13th ANNUAL DRUG DISCOVERY FOR NEURODEGENERATION CONFERENCE:
An Educational Course on Translating Research into Drugs

March 17-19, 2019 • Long Beach, CA

Presented by the Alzheimer’s Drug Discovery Foundation

www.alzdiscovery.org
#CNSDrugCourse
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LIST OF ABBREVIATIONS

• ADMET (absorption, distribution, metabolism, excretion, toxicity)
  o Absorption-ability of drug to penetrate the GI tract to the circulatory system
  o Distribution-solubility of drug in blood, binding to plasma proteins
  o Metabolism-chemical modifications of drug (e.g. by cytochrome P), amount available to reach target
  o Excretion-mechanisms of drug elimination from the body
  o Toxicity-deleterious on- or off-target effects of drug
• API-Active pharmaceutical ingredient
• AUC (Area Under the Curve)-The definite integral of the plot of drug concentration versus time in blood plasma. It is used to represent the total drug exposure over time, and can be helpful when comparing the total drug exposure from different formulations of the same drug
• BBB-Blood brain barrier
• CMC-Chemistry, manufacturing, control
• CNS-Central nervous system
• CRO-Contract research organization
• CSF-Cerebral spinal fluid
• CYP450-Cytochrome P450 enzyme family
• DMPK-(Drug Metabolism and Pharmacokinetics)- Usually a part of ADMET (Absorption, Distribution, Metabolism, and Excretion, Toxicity) studies
• FDA-Food and Drug Administration
• EC50 – Effective concentration – median concentration that causes 50% of the maximal response
• EMA-European Medicines Agency
• FBLD-Fragment based lead discovery
• FDG-PET- fludeoxyglucose positron emission tomography
• FTE-Full time employee
• FIH-First-in-humans
• GCP-Good clinical practice
• GLP-Good laboratory practice
• GMP-Good manufacturing practices (cGMP)
• HCS-High content screening
• hERG-Human ether-a-go-go gene hERG ion channel binding assay is an indicator of cardiotoxicity and predicts cardiac channel blockade through automated patch clamp.
• IC50 – Inhibition concentration – concentration that reduces activity by 50%
• IHC – International Conference on Harmonisation-A set of guidelines enacted by the regulatory agencies of several different countries and the European Union
• HTS-High throughput screening
• IND-Investigational new drug
• IRB-Institutional review board
• K_i-Inhibition constant- an indication of how potent an inhibitor is
• LC-MS/MS-Liquid chromatography coupled with tandem mass spectrometry
• LOAEL-Lowest observable adverse effect level-The lowest dose of a drug that causes an adverse (harmful) event in the test subject, animal or human.
• LOEL-Lowest observed effect level
• logP-Octanol-water partition coefficient
• MW-Molecular weight
• Magnetic Resonance Imaging (MRI)-A non-invasive imaging technique that allows the study of structural elements of tissues within the human body
• Magnetic Resonance Spectroscopy (MRS)- A non-invasive imaging technique that allows the study of certain types of metabolic activity w/in tissues
• MTD-Maximum tolerated dose-The highest dose that can be administered without the subject experiencing unacceptable side effects
• MOA-Mechanism of action-How the drug acts to affect the biological pathways in the organism that lead to its therapeutic affect
• MW-Molecular weight-The size of a molecule, for drugs, normally given in Daltons (da)
• MDR1-MDCK cells-Madin Darby Canine Kidney cells, that stably express the Multi-drug resistance protein 1 (MDR1), otherwise known as P-glycoprotein 1 (P-gp)
• NCE-New chemical entity
• NDA-New drug application
• NIA-National Institute of Aging
• NIH-National Institutes of Health
• NINDS-National Institute of Neurological Disorders and Stroke
- NOAEL-No observable adverse effect level
- NOEL-No observable effect level
- MOA-Mechanism of action
- MTD-Maximum tolerated or minimally toxic dose
- PD-Pharmacodynamics
- PK-Pharmacokinetics
- POC-Proof of concept
- PET-Positron Emission Tomography- An imaging technology that detects gamma rays emitted by certain radioactive isotopes. Radioactive isotopes can be incorporated into a number of compounds, allowing imaging of different structures and processes in the body. PET imaging is especially valuable for assessing metabolic changes and target engagement of drugs in the CNS
- P-gp- p-glycoprotein- I, which is responsible for transporting many foreign substances out of cells.
- PSA-Polar surface area
- QSAR-Quantitative structure activity relationship
- SAR-Structure-activity relationship
- SBIR-Small Business Innovation Research Award
- SPR (surface plasmon resonance)- A powerful biophysical technique used for measuring the interaction of proteins and ligands
- SWOT (Strength Weaknesses Opportunities and Threats) Analysis- An evaluation undertaken by a company to understand its position in the market
- SOP-Standard operating procedure
- STTR-Small Business Technology Transfer
- TI-Therapeutic index, ratio between the dose that produces toxic effects to the dose needed for therapeutic response.
- Toxicokinetic parameters:
  - $AUC = \text{area under the plasma concentration vs. time curve}$
  - $C_{\text{max}} = \text{max. plasma concentration}$
  - $T_{\text{max}} = \text{time to achieve maximum plasma concentration}$
  - $T_{1/2} = \text{elimination half-life}$
  - $F = \text{percent bioavailability}$
- TPP-Target product profile
ABOUT THE ALZHEIMER’S DRUG DISCOVERY FOUNDATION

CONQUERING ALZHEIMER’S THROUGH DRUG DISCOVERY

Our mission: To accelerate the discovery of drugs to prevent, treat, and cure Alzheimer’s disease, related dementias and cognitive aging.

