



# THE OPPORTUNITY OF A GENERATION

*Celebrating the Achievements of the Epstein Family  
Alzheimer's Research Collaboration in its Third Year*

IMPACT REPORT 2024

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## DIRECTORS' REPORT

Dear Friends and Supporters,

Now in its third year, the **Epstein Family Alzheimer's Research Collaboration** continues to deliver on its bold commitment to pursuing innovative approaches to Alzheimer's disease (AD) therapeutics. We are proud to share the significant progress made over the past year in partnership with our fellow collaboration leaders at the University of Southern California (USC), Dr. Paul Aisen and Dr. Michael Rafii.

This work would not have been possible without philanthropy. We are grateful for the role you play in advancing research that has the potential to transform lives.

As you will see in this report, the **Gene Therapy Program** continues to make headway toward a first-in-human gene therapy for the treatment of Alzheimer's disease with a focus on the Jalisco mutation. Patients with this mutation develop early onset of the disease, sometimes as early as in their 30s. This gene therapy offers real hope to families affected by this devastating diagnosis and will serve as proof of concept that specific genes can be targeted to treat AD. Importantly, half of the researchers funded through the Gene Therapy Program have secured larger external grants.

The **Powder for Pennies Program** aims to identify safe and effective medications that are accessible in treating AD. With the goal of repurposing existing FDA-approved medications, this program has a number of targets under investigation. For example, atomoxetine (ATX), an attention-deficit/hyperactivity disorder (ADHD) medication, shows promise in slowing the progression of AD, particularly in individuals with mild cognitive impairment. Powder for Pennies spans from large-scale pharmacoepidemiology studies to advanced preclinical models. Meanwhile, a clinical trial exploring benfotiamine — a high-dose thiamine intervention — was launched in 2024 with funding from the National Institute on Aging, further expanding our therapeutic pipeline.

The collaboration between investigators at UC San Diego and USC continues to be the backbone of our progress. In 2024, we hosted an **Investigators Meeting** that brought together roughly 90 researchers in person and online, fostering meaningful scientific exchange and exciting new research directions.

As we look to the future, the Epstein Family Alzheimer's Research Collaboration is well-positioned for even greater achievements. From innovative treatment strategies to smarter trial designs and dedicated training for the next generation of scientists and clinicians, your support is helping shape a better future for individuals and families affected by Alzheimer's disease.

**Thank you** for your interest in the progress made possible through the Epstein Family Alzheimer's Research Collaboration. We are honored to have you as partners in this critical work.

With gratitude,

**Howard Feldman**

*Co-Director, Alzheimer's Disease Cooperative Study  
and Epstein Family Alzheimer's Research Collaboration*

**Judy Pa**

*Co-Director, Alzheimer's Disease Cooperative Study  
and Epstein Family Alzheimer's Research Collaboration*

# PROGRESS ON ALL FRONTS

## TOP ACHIEVEMENTS OF YEAR THREE

### GENE THERAPY PROGRAM (GTP)

- » **Advancing gene-based therapy:** We are advancing collective program efforts toward the first-in-human gene therapy for the Jalisco mutation, a form of early-onset AD with nearly 100% genetic penetration and virtually certain clinical expression of disease for those who carry the mutation. This mutation offers a unique treatment opportunity due to its early onset, associated cognitive and mobility issues, and the potential for intervention before symptoms manifest.
- » **Acquiring additional outside funding:** Half of funded principal investigators (four of eight) have parlayed their initial Epstein Family Collaboration research findings into larger grants from external agencies, demonstrating the significance of their novel research approaches. UC San Diego Health researchers Dr. Stephanie Cherqui, Dr. Subhojit Roy and Dr. Matthew Shtrahman, together with Dr. Bart De Strooper of KU Leuven, have secured continued funding for their work. In return, they share their gratitude for the opportunity to launch these projects through the Epstein Family Collaboration.
- » **Spurring collaboration:** Our partnerships with USC and the University of Guadalajara (UDG) have flourished.
  - Year three saw important evolution of the Family Engagement Initiative through key collaborations and family meetings that were hosted throughout Jalisco by UDG.
  - A computational genetics training course, which was taught in Spanish for UDG students, expanded beyond Mexico with 40 participants. Taught by experts Dr. Iris Broce from UC San Diego and Dr. Juliana Acosta Uribe from UC Santa Barbara, this program strengthened collaborations across the region and will offer binational in-person training opportunities in 2025.

### POWDER FOR PENNIES (P4P) PROGRAM

- » **Advancing our investigation of atomoxetine (ATX):** The P4P program has prioritized this medicine, which is licensed for treatment of ADHD, to determine its effectiveness in treating AD. Multiple funded projects were launched in 2024:
  - A comprehensive review of ATX's pharmaceutical properties for use in AD is being undertaken by the **P4P Pharmaceutical Team**, including Dr. Vivian Hook of UC San Diego and collaborators at Emory University. They are preparing findings for submission, peer review and publication. This project provided an opportunity for several UC San Diego graduate and medical students to play important contributing roles.
  - An ATX target emulation trial is being undertaken by the **P4P Pharmacoepidemiology Team**, which includes Dr. Aladdin Shadyab of UC San Diego, Dr. Adam Bress of University of Utah, and Dr. Zachary Marcum of Medicus Economics. This project, which launched in early 2025, will investigate the utility of ATX in preventing AD for those who have used it after age 65.

- The **P4P Design Team** has undertaken a statistical and modelling project to advance the most efficient designs for single-arm, lead-in with multiple measures (SLIM) trials with leadership from Dr. Hiroko Dodge of Harvard University and Dr. Steven Edland of the Alzheimer's Disease Cooperative Study (ADCS) at UC San Diego. This project contributed to the submission of an application for National Institutes of Health (NIH) research funding in October for an ATX clinical trial. That application is currently still under consideration.
  - Dr. Anne Bang of Sanford Burnham Prebys is using a state-of-the-art approach to the preclinical study they are leading, which uses human model systems to study ATX and its effects on electrical activity, neuroinflammation and neuroprotection in AD. Dr. Bang's model system of networked human pluripotent stem cells moves disease modelling toward human disease and away from mouse models.
- » **Launching a benfotiamine trial for AD:** One of the highlights of P4P in 2024 was the successful launch of the NIA-funded BenfoTeam clinical trial. This investigation of the efficacy and safety of high-dose thiamine aims to address its deficiency as a brain co-enzyme factor to metabolic pathways in AD. This collaboration involves researchers from the ADCS at UC San Diego, Cornell and Columbia. It includes 28 participating sites across the U.S. where 258 participants were screened and 101 were randomized for treatment with either benfotiamine or placebo.
- » **Expanding the P4P pipeline:** Five additional compounds were added to prescreening. Grant funding is being sought for two green-lighted repurposed medicines (efavirenz and atomoxetine) in early-stage trials.
- » **Developing and validating an evaluation framework:** This new framework will aid in the assessment and prioritization of repurposing compounds for the P4P pipeline. When complete, this initiative will provide an essential reference framework for the entire AD therapeutic field.
- » **Sharing work products through publications:** We are actively sharing our findings on P4P pipeline candidate medications and how they may contribute to future research in AD and other neurodegenerative diseases.



# THREE POWERFUL INVESTMENTS IN THE FUTURE

## THE EPSTEIN FAMILY CHANCELLOR'S ENDOWED CHAIRS IN ALZHEIMER'S DISEASE RESEARCH

Thanks to the generous contribution from the Epstein family in conjunction with UC San Diego Chancellor Pradeep K. Khosla, three prestigious endowed chairs for the Epstein Family Research Collaboration at UC San Diego have been established. These positions, the highest honors in academia, empower our faculty to sustainably dedicate their efforts to groundbreaking treatments and cures for AD.

In 2023, Dr. Feldman was honored as the inaugural holder of the first Epstein Family Chancellor's Endowed Chair in Alzheimer's Disease Research. This funding has been instrumental in supporting Dr. Feldman's leadership of the P4P program, including mentoring faculty and students.

The appointment and arrival of Dr. Hyunkeun (Ryan) Cho as the second Epstein Family Chancellor's Endowed Chair in Alzheimer's Disease Research marks a major milestone in our ongoing quest for breakthroughs in AD therapeutic research. He adds much-needed statistical expertise to our work — a critical piece of the puzzle.

