ANNUAL REPORT

ALS Therapy Development Institute

2021

THE DRUG DISCOVERY ENGINE FOR ALS

ALS
THERAPY DEVELOPMENT
INSTITUTE

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

Dear Friend,

In April of 2021, I was appointed CEO of the ALS Therapy Development Institute (ALS TDI). Over the past 8 months, I have been incredibly proud to lead this dedicated team with an amazing community of supporters. Together, we have persisted and made important gains in ALS research – gains which continue to get us closer to fulfilling our mission to end ALS.

This past fall, I stated that as the ALS Drug Discovery Engine, our goal moving forward is to advance an ALS treatment to human trials every two years. This is an incredibly ambitious goal, but I am more encouraged than ever by the progress that we are making.

Because of your unwavering support, the team of scientists at ALS TDI has been able to continue our vital work to fulfill this mission. We currently have two promising programs that are poised to advance toward clinical trials, and we will continue to build on this progress. Thanks to the data that many of you share with us through our Precision Medicine Program, our team is learning more about ALS and how it affects individuals, enabling us to invent more effective and targeted treatments.

I have been studying ALS for two decades and I believe that we are at a pivotal moment in research. New knowledge is revealing unexplored therapeutic pathways, and new technologies hold the profound potential to help us address the needs of people with ALS.

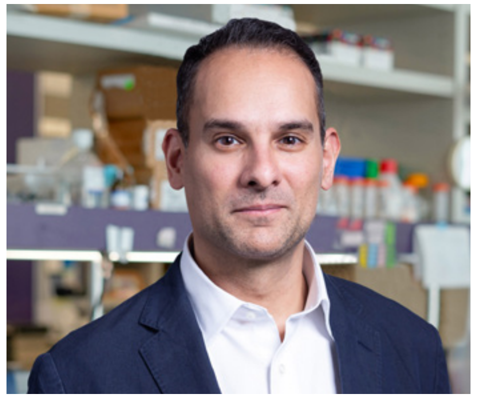
As long as research remains a top priority, these advances in knowledge and technology will lead to treatments. But no one treatment will address the needs of all people with ALS. So, while the current therapeutic pipeline is promising, if we want to change the future of ALS, we must continue to fuel this pipeline with new treatments.

As CEO of ALS TDI, and as a person driven by the loss of my best friend to ALS, I pledge my dedication to fulfilling our mission. With your support, we will overcome the challenges. We will not stop until we end ALS.

With sincere thanks for your continued support,

Fernando Vieira, M.D.

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



FUNDRAISING HIGHLIGHTS

Following a year marked by canceled events and virtual alternatives brought about by the Covid-19 pandemic, ALS TDI's fundraising programs began a gradual return to normalcy in 2021.

While events continued to adapt with hybrid formats and limited capacities, some in-person gatherings were possible, and fundraising continued to bounce back closer to pre-pandemic levels.

Ales for ALS™

In 2021, despite COVID complicating things like brew fests and beer release parties, the Ales for ALS™ program enrolled 221 brewers, each of whom crafted delicious beers to support ALS research. These efforts were further supported by creative virtual Brewfest events and even some in-person parties around the country.

The program raised $550,000 for research at ALS TDI through brewer revenue, sponsorships, and events throughout the year.

Bryan Meyer Golf Invitational

This event was organized by Bryan Meyer, who has been living with ALS since 2020, and his family. It was a particularly successful example of our Driving for Life program, which helps people all over the country organize golf tournaments to raise funds for ALS Research.

The tournament brought a full field of golfers to the Indian Wells course in Palm Springs, CA, raising $315,000.

Top: Balebreaker's brew fest celebrating their Ales for ALS™ brew. Bottom: Players at the Bryan Meyer Golf Invitational event.

Brothers Scott and David Lloyd attending one of their successful Racing for ALS events.

Racing for ALS

Dave's Race 3 was held on May 8, 2021 at Virginia International Raceway in Alton, VA. After raising more than $50,000 in 2020, David and Scott Lloyd's third annual high-performance driving event raised the bar yet again – challenging the drivers and supporters in their racing community to double their support.

Amazingly, Dave's Race 3 achieved that goal and then some, raising over $105,000 for ALS in 2021.

Tri-State Trek

Following the pivot to an online-only fundraising ride in 2020, the Tri-State Trek returned as an in-person event in 2021. The modified one-day, 100-mile ride began and ended at the ALS TDI lab in Watertown, MA. Though attendance was limited, the enthusiasm of the #TrekFamily was palpable and the event was a success. In addition to the in-person ride, there was an online "Virtual Trek" option and "Trek Your Way" option for those who preferred to fundraise through an activity other than cycling.