Founded in 1998 by Co-Chairmen Leonard and Ronald Lauder, the Alzheimer’s Drug Discovery Foundation (ADDF) awards grants to leading scientists conducting breakthrough drug discovery and early clinical research. The ultimate goal of our unique organization is to support the science that will drive the development of drug therapies for Alzheimer’s.

WHAT WE’VE ACCOMPLISHED

- The ADDF has granted more than $120 million to fund more than 590 Alzheimer’s drug discovery programs and clinical trials in academic centers and biotechnology companies in 18 countries.
- In 2018, the ADDF committed $20 million to support clinical, preclinical, biomarker, and prevention programs.

OUR CONFERENCES

The Alzheimer’s Drug Discovery Foundation organizes two annual scientific conferences as part of our ongoing efforts to increase researchers’ knowledge about Alzheimer’s disease and the drug discovery process. The ADDF also plans smaller “catalyst conferences” that center on a relevant topic in the field of neurodegeneration.

Our International Conference on Alzheimer’s Drug Discovery, held each year in fall, in Jersey City, NJ, brings together academic and industry scientists intent on accelerating the development of innovative treatments for Alzheimer’s disease and related dementias. Top-level scientists in the field and the ADDF’s funded investigators present on their current research progress and stimulate discussion.

And our Drug Discovery for Neurodegeneration Conference held each year in spring, is designed as a comprehensive course on the drug discovery process, from target validation through to clinical development. This annual conference provides participants with the fundamental knowledge and resources to translate their research into new drugs to treat and prevent Alzheimer’s disease and related neurodegenerative diseases.
SCIENTIFIC ADVISORY COMMITTEE

Kurt Brunden, PhD, University of Pennsylvania

Kuldip Dave, PhD, Michael J. Fox Foundation for PD Research

Howard Fillit, MD, Alzheimer’s Drug Discovery Foundation

Lauren Friedman, PhD, Alzheimer’s Drug Discovery Foundation

Marcie Glicksman, PhD, Orig3n, Inc.

Walt Kostich, PhD, National MS Society

Frank Longo, MD, PhD, Stanford School of Medicine & Pharmacophix

Suzana Petanceska, PhD, National Institutes of Health, National Institute on Aging

Edward Spack, PhD, MedaRed, Inc.

Alessio Travaglia, PhD, Alzheimer’s Drug Discovery Foundation

D. Martin Watterson, PhD, Northwestern University

CONFERENCE DELIVERABLES

A webcast of the entire conference will be made available on the Alzheimer’s Drug Discovery Foundation Conference website (http://www.worldeventsforum.com/addf/drugdiscovery/videocasts), where you may also access a webcast of past year conferences.
WELCOME REMARKS

On behalf of the Alzheimer’s Drug Discovery Foundation (ADDF), I am pleased to welcome you to the 13th Drug Discovery for Neurodegeneration Conference: An Educational Course on Translating Research into Drugs.

Designed as a comprehensive course on the drug discovery process, from target validation through to clinical development, this annual Drug Discovery for Neurodegeneration conference provides participants with the fundamental knowledge and resources to translate their research into new drugs to treat and prevent Alzheimer’s disease and related neurodegenerative diseases.

I would like to personally thank our scientific advisory committee session chairs, and speakers for their dedication and commitment to this meeting. Your expertise in the field and willingness to share lessons learned has helped to make this course possible.

We encourage you to visit the poster presentations which showcases our talented Young Investigator Award winners. Poster presentations are scheduled for 30 minutes before the lunch breaks.

Our meeting is made possible by the generous support of our sponsors: National Institute of Aging, Merck, The National Multiple Sclerosis Society, and our exhibitors: Bachem, Charles River, InterVivo Solutions Inc., MagQu, and NanoString.

This year, we are pleased to host the meeting in Los Angeles metro area, home to around 230 colleges and universities and 43 Nobel Laureates in the sciences. The area boasts 311,226 life sciences employees, 1,570 biotech and pharma companies, $7.6 Billion venture capital attracted in 2018 (#1 in the nation), and $3.9 Billion NIH Grants attracted in 2018. We are thrilled to be able to participate in this community and bring our conference to this progressive state.

Looking forward to a stimulating and educational two and half days, we thank you for joining us!

Howard Fillit, MD
Founding Executive Director and Chief Science Officer
Alzheimer’s Drug Discovery Foundation
### PROGRAM

**SUNDAY, March 17, 2019**

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<tr>
<td>2:00pm-5:10</td>
<td>Registration</td>
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| 2:00-3:00  | **EARLY CAREER INVESTIGATORS PANEL: Job Opportunities in Drug Discovery** (Q&A after panel)  
Moderator: Alessio Travaglia, PhD—Alzheimer’s Drug Discovery Foundation  
Foundation Representatives: Walt Kostich, PhD—National MS Society and Kuldeep Dave, PhD—MJFF for PD Research  
Government Representative: Zane Martin, PhD—NIA  
Biotech Representative: Marcie Glicksman, PhD—Orig3n Inc.  
Academic Drug Discovery: Kurt Brunden, PhD—University of Pennsylvania |
| 3:00-3:50  | **How to Land the Job: Cover Letter, Resume and Interview Skills Workshop** |
| 4:00-4:20  | **Welcome & Opening Remarks: Challenges and Opportunities in Academic Drug Discovery**  
Lauren Friedman, PhD—Alzheimer’s Drug Discovery Foundation |
| 4:20-5:00  | **KEYNOTE: Increasing Efficiency, Safety, and Speed in Clinical Trials for Neurodegenerative Diseases**  
Diane Stephenson, PhD—Critical Path Institute |
| 5:00-5:10  | Q&A                                                                 |
| 5:10-7:00  | Welcoming Reception                                                  |