The third chair will be held by an outstanding scientist with complementary expertise who is focused on accelerating therapeutic progress to achieve the vision and goals of the Epstein Family Collaboration.

### **Hyunkeun (Ryan) Cho**

#### ***Director of Biostatistics, Alzheimer's Disease Cooperative Study (ADCS)***



Hyunkeun (Ryan) Cho joined the ADCS as the director of the biostatistics core in January 2025, while also holding joint faculty appointments in the Department of Neuroscience and the Division of Biostatistics at UC San Diego. With a deep-seated passion for collaborative research and education, Dr. Cho is actively involved in several NIH grants, as well as grants from the Department of Defense and the Department of Veterans Affairs, demonstrating his wide-ranging collaborative efforts across multiple disciplines, including clinical trials. He is honored to be an Epstein Family Chancellor's Chair in Alzheimer's Disease Research.

Before his tenure at UC San Diego, Dr. Cho was a faculty member at the University of Iowa, where he honed his expertise in longitudinal and functional data analysis, causal inference and machine learning, focusing on neurodegenerative diseases, aging and mental health disorders. His research employs innovative biostatistical methods to tackle complex research questions in both observational studies and clinical trials, enhancing our understanding of disease progression and treatment outcomes. Dr. Cho is also a committed educator driven by a love for teaching and mentoring to help shape the next generation of researchers in biostatistics and neuroscience.

Dr. Cho's commitment to advancing AD research through rigorous statistical analysis, collaborative research, education and clinical trials is pivotal to ADCS's mission. He is dedicated to scientific discovery and to ensuring that his findings lead to practical and impactful interventions for AD and related conditions.

# TWO INSPIRED PROGRAMS WITH ONE SHARED GOAL

## ACCELERATING THERAPEUTICS FOR ALZHEIMER'S DISEASE

The GTP and P4P programs under the Epstein Family Collaboration are both squarely focused on driving research, accelerating the search for treatments, and finding a cure. Both are supported by the ADCS infrastructure and are international and inter-institutional in scope to harness the best talent and resources to push this mission forward.

### THE GENE THERAPY PROGRAM

#### 2024 DEVELOPMENTS

The GTP is committed to advancing research and development efforts that support innovative gene therapy approaches, with an initial focus on creating the first-in-human gene-based therapy for the Jalisco mutation (PSEN1 A431E). The Jalisco mutation is a particularly tragic variant of AD caused by an autosomal dominant single genetic substitution, which manifests with an unusually early onset (a mean age of 41 years) and distinct neurological features such as spastic paraparesis. The broader objective is to generate findings applicable to both genetic and sporadic forms of AD. To this end, the GTP actively seeks projects in the following areas:

- » Model systems to clarify targets and screening of therapeutics
- » Neuropathology studies
- » Familial studies
- » Candidate gene therapy approaches

A fundamental strength of the Epstein Family Collaboration has been its agility in adapting to emerging research opportunities. This flexibility proved particularly valuable in year three, as Jalisco family engagement initiatives evolved to include a comprehensive capacity-building effort aimed at training Mexico's next generation of geneticists.

### THE JALISCO FAMILY STUDY

Since our inception, UC San Diego has collaborated with USC on developing a longitudinal research initiative entitled Population Engagement Towards Enabling Translation of Gene-Targeted Interventions in Autosomal Dominant Alzheimer Disease, known as the Jalisco Family Study.

In May 2023, members of the UC San Diego GTP and Dr. John Ringman's USC team attended the Alzheimer's Association International Conference (AAIC) Satellite Symposium in Mexico City. This year two engagement yielded significant progress in year three through collaborations initiated at this symposium.

In April 2024, Dr. Feldman and Dr. Pa, along with other GTP researchers, met with Dr. Jorge Llibre Guerra, assistant director of the Dominantly Inherited Alzheimer's Network-Trials Unit (DIAN-TU) in San Diego. Bringing together the GTP with DIAN-TU is particularly exciting because it adds a new collaboration to the largest global study of families with inherited forms of AD.

**Collaborative Capacity Building Between the U.S. and Mexico**

Dr. Broce, a geneticist and faculty member at UC San Diego and an active participant in the Jalisco roundtable, led the development and implementation of a 21-week Zoom-based computational genetics course. The course, which launched in July 2024, attracted 40 students, with an average of 20 attendees per session. Its reach extended across five institutions in four Latin American countries.

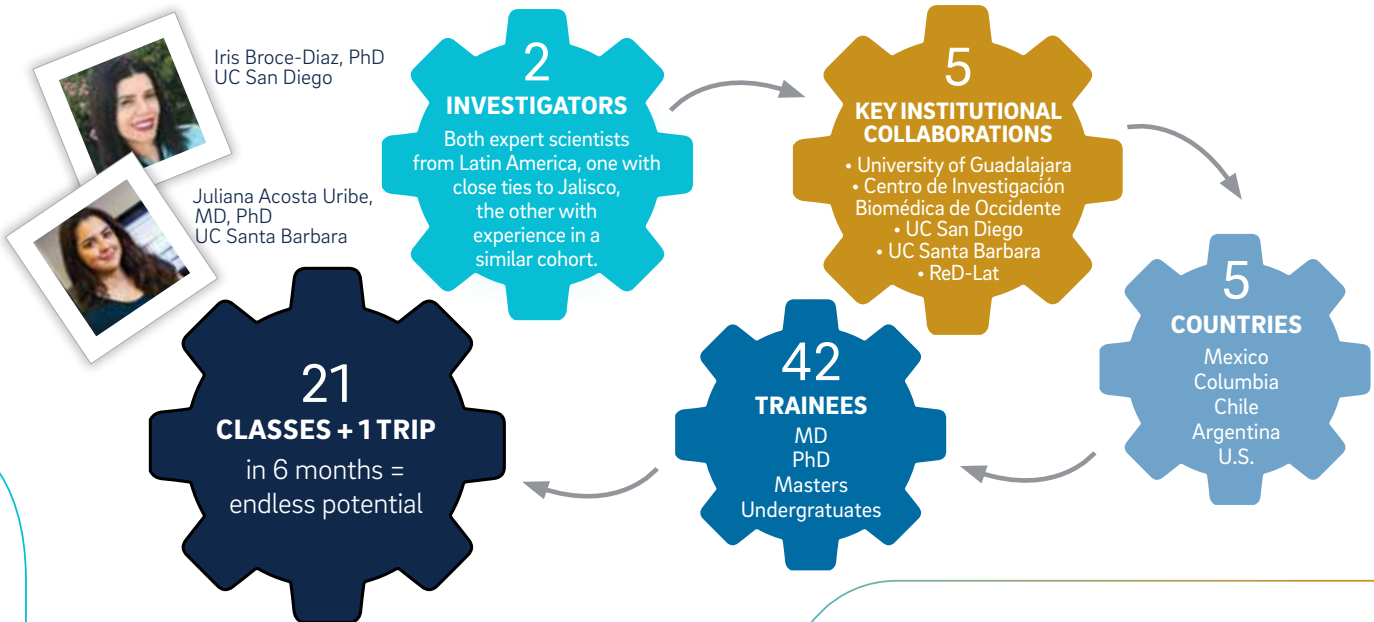
Dr. Broce shares teaching responsibilities with Dr. Juliana Uribe, a researcher at the UC Santa Barbara who trained under both Dr. Francisco Lopera and Dr. Kenneth Kosik. Dr. Uribe developed a web-based GitHub platform to house the syllabus, recorded lectures, reading materials and additional resources. She also established a Slack channel for real-time communication, which facilitated a dynamic and interactive learning experience. The course concluded successfully in December 2024.



*Computational genetics students first connected by Zoom then met in person in Guadalajara. Dr. Broce, UC San Diego neuroscientist (standing, far left), co-led the course.*

**COMPUTATIONAL GENETICS TRAINING**

**COLLABORATION AND EFFICIENCY: JUNE – DECEMBER 2024**



## Strengthening Our Ties with Impacted Families

In December 2024, Dr. Broce spearheaded a trip to the University of Guadalajara (UDG) during its annual family meetings. The trip involved both the launch of the computational genetics course and the evolving family engagement project, including a series of informational and support sessions for families affected by the Jalisco mutation who also participate in research with UDG. Dr. Broce and ADCS program manager Michelle Herman were graciously received by members of the UDG faculty and members of the Jalisco roundtable, along with Dr. Ringman and his USC research team. They participated in three days of meetings with students in the computational genetics program and families impacted by the Jalisco mutation.