Altogether, Trek participants raised $600,000 for research at ALS TDI.

ALS TDI RESEARCH HIGHLIGHTS

2021 was a year of big changes for the ALS Therapy Development Institute. We moved into a new, state-of-the-art laboratory in Watertown, MA.

We worked to safely bring back all of our researchers to the lab after a year of learning to adapt to the continuing challenges of the COVID-19 pandemic. All the while, we continued pushing the pace of ALS research forward – yielding many promising results.

Promising new discoveries for the future of ALS Treatments

We discovered “redox metabolism modulators” – a collection of drug-like molecules that we believe can protect against ALS-related cell death

We worked to further unlock the potential of our new drug target discovery, Type-1 PRMTs, for C9orf72-related ALS. We began testing treatments against this target, with the hope of identifying one that we can advance to animal testing. Findings may also be transferable to other forms of ALS.

Continuing the search for the next potential treatments

While continuing to move our promising drug discoveries forward, we also tested 26 treatments in animal models of ALS. Those that showed potential will be assessed for tolerability, side effects, and efficacy. The treatments that show the most promise will be further advanced - allowing us to continue to fuel our pipeline.

Our dedicated ALS TDI researchers working in the lab.

Important collaborations to expand the Precision Medicine Program

We announced a partnership with Dr. Rick Bedlack and the Duke ALS Clinic to enroll people who represent the rare instances of ALS reversals into the Precision Medicine Program (PMP). We aim to learn more about the underlying biological pathways behind these reversals and use this understanding to inform treatment discovery and development.

We also continued to collaborate with Google to apply a voice scoring algorithm to recordings contributed by Precision Medicine Program (PMP) participants. We began sharing these scores with PMP participants to give them a numerical measure of their own speech wellness.

We look forward to continuing to build upon these accomplishments in 2022, with the ultimate goal of advancing a new drug to clinical trial every two years.

As the Drug Discovery Engine for ALS, our role is to continue to invent and discover drugs until there are treatments for everyone with 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.

LEADERS IN THE COMMUNITY

David & Scott Lloyd

Stephen Heywood Patients Today Award

David and Scott Lloyd took a few powerful engines, created Racing for ALS, and have not stopped helping accelerate ALS research ever since! It all started with a simple live video on Facebook, showing them picking up their dream car in Texas and driving it home to North Carolina. David and Scott thought "Let's see if anyone will make donations to research while we drive this beast home," planting the seed for what would become Racing for ALS. The Lloyd brothers have been able to engage so many different communities to learn more about ALS and the importance of research at ALS TDI. In 2018, they put together the first Dave's Race event in just a few short weeks, despite never having hosted an event like it before, and were able to raise just under $40,000! They have now grown the Racing for ALS program to over $250,000 raised and generated a lot of awareness as they continue to build their brand. David has inspired hundreds of drivers to take on our cause due to his unwavering faith in the science at ALS TDI. Racing For ALS continues to be active through social media, news outlets, and print media to engage and support ALS patients through their love and experiences for racing.

Rahul Desikan M.D., Ph.D.

Stephen Heywood Patients Today Award

Rahul was diagnosed with bulbar-onset amyotrophic lateral sclerosis (ALS) in February 2017 and passed away from complications due to ALS on July 14, 2019. In the span of two years, Rahul developed a research program focused on the genetic architecture of ALS, became an influencer on Twitter gaining more than a thousand followers while raising awareness of ALS. In 2017, Rahul had been studying the polygenic architecture of ALS when he himself unimaginably received a diagnosis of ALS. Within four months of his diagnosis, he was unable to walk, use his hands or speak. He relied on his wheelchair for mobility and used a hands-free speech device to communicate. As devastating as it was for Rahul to receive this diagnosis, he did not let it govern his life. Despite his severe disabilities, Rahul worked tirelessly until the day he died.

Rahul set a high bar with his record of scientific accomplishments and his skill in bridging science and advocacy to spur innovations in ALS research and policy. Many words have been used to describe Rahul including, "genius", "brilliant", "funny", and "hero." His quintessential trait was his ability to connect.