**MONDAY, March 18, 2019**

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<tr>
<td>7:30am-5:00pm</td>
<td>Registration</td>
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<tr>
<td>7:30am-8:30</td>
<td>Breakfast</td>
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| 8:30-8:40  | **Opening Remarks and ADDF Funding Opportunities**                     
Meriel Owen, PhD—Alzheimer’s Drug Discovery Foundation |
| 8:40-8:50  | **NIA Opportunities for Translational Research Funding**              
Zane Martin, PhD—National Institutes of Health, National Institute on Aging |
| 8:50-9:00  | **NINDS Opportunities for Translational Research Funding**            
Charles Cywin, PhD—National Institutes of Health, National Institute of Neurological Disorders and Stroke |

**Session I. EMBARKING ON A DRUG DISCOVERY CAMPAIGN**  
Chair: Marcie Glicksman, PhD—Orig3n, Inc.

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| 9:00-9:05  | **Session Overview:**  
Marcie Glicksman, PhD—Orig3n, Inc. |
| 9:05-9:25  | **What Makes a Good Drug Target? A Perspective in Neurodegenerative Disease Therapeutic Discovery**  
Samuel Hasson, PhD—Amgen Neuroscience |
| 9:25-9:35  | **Q&A**                                                             |
| 9:35-9:55  | **High Throughput Screening and Assay Development**                  
Scott Sneddon, JD, PhD—Sharp Edge Labs |
| 9:55-10:05 | **Q&A**                                                             |
| 10:05-10:25| **Ask Your Chemist Which Chemical Series Is Right for You**          
Amy Ripka, PhD—Lucy Therapeutics |
| 10:25-10:35| **Q&A**                                                             |
| 10:35-11:00| **EXHIBITOR SESSION AND BREAK**                                    |

**Session II. DRUG DISCOVERY: FROM LEAD TO CLINICAL CANDIDATE**  
Chair: D. Martin Watterson, PhD—Northwestern University

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| 11:00-11:05| **Session Overview:**  
D. Martin Watterson, PhD—Northwestern University |
| 11:05-11:25| **Secondary Pharmacology in Lead Compound Development and Risk Reduction in CNS Disease Drug Discovery**  
D. Martin Watterson, PhD—Northwestern University |
| 11:25-11:35| **Q&A**                                                             |
| 11:35-11:55| **PK/PD in Preclinical Development**                                 
Isabel Gonzalez, PhD—Drug Discovery and Development Consultants Ltd |
| 11:55am - 12:05pm | **Q&A**                                      |
| 12:05-12:25| **Predictive Disease Models for CNS Drug Development**               
Birgit Hutter-Paier, PhD—QPS |
| 12:25-12:35| **Q&A**                                                             |
| 12:35-1:00 | **YOUNG INVESTIGATOR SCHOLARSHIP POSTER SESSION**                   |
| 1:00-2:00  | LUNCH                                                               |

**Session III. ACCELERATING THERAPIES INTO CLINICAL TRIALS**  
Chair: Edward Spack, PhD—MedaRed, Inc.

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| 2:00-2:05  | **Session Overview:**  
Edward Spack, PhD—MedaRed, Inc. |
| 2:05-2:25  | **Requirements for an IND**                                          
Edward Spack, PhD—MedaRed, Inc. |
| 2:25-2:35  | **Q&A**                                                             |
| 2:35-2:55  | **The Role of Fluid Biomarkers in Clinical Trials**                  
Robert Fox, MD—Cleveland Clinic |
<p>| 2:55-3:05  | <strong>Q&amp;A</strong>                                                             |</p>
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<tr>
<td>3:05-3:25</td>
<td>The Role of PET Biomarkers in Clinical Trials</td>
<td>Adam Fleisher, MD—Avid Radiopharmaceuticals</td>
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<td>3:25-3:35</td>
<td>Q&amp;A</td>
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<tr>
<td>3:35-3:55</td>
<td>Using Wearable, Sensor, and Behavior Signals to Develop Digital Biomarkers for Neurodegenerative Diseases</td>
<td>Ernesto Ramirez, PhD—Evidation Health</td>
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<td>Q&amp;A</td>
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<td>4:05-4:25</td>
<td>EXHIBITOR SESSION and BREAK</td>
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<tr>
<td>4:25-4:45</td>
<td>Designing Early Stage Clinical Trials for Neurodegenerative Diseases</td>
<td>Suzanne Hendrix, PhD—Pentara Corporation</td>
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<td>4:45-4:55</td>
<td>Q&amp;A</td>
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<td>4:55-5:15</td>
<td>Selecting the Right Subjects for Clinical Trials in Neurodegenerative Diseases</td>
<td>Richard Margolin, MD—CNS Research Solutions LLC</td>
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<td>5:15-5:25</td>
<td>Q&amp;A</td>
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<td>5:25-5:30</td>
<td>Young Investigator Scholarship Awards Presented</td>
<td>Nicole Bjorklund, PhD—Alzheimer’s Drug Discovery Foundation</td>
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<td>5:40-6:30</td>
<td>Mentoring Session (pre-registration required)</td>
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<td>6:30</td>
<td>Networking Reception</td>
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**TUESDAY, March 19, 2019**

