



**CRITICAL PATH  
INSTITUTE**

*collaborate · innovate · accelerate*

**ACCELERATING THE PATH  
TO A HEALTHIER WORLD**

**2013**  
ANNUAL REPORT



**MARTHA A. BRUMFIELD, PHD**  
President and CEO

## Dear Friends and Supporters,

Reflecting on the past year, I am very proud of the accomplishments Critical Path Institute (C-Path) has achieved in leading the charge to transform drug development. This was a banner year for C-Path. We announced a breakthrough modeling tool for Alzheimer's disease, made steady progress in reaching key regulatory milestones, launched a new consortium to qualify a neuroperformance measure for multiple sclerosis (funded by the National Multiple Sclerosis Society), and increased recognition of C-Path as an organization that accelerates new approaches for drug development.

This past summer, the Coalition Against Major Diseases (CAMD) received a positive decision by the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) on the first clinical trial simulation tool they have endorsed. Five years in the making, this tool is the result of one of the most collaborative efforts the biopharmaceutical industry has ever undertaken. Starting in 2008, CAMD created a groundbreaking roadmap for data acquisition and curation, developed an Alzheimer's disease data standard, developed the mathematical structure, and validated the model – all to standards which regulatory agencies would accept. The tool is now freely available for use by any drug developer to inform trial design for studying treatment effect in mild to moderate Alzheimer's disease. This new pathway for studying treatments for one of our most pressing health needs is evidence of the value that the C-Path public-private partnership model creates.

C-Path is using its regulatory, scientific, and project management expertise to lead seven global scientific consortia across multiple disease areas/methodologies, including Alzheimer's disease, Parkinson's disease, multiple sclerosis, tuberculosis (TB), polycystic kidney disease, patient-reported outcome measures, and safety biomarkers. C-Path's modeling experience in Alzheimer's disease has been extended to develop a disease model for the Polycystic Kidney Disease Outcomes Consortium (which will establish evidence for a new biomarker: imaging of total kidney volume), and to improve quantitative tools for measuring infectious agents for the tuberculosis consortium. With growing interest in developing models for other diseases, C-Path, the FDA, and the International Society of Pharmacometrics co-sponsored a modeling and simulation workshop in the fall of 2013, another first for C-Path.

In our eighth full year of operation, C-Path is now recognized as a catalyst to deliver results. This recognition has spurred further investment in C-Path and new collaborative efforts. The Bill and Melinda Gates Foundation recently awarded C-Path two additional multi-year grants to develop TB modeling projects and spur development of a diagnostic to detect drug resistance. This will be C-Path's first program in the diagnostics arena, and we are very excited about the opportunity.

As an independent non-profit organization, the financial and in-kind support we receive allows C-Path to continue catalyzing global efforts to develop new approaches to accelerate the process of getting new medicines to patients who need them. We encourage our supporters and collaborators to stay engaged as we continue to accelerate progress in areas of unmet need.

Respectfully,

Martha A. Brumfield, PhD

President and CEO

# NEWS AND ACCOMPLISHMENTS

**DEC 6  
2012** C-Path and the National Multiple Sclerosis Society launch the MS Outcome Assessments Consortium

**JAN 29  
2013** C-Path and Clinical Data Interchange Standards Consortium announce Parkinson's Disease Drug Development Milestone: Release and Availability of a PD Therapeutic Area Data Standard

**FEB 21  
2013** Critical Path Institute Names Martha A. Brumfield, PhD, CEO

**MAR 6-8  
2013** Brussels, Belgium joint IMI and C-Path meeting entitled: "Collaborating for Cures - Leveraging Global Public-Private Partnerships to Accelerate Biopharmaceuticals Development"

**MAY 23  
2013** Critical Path Institute and Innovative Medicines Initiative Sign Agreement on Development of Important New Drug Safety Tests

**JULY 10  
2013** U.S. Food and Drug Administration and European Medicines Agency Reach Landmark Decision on Critical Path Institute's Clinical Trial Simulation Tool for Alzheimer's Disease





## VISION

Accelerating the Path to a Healthier World

## MISSION

Critical Path Institute is a catalyst in the development of new approaches to advance medical innovation and regulatory science. We achieve this by leading teams that share data, knowledge, and expertise resulting in sound, consensus-based science.

