ANNUAL REPORT

ALS Therapy Development Institute
2022

THE DRUG DISCOVERY ENGINE FOR ALS

ABOUT US

As the Drug Discovery Engine for ALS, the ALS Therapy Development Institute (ALS TDI) discovers and invents ALS treatments and partners to advance them into clinical trials.

It is the first and largest nonprofit biotech focused 100 percent on ALS research. ALS TDI incorporates all aspects of drug discovery under one roof to find treatments as quickly as possible.

Located in Watertown, MA, ALS TDI employs researchers with over 300 years of combined experience and expertise across all areas of drug discovery. ALS TDI is recognized as an international leader in preclinical and translational ALS research, and partners with pharmaceutical companies and biotechs around the world. Awarded the highest nonprofit rating – four stars – on Charity Navigator, ALS TDI spends 87 cents of every dollar raised on finding effective treatments and cures for ALS.

Learn more at www.als.net.

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LETTER

FROM THE CEO

As 2022 comes to a close, I feel profoundly grateful for your steadfast support of the ALS Therapy Development Institute (ALS TDI). This year, your generosity and commitment have been foundational to a year of remarkable progress and invaluable discoveries.

When it comes to testing and discovering drugs, ALS TDI has always been focused on “getting more shots on goal.” That is because more shots on goal tend to produce more goals. But it is also because we recognize that no single treatment will be enough to address the needs of people with ALS. So, our mandate is broader, more ambitious. We are committed to creating a pipeline of treatments, a range of options to change the future for everyone living with ALS.

Throughout the past year, your unwavering support has enabled us to achieve numerous milestones. We’ve accelerated our preclinical research by screening hundreds of compounds and assessing dozens of drug candidates in pharmacology studies. We are working to advance he most promising candidates, such as Type I PRMT inhibitors and copper complexes, toward clinical trials.

We are also on the brink of launching a cloud-based platform in early 2023, part of our multifaceted program to collect and share comprehensive data about ALS. This will offer researchers worldwide access to an extensive natural history and genomics database that we have compiled through the Precision Medicine Program (PMP). Moreover, thanks to a $281,000 grant from the ALS Research Program at the Department of Defense, we're using cutting-edge proteomics technology to identify new biomarkers and targets for ALS.

Looking ahead to 2023, I am filled with optimism and anticipation for what we can achieve together. Your continued support not only fortifies our ongoing work but also emboldens us to aim ever higher. As we navigate through the year, we look forward to sharing further updates that will illuminate the power and potential of our joint efforts.

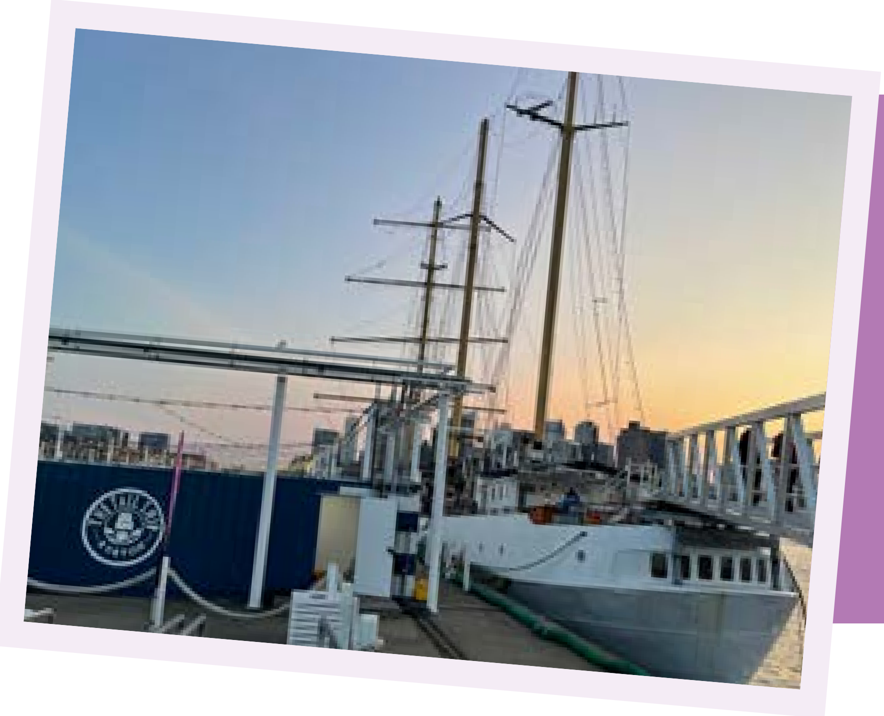
In closing, thank you once again for your commitment to this cause, for being a part of this incredible community, and for helping us move ever closer to fulfilling our shared mission: to end ALS.

