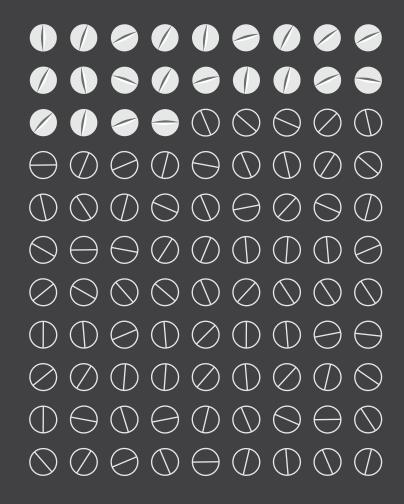


OF ALL THE DRUG DISCOVERY PROGRAMS NOW IN CLINICAL TRIALS

WE'VE SUPPORTED MORE THAN 20%

Effective treatments for Alzheimer's are now just years, rather than decades, from becoming a reality. The Alzheimer's Drug Discovery Foundation is proud to have contributed to over 20% of the drugs now in clinical trials. Over 15 years ago, we seed funded drug discovery by **Frank M. Longo, MD, PhD,** featured on the cover. And we continued that support, helping him found the biopharmaceutical company PharmatrophiX and develop his drug, LM11A-31. Earlier this year, that drug, which is about to begin Phase 2a clinical trials, was featured on the cover of *Time* magazine and called a potential "game changer." *Read more about his work on page 7.*



"WE ARE NEARING THE FINISH LINE"

Dear Friends,

At our Fall Symposium & Luncheon in November, we stated an ambitious goal—to be able to treat Alzheimer's within our lifetimes. Thanks to the Alzheimer's Drug Discovery Foundation (ADDF), the scientists we fund, and supporters like you, we can and will get there.

By any measure, 2015 was the most successful year in the ADDF's history. We raised over \$22.5 million, more than doubling our fundraising total from 2014. And 100% of donations fund drug discovery programs.

Because of your tremendous support, we are able to invest in even more promising drug programs. And many more of these programs are in human clinical trials—the final stages of development.

We are nearing the finish line. Together we will conquer Alzheimer's disease.

With our deepest thanks,



Jeons fander

LEONARD A. LAUDER

Co-Chairman and Co-Founder

ADDF'S STRATEGY:

BRIDGING THE GAP

BASIC SCIENCE

DRUG DISCOVERY

IND ENABLING

CLINICAL TRIALS

INNOVATIVE PROGRAMS

The ADDF bridges a critical gap in research funding—often called "the valley of death"—between basic research supported by government and traditional philanthropy and late-stage clinical trials funded by venture capitalists and pharmaceutical companies. The ADDF's funding ensures innovative ideas for drugs to treat Alzheimer's get a chance.

BIOTECHS

The ADDF is a pioneer in biomedical venture philanthropy. We fund scientists in both academia and the biopharmaceutical industry. Through the ADDF Biotechnology Founders program, we help researchers create new companies to further their drug development efforts.

CLINICAL RESEARCH

With many of our early investments and repurposing studies now in clinical trials—the final stages of drug development—the ADDF is allocating a larger portion of our funding to programs with the potential to reach patients within the next five years.

Dear Friends,

Over the course of my 35-year career as both a physician and a scientist, I've seen the toll that Alzheimer's disease takes on patients and their families. The ADDF was founded to end that unnecessary suffering, and we are getting closer than ever to fulfilling our goal.

I'm proud to say that with your support, the ADDF has become a world leader in Alzheimer's drug discovery. Our funded scientists are translating new findings about the causes of Alzheimer's disease into drugs to prevent and treat it.

Today, there are over 100 treatments for Alzheimer's in clinical trials—the last stages of development before a drug is approved for patients. The ADDF has helped support more than 20% of them. Without our funding, promising treatments from biopharmaceutical companies such as PharmatrophiX and Oryzon Genomics—which is developing the very first epigenetic treatment for Alzheimer's—would not have made it this far. And we're not resting on our laurels.

In 2015, we invested nearly \$13 million in drug discovery programs, the most in our history. We're directing more of those investments toward clinical trials because the drugs we picked early on have proven to be among the best candidates for a breakthrough.

The ADDF is inspired by the remarkable progress made by drug discovery researchers and proud of the role we've played in advancing the field, but we know there's still work to be done. That's why we will continue to fund the best ideas in the world for treating Alzheimer's.