## VALUE

As an independent and trusted partner, we value integrity, innovation, and teamwork.

### HISTORICAL TIMELINE

The U.S. Food & Drug Administration releases the Critical Path Initiative report.

**2004 - MAR 1**



**2004 - Nov 30**

State of Arizona awards C-Path a planning grant. C-Path files articles of non-profit incorporation.

C-Path begins first fiscal year with four full-time employees.

**2005 - JUL 1**

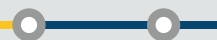


**2005 - DEC 10**

C-Path hosts Tucson ribbon-cutting ceremony to officially launch Institute.

FDA announces first-of-its-kind partnership with C-Path to fulfill mission of U.S. Government's "Critical Path Initiative."

**2005 - DEC 16**



**2006 - MAR 16**

C-Path creates unprecedented collaboration between pharmaceutical companies and the FDA to form the Predictive Safety Testing Consortium (PSTC).





## WE COLLABORATE, INNOVATE, AND ACCELERATE ON A GLOBAL SCALE



The Critical Path Institute is an independent, non-profit organization that brings together pharmaceutical, academic, government, and non-profit organizations to work on important drug and medical product development challenges.

The work of the Critical Path Institute advances the innovative and progressive work of the medical devices and pharmaceutical industries. C-Path teams catalyze innovative ideas that accelerate the speed of drug and other medical product development. Our work makes a lasting difference in future treatment options for physicians and patients across the globe.

C-Path leverages the depths of its scientific knowledge and experience to break down the barriers in drug and medical product development. By addressing the inherent challenges in these processes, C-Path creates pathways to facilitate the creation of treatments for unmet and under-addressed medical needs.

## WHO WE ARE

## WHAT WE DO

## HOW WE DO WHAT WE DO

C-Path receives monetary award from FDA for a collaboration.

**2006 - SEP 13**

Science Foundation Arizona (SFAz) awards grant to C-Path and industry-partner Ventana Medical Systems to collaborate on personalized medicine initiative.

**2007 - AUG 16**

**2007 - JUN 7**

C-Path hosts ribbon-cutting ceremony at the Library of Congress to announce opening of its Rockville, Maryland office.

**2007 - SEP 27**

President George W. Bush signs bill that authorizes FDA to create "Critical Path Public/Private Partnerships." The first (and most successful) of these is the collaboration between the FDA and C-Path.

# C-PATH CONSORTIA AND PROGRAMS



SHARING KNOWLEDGE  
THAT LEADS TO  
INNOVATION

## Coalition Against Major Diseases (CAMD)

CAMD develops innovative approaches and processes to accelerate drug development for the treatment of chronic neurodegenerative diseases.



## Polycystic Kidney Disease Outcomes Consortium (PKDOC)

The PKD Outcomes Consortium is a collaboration between the PKD Foundation, the FDA, C-Path, and clinical scientists to address the significant unmet need for effective drug therapies for Polycystic Kidney Disease.



## HISTORICAL TIMELINE

C-Path officially announces its collaboration with Ventana Medical Systems to develop standardized evaluation of companion diagnostic tests and targeted cancer therapies.

**2007 - OCT 10**

Arizona's Governor Janet Napolitano honors C-Path with an "Arizona Innovation Award" to recognize its ground-breaking approach to speeding the development of safe, innovative medicines and medical devices.

**2007 - OCT 18**

**2007 - OCT 16**

C-Path receives grant from Agency for Healthcare Research and Quality (AHRQ) to continue support for the Arizona Center for Education and Research on Therapeutics (AzCERT) initiative.

**2008 - JUN 12**

C-Path leads novel transatlantic drug safety effort which yields FDA/EMA qualification of new drug tests for kidney safety. C-Path qualifies first set of preclinical safety biomarkers.

## Electronic Patient-Reported Outcome (ePRO) Consortium

The ePRO Consortium facilitates the implementation of patient-reported outcome instruments onto electronic platforms such as smart phones, tablet computers, the web, or interactive voice response systems.

ePRO Solution Providers 8

## Patient-Reported Outcome (PRO) Consortium

PRO Consortium develops and qualifies PRO Instruments for use as primary or key secondary endpoints in clinical trials.