With deepest appreciation and heartfelt thanks,

Fernando Vieira, M.D.

President, Chief Executive Officer, and Chief Scientific Officer,
ALS Therapy Development Institute

FUNDRAISING HIGHLIGHTS



Tall Ship Party to #EndALS

In 2022, longtime supporters, Eric and Rachel Engdahl, hosted their inaugural Tall Ship Party to #EndALS. The event took place at The Tall Ship in Boston, looking over the famous Boston Harbor. Guests joined for oysters, cocktails, and a gorgeous sunset, all to support ALS research. This incredible event ended up raising over $55,000 in its first year!

Acing ALS

Becky Wetzel and Kristen Segal created Acing ALS in 2021 to raise awareness and funds for ALS. They brought together women from their local racquet community for a day of paddle fun in the spirit of hope and giving. In 2022, they hosted three tournaments across the country that raised a combined $152,000 for ALS research!

Walk for Research

As a reimagined version of ALS TDI's "Race 4 Research" the ALS TDI Walk for Research had its inaugural year in 2022. The event was a four mile walk in Newton, MA, paying homage to the town where ALS TDI was founded. The Walk for Research united those in the area impacted by ALS while raising $54,000 for ALS research!

ALS TDI RESEARCH

In 2022, ALS TDI worked to build on past achievements and innovate new programs to accelerate ALS Research.

The year saw an important milestone for tegoprubart, a drug invented at the institute, as well as continued progress on the promising treatments currently in our pipeline. We laid the groundwork for a major new initiative to share essential data from people with ALS with researchers around the world. We collaborated with prestigious organizations to advance important research about how to track ALS progression. All the while, we continued our mission to fill the ALS clinical pipeline and test more potential ALS treatments than any other research lab in the world.

Continuing to Fuel the Pipeline

In 2022, ALS TDI researchers worked tirelessly to move forward the two most promising potential ALS treatments in our pipeline. The ALS TDI clinical pharmacology team tested several copper complex molecules in animal models of ALS, moving us closer to identifying a lead candidate for clinical trials. Meanwhile, members of the Cell Biology team continued to work toward identifying promising type-1 PRMT inhibitors – a class of drugs that affects a target discovered at ALS TDI for C9orf72-related ALS – to advance toward animal testing.

Additionally, tegoprubart, a treatment invented at ALS TDI, successfully completed a Phase 2a clinical trial – an important step for the first potential ALS drug invented by a nonprofit to reach human clinical trials.

HIGHLIGHTS

Building Solutions to Advance Research

One of the major challenges in the field of ALS research is the lack of a widely accessible, shared source of data from people living with the disease. **In 2022, ALS TDI worked to address this by building the ALS Research Collaborative (ARC) Data Commons** – an online portal through which researchers anywhere in the world can access and analyze the wealth of data collected through the ARC study, the longest running natural history study in ALS.