These engagements provided critical insights into the computational limitations faced by students in Jalisco, including a lack of access to the computing power necessary to analyze genomic data effectively. Dr. Broce integrated these findings into a proposal submitted to the Epstein Family Collaboration in January 2025, which sought funding to enhance computational resources and expand training opportunities.

The proposal was well received by the scientific advisory board, which endorsed an even more expansive training initiative. This proposal now includes two six-month training opportunities in the U.S. for two promising students from UDG and several weeks of data set support from Dr. Broce in Guadalajara for interested students. Additionally, a specialized server will be established to support more extensive computational genetics research within Jalisco.

*Dr. Esmerelda Matute's and Dr. Ringman's teams after the meeting in Poncitlán.*



## 2024 University of Guadalajara Family Meetings

The second annual series of family meetings hosted by UDG were held from December 13 to 15. These gatherings play a crucial role in sustaining familial participation in this multiyear study aimed at characterizing the physical and cognitive effects of the Jalisco mutation. This research is funded by an NIH Fogarty grant under the leadership of Dr. Matute (UDG) and Dr. Ringman (USC).

The meetings provided a structured environment for family members to engage in discussions on deeply personal and significant topics, including:

- » The **emotional impact** of hereditary AD.
- » The **value of participating** in genetic research.
- » Future **hopes and expectations**.
- » Understanding the **hereditary nature** of the condition.
- » Strategies for **personal and familial care**.
- » **Lessons learned** through participation in the study.

Dr. Matute's research team facilitated these discussions. They fostered a strong rapport with participants and reinforced the study's commitment to community engagement and building trust.



*Groups answering emotional questions and supporting each other in Guadalajara.*

## Future Directions: Family Engagement in the United States

As the GTP enters year four, its focus is shifting toward engaging families originally from Jalisco who now reside in the U.S., which is where most initial human gene therapy trials are conducted. By leveraging the infrastructure of the ADCS, we will aim to identify and connect with U.S.-based families who may be suitable trial candidates. All progress will be shared with our collaborators in Mexico.

The overarching goal of this long-term family study is to cultivate trust and collaboration within affected communities. Essential components of this initiative include genetic counseling, caregiving support and education, all of which are fundamental to fostering informed and willing participation in future trials.

In 2025, the Epstein Family Collaboration scientific advisory board invited three investigators to submit proposals aimed at advancing their research toward clinical application. An open call for proposals is also under consideration for later in the year to expand research that will further accelerate progress in gene therapy research for AD.

## REMEMBERING A LEADER IN ALZHEIMER'S RESEARCH



We would like to commemorate the passing of Dr. Francisco Lopera, a distinguished clinician and researcher known for his groundbreaking studies and clinical trials involving a similarly extensive cohort of families with a PSEN1 autosomal dominant AD in Colombia. He actively engaged with the GTP, offering his deep expertise and knowledge to the Epstein Family Collaboration. His legacy endures through the generations of trainees he mentored. This legacy will be further reinforced through GTP collaborations he supported and bolstered, including a computational genetics training course for students in Jalisco, Mexico, delivered in Spanish by one of his trainees.

*Jalisco roundtable dinner in Mexico City, May 2023. The late Dr. Lopera is in the front row in khaki green.*

# GENE THERAPY PROGRAM RESEARCH IMPACT

## YEAR ONE FUNDED PROJECTS



**Project:** Hematopoietic stem cell gene therapy for AD (ending May 2025)

**Principal investigator:** Dr. Stephanie Cherqui, Department of Pediatrics, UC San Diego

**Epstein Family Collaboration funds received:** \$350,000 over two years

**Return on investment:** 6x

- » "Rescue of Alzheimer's disease phenotype in a mouse model by transplantation of wild-type hematopoietic stem and progenitor cells" published in Cell Reports (August 2023).
- » Received NIH RO1 research award in 2024 based on her Epstein Family Collaboration project. The project, "Understanding the mechanism of rescue of Alzheimer's disease by hematopoietic stem cell (HSPC) transplantation," was granted \$1,975,00 over five years and will investigate how an HSPC transplant prevents neuroinflammation and leads to the preservation of the neurocognition function in AD.
- » Serving as co-lead of the Gene Therapy Initiative at UC San Diego, which is also philanthropically funded by the Nancy and Geoffrey Stack Family Foundation. The Stacks' daughter received an HSPC therapy that successfully treats cystinosis and was developed by Dr. Cherqui.



**Project:** Characterization of a novel knock-in PSEN1 A431E (Jalisco) mouse model (completed October 2024)

**Principal investigator:** Dr. Bart De Strooper, UK Dementia Research Institute, University College London and the VIB-KU Leuven Center for Brain & Disease Research

**Epstein Family Collaboration funds received:** \$303,357 over two years

**Return on investment:** 3.5x

- » With Epstein Family Collaboration funding, De Strooper developed a knock-in mouse model with the Jalisco mutation as well as the required control.
- » This mouse has been shared with Dr. Cherqui and is available to other Epstein Family Collaboration investigators.
- » With a letter of support from the GTP, De Strooper received a competitive and prestigious Belgian award of €1 million for use in 2026 through 2030 to study antisense oligonucleotides (ASOs) as therapeutics for autosomal dominant AD.



**Project:** Developing a synthetic adeno-associated virus (AAV) for engineering safer gene therapies

**Principal investigator:** Dr. Matthew Shtrahman, Department of Neurosciences, UC San Diego

**Epstein Family Collaboration funds received:** \$177,419 over two years

**Return on investment:** 10x

- » Dr. Shtrahman used his funding to hire an expert in AAV engineering.
  - » Thanks to the work accomplished with Epstein Family Collaboration funding, he was able to successfully apply for an NIH Katz Early-Stage Investigator award of \$1,222,811 over three years for developing a synthetic AAV for engineering safer gene therapies.
  - » Due to a discovery made during his first Epstein Family Collaboration project, Dr. Shtrahman will be applying for additional support to better integrate AAV vectors with CRISPR gene editing.
- 



**Project:** Therapeutic CRISPR editing of amyloid precursor protein (APP) and proposed application to the Jalisco mutation

**Principal investigator:** Dr. Subhojit Roy, Departments of Pathology and Neurosciences, UC San Diego

**Epstein Family Collaboration funds received over two projects:** \$414,386 over two years

**Return on investment:** 5x

Dr. Roy has been continuing his groundbreaking work in advancing CRISPR-based therapeutics for the APP with potential to impact the Jalisco mutation.

- » With Epstein Family Collaboration funding, Dr. Roy and team are testing a single AAV-vector CRISPR delivery system in human organoids with PSEN1/APP mutations including the Jalisco mutation and Down syndrome.
  - » Dr. Roy received two years of continued Epstein Family Collaboration funding for this work. He has leveraged his results to successfully apply for NIH funding for similar work in other mutations.
  - » Epstein Family Collaboration funds supported the purchase of a Meso Scale Discovery machine that is needed to measure A $\beta$  fragments to understand different cleavage patterns unique to a mutation. This equipment is available to all Epstein Family Collaboration investigators.
-



**Project:** Molecular analysis of central nervous system (CNS) blood vessels from AD patients with the Jalisco mutation

**Principal investigator:** Dr. Richard Daneman, Departments of Pharmacology and Neurosciences, UC San Diego

**Epstein Family Collaboration funds received:** \$225,000

**Return on investment:** TBD

Dr. Daneman's interest is in the molecular mechanisms that regulate blood-brain barrier (BBB) function in various disease processes.

- » With the funding received from the Epstein Family Collaboration, Dr. Daneman and his lab apply techniques used to understand BBB function in stroke, edema, trauma and multiple sclerosis. These same techniques are being applied to Jalisco mutation autosomal dominant Alzheimer's disease (ADAD) to identify whether targeting the BBB may be therapeutic.
- » He has collaborated with the USC neuropathology team and the U.S. Department of Veterans Affairs health system to acquire needed brain tissues. Dr. Daneman is completing his work this year and his report is eagerly anticipated.