Gov & Reg Agencies 3  
Pharmaceutical Industry 25

## Predictive Safety Testing Consortium (PSTC)

PSTC brings together pharmaceutical companies to share and qualify innovative safety testing methods under advisement of the FDA, EMA, and the Japanese Pharmaceuticals Medical Devices Agency (PMDA).

Gov & Reg Agencies 4  
Non-Profit Research Organizations 2  
Pharmaceutical Industry 19

## Critical Path to TB Drug Regimens (CPTR)

The CPTR initiative is a public-private partnership led by the Critical Path Institute, the Bill & Melinda Gates Foundation, and the Global TB Alliance, focused on enabling the accelerated development of new treatment regimens for Tuberculosis. Related work being conducted includes advancing novel biomarkers and data standards, developing a TB disease progression model and clinical trial simulation tool as well as enhancing global regulatory pathways for new TB drug regimens.

Founding Partners 3  
Academic Institutions 7  
Gov & Reg Agencies 4  
Non-Profit Research Organizations 11  
Pharmaceutical Industry 17

## Multiple Sclerosis Outcome Assessments Consortium (MSOAC)

The primary purpose of the MSOAC is to achieve qualification from the FDA and EMA of a performance measurement instrument as a primary or secondary endpoint in clinical trials of MS therapies.

Academic Institutions 22  
Gov & Reg Agencies 3  
Non-Profit Research Organizations 7  
Pharmaceutical Industry 10

## Coalition for Accelerating Standards and Therapies (CFAST)

CFAST is a partnership between C-Path and the Clinical Data Interchange Standards Consortium to accelerate clinical research and medical product development by creating and maintaining data standards and regulatory reviews.

Founding Partners 2  
Gov & Reg Agencies 2  
Non-Profit Research Organizations 1

Science Foundation Arizona (SFAz) awards C-Path a grant to assist in developing better testing methods to accelerate drug development for major diseases including Alzheimer's disease and Parkinson's disease.

2008 - Nov 12

C-Path launches Coalition Against Major Diseases (CAMD) as a consortium with pharmaceutical companies, patient groups, FDA, and National Institutes of Health (NIH) to address clinical trial needs in neurological diseases.

2009 - FEB 3

C-Path launches Critical Path to TB Drug Regimens (CPTR).

2010 - MAR 24

2008 - Nov 30

Reader's Digest lists C-Path as No. 7 on its list of "18 Big Ideas to Fix Healthcare Now!"

2009 - MAR 31

C-Path launches the Patient-Reported Outcome (PRO) Consortium.

# PROJECT PIPELINES



TITLE	DESCRIPTION	FEASIBILITY <sup>1</sup>	SCOPING <sup>2</sup>	RESEARCH <sup>3</sup>	SUBMITTED <sup>4</sup>	QUALIFIED/ ENDORSED <sup>5</sup>
<b>Alzheimer's Disease (AD)</b>						
Alzheimer's Disease (AD) Imaging	An imaging biomarker of low baseline hippocampal volume for selection of subjects to enroll in pre-dementia AD clinical trials					
AD Cerebrospinal Fluid (CSF)	The baseline measures of $\beta$ -amyloid protein, tau and phosphotau levels in CSF as biomarkers for selection of subjects to enroll in pre-dementia AD clinical trials					
AD Clinical Trial Modeling and Simulation Tool	An empirical model and simulation platform for simulating clinical trials to determine optimal clinical trial design					
AD Cognition Clinical Outcome Assessment	A novel composite clinical outcome assessment instrument for use in pre-dementia AD trials					
<b>Parkinson's Disease (PD)</b>						
Parkinson's Disease Imaging	A neuroimaging biomarker of dopamine transport activity to exclude certain subjects in clinical trials of early motor PD subjects					
<b>Polycystic Kidney Disease</b>						
Imaging of Kidney Volume	The use of total kidney volume (TKV) as a prognostic biomarker to identify select patients likely to respond to therapy in clinical trials					
<b>Tuberculosis</b>						
In Vitro Hollow Fiber Model for Tuberculosis (HFS-TB)	Pre-clinical, <i>in vitro</i> hollow fiber pharmacokinetic/pharmacodynamic efficacy model for TB to inform selection of dose and optimal drug regimens to support early clinical combination testing					
Liquid Culture	Quantitative utility of time-to-positivity as determined by liquid culture for assessment of durable cure or potential for relapse for new TB drugs and drug regimens					

## HISTORICAL TIMELINE

Nature Biotechnology features PSTC's evaluation of seven kidney biomarkers for use in drug safety assessment.