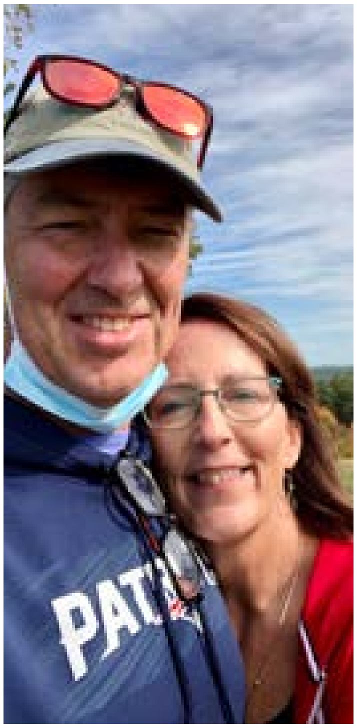
This platform, which was launched in early 2023, **allows researchers to log in from anywhere in the world and easily search, analyze, and download the wealth of de-identified data.** By providing a large, ever-expanding dataset, and powerful tools to filter and visualize the data, the ARC Data Commons can provide scientists with key insights – that previously might have required months or years of research – in a matter of minutes.

Learning More About ALS

In collaboration with Google, ALS TDI analyzed data gathered through the ARC Study using machine learning techniques to develop new digital biomarkers of ALS – tools that can objectively measure ALS symptom progression over time. These tools could potentially provide researchers and clinicians with more accurate ways to track progression and measure the effectiveness of treatments in clinical trials.

Supported by a $281,000 grant from the Department of Defense's ALS Research Program, **we initiated a project to identify new protein-based biomarkers for ALS.** Leveraging data from ARC and cutting-edge proteomics technology, this study represents an unprecedented opportunity in the pursuit of ALS biomarkers.

LEADERS IN THE COMMUNITY



Rebecca Mourey Stephen Heywood Patients Today Award

Rebecca "Becky" Mourey was diagnosed with ALS in November of 2020. From the moment of her diagnosis, she channeled her natural strength and determination into becoming an eloquent and indomitable advocate for the ALS community. Nearly two years after diagnosis, wheelchair-bound and requiring a Tobii to communicate, she continued to live her life by the following tenet: "Now, and for the rest of my life, my absolute focus is to do everything in my power to help change the trajectory of this disease from 100% fatal to treatable."

Becky worked with MGH, I AM ALS, ALS ONE, and countless politicians during the passing of ACT for ALS. After December of 2021, her advocacy work continued, with a focus on getting ALS patients access to the promising drug AMX0035.

Even when she felt sick or needed extra help, Becky continued to demonstrate to the world that an ALS-ridden body is not a useless body. She showed tremendous resilience, always putting the good of the greater ALS community before her immediate comfort. Becky passed from ALS in February 2023, but her selfless actions have triggered a chain reaction of compassion, courage, and strength, pushing the needs of the ALS community to the forefront of ALS research.

Her ALS Story Stephen Milne Adventurous Spirit Award

For the first time in the history of these awards, ALS TDI is honoring a group – Her ALS Story. Her ALS Story is a group of 32 women, all diagnosed with ALS before their 35th birthday. Their mission is to challenge the stereotype that ALS only affects older, mostly white, men. The women of Her ALS Story have fostered a candid dialogue about their declining health in female-centric media outlets, cultivated relationships with women lawmakers to improve insurance and Medicare standards for people with ALS, and introduced legislation to speed up the ALS drug pipeline.

They have also raised money to support the pursuit of unbiased ALS research to ultimately end this devastating disease. We are constantly inspired by the work of these women, many of whom have individually received nominations for leadership awards themselves, and we know their efforts will help change the trajectory of ALS.

As part of this year's ALS TDI Summit, a free conference about ALS TDI's latest research, we recognized a few community members, nominated by their peers, whose efforts truly stood out this year.

Sandra Marlowe

Mary Lou Krauseneck Courage & Love Award

Sandra Marlowe is a mother, grandmother and, like ALS TDI's CEO Dr. Fernando Vieira, a Florida Gator (Go Gators!). She and her husband Wayne have been married for 45 years. They have five children and 13 grandchildren.

The Marlowes are a close-knit family who love spending time together and going on travel adventures. Prior to her diagnosis, Sandra maintained an active lifestyle of recreational biking, hiking, walking, and competitive swimming with US Masters Swimming. In 2019, Sandra experienced an unusual choking episode at a family Thanksgiving dinner. Just a few months later, in March of 2020, she was diagnosed with bulbar ALS.