Teresa Thurtle

Stephen Milne Adventurous Spirit Award

Teresa Thurtle has one heck of an Adventurous Spirit and inspires the entire ALS community with it! Teresa has traveled the globe spreading ALS awareness on all seven continents. An Air Force veteran and professor, Teresa spends whatever spare time she has jumping into programs like Ragnar for Research and the Tri-State Trek to help end this disease. Even with little time to train, and a bunch of injuries, Teresa's adventurous spirit lead her to TWO runs, just weeks apart, in New Jersey and Texas this year....bears and all! Teresa comes from a familial ALS family, having lost her father and grandmother to this disease. And, beyond all of her physically adventurous efforts to help fund research, she is also the founder of Bottoms Up to Down ALS, a Young Faces of ALS ambassador, and has helped us bring new brewers into the Ales for ALS program.

Katie Bauer

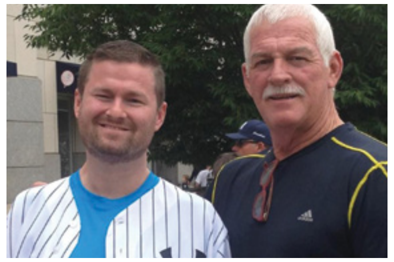
Mary Lou Krauseneck Courage & Love Award

Katie lost her best friend, her husband, Charlie, to ALS, in 2016. And despite that, she has become, truly, the heart of the ALS community. Being with Katie, is like getting a big hug. A lawyer, a mother, a caregiver, and a friend to all who need her. Katie has chosen to 'celebrate' the anniversary of Charlie's passing, each year, by coming to the ALS lab, and treating all of us to breakfasts, and lunches, and personalized gifts, and some of the best lemon cookies you could ever imagine. Katie not only rides the Tri-State Trek, but also jumps in, at the last minute, when she's needed, into a 24-hour run through the back woods of New Jersey through Ragnar for Research. This year she is also representing ALS TDI at the TCS New York City Marathon! Her poignant blogs allow the entire community into the life of, and after ALS. She is the pinnacle of Love and Courage.

Mac and Bailey Brown

Fran Delaney Challenge & Respect Award

Mac and Bailey Brown have been fundraising for ALS research at ALS TDI since 2012 through their ALS "Awesome Lemonade Stand." What started out as a small lemonade stand on the corner of their street has turned into a nationwide effort where community is formed through support and sharing. Mac has used his position as a football player at Ole Miss University to generate ALS awareness. Bailey is Mac's proud older sister and a behind the scenes helper to help him spread awareness and carry it through. Bailey graduated from Boston Collage where the infamous Pete Frates attended. She now lives in Chicago but that does not keep her from being present at Ole Miss games and ALS fundraising events. Their spirit, fueled by the selflessness of a family friend, Michael Brandt, who in his hardest days with ALS taught Mac and Bailey the power of giving back. They have inspired others to host their own lemonade stands and contribute their earnings to support ALS TDI. To date, they have raised over $135,000, and funds continue to increase every year.



Patrick Liam Quinn

Mary Lou Krauseneck Courage & Love Award

Pat Quinn Sr. (Big Pat) has exemplified love and courage since his son, Pat Quinn, was diagnosed with ALS at the age of 30. He was Pat's biggest fan and pledged to be alongside his son throughout his journey. Early on, they launched Quinn 4 The Win to help support Pat and countless others facing ALS. Then came August 2014, when Pat co-founded the ALS Ice Bucket Challenge with Pete Frates. Big Pat was there, as always, making it possible for his son to march in parades, conduct countless television interviews, and raise $300 million for ALS care and research across the globe. Even after we lost Pat one year ago, Big Pat has kept the fight going. He spends his days collecting and delivering equipment for local people with ALS and offering help and advice to so many who need it. He runs countless events to ensure funds are there for people with ALS in need, and for research at ALS TDI. He keeps his son's incredible spirit alive, despite facing a loss that no parent should have to bear.

FINANCIAL REVIEW

ALS TDI financial information for fiscal year ending in December 31, 2021

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	$10,732,566	Property & Equipment, Net	$251,537
	Pledges & Accounts Receivable	$1,049,523	Patents	$662,622
	Other Current Assets*	$233,017	Investment in Subsidiary	$5,845,830
			Other Long Term Assets	$226,916
	Total Assets			**$19,047,011**

Liabilities & Net Assets	Current Liabilities	$657,736
	Long Term Liabilities	$1,867,513
	Net Assets	$16,521,762
	Total Liabilities & Net Assets	**$19,047,011**

Operating Income	Grants	$300,620
	Special Events, Net	$8,025,788
	Contributions	$2,507,818
	Released from Restrictions	$250,000
	Fee for Service	$628,036
	Donated Goods & Services	$6,798
	Interest & Other	$11,989
	Total Public Support	**$11,731,049**