**Project:** Delivery of prime DNA base editors to treat AD

**Principal investigator:** Dr. Stephen Dowdy, Department of Cellular and Molecular Medicine, UC San Diego

**Co-investigators:** Dr. William Mobley, Dr. Alexis Komor, and Dr. Subhojit Roy

**Epstein Family Collaboration funds received:** \$303,357 over two years

**Return on investment:** TBD

Dr. Dowdy and his lab focus on the targeted delivery of RNA interference (RNAi) and ASO therapeutics for treating cancer and infectious and central nervous systems diseases.

- » Together with Dr. Mobley of the Department of Neurosciences, Dr. Komor of the Department of Chemistry and Biochemistry, and with the support of Dr. Roy of the Departments of Pathology and Neurosciences, the research team has taken on the issue of delivering gene editors safely to brain neurons.
- » After several failed attempts at messenger RNA (mRNA) delivery of prime edited genes, they will test two new theories in 2025, including mutant selective RNAi and splitting the prime editor into two AAVs.
- » This team received continuation funding for a second year for this work.



**Project:** Neuropathology of the A431E PSEN1 mutation

**Principal investigator:** Dr. John Ringman, Department of Neurology, USC

**Epstein Family Collaboration funds received:** \$542,599

**Return on investment:** TBD

Dr. Ringman is caring for those afflicted with the Jalisco mutation ADAD, having worked with and for families afflicted with this mutation for over 20 years.

- » During this time, he has worked to collect brain and spinal cord samples for study of the neuropathology of this unique early-onset AD.
- » With the support of the Epstein Family Collaboration funding, Dr. Ringman and the team of experts he has assembled hope to answer the basic questions of how the brains and spinal cords of those with the Jalisco mutation differ from those with sporadic AD in terms of A $\beta$  and tau pathology as well as the cell loss, alpha-synuclein pathology and inflammatory changes.
- » They also hope to define the neuropathological correlates of spastic paraparesis (weakness and stiffness of the legs).
- » This work continues in year two with a no-cost extension. We look forward to final reports in 2025.

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## YEAR TWO FUNDED PROJECTS



**Project:** Mechanisms underlying atypical neuronal phenotypes of Latin American familial AD

**Principal investigator:** Dr. Jerome Mertens, Department of Neurosciences, UC San Diego

**Epstein Family Collaboration funds received:** \$150,000

**Return on investment:** TBD

Dr. Mertens' lab is dedicated to the study of neuronal aging.

- » In this project, Dr. Mertens and his team have been developing cellular models of Jalisco mutation AD using patient-specific induced neurons, or iNs, in contrast to induced pluripotent stem cells (iPSC), which are already under study.
- » These iNs are being generated in a patient-specific and age-equivalent manner and more closely resemble the adult human brain.
- » This work characterizes and analyzes synapses, tau species and  $\beta$ -amyloid isoform secretion, to decipher the epigenetic and functional underpinnings of Jalisco mutation AD.
- » In addition, the cellular phenotypes of the spastic paraplegia unique to this illness are being explored with the hope of starting to understand how this component of the disease overlaps with the cognitive components.



**Project:** Safety considerations for gene therapy in central nervous system disorders

**Principal investigator:** Dr. Gabriel Léger and Dr. Elizabeth Bevins, Department of Neurosciences, UC San Diego

**Epstein Family Collaboration funds received:** \$34,215



**Return on investment:** TBD

As gene therapies have shown more promise in treating neurologic diseases such as AD, the ADCS recognizes the need to develop expertise in the challenges and safety issues to be considered in delivering such treatments.

- » In this project, Dr. Léger and Dr. Bevins, ADCS medical safety faculty, are completing a comprehensive literature review of medical safety considerations and are describing specific clinical outcomes and safety data in existing gene therapy trials for AD and other related neurodegenerative disorders.
  - » In year three, safety data for 14 gene-based therapy trials from 2003 to 2024 for AD were evaluated. The literature on seven other trials of gene-based therapies for neurodegenerative disorders were also collected for comparison and study.
  - » In year four, we are looking forward to an impactful publication on the tolerability and safety of gene therapy in AD and other neurodegenerative diseases.
  - » The ultimate goal is to establish a framework to systematically gather and evaluate available safety and tolerability data and recommend an approach to addressing safety as this form of treatment evolves.
-

# THE POWDER FOR PENNIES PROGRAM

## 2024 DEVELOPMENTS

During the past year, the P4P program has focused on pipeline development and clinical trials. As seen in Figure 1, each of the critical research working groups contribute to either the shaping of the pipeline, the evaluation of candidate medicines, or the development of clinical trials that are selected from the pipeline. These are fundamental activities and the success of the P4P program depends on the strength and progress of this pipeline.

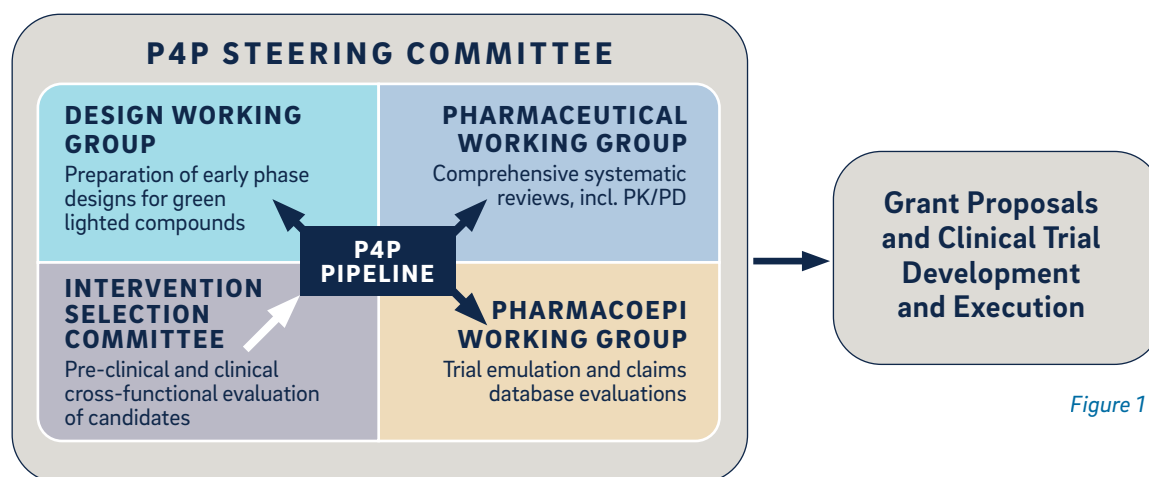


Figure 1

## P4P PIPELINE UPDATES

In 2024, significant progress was made in advancing atomoxetine to be ready for repurposed use in AD clinical trials. This effort included the intervention selection committee, which reviewed this medication and recommended its prioritization. An ADCS network-wide webinar convened on April 26, 2024, with presentations by principal investigators Dr. Allan Levey and Dr. David Weinsheinker of Emory University with 72% of the ADCS network sites indicating their support for participating in clinical trials of this medication. The pharmaceutical team has been assessing ATX properties as an AD drug and the work product of its review will be completed and submitted for publication in 2025. This work is foundational for the ATX program because it will explain the scientific rationale and supporting data for its use.