It is a true privilege to work with the ADDF's committed donors and partners to overcome Alzheimer's disease. With your continued support, I know we will succeed.

Sincerely,

HOWARD FILLIT, MD

Founding Executive Director and Chief Science Officer

LETTER FROM OUR EXECUTIVE DIRECTOR



ACCELERATING PROGRESS

In 2015, the Alzheimer's Drug Discovery Foundation made significant progress toward our goal of finding effective treatments for Alzheimer's disease. Our strategy is simple. Led by a team of neuroscientists, the ADDF invests in a diverse portfolio of the best ideas to conquer Alzheimer's.



SEED FUNDING NOVEL PROGRAMS

We fund scientists as they discover and then develop new ways to prevent and treat Alzheimer's and related dementias. During 2015, we funded 27 such early-stage programs, including scientists working on revolutionary gene therapy and epigenetic treatments.



INVESTING IN BIOTECHS

Often, researchers developing novel drug programs spin off biotechnology companies as they move toward clinical trials. This can aid in establishing intellectual property and partnerships and in attracting investors. In 2015, we funded 8 new biotechs, including 3 that we helped create through the ADDF Biotechnology Founders Program.



SUPPORTING CLINICAL TRIALS

Many of our investments—including early funding for programs targeting inflammation—have moved through the drug pipeline and are now in clinical trials. We continue to support these as well as trials for drugs approved for other conditions that show promise for treating Alzheimer's—a process called "repurposing." In 2015, we supported 8 new programs in clinical trials, which included 6 repurposing programs.



FORGING PARTNERSHIPS

Developing drugs requires a diverse array of skills and significant time and money. Since our earliest days, the ADDF has partnered with like-minded organizations to leverage our combined resources and provide grantees with the expertise they need. We were proud to be working with 8 partners in 2015.



PROVIDING RESOURCES

The ADDF works to expand the number of scientists in drug discovery and support those already in the field. Our resources include the ACCESS website, which connects researchers with high-quality contract research organizations, as well as annual conferences and courses. At CognitiveVitality.org, we empower the public to make informed decisions about brain health by evaluating various strategies.



Spotlight on Epigenetics

Early-stage drug discovery is challenging. It involves a high degree of risk and requires a nuanced understanding of the latest research into the causes of Alzheimer's. Every new finding about the mechanisms of the disease is also an opportunity to try to prevent or treat it.

Scientists have identified genes that increase risk for Alzheimer's, such as APOE4, and others that decrease risk. Gene therapy tries to alter genes for the better. Epigenetics—an emerging area for drug discovery—is different. Rather than trying to change actual genes, epigenetics changes how, and how much, those genes are expressed. Think of it like a dimmer switch: you can turn genes on and off and also increase or decrease their intensity.



The ADDF is funding several biotechnology companies trying to "adjust the dimmer" on genes that enhance learning and memory and may slow down the progression of Alzheimer's disease. In 2015, we made our second investment in Oryzon Genomics, a biotech based in Barcelona, Spain, that we initially funded in 2010. Dr. Tamara Maes and her colleagues at Oryzon are developing ORY-2001, which may become the first epigenetic treatment for Alzheimer's. Oryzon recently initiated a Phase 1 study of ORY-2001 in healthy subjects, which should lay the groundwork for a planned Phase 2 study in Alzheimer's patients in 2017. In 2015, the ADDF also made a second grant to the team at Rodin Therapeutics in Cambridge, Massachusetts, which is developing an epigenetic treatment targeting a different set of genes.



INVESTING IN BIOTECHS

Spotlight on Klogene Therapeutics

Founding a biotechnology company can be a difficult but important step for scientists who are developing novel drugs. As drugs move toward clinical trials, the scientists developing them face intellectual property questions and require significant financial backing. The ADDF created the Biotechnology Founders Program to help academic scientists meet these challenges.

In 2015, our grantee Carmela Abraham, PhD, a professor at Boston University School of Medicine, founded Klogene Therapeutics, the 10th company created through the ADDF's program. With five years of previous support from the ADDF, she developed compounds that boost Klotho, a protein that she found is low in the brains of people with Alzheimer's disease and multiple sclerosis. Studies have also shown that mice with higher levels of Klotho live up to 30 percent longer than normal mice and have better memory.