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<td>7:30am-8:00</td>
<td>Mentoring Session (pre-registration required)</td>
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<tr>
<td>7:30-8:20</td>
<td>Continental Breakfast</td>
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<tr>
<td>8:20-8:25</td>
<td>Welcome &amp; Opening Remarks</td>
<td>Betsy Mills, PhD—Alzheimer’s Drug Discovery Foundation</td>
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<tr>
<td>8:25-9:05</td>
<td>KEYNOTE: Therapeutic Strategies from the Plasma Proteome for Age-related Disorders</td>
<td>Steven Braithwaite, PhD—Alkahest, Inc</td>
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<td>9:05-9:15</td>
<td>Q&amp;A</td>
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**Session IV. STRATEGIES FOR CHALLENGING CNS TARGETS: CASE STUDY EXAMPLES**
Chair: Kurt Brunden, PhD—University of Pennsylvania

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<tr>
<td>9:15-9:20</td>
<td>Session Overview:</td>
<td>Kurt Brunden, PhD—University of Pennsylvania</td>
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<tr>
<td>9:20-9:40</td>
<td>Case Study on Stem Cells</td>
<td>Marcie Glickman, PhD—Orig3n Inc.</td>
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<td>9:40-9:50</td>
<td>Q&amp;A</td>
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<tr>
<td>9:50-10:10</td>
<td>Designing Combination Therapies Trials for ALS and Alzheimer’s Disease</td>
<td>Kent Leslie, MS—Amylyx Pharmaceuticals</td>
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<td>10:10-10:20</td>
<td>Q&amp;A</td>
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<td>10:20-10:40</td>
<td>EXHIBITOR SESSION and BREAK</td>
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<tr>
<td>10:40-11:00</td>
<td>NLRP3 Inflammasome Inhibitors to Arrest Neuroinflammation in CNS Diseases</td>
<td>David Miller, PhD—Inflazome</td>
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<td>11:00-11:10</td>
<td>Q&amp;A</td>
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<tr>
<td>11:10-11:30</td>
<td>The Intersection of the Brain, Immune, and Vascular Systems</td>
<td>Katerina Akassoglou, PhD—Gladderstone Institutes, University of California San Francisco</td>
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<td>11:30-11:40</td>
<td>Q&amp;A</td>
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<tr>
<td>11:40-12:00pm</td>
<td>Lessons Learned in Drug Development from an Academic and Small Biotech Perspective</td>
<td>Frank Longo, MD, PhD—Stanford University &amp; PharmatrophiX</td>
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<td>12:00-12:10</td>
<td>Q&amp;A</td>
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<td>12:10-12:40</td>
<td>YOUNG INVESTIGATOR SCHOLARSHIP POSTER SESSION</td>
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<td>12:40-1:40</td>
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**Session V. BUILDING THE INFRASTRUCTURE TO COMMERCIALIZE SCIENCE INTO PRODUCTS**
Chair: Frank Longo, MD, PhD—Stanford University & PharmatrophiX

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<td>1:40-1:45</td>
<td>Session Overview:</td>
<td>Frank Longo, MD, PhD—Stanford University &amp; PharmatrophiX</td>
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<tr>
<td>1:45-2:05</td>
<td>Working with Your Tech Transfer Office to Commercialize Technologies</td>
<td>Lukasz Kowalk, PhD—University of California, Los Angeles, Technology Development Group</td>
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<td>2:05-2:15</td>
<td>Q&amp;A</td>
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<td>2:15-2:35</td>
<td>How to Pitch an Idea to Investors with Total Confidence</td>
<td>Shobha Parthasarathi, PhD—Harrington Discovery Institute</td>
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<td>2:35-2:45</td>
<td>Q&amp;A</td>
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<td>2:45-3:05</td>
<td>The View from Here—a Corporate Venture Capital Perspective</td>
<td>Rana Al-Hallaq, PhD—Pfizer Inc.</td>
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<td>3:05-3:15</td>
<td>Q&amp;A</td>
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<tr>
<td>3:15-3:20</td>
<td>Closing Remarks</td>
<td>Lauren Friedman, PhD—Alzheimer’s Drug Discovery Foundation</td>
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Funding for this conference was made possible, in part by Cooperative Agreement 1U13AG052268-01 from the National Institute on Aging.

The views expressed in written conference materials or publications and by speakers and moderators do not necessarily reflect the official policies of the Department of Health and Human Services; nor does mention by trade names, commercial practices, or organizations imply endorsement by the U.S. Government.
2019 ADDF SCHOLARSHIP AND AWARD WINNERS

Congratulations to the 2019 ADDF Young Investigator Scholarship and Award winners! These scholarships recognize the early achievements of talented young investigators and seek to encourage the career development of the next generation of research scientists in the field of drug discovery for neurodegenerative diseases.

OUTSTANDING YOUNG INVESTIGATOR AWARDS

Chantal Ferguson—University of Massachusetts Medical School
Manoj Govindarajulu, PhD (cand.)—Auburn University
Zhibin Liang, PhD—The Salk Institute for Biological Studies
Jie (Daniel) Luo, PhD—Iowa State University
Nicole Maphis, PhD (cand.)—University of New Mexico

YOUNG INVESTIGATOR SCHOLARSHIPS

Danielle Beckman, PhD—University of California, Davis
Victor Ekuta—Beth Israel Deaconess Medical Center/Harvard Medical School
Joel Frandsen, PhD (cand.)—University of Nebraska Medical Center
Ruben Gomez-Gutierrez, PhD (cand.)—University of Texas Health Science Center at Houston
Hannah Johnson, MD, PhD—University of Arizona
Shelby Johnson, PhD (cand.)—The University of Rhode Island
Celina Liu, BS - University of Toronto
Sylvia Lombardo, PhD—Tufts University School of Medicine
Arshnous Marandi, PhD (cand.) —The University of Sheffield
Aarti Mishra, MS—University of Southern California
Kelsey Murphy, PhD (cand.)—University of Toledo
Priyanka Pinky—Auburn University
Sindhu Ramesh, PhD—Auburn University-Harrison School of Pharmacy
Paul Seidler, PhD—University of California, Los Angeles
Yuan Shang, PhD—University of Arizona
Jiahong Sun, PhD—Keck Graduate Institute
Yulong Xu, PhD—Massachusetts General Hospital, Harvard Medical School
Gabrielle Zuniga, PhD (cand.)—UT Health San Antonio
CHAIRS AND SPEAKERS