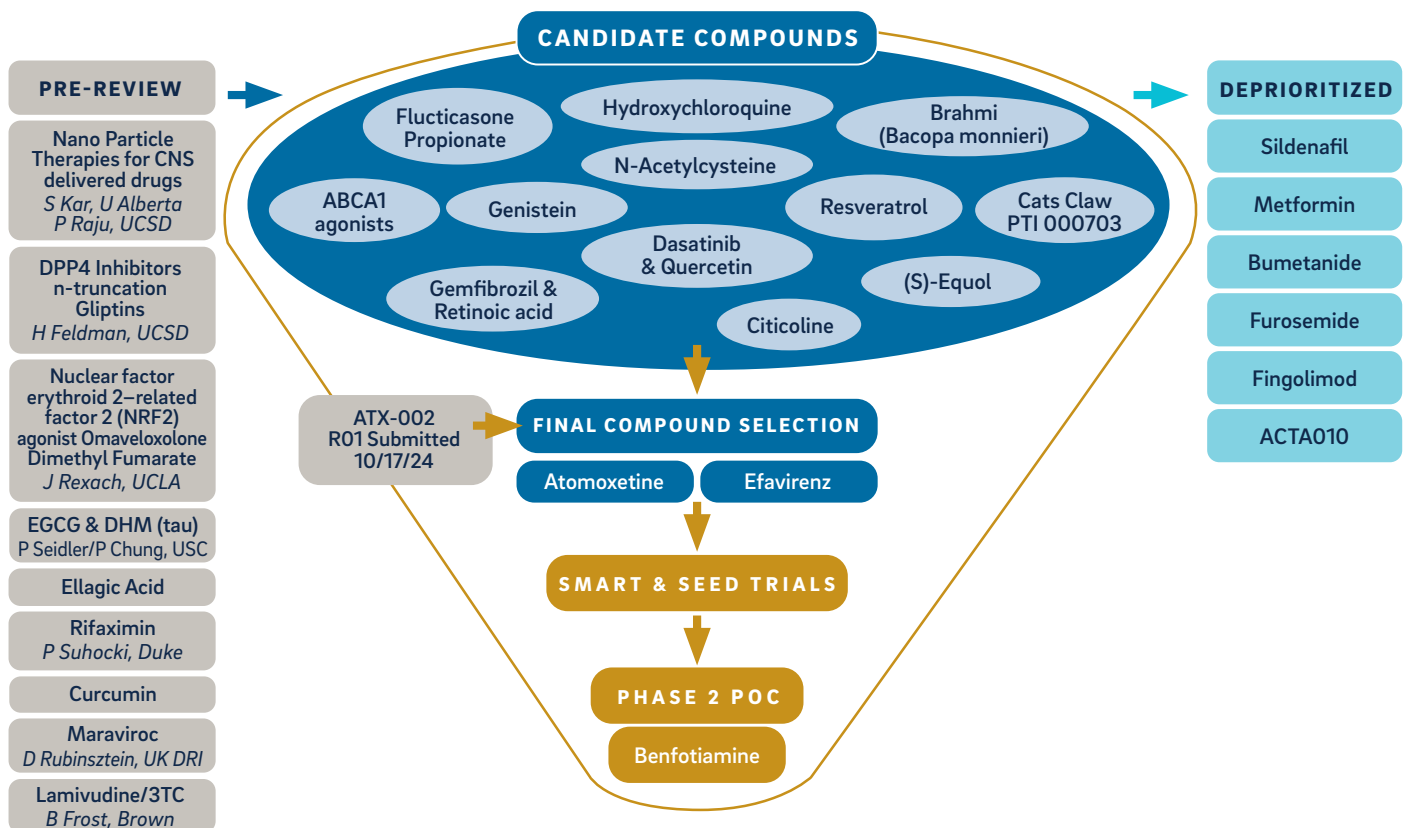
In addition, the pharmaceutical team reviewed and assessed the suitability of efavirenz, an approved HIV drug, for AD. Following peer review, the findings were published in 2024 in an article entitled "Challenges and Opportunities for Consideration of Efavirenz Drug Repurposing for Alzheimer's Disease Therapeutics"<sup>1</sup> (Boyarko et al., ACS Pharmacol Transl Sci., 2024). This review highlighted some of the important challenges identified in repurposing this reverse transcriptase inhibitor for AD.

Two other HIV drugs were evaluated this year: maraviroc, which was proposed by Dr. David Rubinzstein of Cambridge University, and lamivudine (or 3TC), which was proposed by Dr. Bess Frost of Brown University. Each of these HIV drugs has a different scientific rationale for its use: efavirenz promotes cholesterol efflux and lowering tau

hyperphosphorylation; maraviroc blocks the chemokine receptor type 5 (CCR5) with potential anti-inflammatory, immunomodulatory and neuroprotective effects; and 3TC inhibits the retrotransposition of DNA elements or long interspersed nuclear elements-1 (LINEs-1 or L1s), which are promoted by pathogenic tau protein.

The other emerging medication class for P4P repurposing includes drugs which increase nuclear factor erythroid 2-related factor 2 (Nrf2), a master cellular antioxidant response. There are numerous drugs which activate this pathway and potentially help the brain respond to increased reactive oxygen and nitrogen species as they occur in AD to lower abnormal oxidative damage and inflammation. The pharmaceutical team and Dr. Jessica Rexach at UCLA are evaluating several leading compounds including omaveloxolone (Skyclarys®), which is otherwise approved for Friedrich's ataxia; and dimethyl fumarate (Tecfidera®), approved for relapsing remitting multiple sclerosis (RRMS).

## PIPELINE HEAT MAP



## STREAMLINING RAPID DRUG EVALUATION

### The ADCS Intervention Selection Evaluation Framework Project

In partnership with P4P, the ADCS has developed an intervention selection evaluation framework to assist in unbiased screening and ranking of P4P and other drug candidates that are being considered for clinical advancement. This framework is intended to facilitate screening and scoring of prospective repurposed drugs and other compounds for AD clinical trials. Members of the ADCS intervention selection committee (ISC) include a distinguished team of preclinical scientists, translational pharmacologists, and clinical trial experts who have come together from both academic and industry institutions across North America to advance this framework for our P4P pipeline evaluation. Given the multiple candidates identified in the P4P pipeline, a robust review process can provide comparative ratings and rank ordering to prioritize repurposed medicines and more efficiently bring effective treatments to patients. It also helps direct resources and efficiencies in advancing repurposed medicines to allow them to successfully follow the “rights” of AD drug development (the right target, right drug, right biomarker, right participant and right trial) (Cummings J, Feldman HH, Scheltens P. The “rights” of precision drug development for Alzheimer’s disease. *Alzheimers Res Ther.* 2019).

In 2024, P4P supported a project that rigorously evaluates this framework of ranking drug candidates for unbiased screening methods. Four established compounds (semagacestat, verubecestat, donepezil and lecanemab) and three prospective compounds (sildenafil, levetiracetam and bumetanide) are being evaluated in this project. Six ISC members initially evaluate and rate each compound independently within the framework and submit their scores prior to a consensus meeting where they are reviewed and discussed. The scores are finalized and set against a Monte Carlo simulation to evaluate cutoff points and enable rank ordering. Compounds are assessed on scientific rationale and potential for clinical development; preclinical evidence that the drug effectively engages the proposed target or pathway in preclinical models; clinical evidence of safety and pharmaceutical properties; and any additional documentation which supports conducting clinical studies.

Since the project was launched in July 2024, the ISC has reviewed six of the seven selected compounds and held seven consensus meetings. They are anticipating completing all reviews by April 2025. A manuscript detailing this project is in development and will be submitted for publication in a peer-reviewed journal to share with the broader field. Additionally, the framework will be made available to all principal investigators or organizations who wish to bring a pharmaceutical program to P4P or the ADCS.

**Ensuring the “rights” of AD drug development:  
the right target, right drug, right biomarker,  
right participant and right trial.**

—J. CUMMINGS ET AL.

*Alzheimer's Research & Therapy*

## P4P CANDIDATE: BENFOTIAMINE

### Launching the Nationwide BenfoTeam Trial

In April 2024, our Seamless Phase 2A-Phase 2B Multicenter Trial to Test the Benefits of Benfotiamine on the Progression of Alzheimer's Disease (BenfoTeam) enrolled its first participant in a nationwide clinical trial. This is being undertaken within a funding period of 2022 to 2027 and a total NIA award of \$46 million. BenfoTeam will test high dose vitamin B1 (thiamine) as a P4P-endorsed repurposed medicine for the treatment of AD.



One of the trial's principal investigators, Dr. Gary Gibson of Cornell University, has done decades of groundbreaking scientific preclinical work uncovering the deficit in thiamine-dependent brain enzymes needed for brain glucose and energy metabolism. Through the administration of a thiamine prodrug, thiamine can be raised to pharmacological levels as high as 100 times more than normal to restore brain thiamine-dependent processes. The prodrug is formulated to restore the activity of thiamine-dependent enzymes and to bring them to a sufficient level of functional activity, improving energy and glucose metabolism deficits in the brain.

