFTD, announced in 2019, resulted in funding for six pharma/biotech-led projects working to find treatments or biomarkers for both ALS and FTD. One of these projects has already resulted in the launch of a clinical trial for ALS (in 2021).

▶ We also funded five new projects to test new drug targets, utilizing an animal model for ALS. A beneficial effect of a drug in an animal model of the disease is a key step in its progress toward the clinic.

Groundbreaking Partnership

Working with Gates Ventures and The Alzheimer's Drug Discovery Foundation to Accelerate Biomarker Discovery and Development



Alzheimer's
Drug Discovery
Foundation

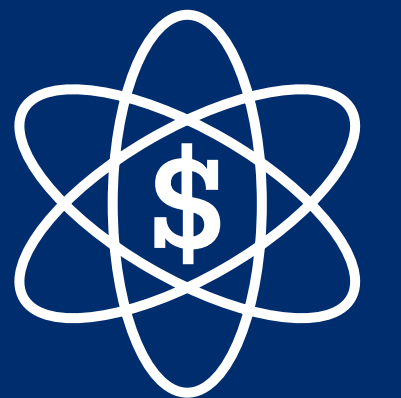


Groundbreaking Partnership

In December 2021, Target ALS announced an innovative new partnership with Gates Ventures and the ADDF focused on identifying and developing biomarkers for ALS, along with other neurodegenerative diseases like AD and FTD.

The goal is to encourage cross-pollination of ideas across different research communities. Biomarkers can help diagnose neurodegenerative diseases earlier, reliably track their progression, and assess the effects of new drugs, leading to more efficient clinical trials.

The partnership funds four biomarker-focused collaborative research projects led by a researcher from a pharma/biotech company in collaboration with academic scientists.



Groundbreaking Partnership

Partnership with the Association for Frontotemporal Degeneration Results in New Clinical Trial

Capping a highly successful two-year partnership with AFTD, Target ALS has co-funded six research groups doing critical work in ALS and FTD. One has already launched a clinical trial, and the other five are moving forward despite challenges posed by the pandemic.

Because ALS and FTD share overlapping genetic causes and mechanisms, the partnership incentivized pharma/biotech scientist-led collaborative projects to work on therapeutic approaches or biomarkers applicable to both ALS and FTD.



Update on Target ALS Diagnosis Initiative

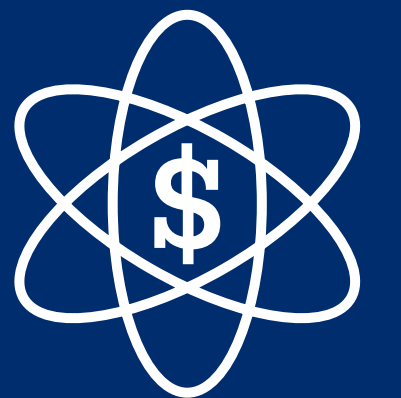
The Target ALS Diagnosis Initiative, launched in 2020, is funding research and creating scientific resources to discover and develop critically needed biomarkers.

Under this initiative, we funded four biomarker-focused collaborative projects led by a pharma/biotech-based scientist. The projects have, by now, completed the first year of their funding period.

We also funded precompetitive biomarker projects focused on understanding the forms of TDP-43 and developing new tests to measure its levels present in the cerebrospinal fluid of ALS patients. The data and tools generated from these projects will be shared with the ALS research community worldwide.

TDP-43 pathology is the most common neuropathologic hallmark in ALS, occurring in greater than 90 percent of all cases. It is also a common neuropathologic feature in other neurodegenerative diseases, including AD and FTD.

With Target ALS serving as the hub of this collaboration, the project has brought together a cross-sectoral group that includes 14 pharma/biotech groups and a panel of 10 academic experts and six nonprofit foundations. Members of this initiative have worked together over the past two years to formulate and launch the two TDP-43-focused projects.



Target ALS Launches Longitudinal Biofluid Core

The suite of our scientific cores continues to expand to provide access to critically needed research tools and resources.



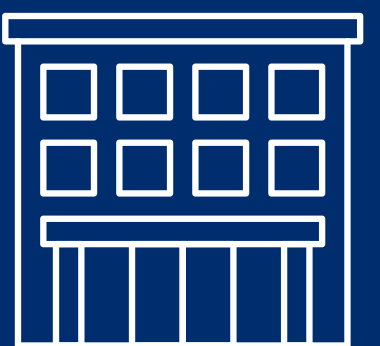
Target ALS has successfully launched a Longitudinal Biofluid Core and established a new inventory management system across the Biofluid and Postmortem Tissue Cores, which will significantly increase the efficiency of sample management and distribution.