BIOS AND ABSTRACTS
DAY 1: Early Career Investigators’ Panel

Alessio Travaglia, PhD, Alzheimer’s Drug Discovery Foundation

Alessio Travaglia, PhD, is a member of the ADDF’s Scientific Affairs team. He supports the scientific portfolio through strategic review of funding proposal and program management.

Dr. Travaglia completed his postdoctoral training at New York University, where he studied mechanisms underlying memory formation during infancy. He earned a doctorate in nano science at the University of Catania (Italy), where he worked on synthesis and characterization of new potential drugs for Alzheimer's disease. Dr. Travaglia has authored numerous peer-reviewed publications, including articles in Nature Neuroscience and Journal of Neuroscience.

Walt Kostich, PhD, National MS Society

Walt Kostich, PhD, is the Director of Commercial Research at the National MS Society. He manages commercial research partnerships developed through the Fast Forward program. Fast Forward bridges the preclinical commercial funding gap by targeting funds to de-risk therapeutic development for MS. Walt also serves as a program officer for the academic research grant program, where he is responsible for grants with a clinical component.

A Neuroscientist by training, he joined the National MS Society in 2015 following a twenty-year career in the pharmaceutical industry in neuroscience drug discovery. He was most recently a Senior Research Investigator at Bristol-Myers Squibb. In that role he provided leadership for several preclinical drug discovery programs in neurologic and psychiatric disorders. Dr. Kostich earned a Masters degree from Washington University and a Doctoral degree from the University of Maryland.

Kuldip Dave, PhD, The Michael J Fox Foundation for Parkinson’s Research

Kuldip Dave, PhD, joined the Michael J Fox Foundation in 2010. As Director, Research Programs, he stays closely linked to the Parkinson’s community in order to develop an aggressive and innovative agenda for accelerating research and drug development for Parkinson’s disease.

Dr. Dave regularly meets with academic and industry scientists around the world to identify promising proposals to support, providing troubleshooting and ongoing management of projects as they go forward. He supports the Foundation’s priority interest in alpha-synuclein, an important protein linked genetically and pathologically to Parkinson’s disease. He also oversees the emerging targets portfolio to identify and validate novel targets for PD.

Dr. Dave earned an undergraduate degree in biology from Rutgers University and a PhD in Pharmacology & Physiology from the MCP-Hahnemann University. He completed his postdoctoral fellowship at a small biotechnology firm Adolor Corporation investigating opioid-receptor regulation of pain and inflammation pathways. Dr. Dave went on to work for the pharmaceutical company Wyeth managing programs within the Women’s Health Department focusing on the hormonal regulation of mood and sexual disorders. He brings this broad CNS drug-discovery experience and knowledge to the MJFF to help bring new treatments to people with Parkinson’s.

Zane Martin, PhD, National Institute on Aging

Zane Martin, PhD, is Program Director for Alzheimer’s Disease and Related Dementias Translational Research in the Division of Neuroscience at the National Institute on Aging (NIA). She oversees SBIR and STTR grants focused on drug discovery, drug development, and clinical trials aimed to ameliorate various dementias of aging. Before being hired as Program Director, Zane was a AAAS Science & Technology Policy Fellow at NIA. During that time, she was awarded the National Institutes of Health Award of Merit for helping with the development and implementation of the Alzheimer’s Disease Preclinical Efficacy Database (AlzPED). AlzPED is a publicly available data resource that aims to increase reproducibility, transparency, and translatability of preclinical Alzheimer’s drug discovery studies with the goal of improving the drug pipeline to human clinical
Dr. Martin has a PhD in Neuroscience and MS in Pharmacology from the University of Texas Medical Branch. She received postdoctoral training in the Department of Neurochemistry at the New York State Institute for Basic Research in Developmental Disabilities. Her research career has primarily focused on drug discovery strategies to combat Alzheimer’s disease and related dementias. She has investigated a wide range of therapeutic targets, including tau hyperphosphorylation, synaptic dysfunction, and amyloid aggregation.

Marcie Glicksman, PhD, Orig3n, Inc.

Marcie Glicksman, PhD, is the Chief Scientific Officer at Orig3n, Inc.; a biotechnology company that has established the world's largest uniformly consented HLA-matched cell repository to be used for cell therapy and to better understand the cellular and molecular foundations of disease. Dr. Glicksman has been in the field of drug discovery for more than 20 years.

Previously, Dr. Glicksman was Co-Director of the Laboratory for Drug Discovery in Neurodegeneration (LDDN) at Harvard Medical School and Brigham and Women’s Hospital. LDDN was focused on accelerating the identification of new therapeutics. While at LDDN, she helped spin out 8 new companies. Previously, she was at the company, Descartes Therapeutics focused on pain therapeutics and Cubist focused on novel antibiotics. Prior to these positions, she was at DuPont-Merck and at Cephalon, Inc. She has led multiple advanced programs for neurodegenerative diseases including co-inventor of CEP1347, a kinase inhibitor that has been in Phase III clinical trials. She has also been part of the team to prepare an IND for a drug for neuropathic pain that has completed Phase II clinical trials. She was elected (2005-2009) to the Board of Directors and served as Chairman of the Board for the Society for Biomolecular Sciences (now Society for Laboratory Automation and Screening). She is on the science advisory board for the Alzheimer’s Drug Discovery Foundation (ADDF) and the California Institute for Regenerative Medicine (CIRM), and reviews grants for NIH, Department of Defense, SBIR, the Michael J Fox, Alzheimer’s Association, and Rett Foundation.