If you haven't met Sandra Marlowe in real life, you have very likely interacted with her on Twitter. Every day her unwavering positivity is an inspiration to many as she navigates the "new normal" of living with ALS. Sandra's active Twitter and Facebook feeds have always shown her incredible attitude and heart. She always provides great examples of the hardships of living with ALS while also demonstrating hope and positivity.

"As symptoms progress, many people living with ALS become homebound," Sandra says. "Out of sight, out of mind. The public have no idea of our struggles. I live next to a park with a walking trail. I get stares, and smiles. I can't speak, but I'm a rolling ambassador."

Lori Larson Heller

Fran Delaney Challenge & Respect Award

On September 6th, 2018, Lori Larson Heller's life changed forever when her beloved husband, Jim, was diagnosed with ALS. Lori and Jim were both commercial real estate executives. Despite her robust career, Lori made the decision that fateful day to leave her job and become Jim's full-time caregiver. It was just a year and a half later that Jim passed away.

Despite her loss, Lori chose to dedicate her life to changing the future of ALS for others. Her goal is to ensure that a cure is found in her lifetime. She connected with almost every ALS organization and advocate she could to identify opportunities to get involved. For the past two years, Lori has been a tireless advocate for ALS research and ALS TDI. She generously provided the funding to establish the Jim Heller Mouse Investigation Room at ALS TDI, while visiting clinics to educate staff on the Precision Medicine Program. In her little free time, Lori has taken classes on the role of Expanded Access Programs, hosted fundraisers, and supported many people living with ALS with her warmth and kindness.

FINANCIAL REVIEW

ALS TDI financial information for fiscal year ending in December 31, 2022

This financial information is derived from audited financial statements. Copies of audited financial statements are available upon request. For a complete copy of our IRS Form 990 or Independent Auditors Report, please call us at 617.441.7200.

Assets

Current Assets		**Other Assets**	
Cash And Cash Equivalents	$10,028,667	Property & Equipment, Net	$380,524
Pledges & Accounts Receivable	$1,053,475	Patents	$775,666
Other Current Assets*	$584,567	Investment in Subsidiary	$3,022,334
		Other Long Term Assets	$5,206,292
Total Assets			**$21,051,525**

Liabilities & Net Assets

Current Liabilities	$1,477,146
Long Term Liabilities	$4,345,898
Net Assets	$15,228,481
Total Liabilities & Net Assets	**$21,051,525**

Operating Income

Grants	$337,846
Special Events, Net	$7,968,545
Contributions	$1,211,001
Released from Restrictions	
Fee for Service	$636,927
Donated Goods & Services	$4,801
Interest & Other	$1,69,975
Total Public Support	**$10,329,095**

Operating Expenses

Program		**Support**	
R&D		General Fund	$537,070
Science	$6,575,538	Fundraising	$459,735
Informatics	$702,353	**Total Support**	**$996,805**
Patient Services	$80,945		
Communications	$1,440,736		
Business Development	$37,963		
Total Program	**$8,837,535**		
Total Expenses			**$9,834,340**