**2010 - MAY 11**

First-ever biomarker qualification decision announced by the Japanese Pharmaceuticals and Medical Devices Agency (PMDA) to accept PSTC's new kidney biomarkers.

**2010 - JUN 21**

**2010 - JUN 11**

C-Path announces the availability of its database of 11 industry-sponsored clinical trials that included data from more than 4,000 Alzheimer's disease patients. This database is the first effort of its kind to aggregate clinical trial data from multiple companies in a common CDISC data standard.

**2010 - SEP 9**

With support and funding from the Polycystic Kidney Disease Foundation, C-Path launches Polycystic Kidney Disease Outcome Consortium (PKDOC).



- U.S. Food & Drug Administration (FDA)
- European Medicines Agency (EMA)
- Pharmaceutical & Medical Devices Agency (PMDA) Japan

TITLE	DESCRIPTION	FEASIBILITY <sup>1</sup>	SCOPING <sup>2</sup>	RESEARCH <sup>3</sup>	SUBMITTED <sup>4</sup>	QUALIFIED/ ENDORSED <sup>5</sup>
<b>Drug Safety</b>						
Nonclinical Kidney : Phase I	A set of urinary biomarkers for use in addition to serum creatinine and blood urea nitrogen in rat toxicology studies to monitor drug-induced kidney injury	●	●	●		
Nonclinical Kidney: Phase II	Rat urine safety biomarkers for use in addition to serum BUN and serum creatinine to identify cases of drug-induced kidney tubule degeneration/necrosis	●	●	●		
Clinical Nephrotoxicity	Human urine safety biomarkers to monitor for renal tubular safety	●	●	●		
Nonclinical Skeletal Myopathy	Rat plasma and serum safety biomarkers to identify cases of drug-induced skeletal muscle degeneration/necrosis	●	●	●		
Nonclinical Liver Toxicity	Rat plasma and serum safety biomarkers to detect various drug-induced kidney injuries	●	●	●		
Nonclinical Cardiac Hypertrophy	Rat plasma and serum safety biomarker to detect drug-induced cardiac hypertrophy	●	●	●		
Nonclinical Vascular Injury	A panel of nonclinical plasma and serum safety biomarkers to identify cases of histologically apparent acute vascular injury	●	●	●		
Nonclinical Biomarkers of Testicular Toxicity	A nonclinical plasma and serum safety biomarker to detect drug-induced damage to the seminiferous epithelium of the testis	●	●	●		
<b>Multiple Sclerosis</b>						
Multiple Sclerosis Outcome Assessments	Combination of performance measures for use as a primary endpoint in trials of MS therapies	●	●	●		

<sup>1</sup>Feasibility: Determine if the drug development tool has sufficient support and data to justify launching a project toward a regulatory submission.

<sup>2</sup>Scoping: Develop the project's goals, objectives, deliverables, timeline, and budget.

<sup>3</sup>Research: Carry out the necessary actions to execute the research plan.

<sup>4</sup>Submitted: Prepare the qualification dossier containing the evidence supporting the context of use for submission to the regulatory agencies.

<sup>5</sup>Qualified/Endorsed: Final review by the regulatory agencies in order to issue an opinion regarding the proposed utility of the novel drug development tool.

C-Path and industry-partner Ventana Medical Systems receive award from Science Foundation Arizona to develop national resource for clinical research standardization.

**2010 - OCT 28**

C-Path announces formation of the Electronic Patient-Reported Outcome (ePRO) Consortium.


**2011 - JUN 1**

**2011 - JAN 10**

C-Path and Clinical Data Interchange Standards Consortium (CDISC) announce partnership.