Dr. Abraham is currently gearing up to conduct preclinical tests of her Klotho-enhancing compounds and plans to develop the most promising candidates into oral drugs for testing in human clinical trials.

SUPPORTING CLINICAL TRIALS

Spotlight on LM11A-31

Human clinical trials are the final stages of drug development. Here, scientists determine the safest dose of their compound and whether and how it is effective, first in small groups and then in very large trials with thousands of participants.

Many drugs that have been tested for Alzheimer's targeted amyloid plaques. But in the last few years, the treatments reaching clinical trials for Alzheimer's disease have had new, more diverse targets, such as inflammation and neuroprotection (i.e., keeping neurons from being injured or dying). The ADDF has helped fund over 20 percent of the treatments now in clinical trials, which includes novel programs we seed-funded over a decade ago.

One of the most promising drugs in clinical trials is LM11A-31, developed by Frank Longo, MD, PhD, and his colleagues. The ADDF funded the earliest stages of Dr. Longo's drug discovery work in 2000, and since then has awarded him over \$2 million to continue development. The resulting drug, LM11A-31, counteracts abnormal signals in the brain that lead to the accumulation of toxic forms of the tau protein and to the degeneration of neurons and their synaptic connections. Inhibiting these processes prevents memory loss and other cognitive issues that occur in Alzheimer's disease. A Phase 2a trial of LM11A-31, which the ADDF helped fund, is scheduled to begin in summer 2016 at sites in Europe.

For his groundbreaking work, Dr. Longo was chosen by an independent selection committee as the winner of our inaugural Melvin R. Goodes Prize for Excellence in Alzheimer's Drug Discovery in 2015.



FORGING PARTNERSHIPS

Harrington Discovery Institute



The ADDF has established numerous partnerships to bring additional funding and expertise to our grantees. Our partners include nonprofit organizations, government agencies, pharmaceutical companies, venture funds, and others who are working to accelerate drug discovery. As you'd expect, developing a novel drug requires a team with diverse scientific skills—including neurobiology, medicinal chemistry, pharmacology, and toxicology. But to be successful, the team will also need experience in patent law, business development, commercialization, and marketing—skills more associated with a MBA than a PhD.

To help grantees access the expertise they need to find success, we began a partnership with the Harrington Discovery Institute at University Hospitals in Cleveland, Ohio, in 2013. To advance their research, investigators funded through the partnership receive help from Harrington's Innovation Support Center in drug discovery project management, regulatory processes, intellectual property, and business development.

In 2015, Carol Colton, PhD, and her colleague James Burke, MD, PhD, received funding through the ADDF-Harrington partnership for preclinical studies on difluoromethylornithine (DFMO), a drug currently being investigated in human clinical trials to treat cancer. The investigators have found that DFMO blocks an immune response in the brain that diminishes arginine, a vital nutrient. Blocking this response prevents the death of neurons and associated memory loss found in Alzheimer's disease.

PROVIDING RESOURCES

An important part of our mission is providing researchers with the resources they need for drug discovery and development. The ADDF is also committed to providing unbiased information to the public about options to improve brain health and possibly prevent dementia.

CONFERENCES

In 2015, the Alzheimer's Drug Discovery Foundation organized our 9th Drug Discovery for Neurode-generation Conference to train researchers in the process of drug discovery and development. And we convened those already working in the field at our 16th International Conference on Alzheimer's Drug Discovery to share findings, network, and forge partnerships. We also held two meetings that brought together researchers working on Alzheimer's with others working on cancer, diabetes, and heart disease to help each community learn from the others. AlzDiscovery.org/events

ACCESS

The ACCESS website advanced our mission in 2015 by adding more vendors and resources. ACCESS connects scientists with high-quality contract research organizations (CRO), online project management tools, and educational resources. ADDFaccess.ondeckbiotech.com

COGNITIVE VITALITY

The neuroscientists in our Aging and Alzheimer's Disease Prevention program evaluate current strategies to promote brain health and prevent dementia and make their findings available to the public at CognitiveVitality.org. In 2015, they shared 18 new reports and 26 blog articles on topics ranging from the risks of concussions and surgery to evaluations of the potential benefits of vinpocetine and astragalus.