Dr. Glicksman co-founded the Academic Drug Discovery Consortium to build a collaborative network for the academic drug discovery community. Dr. Glicksman co-designed and developed an annual drug discovery course supported by NIH. Dr. Glicksman received a bachelor’s degree from Brown University and a Ph.D. degree in Neuroscience from Washington University. Dr. Glicksman has over 80 publications and 16 issued patents.

Kurt Brunden, PhD, University of Pennsylvania

Kurt Brunden, PhD, is Director of Drug Discovery and a Research Professor in the Center for Neurodegenerative Disease Research (CNDR) at the University of Pennsylvania, where he oversees drug discovery programs in the areas of Alzheimer’s disease (AD), frontotemporal lobar degeneration and Parkinson’s disease.

Prior to joining CNDR in 2007, Dr. Brunden was an executive in the biotechnology sector, where he served as VP of Research at Gliatech, Inc. and later as Sr. VP of Drug Discovery at Athersys, Inc. In these positions, he initiated and managed drug discovery programs in AD, cognitive enhancement, schizophrenia, inflammation, metabolic disease and cancer. Prior to his time in industry, Dr. Brunden was an NIH-funded faculty member within the Biochemistry Department at the University of Mississippi Medical Center, with a research focus on the regulation of myelination.

He obtained his BS degree (magna cum laude) from Western Michigan University, with dual majors of Biology and Health Chemistry, and his PhD in Biochemistry from Purdue University, with a post-doctoral fellowship at the Mayo Clinic. Dr. Brunden has over 100 scientific publications, and multiple issued and pending U.S. and PCT patents.
Lauren Friedman, PhD, is the Director of Scientific Programs at the Alzheimer’s Drug Discovery Foundation (ADDF) where she supports the management of the ADDF’s drug discovery portfolio by providing scientific and strategic review of preclinical drug discovery proposals and tracking program progress.

Additionally, she manages the ADDF ACCESS program, which provides a virtual network of contract research organizations (CRO) and consultants, and offers educational resources on drug discovery and CRO selection and management. Dr. Friedman completed her postdoctoral training at Columbia University where she studied modulators of autophagy in Alzheimer’s disease. She earned a PhD in Neuroscience at the Icahn School of Medicine at Mount Sinai where she studied molecular mechanisms underlying the development and degeneration of brain circuits involved in autism and Parkinson’s disease.

Dr. Friedman completed her postdoctoral training at Columbia University, where she studied modulators of autophagy in Alzheimer’s disease. She earned a doctorate in neuroscience at the Icahn School of Medicine at Mount Sinai, where she focused on molecular mechanisms underlying the development and degeneration of brain circuits involved in autism and Parkinson’s disease. She received a bachelor’s degree in biopsychology from Tufts University. Dr. Friedman has authored numerous peer-reviewed publications and is a member of the Society for Neuroscience, New York Academy of Sciences and the Association for Women in Science.
DAY 1: KEYNOTE

Increasing Efficiency, Safety, and Speed in Clinical Trials for Neurodegenerative Diseases

Diane Stephenson, PhD, Critical Path Institute

Diane Stephenson, PhD, is a neuroscientist by training with 30 years combined experience in academic neuroscience and drug discovery. She is passionate about translational science and has a long-time dedication to the discovery of therapies to treat diseases of the nervous system. Dr. Stephenson received her undergraduate degree in Biochemistry at University of California, Santa Barbara and her PhD in Medical Neurobiology from Indiana University.

In her academic career, she focused her research on Amyotrophic Lateral Sclerosis and Alzheimer’s disease (AD), while in industry she focused on drug discovery for Alzheimer's disease, stroke, Parkinson’s disease and Autism Spectrum Disorders. From 1981-1989, Dr. Stephenson was an associate research scientist at the ALS and Neuromuscular Research Foundation in San Francisco. During her career in industry, focus included animal model characterization and evaluation of drug candidates for Neurodegenerative diseases.

Dr. Stephenson joined Critical Path Institute in 2011 and is the Executive Director of Critical Path for Parkinson’s, a multinational consortium comprised of academic experts, industry scientists, patient advocacy groups and regulatory experts collectively aimed at accelerating treatments for Parkinson’s disease.

Increasing Efficiency, Safety, and Speed in Clinical Trials for Neurodegenerative Diseases

Diane Stephenson

Critical Path Institute, Tucson, AZ, US

The lack of success in development of disease modifying therapeutic candidates for Neurodegenerative diseases have led to the recommendation of public private partnerships to tackle the challenges and share costs and risks amongst diverse stakeholders. Critical Path Institute (C-Path) is a nonprofit organization that is dedicated to accelerating drug development by delivering on the mission outlined by the U.S. Food and Drug Administration’s (FDA’s) Critical Path Initiative. Fundamental to the mission of C-Path consortia is the sharing of patient level data from longitudinal natural history studies and clinical trials, and transformation of those data into generalizable and applicable knowledge to advance therapies for specific diseases. C-Path consortia are comprised of industry members, regulatory agencies, academic experts, government agencies and patient advocacy organizations that collaborate to achieve regulatory milestones not achievable by any one organization. Diseases to date that are aligning with both European Medicines Agency and FDA enabled by C-Path’s consortia include Alzheimer’s disease, Parkinson’s disease, Multiple Sclerosis and Huntington’s disease. This presentation will focus on the progress of The Critical Path for Parkinson’s consortium launched in 2015 with the goal of achieving regulatory endorsement for biomarkers and disease progression modeling tools to streamline the efficiency of PD clinical trials. Regulatory science strategies enabled by active collaboration of stakeholders around the world promises to accelerate the approval of therapies for neurodegenerative diseases.
DAY 2: Opening Remarks and ADDF Funding Opportunities

**Meriel Owen, PhD, Alzheimer’s Drug Discovery Foundation**

Meriel Owen, PhD, is a member of the ADDF’s scientific affairs team. She supports the scientific portfolio through strategic review and program management.