**2011 - JUN 14**

C-Path and Innovative Medicines Initiative (IMI) announce formal collaboration to further the mission of both organizations and to prevent duplication of efforts.

TITLE	DESCRIPTION	FEASIBILITY <sup>1</sup>	SCOPING <sup>2</sup>	RESEARCH <sup>3</sup>	SUBMITTED <sup>4</sup>	QUALIFIED/ ENDORSED <sup>5</sup>
 <b>Patient-Reported Outcome Instruments</b>						
Asthma	A patient-reported symptom measure for use as an endpoint in clinical trials to document treatment benefit in patients age 12 and older with persistent asthma					
Cognition	A patient-reported outcome instrument for use as an endpoint in clinical trials to measure performance of complex activities of daily living and interpersonal functioning in adults with mild cognitive impairment due to Alzheimer's disease					
Depression	A patient-reported symptom measure for use as a primary endpoint in clinical trials to document treatment benefit in adult patients with major depressive disorder					
Functional Dyspepsia (FD)	A patient-reported symptom measure for use as a primary endpoint in clinical trials to document treatment benefit in adult patients with FD					
Irritable Bowel Syndrome (IBS)	A patient-reported symptom measure for use as a primary endpoint in clinical trials to document treatment benefit in adult patients with IBS					
Non-Small Cell Lung Cancer (NSCLC)	A patient-reported symptom measure for use as an endpoint in clinical trials to document treatment benefit in adult patients with NSCLC					
Rheumatoid Arthritis (RA)	A patient-reported symptom measure for use as a secondary endpoint in clinical trials to document treatment benefit for fatigue in patients with RA					

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## HISTORICAL TIMELINE

C-Path and CDISC announce release of data standards for Alzheimer's disease research; the first in a series of therapeutic area common data standards.

**2011 - Oct 17**

C-Path and The Hamner Institutes for Health Sciences (The Hamner) announce formal collaboration.

**2011 - Dec 20**

**2011 - Nov 30**

C-Path, CDISC, and FDA host global two-day conference on drug development, "Creating Consensus Science: Tools and Tactics for Next-Gen Drug Development."

**2011 - Dec 23**

The National Institute of Mental Health selects C-Path as "One of the Top 10 Research Advances of 2011."



# STRATEGIC DIRECTION

Critical Path Institute's (C-Path's) mission is to be a catalyst in the development of tools to advance medical product innovation and regulatory science. This is achieved by leading teams of experts that share data, knowledge, and expertise, resulting in sound, consensus-based science. The work of C-Path is driven by the need to address challenges faced across the spectrum of drug development decision making, with the goal of decreasing the amount of uncertainty as to regulatory outcome.

As C-Path's leadership looks to the future, we are excited to take on new programs that focus on unmet needs in specific disease areas or disciplines such as model-based drug development, biomarker qualification, or clinical outcome assessment instrument development, where our expertise can make significant impact.

Decisions regarding new projects to be undertaken will be compatible with the vision, mission, and values of C-Path, and will be grounded in our core competencies. Additionally, all C-Path programs must involve an array of stakeholders. Maintaining neutrality is of paramount importance in our work.

C-Path has established its credibility in catalyzing change and driving results through our consortia model as evidenced by the growing number of requests from external organizations for assistance in achieving their objectives. This is further evidenced by the additional funding that C-Path received in 2013. We are prepared to expand our work to encompass new areas of cutting-edge regulatory science.

We are committed to bringing even more global expertise to bear on our work and to seeking new strategic alliances that will benefit ongoing programs or that open new doors to enter areas of unmet need where C-Path has not yet engaged and which are compatible with our mission and values.

C-Path receives approval from the European Medicines Agency (EMA) for imaging biomarker as a qualified measure to identify patients with early stage cognitive impairment for Alzheimer's disease clinical trials.

**2012 - JAN 23**

**2012 - DEC 6**

C-Path and the NMSS launch the MS Outcome Assessments Consortium (MSOAC)

C-Path names Martha A. Brumfield, PhD, as President and CEO.

**2013 - FEB 21**

FDA and EMA reach landmark decisions on Critical Path Institute's Clinical Trial Simulation Tool for Alzheimer's disease.