This trial will evaluate its participants over 18 months at 50 sites nationwide. There are 406 participants between the ages of 50 and 89 who have mild cognitive impairment or mild dementia due to AD. The trial will determine the highest safe and well-tolerated dose of benfotiamine and whether it can improve function and cognition over 18 months. At the time of this report, 121 of 406 participants (30%) were randomized, 184 of 333 participants (55%) failed the trial screening, and 28 participants are currently being screened.

## P4P CANDIDATE: ATOMOXETINE (ATX)

### Exploring an Established ADHD Drug to Treat AD

In 2024, the focus on repurposing ATX attracted P4P support due to the accumulation of decades of compelling preclinical and preliminary clinical evidence concerning the role of the norepinephrine neurotransmitter system in AD. Prior to symptom onset, the first pathological signs of AD are evidenced by the appearance of deposits of hyperphosphorylated tau (p-tau) and neurofibrillary tangles (NFTs) in the locus coeruleus (LC), a small but dense cluster of roughly 40,000 neurons in the brainstem. The LC's noradrenergic neurons project throughout the brain and are the principal central source for norepinephrine (NE), a key regulator for attention, arousal, stress responses, learning and memory. These pathways are also implicated in regulating neuroprotection and anti-inflammatory responses in AD. Early disturbances in the NE transmitter system are further supported by pharmacological strategies that augment the system's levels and promote neuroprotection and prevention of tau spread and synaptic loss in AD.

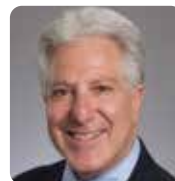
A preliminary trial by Dr. Levey that uses ATX as a neuroprotective treatment showed very encouraging results (Dr. Levey et al. A phase II study repurposing atomoxetine for neuroprotection in mild cognitive impairment, *Brain*, 2022). The early disturbances in LC integrity also coincide with the emergence of noncognitive behavioral problems including anxiety, depression, aggression, apathy and sleep disturbances. Furthermore, the feasibility of testing target engagement of the LC has become more feasible with the advent of sensitive neuroimaging sequences with MRI that can visualize this structure and its degeneration in the disease. Based on this scientific progress in 2024, P4P endorsed proceeding with testing ATX in the projects that follow.

## POWDER FOR PENNIES RESEARCH IMPACT

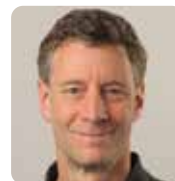
### P4P biomarker platform trial design: ATX-002 NIA R01

(currently under NIA review)

In collaboration with Dr. Levey and Dr. Weinshenker, Dr. Feldman led the submission of an NIA grant application for “A Phase 2A Clinical Trial of ATX as a Repurposed Medicine in the Treatment of Early Alzheimer’s Disease.” This proposal brings together a skilled team of investigators from various institutions for a clinical trial of ATX-002. The trial incorporates a novel and efficient SLIM design, state-of-the-art biomarkers and multimodal neuroimaging as well as PET and MRI. NIA study sections are reviewing and scoring the ATX-002 study concept this spring. If funded in July, we expect to begin enrollment in 2025.



Allan Levey



David Weinshenker

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### P4P design team, ATX study working group

The trial design for ATX-002 emerged out of the collaborative planning discussions with preeminent biostatisticians including Dr. Edland (UC San Diego), Dr. Dodge (Massachusetts General Hospital and Harvard University), and Dr. Gary Cutter (University of Alabama at Birmingham). This is the first application of an innovative study design (single-arm, repeated measures run-in and run-out) that will improve study efficiency and speed to potentially complete this and future phase two drug repurposing trials. The design exploits the value of measuring intra-individual change to sharpen the measurement of treatment benefits. By using the individual as their own control, we alleviate the need for a placebo to be used as a control condition. Our foundational work is being presented by Dr. Dodge at the Alzheimer’s and Parkinson’s diseases conference in April 2025. We intend to validate this study design with the ATX-002 clinical trial.



Steve Edland



Hiroko Dodge



Gary Cutter

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### P4P pharmaceutical team, ATX pharmacologic review and analysis

Building on their earlier work repurposing bumetanide and efavirenz for AD, Dr. Vivian Hook at UC San Diego and her team are now evaluating ATX as a potential AD treatment. With support from the P4P program, they are preparing a new review manuscript focused on ATX. Student lead Laura Demsey shared early findings at the February 2025 Epstein Family Research Collaboration Investigators Meeting. The review explored how ATX affects the brain’s locus coeruleus-norepinephrine (LC-NE) system, which plays a key role in brain function and is one of the first areas affected in AD. It also summarized evidence from animal models showing ATX’s potential to improve memory and reduce brain inflammation. Finally, the review discussed past ATX use in both Alzheimer’s and Parkinson’s studies, its effects on biomarkers, and its safety in older adults.



Vivian Hook

### **P4P Pharmacoepidemiology Team, ATX Target Trial Emulation (TTE)**

The P4P pharmacoepidemiology team, led by Dr. Shadyab in collaboration with Dr. Bress and Dr. Marcum, are undertaking a study to evaluate whether long-term use of ATX delays or significantly reduces the incidence rate of AD.

They will be using the entire 2007 – 2023 Medicare fee-for-service claims database, with over 30 million Medicare beneficiaries, to design and emulate a pragmatic randomized trial (i.e., the target trial) to address this important question. The results will add significantly to the evidence base of clinical trials undertaken in AD. This is the first target trial emulation (TTE) that the ADCS is undertaking.

Unlike a typical randomized, controlled clinical trial that prospectively enrolls its participants, the TTE identifies subjects or beneficiaries for whom data is already present. The trial is then undertaken with a large amount of data spanning many years already in hand. It is well positioned to evaluate whether ATX treatment is associated with reduced AD and all-cause dementia risk. One of the remarkable opportunities with this trial will be our ability to undertake it from start to completion in 12 to 18 months compared to the usual four to five years.



*Aladdin Shadyab*



*Adam Bress*



*Zachary Marcum*

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### **P4P ATX Translational Research Projects**

In 2024, scientific approval and funding was allocated for two additional collaborative linked translational research projects which utilize ATX, one from Dr. Bang and the other from Dr. Hook.



*Anne Bang*



*Vivian Hook*

Dr. Bang's project entitled "Development of a Human Induced Pluripotent Stem Cell (hiPSC) Model to Study the Effects of Atomoxetine on Neuronal Network Activity, Neuroinflammation, and Neuroprotection" will examine the balance of excitation and inhibition in a networked model system of AD using hiPSCs. The finding of imbalance between excitation and inhibition is seen as an increasingly important problem in AD, as the disease leaves potential for pharmacological treatment to rebalance the system. Dr. Bang will examine the balance in this model system, which evaluates the presence and absence of the oligomeric  $\beta$ -amyloid 42 and with both noradrenergic agonists and antagonists. She will also evaluate these effects on neuroinflammation and neuroprotection through co-cultures of neurons, astrocytes and microglia to gauge the effects on cellular function within perturbations of network activity.

To date, Dr. Bang has expanded and banked the control (KOLF induced pluripotent stem cells [iPSC] and H9 human embryonic stem cells) and has started the LC-NE and microglial differentiations. She is currently assessing and confirming intermediate stage markers.

Dr. Hook's research project, "CSF Neuropeptide Transmitter Biomarkers in Alzheimer's Disease and Regulation by the FDA Drug Atomoxetine," is centered on measuring novel and potentially responsive biomarkers according to the ATX mechanism of action. In the first phase of her work, which was funded in February 2025, she will evaluate some of the data acquired in Dr. Levey's ATX study to quantify dysregulation of the nerve growth factor inducible (VGF) granin family of neuropeptide transmitters in cerebrospinal fluid (CSF) and to assess how ATX treatment affects the regulation of VGF granin neuropeptides in the CSF from AD patients and controls. In the second phase of this project, Dr. Hook will measure the same factors in media from Dr. Bang's AD iPSC-derived neuronal cultures to evaluate ATX regulation and release of these proteins. Should the findings from the AD iPSC-derived neurons replicate the findings from the AD patients' CSF in response to ATX treatment, these results would support the development of VGF granin neuropeptides as a novel biomarker for AD specifically well suited for measuring treatment effects of ATX.