Dr. Owen earned her doctorate in neuroscience from Northwestern University, where she used neuroimaging and robotic techniques to better understand the neural mechanisms underlying motor impairment after stroke. She received a MSc from University College London in clinical neuroscience and a bachelor’s degree in cognitive science from the University of California, Berkeley. Dr. Owen is also interested in the intersection between neuroscience and entrepreneurship. During her graduate studies, she completed the Kellogg Management Program for scientists and engineers, was selected as a Northwestern Leadership Fellow, and co-founded a startup company that won the Neuro Startup Challenge.

**ADDF Funding Opportunities**

Dr. Owen will present Alzheimer’s Drug Discovery Foundation’s spectrum of funding opportunities and programs.

**Zane Martin, PhD, National Institute on Aging**

Zane Martin, PhD, is Program Director for Alzheimer’s Disease and Related Dementias Translational Research in the Division of Neuroscience at the National Institute on Aging (NIA). She oversees SBIR and STTR grants focused on drug discovery, drug development, and clinical trials aimed to ameliorate various dementias of aging. Before being hired as Program Director, Zane was a AAAS Science & Technology Policy Fellow at NIA. During that time, she was awarded the National Institutes of Health Award of Merit for helping with the development and implementation of the Alzheimer’s Disease Preclinical Efficacy Database (AlzPED). AlzPED is a publicly available data resource that aims to increase reproducibility, transparency, and translatability of preclinical Alzheimer’s drug discovery studies with the goal of improving the drug pipeline to human clinical trials. Dr. Martin has a Ph.D. in Neuroscience and M.S. in Pharmacology from the University of Texas Medical Branch. She received postdoctoral training in the Department of Neurochemistry at the New York State Institute for Basic Research in Developmental Disabilities. Her research career has primarily focused on drug discovery strategies to combat Alzheimer’s disease and related dementias. She has investigated a wide range of therapeutic targets, including tau hyperphosphorylation, synaptic dysfunction, and amyloid aggregation.

**National Institute on Aging Alzheimer’s Disease Translational Research Program**

The talk will provide an overview of the NIA Translational Research Program, focusing on a number of funding opportunities and initiatives available to investigators.

**Charles Cywin, PhD, National Institute of Neurological Disorders and Stroke (NINDS)**

Charles L. Cywin, PhD, joined the National Institute of Neurological Disorders and Stroke (NINDS) in 2011 in the Office of Translational Research and currently serves as the Program Director for the Blueprint Neurotherapeutics Network (BPN) https://neuroscienceblueprint.nih.gov/bpdrugs/index.htm.

He is providing project leadership and coordination for a portfolio of neuroscience drug discovery projects ranging from early discovery to Phase I trials. He is the Contract Officer Representative for our Medicinal Chemistry, DMFP and Clinical contracts. Prior to joining NIH he spent 17 years at Boehringer Ingelheim Pharmaceuticals where he was Director, Medicinal Chemistry and was responsible for Hit to Lead and Lead Optimization programs focused on clinical candidate selection in a number of therapeutic areas. He created the lead discovery team, the parallel synthesis group and led the efforts to identify and implement new technologies, infrastructure and outsourcing in medicinal chemistry.
Dr. Cywin received his Bachelor’s degree in chemistry from Providence College, performed his doctoral training at Syracuse University focused on natural product synthesis where he was a University Fellow, and completed his postdoctoral fellowship with Professor E.J. Corey at Harvard focusing on asymmetric catalysis.

**NINDS Opportunities for Translational Research Funding**

The Division of Translational Research (DTR) at the National Institute of Neurological Disorders and Stroke (NINDS) provides many funding opportunities to accelerate leading-edge preclinical research. DTR helps academic and industry researchers create a bridge through which discoveries made in the lab lead to new and improved medical treatments and options for patient care. DTR provides funding and resources (approximately $100 million annually) through grants, cooperative agreements, and contracts to academic and industry researchers to advance early-stage neurological technologies, devices, and therapeutic programs to industry adoption (i.e., investor funding and corporate partnerships). DTR comprises seven programs that support the design, implementation, and management of research activities to critical translational challenges in neurology. The presentation will cover funding opportunities at DTR/NINDS and provide examples for best practices for converting basic research discoveries into therapeutic modalities for treatment of neurological disorders and stroke.
SESSION I: Embarking on a Drug Discovery Campaign

Chair: Marcie Glicksman, PhD—Orig3n, Inc.

What Makes a Good Drug Target? A Perspective in Neurodegenerative Disease Therapeutic Discovery
Samuel Hasson, PhD—Amgen Neuroscience

High Throughput Screening and Assay Development
Scott Sneddon, JD, PhD—Sharp Edge Labs

Ask Your Chemist Which Chemical Series Is Right for You
Amy Ripka, PhD—Lucy Therapeutics
Marcie Glicksman, PhD, Orig3n, Inc.