**2013 - JUL 10**

# FINANCIAL STATUS

FISCAL YEAR ENDING JUNE 30, 2013

Critical Path Institute (C-Path) is extremely grateful to all of the state and local supporters, both public and private, who believe in the vision of improving drug development and have provided financial support. Eight years after our launch, C-Path is a financially sound organization that is transforming drug and medical product development around the world.

In 2013, C-Path was the proud recipient of two new funding awards from the U.S. Food & Drug Administration (FDA) totaling over \$2.4 million to work on Clinical Data Interchange Standards Consortium (CDISC) clinical trial data standards. C-Path is a leader in developing therapeutic area data standards, and the FDA and European Medicines Agency (EMA) increasingly require new drug submissions to use these standards. Data standards enable the sharing and combining of clinical trial data and facilitate the review process of new drugs by the regulatory authorities.

C-Path is a widely recognized leader in regulatory science, and is making a significant impact in many therapeutic areas, in both the United States and around the world. In September of 2012, C-Path formed a new consortium working on multiple sclerosis (MS). In partnership with the National MS Society, C-Path is leading a four-year effort with industry and academia to create a new data standard for MS, develop a database for MS clinical trial data contributed by several pharmaceutical companies, and to use these data as the primary source of support to develop a new clinical outcome assessment instrument for use in clinical trials for new MS therapies. The Polycystic Kidney Disease (PKD) Foundation approved two extensions to the current grant and awarded a second grant to support the work of the PKD consortium. Additionally, the Bill & Melinda Gates Foundation has provided another grant for C-Path to lead an effort to develop a diagnostic to quickly determine if a patient has a drug-resistant form of tuberculosis. Other innovative potential projects are in the exploratory stages.

Between the initial investment from the Arizona community and the significant funding received from Science Foundation Arizona, which concluded this year, C-Path has become an established and growing member of the Arizona biomedical community. The initial investment by the local community has resulted in 440 percent additional revenue during the last seven years.

This coming year promises to be one of growth; our team is currently expanding, as is the scope and number of projects underway. Additionally, several organizations are approaching C-Path to form partnerships and fund new areas of research. C-Path is financially sound and strongly positioned for the future. We look forward to this year with excitement.

## ASSETS

Cash and Cash Equivalents	\$ 4,959,918
Certificates of Deposit	\$ 2,403,428
Accounts Receivable	\$ 1,102,425
Property and Equipment	\$ 176,191
Other	\$ 74,899
<b>TOTAL ASSETS</b>	<b>\$ 8,716,861</b>

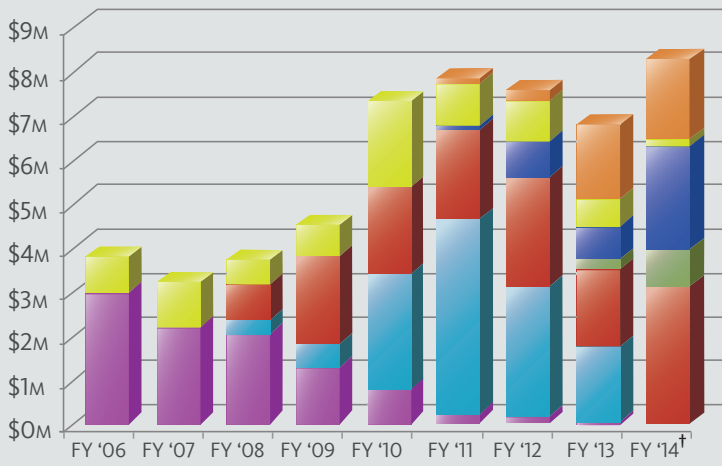
## LIABILITIES AND NET ASSETS

Accounts Payable	\$ 357,235
Accrued Expenses	\$ 225,154
Deferred Revenue*	\$ 4,558,010
Deferred Rent	\$ 64,841
Total Liabilities	\$ 5,205,240
Unrestricted Assets	\$ 1,112,979
Board Designated Funds**	\$ 2,167,956
Property And Equipment	\$ 176,191
Temporarily Restricted	\$ 54,495
Total Net Assets	\$ 3,511,621
<b>TOTAL LIABILITIES AND NET ASSETS</b>	<b>\$ 8,716,861</b>