## P4P Supported Publications in 2023-24

1. Boyarko B, Podvin S, Greenberg B, Momper JD, Huang Y, Gerwick WH, Bang AG, Quinti L, Griciuc A, Kim DY, Tanzi RE, Feldman HH, Hook V. Evaluation of bumetanide as a potential therapeutic agent for Alzheimer's disease. *Front Pharmacol*. 2023 Aug 4;14:1190402. doi: 10.3389/fphar.2023.1190402. PMID: 37601062; PMCID: PMC10436590.
2. Morales J, Gabriel N, Natarajan L, LaCroix AZ, Shadyab AH, Xu R, Silverman J, Feldman HH, Hernandez I; Powder for Pennies Collaboration. Pharmacoepidemiology evaluation of bumetanide as a potential candidate for drug repurposing for Alzheimer's disease. *Alzheimers Dement*. 2024 Aug;20(8):5236-5246. doi: 10.1002/alz.13872. Epub 2024 Jun 21. PMID: 39030734.
3. Feldman HH, Luchsinger JA, Léger GC, Taylor C, Jacobs DM, Salmon DP, Edland SD, Messer K, Revta C, Flowers SA, Jones KS, Koulman A, Yarasheski KE, Verghese PB, Venkatesh V, Zetterberg H, Durant J, Lupo JL, Gibson GE; ADCS BenfoTeam Study Group. Protocol for a seamless phase 2A-phase 2B randomized double-blind placebo-controlled trial to evaluate the safety and efficacy of benfotiamine in patients with early Alzheimer's disease (BenfoTeam). *PLoS One*. 2024 May 29;19(5):e0302998. doi: 10.1371/journal.pone.0302998. PMID: 38809849; PMCID: PMC11135745.
4. Boyarko B, Podvin S, Greenberg B, Arnold S, Juanes AM, van der Kant R, Goldstein L, Momper JD, Bang A, Silverman J, Feldman HH, Hook V. Challenges and Opportunities for Consideration of Efavirenz Drug Repurposing for Alzheimer's Disease Therapeutics. *ACS Pharmacol Transl Sci*. 2024 Sep 6;7(10):2924-2935. doi: 10.1021/acsptsci.4c00229. PMID: 39421657; PMCID: PMC11480897.
5. Dodge HH, Chen L, Edland SD, Feldman HH, Arnold S. Seeking Optimal Repeated Fluid Biomarker Assessments to Enhance Precision and Statistical Power in Clinical Trials: SLIM Approach. Poster presentation at AD/PD International Conference on Alzheimer's and Parkinson's Disease and Related Neurological Disorders in April 2025.

## FOSTERING TOMORROW'S AD RESEARCHERS

### THE EDUCATIONAL IMPACT OF P4P

Meet some of the students who are contributing to the ATX review with mentorship from Dr. Hook and the collaborative ADCS team:



**Ben Boyarko**

*Class of 2026*

*Drexel University College of Medicine*

*"My experience with the Epstein program has been transformative. Collaborating with the P4P team has taught me to approach medical research through a multidimensional lens and helped me gain a deeper understanding of the many facets involved in evaluating therapeutics. Literature evaluations have refined my ability to critically assess medical research and evaluate research methodologies with a healthy degree of skepticism. Most importantly, this experience has reinforced the value of bold, innovative research. I have come to appreciate the necessity of pushing scientific boundaries in order to transform patient care and improve lives."*

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**Danielle Burch**

*Class of 2027*

*UC San Diego Skaggs School of Pharmacy and Pharmaceutical Sciences*

*"This work has helped expose me to clinical research, pharmaceuticals, drug development, safety trials, animal and human testing, phases of clinical research, and FDA approvals. The knowledge I have gained and the skills I have acquired are preparing me for research during my residency and developing my ability to independently analyze related research and draw informed conclusions. These skills will benefit me both when I graduate and throughout my career. I am truly grateful for the opportunity to collaborate on such important research."*

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**Evan Lin**

*Class of 2028*

**UC San Diego Skaggs School of Pharmacy and Pharmaceutical Sciences**

*"I've appreciated this opportunity to learn how to design a study framework and analyze literature for supporting evidence. Learning how to navigate through scientific databases and assess existing studies has strengthened my ability to find gaps in knowledge and develop research questions. I've been able to see how others approach problem solving and work together to explore different aspects of a research question. I've gained a greater appreciation for drug repurposing as an approach to expand treatment options. This experience has sparked my interest in seeing how other novel therapies can be developed and continuing to connect the fields of pharmaceutical research and clinical practice."*

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**Laura Demsey**

*Class of 2029*

**UC San Diego Skaggs School of Pharmacy and Pharmaceutical Sciences**

*"Working on the atomoxetine project has deepened my understanding of neurodegenerative disease mechanisms and the translational pipeline from bench to bedside. It has taught me how an existing medication can be thoughtfully reconsidered to target noradrenergic dysfunction in Alzheimer's disease. Through the investigator meetings, I gained a deeper appreciation for how the scientific community navigates the complexity of diseases like Alzheimer's and explores each unique aspect of the disease. I now have a more nuanced understanding of how preclinical findings can evolve into clinical applications. This experience has expanded my appreciation for the creative and rigorous scientific inquiry required to make therapies more accessible and has inspired me to continue integrating research into my medical career."*

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**Diana Quach**

*Class of 2028*

**UC San Diego Skaggs School of Pharmacy and Pharmaceutical Sciences**

*"This has been an invaluable opportunity that aligns closely with my passion for psychiatric pharmacy. Observing how research translates into clinical practice has further solidified my appreciation for the role of psychiatric pharmacists in improving patient outcomes through evidence-based interventions. Collaborating with health care professionals and researchers has underscored the importance of interdisciplinary teamwork in advancing treatment strategies. I am sincerely grateful for the support of the Epstein family, whose contributions are enabling promising research."*

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# ONWARD TO YEAR FOUR

## WE'VE BUILT THE MOMENTUM, NOW LET'S MOVE THE NEEDLE

We are in the throes of year four activity for both of our Epstein Family Collaboration programs. We are inspired by the meaningful progress made in year three and we can already see advances toward each of our strategic program goals for the coming year.

Within the Gene Therapy Program, we celebrate a major success that has progressed toward our goal of a gene therapy for individuals with genetic risk of AD: The development of a genetically modified knock-in mouse that represents the A431E Jaisco mutation is the closest model yet to the human disease. It was followed by remarkable progress in the development of a gene-specific ASO therapy that will target the mutated gene function and remove its mechanism for causing disease. Through a close partnership with Dr. De Strooper at KU Leuven in Belgium, we are advancing toward early preclinical work to better understand the safety and utility of this ASO treatment in humans.

Within the Powder for Pennies Program, we continue to make meaningful progress on the NIH-funded benfotiamine trial that seeks to repurpose the existing medication as an AD treatment.

In year three, atomoxetine was selected to advance from the P4P pipeline. It is now poised to be tested in a variety of studies, all of which will contribute to the weight of evidence to determine whether it is a safe, effective, and affordable new treatment for AD.

As we move into our fourth year, the Epstein Family Inspirational Challenge will build on past gifts and continue to seek philanthropic partnerships to support new and exciting AD research programs at UC San Diego. Your support is giving us the freedom to explore some incredibly promising leads in the quest for a cure for AD at a speed and intensity that were simply not possible before. Because of your generosity, some of the greatest minds in science and medicine can now focus their efforts squarely on the quest for solutions and a clearer understanding of this confounding disease.

Now, onward to year four!