We are supporting over

With **\$27 million** in new and ongoing grant funding

SCIENTISTS GLOBALLY

NEW AND ONGOING ADDF GRANTS IN 2015

APOE

Ronald Crystal, MD

Weill Cornell Medical College \$1,000,000

Bradley Hyman, MD, PhD

Harvard Medical School \$250,000

COGNITIVE ENHANCERS & SYMPTOM MODIFIERS

Giacomo Koch, MD, PhD

Santa Lucia Foundation, Italy \$250,000

Krista Lanctôt, PhD

Sunnybrook Research Institute, University of Toronto, Canada \$219,286

Allan Levey, MD, PhD

Emory University School of Medicine \$447,900

Jerri Rook, PhD

Vanderbilt Center of Neuroscience Drug Discovery \$150,000

EPIGENETICS

Martin Jefson, PhD

Rodin Therapeutics \$161,759

Tamara Maes, PhD

Oryzon Genomics, S.A., Spain \$270,000

Pavel Petukhov, PhD

University of Illinois at Chicago \$142,100

Xiang (Simon) Wang, PhD

Howard University College of Pharmacy \$110,000

FRONTOTEMPORAL DEGENERATION

Nigel Cairns, PhD

Washington University in St. Louis \$156,990

Matthew Disney, PhD

The Scripps Research Institute \$150,000

Edward Huey, MD

Columbia University \$263,829 Donald Lo, PhD

Duke University Medical Center \$149,603

Scott Sneddon, PhD

Sharp Edge Labs, Inc. \$188.800

NEUROIMAGING AND BIOMARKERS

Adam Boxer, MD, PhD

University of California, San Francisco \$75,000

Mari DeMarco, PhD, DABCC

University of British Columbia, Canada \$164,990

Steven Estus, PhD

University of Kentucky \$117,000

Els Fieremans, PhD

New York University School of Medicine \$200,184

Massimo Filippi, MD

La Fondazione Centro San Raffaele del Monte Tabor, Italy \$125,000

Sam Gandy, MD, PhD

Icahn School of Medicine at Mount Sinai \$399,822

Lawrence Honig, MD, PhD

Columbia University \$125,000

Jacob Hooker, PhD

Massachusetts General Hospital \$400,000

Daniel Javitt, MD, PhD

Columbia University Medical Center \$300,000

Ashish Raj, PhD

BrainWire LLC \$275,400

Blaine Roberts, PhD

The Florey Institute of Neuroscience and Mental Health, Australia \$140,000

Charlotte Teunissen, PhD

VU University Medical Center, Netherlands \$150,000

Neil Vasdev, PhD

Massachusetts General Hospital \$331,805

Peter Working, PhD

Alzeca Biosciences, LLC \$322,111

Ying Wu, MD

NorthShore University HealthSystem \$85,300

NEUROINFLAMMATION

Carol Colton, PhD

Duke University Medical Center \$155,051

Luca Ferraro, PharmD

University of Ferrara, Italy \$61,400

Joseph Foss, MD

NeuroTherapia, Inc. \$1,600,000 (in contract)

Thota Ganesh, PhD

Emory University \$136,082

Milton Greenberg, PhD

Vivreon Biosciences, LLC \$150,000

Gilles Guillemin, PhD

Macquarie University, Australia \$145,157

Philip Haydon, PhD

GliaCure, Inc. \$1,000,000

Clive Holmes, PhD

University of Southampton, UK \$533,330

Alexandros Makriyannis, PhD

Northeastern University \$175,000

Mohamed Naguib, MB, BCh, MSc, FCARCSI, MD

Cleveland Clinic Foundation \$257,700

Paolo Pevarello, PhD

Axxam SpA, Italy \$350,000

Thadd Reeder, PhD

Glialogix, Inc. \$207,000

John Schetz, PhD

University of North Texas Health Science Center \$216,000

Malu Tansey, PhD

Emory University School of Medicine \$100,000

Paul Thompson, PhD

University of Massachusetts Lowell \$150,000

Linda Van Eldik, PhD

University of Kentucky \$209,364

Shijun Zhang, PhD

Virginia Commonwealth University \$160,000

Danna Zimmer, PhD

University of Maryland School of Medicine \$150,000

NEURONAL ENERGY FAILURE

James Bennett, MD, PhD

Virginia Commonwealth University \$200,000

Paul Edison, MD, MRCP, PhD, FRCPI

Imperial College London, UK \$458,000

Gary Gibson, PhD

Burke Medical Research Institute \$500,000

Christian Holscher, PhD

Lancaster University, UK \$248,000

Michelle Mielke, PhD

Mayo Clinic \$6,960

Eugenia Trushina, PhD

Mayo Clinic \$300,000

NEUROPROTECTION

Carmela R. Abraham, PhD

Klogene Therapeutics, Inc. \$244,850 (in contract)