Access to longitudinal biofluid samples—cerebrospinal fluid, blood, and urine—has been a long-standing barrier to the advance of ALS research. Donated by ALS patients over the course of their disease and by healthy individuals (control cases), these samples offer unique insights into the pathogenic evolution of ALS over time. They will now be available to researchers on an expedited basis beginning in 2023 and will help galvanize biomarker discovery and development for ALS worldwide.

Over the past nine years, Target ALS has successfully launched seven scientific cores that provide no-strings-attached access to crucial research tools and resources for the worldwide ALS research community. Over 500 ALS projects worldwide have used these cores.

OTHER CORE FACILITIES

Projects to create new animal models for ALS have progressed significantly. A mouse model for C9orf72 ALS is in the final phase of evaluation. Projects to create mice that carry genetic mutation on the TDP-43 gene, which would potentially help test new drug targets for familial and sporadic ALS, are also in progress. Evaluation of one of the TDP-43 mouse models to determine features of ALS is currently underway.



Annual Meeting

Bringing together the diverse constituencies of the worldwide ALS research community is an important part of our work to advance ALS drug discovery and development. Attendees immerse in cutting edge ALS research and network, while forging new collaborations across academia and the pharma/biotech industry, venture capital and non-profits.



Key Statistics

► **Over 700**
total attendees



► Newly implemented hybrid option enabled a broader cross-section of the worldwide community to participate



► **100+** networking
meetings occurred



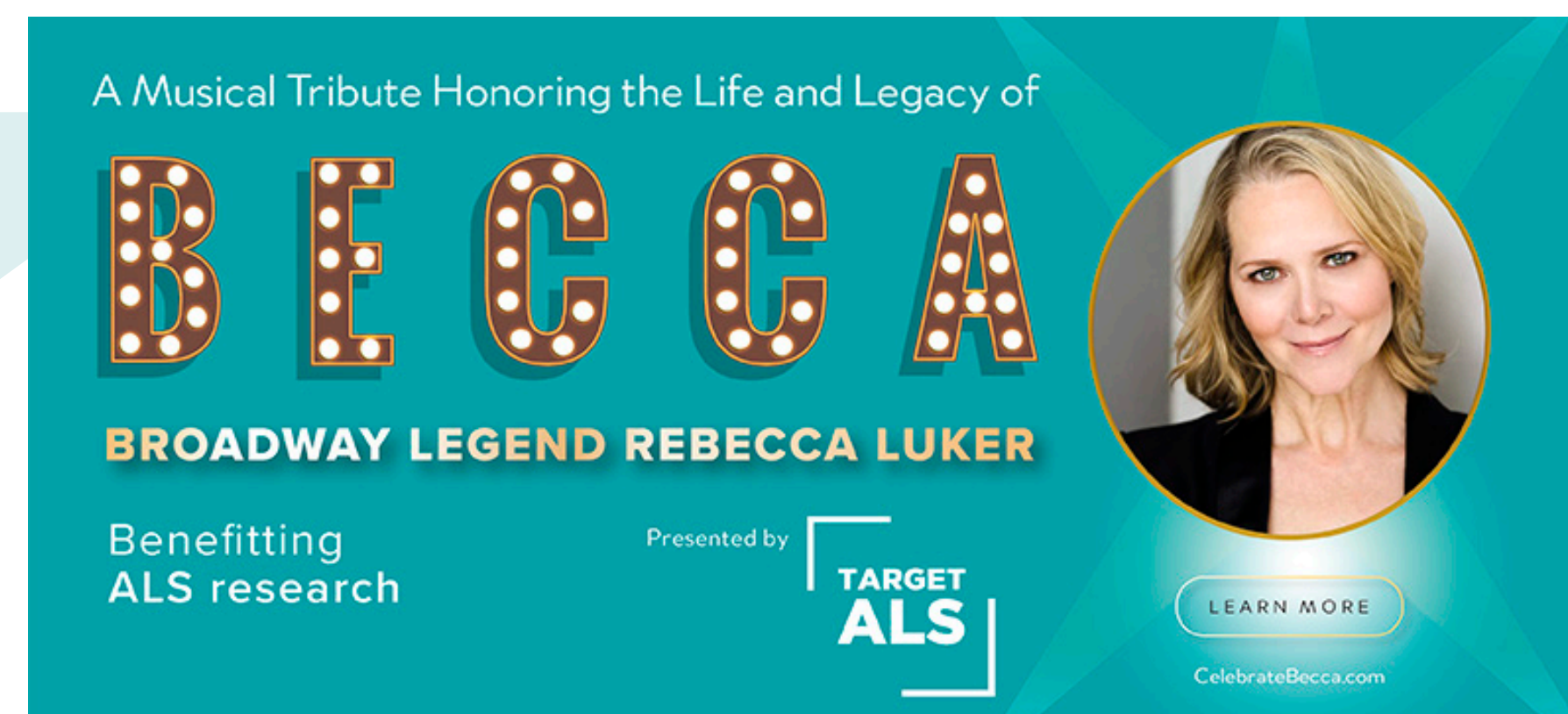
A Star-Studded “Becca”

To honor the life and legacy of Broadway legend Rebecca Luker, Target ALS presented a one-night-only musical tribute called “Becca,” featuring top talent from Broadway, TV, film, and beyond. The concert was partially sponsored by Mitsubishi Tanabe Pharma America (MTPA) and raised more than \$150,000 in immediate funds for ALS projects.