# APPENDICES

## APPENDIX A

### SUMMARY OF FUNDED GENE THERAPY PROJECTS

| PRINCIPAL INVESTIGATOR             | DEPARTMENT / INSTITUTION                      | AMOUNT OF AWARD YEAR ONE | AMOUNT OF AWARD YEAR TWO | AMOUNT OF AWARD YEAR THREE                                                                      | PROJECT TITLE                                                                                       |
|------------------------------------|-----------------------------------------------|--------------------------|--------------------------|-------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------|
| Stephanie Cherqui                  | Pediatrics, UC San Diego                      | \$100,000                | \$250,000                | No-cost extension                                                                               | Hematopoietic stem cell gene therapy for Alzheimer's Disease                                        |
| Richard Daneman                    | Pharmacology and Neurosciences, UC San Diego  | \$225,000                | NCE                      | No-cost extension                                                                               | Molecular analysis of CNS blood vessels from Alzheimer's disease patients with the Jalisco mutation |
| Stephen Dowdy                      | Cellular and Molecular Medicine, UC San Diego | \$304,721                | \$250,000                | No-cost extension                                                                               | Delivery of prime DNA base editors to treat Alzheimer's disease                                     |
| John Ringman                       | Neurology, USC                                | \$311,824                | NCE                      | Complete                                                                                        | Neuropathology of the A431E PSEN1 mutation                                                          |
| Subhojit Roy                       | Pathology, UC San Diego                       | \$310,200                | \$414,386                | Ongoing                                                                                         | Therapeutic CRISPR editing of APP and proposed application to the Jalisco mutation                  |
| Matthew Shtrahman                  | Neurosciences, UC San Diego                   | \$177,419                | NCE                      | Complete. Outside funding received. Submitting another project to Epstein Family Collaboration. | Developing a synthetic adeno-associated virus (AAV) for engineering safer gene therapies            |
| Bart De Strooper                   | UK Dementia Research Institute, UCL           | \$268,157                | \$35,200                 | Complete. Submitting another project to Epstein Family Collaboration.                           | Characterization of a novel knock-in Psen1 A431E (Jalisco) mouse model and control                  |
| Jerome Mertens                     | Neurosciences, UC San Diego                   | N/A                      | \$150,000                | Ongoing                                                                                         | Mechanisms underlying atypical neuronal phenotypes of Latin American familial Alzheimer's disease   |
| Gabriel Leger and Elizabeth Bevins | Neurosciences, UC San Diego                   | N/A                      | \$34,214                 | No-cost extension                                                                               | Safety considerations for gene therapy in central nervous system disorders                          |
|                                    | <b>Total Funds Awarded</b>                    | <b>\$1,697,321</b>       | <b>\$1,133,800</b>       | <b>No new funds granted</b>                                                                     |                                                                                                     |

## APPENDIX B

### EPSTEIN FAMILY ALZHEIMER'S RESEARCH COLLABORATION SCIENTIFIC ADVISORY BOARD MEMBERS



**Claire Clelland**

*Assistant Professor, Department of Neurology  
UC San Francisco*

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**David Holtzman**

*Professor of Neurology  
Washington University in St. Louis  
Scientific Director  
Hope Center for Neurological Disorders*

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**Ken Kosik**

*Co-director, Neuroscience Research Institute  
UC Santa Barbara*

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**Barbara Slusher**

*Professor of Neurology, Pharmacology and Molecular Sciences,  
Psychiatry, Neuroscience, Medicine and Oncology  
Johns Hopkins School of Medicine  
Director, Johns Hopkins Drug Discovery  
Vice-Director, Pedersen Brain Science Institute*

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**Jennifer Yokoyama**

*Associate Professor, Memory and Aging Center  
UC San Francisco*

# APPENDIX C

## WORKING TEAMS

**UC San Diego**

School of Medicine  
Shiley-Marcos Alzheimer's Disease  
Research Center



UC SANTA BARBARA



## GENE THERAPY PROGRAM

### PSEN1

#### Harvard University

Rudy Tanzi

#### Ionis

Hien Zhao

#### Johns Hopkins University

Barbara Slusher

#### KU Leuven

Bart De Strooper  
Inmaculada Sanjuan Ruiz  
Lutgarde Serneels

#### n-Lorem

Tracy Cole  
Stan Crooke

#### Sanford Burnham Prebys

Anne Bang

#### University of Guadalajara

Victor Sanchez

### UC San Diego

Stephanie Cherqui  
Richard Daneman  
Utpal Das  
Steve Dowdy  
Jan Durant  
Carol Evans  
Howard Feldman  
Joe Gleeson  
Michelle Herman  
Anne Hiniker  
Alexis Komor  
Jody-Lynn Lupo  
Hiruy Meharena  
Jerome Mertens  
Priyanka Mishra  
William Mobley  
Nancy Ortega  
Judy Pa  
Carolyn Revta  
Subhojit Roy  
Johannes Schlachetzki  
Matthew Shtrahman  
James Silverman  
Ashley Watson

### UC San Francisco

Claire Clelland  
Aimee Kao  
Jennifer Yokoyama

### UC Santa Barbara

Ken Kosik

### USC

Paul Aisen  
Helena Chui  
John Ringman

### Jalisco Roundtable

Claudia Alvarado, USC  
Lilibeth Barrera, USC  
Luis E. Becerra Solano,  
University of Guadalajara  
Isaac Berumen Ocegueda,  
University of Guadalajara  
Iris Broce, UC San Diego  
Maria Carillo, Alzheimer's Association  
Carol Evans, UC San Diego  
Howard Feldman, UC San Diego

Luis Figuera, Instituto Mexicano  
del Seguro Social, Jalisco, Mexico  
Michelle Herman, UC San Diego  
Ken Kosik, UC Santa Barbara  
Francisco Lopera, University of  
Antioquia, Colombia  
Jody-Lynn Lupo, UC San Diego  
Esmeralda Matute, University of  
Guadalajara  
Jerome Mertens, Salk Institute  
Lucy Montoya, USC  
Maribel Orozco Barajas, University  
of Guadalajara  
Nancy Ortega, UC San Diego  
Judy Pa, UC San Diego  
Karina Perez Rubio, University  
of Guadalajara  
Ana Karen Preciado Baron,  
University of Guadalajara  
John Ringman, USC  
Victor Sanchez, University  
of Guadalajara  
Lon Schneider, USC  
Jennifer Yokoyama, UC San Francisco

## **P4P PROGRAM**

### **Preclinical Team**

Gene Bowman, Harvard University  
Hiroko Dodge, Harvard University  
Ana Griciuc, Harvard University  
Doo Yeon Kim, Harvard University  
Luisa Quinti, Harvard University  
Rudy Tanzi, Harvard University

### **Design Team**

Steven Arnold, Harvard University  
Vahan Aslanyan, USC  
Gary Cutter, University of Alabama  
Steve Edland, UC San Diego  
Douglas Galasko, UC San Diego  
Diane Jacobs, UC San Diego  
Jeffrey Kaye, Oregon Health &  
Science University  
Karen Messer, UC San Diego  
Judy Pa, UC San Diego  
Mary Sano, Mt. Sinai  
Lon Schneider, USC  
Rudy Tanzi, Harvard University

### **Intervention Selection Committee**

Michael Ahljanian, Harrington  
Discovery Institute  
Steven Arnold, Harvard University  
Aaron Burstein, Alzheimer's Drug  
Discovery Foundation  
Xu Chen, UC San Diego  
Doug Galasko, UC San Diego  
Larry Goldstein, UC San Diego

Barry Greenberg, Johns Hopkins  
Medical Institute  
Edward Koo, UC San Diego  
Haakon Nygaard, University of  
British Columbia  
Stacey Rizzo, University of Pittsburg  
Lon Schneider, USC  
Malú Tansey, University of Florida  
Paul Territo, Indiana University

### **Pharmaceutical Team**

Anne Bang, Sanford Burnham Prebys  
Ben Boyarko, Drexel University  
Barry Greenberg, Johns Hopkins  
University  
Bill Gerwick, UC San Diego  
Vivian Hook, UC San Diego  
Jeremiah Momper, UC San Diego  
Kevin Ryneerson, UC San Diego  
Rudy Tanzi, Harvard University

### **Pharmacoepidemiology Team**

Inma Hernandez, UC San Diego  
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Jasmine Morales, UC San Diego  
Aladdin Shadyab, UC San Diego

### **Administrative Team**

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Judy Pa, UC San Diego

### **ADCS Support Staff**

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Tatiana Herold, UC San Diego  
Michelle Herman, UC San Diego  
Leticia Hu, UC San Diego  
Jody-Lynn Lupo, UC San Diego  
Indra Perez-Hall, UC San Diego  
Carolyn Revta, UC San Diego  
James Silverman, UC San Diego



UC San Diego