Carmela R. Abraham, PhD

Boston University School of Medicine \$580,821

Roberta Diaz Brinton, PhD

University of Southern California \$338,898

Jeffrey L. Cummings, MD

Cleveland Clinic, Lou Ruvo Center for Brain Health \$1,000,000

Alpaslan Dedeoglu, MD, PhD

Boston University School of Medicine \$148,954

Pontus Forsell, PhD

AlzeCure Foundation, Sweden \$456,905

Chien-liang Lin, PhD

Ohio State University \$244,008

Frank M. Longo, MD, PhD

PharmatrophiX \$500,000

Giovanna Mallucci, MD, PhD Cambridge University, UK

\$268,634

Peter Nelson, MD, PhD

University of Kentucky \$149,997

Salvatore Oddo, PhD

Banner Sun Health Research Institute \$242,000

Ana Pereira, MD

The Rockefeller University \$50,000

Stephen Salton, MD, PhD

Icahn Institute for Genomics and Multiscale Biology at Mount Sinai \$158,171

Brent Stockwell, PhD

Columbia University \$244,329

Grace Stutzmann, PhD

Chicago Medical School \$257,942

Raymond Scott Turner, MD. PhD

Georgetown University \$2,059,207 (in contract)

Sung Ok Yoon, PhD

Ohio State University \$47,397

Vincent Zurawski, PhD

Varinel Inc. \$239,700

VASCULAR

Hyung Jin Ahn, PhD

The Rockefeller University \$150,000

Narayan Bhat, PhD

Medical University of South Carolina \$230,961

Sandra Black, MD, FRCP(C)

Sunnybrook Research Institute, University of Toronto, Canada \$1,442,388

Atticus Hainsworth, PhD

St George's, University of London, UK \$464,992

Ihab Hajjar, MS, MD

Emory University \$973,777

Ling Li, DVM, PhD

University of Minnesota \$200,000

Olga Meulenbroek, PhD

Radboud University Medical Centre \$380,224

OTHER

Additional Targets

Dirk Beher, PhD

Asceneuron SA \$325,000

Mauro Costa-Mattioli, PhD

Baylor College of Medicine \$150,000

Nathalie Pochet, PhD

Brigham & Women's Hospital \$135,000

Partnerships

David Knopman, MD

National Biomedical Research Ethics Council, Inc. \$100,000

Michael Weiner, MD

University of California, San Francisco \$100,000

David Wholley, MA

Foundation for the National Institutes of Health, Inc. \$100,000

Prevention

Deborah Blacker, MD, ScD Harvard Medical School

Harvard Medical Schoo \$25,000

Marek Brzezinski, MD, PhD

University of California, San Francisco \$300,000

Our Diversified Portfolio of Drug Targets in 2015



APOE



Cognitive Epigenetics



Frontemporal Degeneration



Enhancers





Neuroimaging & Biomarkers

Neuroinflammation

Neuronal Energy Failure







Vascular

Other

Lenore Launer, PhD

Intramural Research Program, National Institute on Aging \$80,264

Galit Wainstein, PhD

Boston University School of Medicine \$82,789

OUR SUPPORTERS

We are moving closer to finding a cure for Alzheimer's disease thanks to your generosity. Many of our supporters—like Nancy Goodes and Christopher Johnson—have had a loved one affected by Alzheimer's or a related dementia and know firsthand how badly treatments are needed. We thank them and all of you for your unwavering dedication to our mission.

"When my husband, Mel, was diagnosed with Alzheimer's disease there was no deliberation about the best organization to work with to find a cure. As the former CEO of Warner-Lambert, Mel knows a lot about developing drugs, and he knows that the ADDF is unrivaled in its scientific expertise and approach to defeating Alzheimer's.

Throughout his career, Mel has been relentless in his search for drugs that improve people's lives. The ADDF is equally relentless in its mission to support the best science in the fight against Alzheimer's.