Operating Expenses	Program		Support	
	R&D		General Fund	$710,102
	Science	$5,933,516	Fundraising	$384,423
	Informatics	$728,765	**Total Support**	**$1,094,525**
	Patient Services	$62,856		
	Communications	$1,146,415		
	Business Development	$28,207		
	Total Program	**$7,899,759**		
	Total Expenses			**$8,994,284**

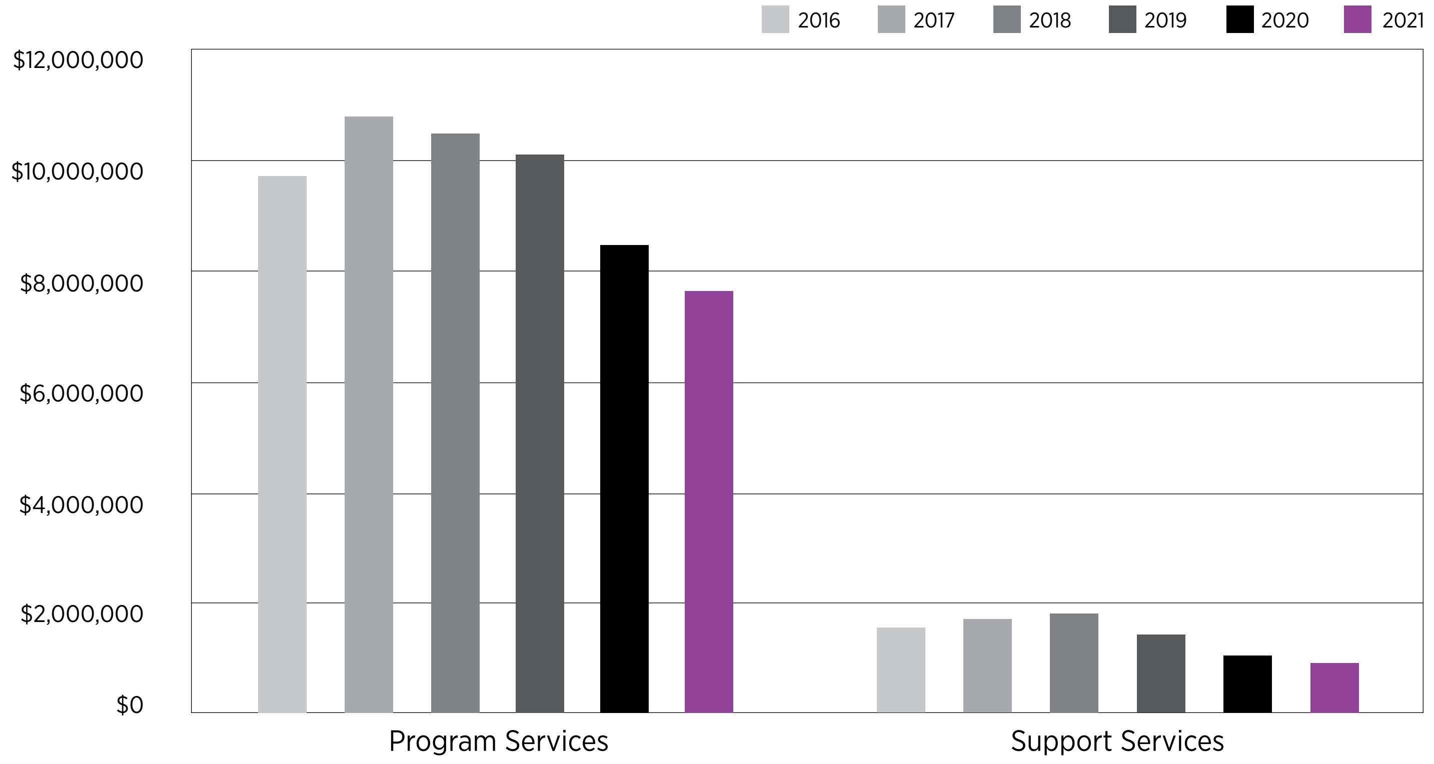
** This financial information is derived from audited financial statements, available upon request.*

2016-2021: 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.

	2016	2017	2018	2019	2020	2021	Total Spent
Program Services	$9,705,301	$10,771,564	$10,587,060	$10,039,201	$8,466,048	$7,899,759	$57,468,933
Support Services	$1,569,649	$1,766,028	$1,815,788	$1,442,668	$1,103,743	$1,094,525	$9,123,003



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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