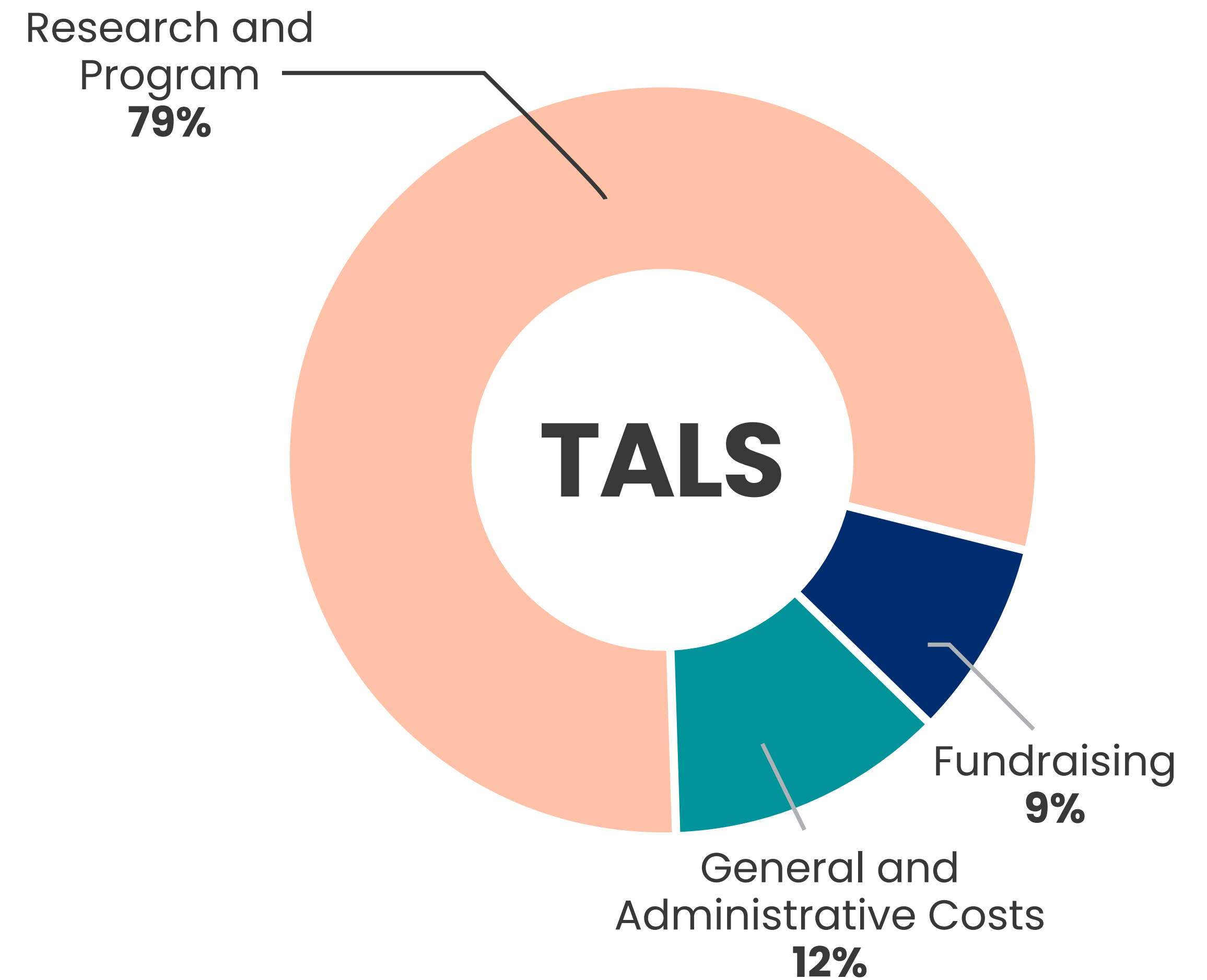
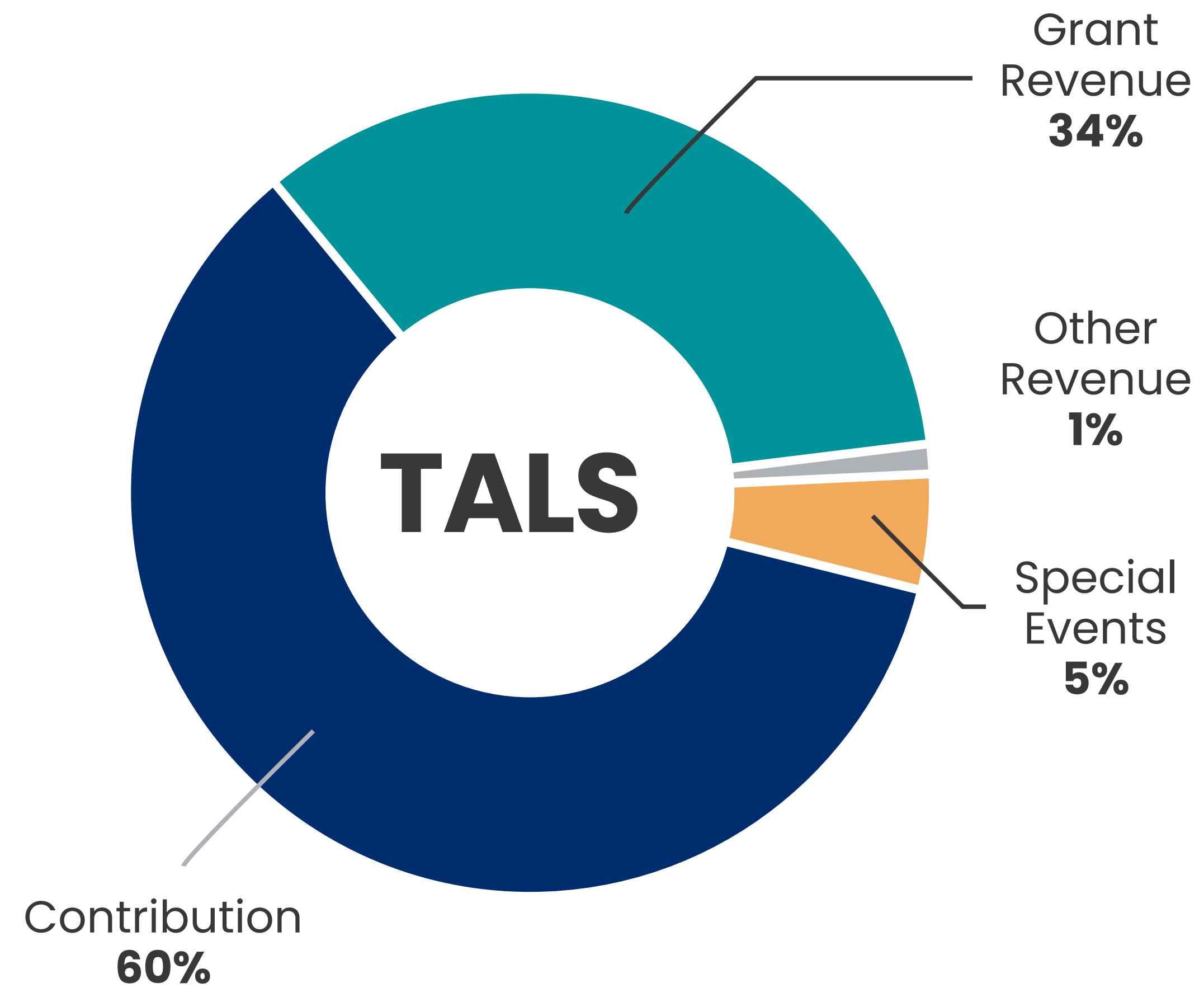
Presented online in May 2021, the concert featured Tony recipients and nominees Kristin Chenoweth, Laura Benanti, and Judy Kuhn. Many remembered performing

alongside Rebecca in musicals, including *Mary Poppins*, *The Music Man*, and *The Sound of Music*.

As a result of the concert’s success, we created a special awards series in Rebecca’s honor—the Rebecca Luker Courage Awards—to commemorate individuals making a remarkable impact in the fight against ALS. This award was created in partnership with MTPA. Winners include leading researchers, ALS advocates, and a generous philanthropist who have all contributed their time, energy, and passion to the fight against the disease.



Financials



Target ALS would like to thank its wide range of donors whose generous contributions help make our work possible.

Jeffrey Altman

Barbara Freitag

Jim Levine

Judith Rubin

Michele Jean Anderson

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John Logan

Judy Rutkowski

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Alan Eustace

Marcia A. Kunstel and Joseph Albright

Richard Rieger

THANK YOU!