Mel and I established the Melvin R. Goodes Prize for Excellence in Alzheimer's Drug Discovery to recognize outstanding scientists in the search for a cure. It is an honor to have our name linked to the ADDF in this way."

NANCY GOODES

ADDF Board of Governors

"When Alzheimer's touched my family I felt compelled to find a way to rid the world of this disease. In the ADDF, I discovered a vibrant community of scientists, volunteers, and professionals who understand and share my urgency to solve Alzheimer's. They know on both a scientific and human level that something can and must be done as quickly as possible, and their devotion is evident in everything they do.

The ADDF is so much more than just an Alzheimer's research nonprofit. It is a community of people devoted to this fight. From the founders who make sure that every dollar raised goes directly to drug discovery to the supporters with personal stories and motivations that mirror my own—everyone at the ADDF shares the unflappable belief that we can and will end Alzheimer's.

If there's one good thing that has come out of my family having to deal with my father's Alzheimer's, it's that we've become closer than we ever were. I'm fortunate to have found an organization that can bring families like mine together with others, and harness our collective desire to make sure that future generations won't have to suffer the effects of this disease."

CHRISTOPHER JOHNSON

ADDF Board of Overseers

CELEBRATING PROGRESS

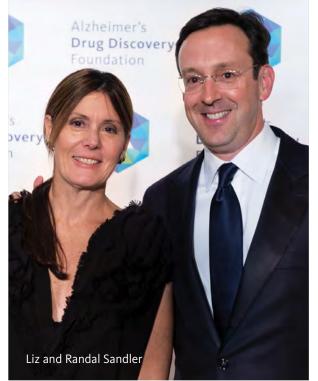
In 2015, the ADDF recognized leaders in Alzheimer's philanthropy and research while celebrating the progress we've made in developing effective treatments for this disease. We thank everyone who came together and supported our events and look forward to seeing you next year.

















THANK YOU

We are deeply grateful to all those who supported our work in 2015. Your generosity gives us hope for a future without Alzheimer's disease.

OVER \$1,000,000

Anonymous (2) The Lauder Foundation -Leonard & Judy Lauder Fund Jo Carole and Ronald S. Lauder

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Irene and Carl Zelinsky

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\$1,000 - \$4,999

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Sam Gandy, MD, PhD

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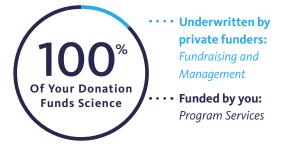
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All lists current as of May 2016.

ASSETS		2015	2014
Cash and cash equivalents		4,903,074	4,923,325
Investments, at fair value		20,649,664	10,809,963
Contributions receivable		4,962,392	4,059,717
Program related investments		536,800	_
Due from Institute for the Study of Aging		82,008	133,215
Other assets		25,366	26,103
Total assets	\$	31,159,304	19,952,323
LIABILITIES AND NET ASSETS			
Liabilities			
Accounts payable and accrued liabilities	\$	100,536	49,324
Grants payable		13,504,012	11,513,136
Deferred revenue		3,680	61,350
Total liabilities		13,608,228	11,623,810
Net assets			
Unrestricted		13,004,344	4,361,805
		4 5 4 6 7 2 2	3,966,708
Temporarily restricted		4,546,732	3,700,700





CHANGE IN NET ASSETS	2015	2014
Support and Revenues		
Support		
Contributions and grants	\$ 17,524,509	6,514,722
In-kind services and contributions		
Contributions of services from the Institute for the Study of Aging, Inc.	3,098,678	2,832,504
Contributions of advertising	440,200	_
Contributions of professional services	35,000	_
Proceeds from special events, net of direct expenses	3,590,294	2,818,092
Revenues		
Grant Returns, net of payments	920,018	1,799,905
Conference registration fees and other income	335,118	226,173
Investment and other (loss) income	(18,367)	106,622
Total support and revenues	25,925,460	14,298,018
Expenses		
Program services	14,460,393	10,850,140
Fundraising	1,772,890	1,236,175
Management and general	469,614	493,156
Subtotal	16,702,897	12,579,471
Expense for uncollected pledge	-	925,000
Total expenses	16,702,897	13,504,471
Change In net assets	9,222,563	793,547
Net assets, beginning of year, as reclassified	8,328,513	7,534,966
Net assets, end of year	\$ 17,551,076	8,328,513



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