\* Pre-awarded funds received for grants

\*\* Consortia fees managed by C-Path to support consortia activities

# Revenue Resources

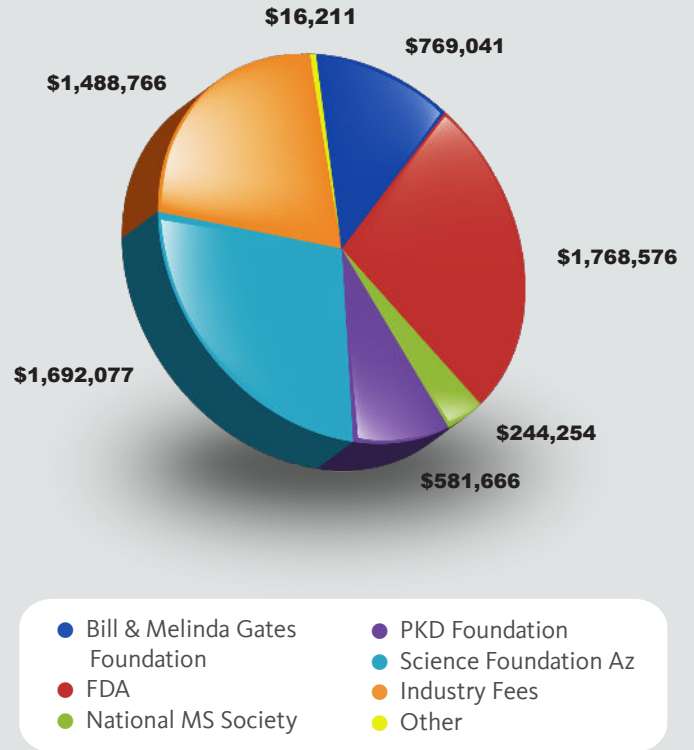


†Projected

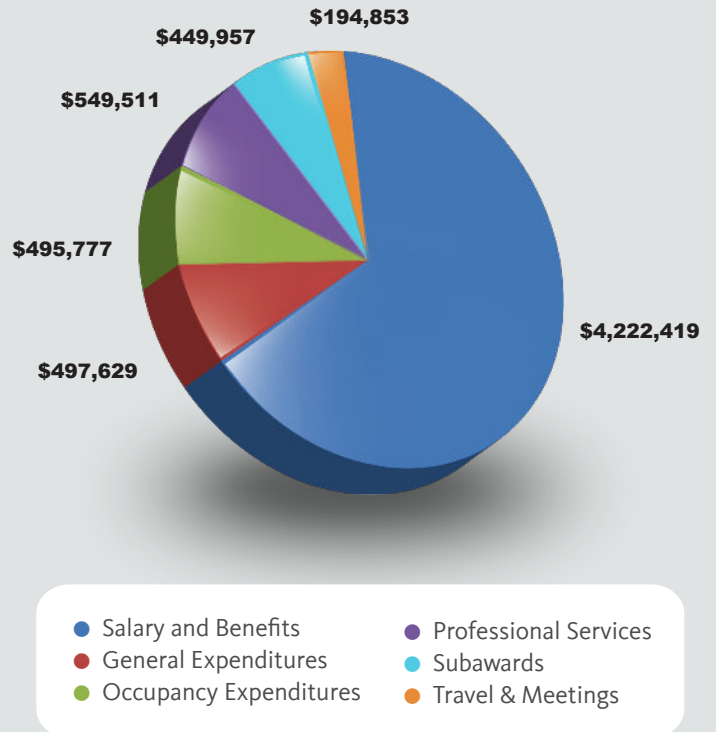


# Revenue \*\*\*

\*\*\* Excluding pass-through funds



# Expenses

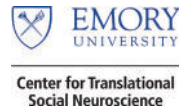




# CONSORTIA MEMBERS



# CONSORTIA PARTNERS



*We want to thank the U.S. Food and Drug Administration and Science Foundation Arizona for their significant funding of our work.*



# CRITICAL PATH INSTITUTE

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