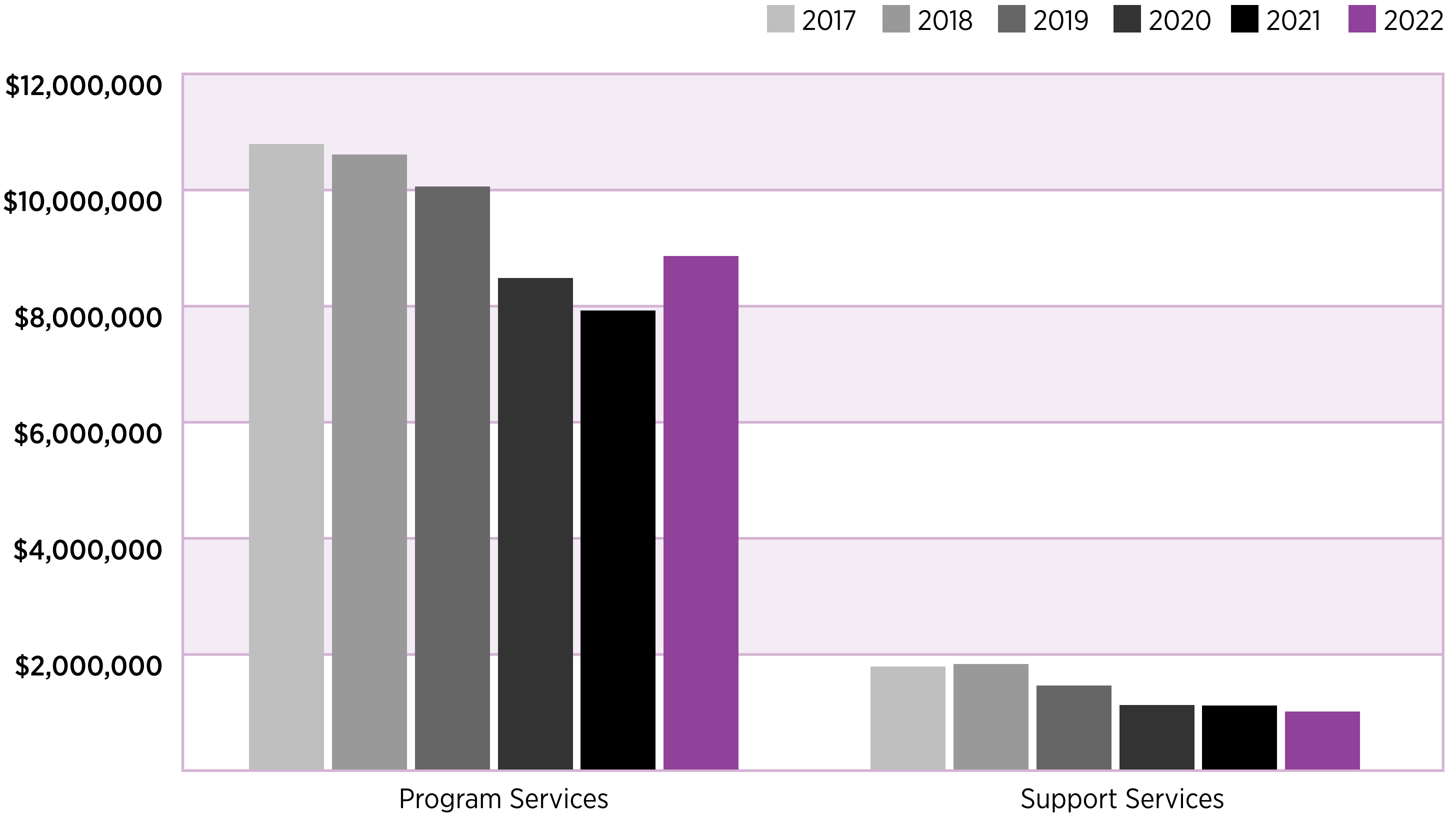
** This financial information is derived from audited financial statements, available upon request.*

2017-2022: A FINANCIAL COMPARISON

As a nonprofit, we rely on donations to accelerate our research.

87 cents of every dollar goes directly to finding treatments and cures at ALS TDI, compared to the average 75 cents** at other research labs, and we have been rated a four-star nonprofit by Charity Navigator for five years in a row.

	2017	2018	2019	2020	2021	2022	Total Spent
Program Services	$10,771,564	$10,587,060	$10,039,201	$8,466,048	$7,899,759	$8,837,535	$56,61,167
Support Services	$1,766,028	$1,815,788	$1,442,668	$1,103,743	$1,094,525	$996,805	$8,219,557



CHARITY NAVIGATOR
★★★★
Four Star Charity

Platinum Transparency 2022
Candid.

Charity Navigator has awarded ALS TDI its highest rating—four stars—for a record six years in a row. This exceptional designation sets ALS TDI apart from its peers.

***Ledford, H. “Keeping the Lights On.” Nature, 20 November 2014*

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