Marcie Glicksman, PhD, is the Chief Scientific Officer at Orig3n, Inc.; a biotechnology company that has established the world's largest uniformly consented HLA-matched cell repository to be used for cell therapy and to better understand the cellular and molecular foundations of disease.

Dr. Glicksman has been in the field of drug discovery for more than 20 years. Previously, Dr. Glicksman was Co-Director of the Laboratory for Drug Discovery in Neurodegeneration (LDDN) at Harvard Medical School and Brigham and Women’s Hospital. LDDN was focused on accelerating the identification of new therapeutics. While at LDDN, she helped spin out 8 new companies. Previously, she was at the company, Descartes Therapeutics focused on pain therapeutics and Cubist focused on novel antibiotics. Prior to these positions, she was at DuPont-Merck and at Cephalon, Inc. She has led multiple advanced programs for neurodegenerative diseases including co-inventor of CEP1347, a kinase inhibitor that has been in Phase III clinical trials. She has also been part of the team to prepare an IND for a drug for neuropathic pain that has completed Phase II clinical trials. She was elected (2005-2009) to the Board of Directors and served as Chairman of the Board for the Society for Biomolecular Sciences (now Society for Laboratory Automation and Screening). She is on the science advisory board for the Alzheimer’s Drug Discovery Foundation (ADDF) and the California Institute for Regenerative Medicine (CIRM), and reviews grants for NIH, Department of Defense, SBIR, the Michael J Fox, Alzheimer’s Association, and Rett Foundation.

Dr. Glicksman co-founded the Academic Drug Discovery Consortium to build a collaborative network for the academic drug discovery community. Dr. Glicksman co-designed and developed an annual drug discovery course supported by NIH. Dr. Glicksman received a bachelor’s degree from Brown University and a PhD degree in Neuroscience from Washington University. Dr. Glicksman has over 80 publications and 16 issued patents.
SESSION I: Embarking on a Drug Discovery Campaign

Samuel Hasson, PhD, Amgen Neuroscience

Sam Hasson, PhD, is a Senior Scientist and lab head in Amgen Neuroscience (Cambridge, Massachusetts). His lab focuses on the deconvolution of human genetics for novel target selection and employs a range of technologies to enable drug discovery. A major goal of his work is to identify modulators of complex neuroimmune phenotypes utilizing innovative assay design strategies such as high content screening.

Prior to joining Amgen Neuroscience in 2018, Sam led a group in Pfizer Neuroscience focused on Alzheimer’s disease drug discovery. As a postdoc, Sam trained with Richard Youle and Jim Inglese at the National Institutes of Health. His work centered on applying functional and chemogenomic methodologies to elucidate factors regulating mitochondrial quality control relevant to Parkinson’s disease.

What Makes a Good Drug Target?  
A Perspective in Neurodegenerative Disease Therapeutic Discovery

Samuel Hasson

Amgen Neuroscience, Cambridge, MA, USA

In therapeutic discovery and development, identification of a target is a universal starting point. Conventionally, a target has referred to a specific protein that exerts control over a pathological process. The term has been extended, however, to encompass a range of factors including nucleotides, metabolites, lipids, in addition to whole biological pathways. Additionally, phenotypic drug discovery methodologies have transformed target concepts into specific transcriptomic, epigenetic, metabolic, and/or proteomic profiles. With the goal of developing therapeutics for neurodegenerative disease, selection of targets is a multifaceted process as there are many challenges in achieving clinical success. New avenues to support target identification for diseases such as Alzheimer’s are emerging from large-scale human genetic studies and efforts to map molecular endophenotypes. Given the changing landscape, the aim is to review considerations surrounding drug targets and practical tools utilized in their selection.
SESSION I: Embarking on a Drug Discovery Campaign

Scott Sneddon, PhD, JD, Sharp Edge Labs

Scott Sneddon, PhD, JD, is President & CEO at Sharp Edge Labs, a company developing therapeutics for genetic diseases including genetic forms of neurodegeneration. Scott holds a PhD in Chemistry & Biophysics from Carnegie-Mellon University, a JD from Columbia University Law School and has over 30 years experience in the drug discovery industry, having held leadership positions at Pfizer and Genzyme. At Pfizer, Dr. Sneddon was a member of the New Leads Discovery group which made pioneering contributions to High Throughput Screening, Compound Library Acquisition and Management, Combinatorial Chemistry, Computational Medicinal Chemistry and Structure-Based Design (as an example, Lipinski’s Rules were developed in the group, as well as the CNS-based rule-set developed later). He went from Pfizer to Genzyme to help establish Genzyme’s small molecule Drug Discovery Program. There he led the Assay Development and High Throughput Screening group and implemented high-throughput functional cellular assays for primary drug screening. At Genzyme he was exposed to the genetic diseases and the many advantages they present, including clinical validation and the advantages of orphan drug development.

He continues this work at Sharp Edge Labs which employs a set of technologies to enable very sensitive cellular assays that monitor the cellular trafficking phenotype (which is disrupted in many genetic diseases). One of the most advanced programs at the company is directed at a genetic subset of Frontotemporal Dementia, and was funded by ADDF.

Dr. Sneddon has also worked as an attorney handling venture financing, licensing and ongoing strategic operation for startup and growth-phase companies in the biotechnology sector. He is a registered patent attorney licensed to practice before the US Patent and Trademark Office.

High Throughput Screening and Assay Development

Scott Sneddon

Sharp Edge Labs, Pittsburgh, PA, USA

In this presentation I will introduce some of the key concepts in High Throughput Screening with an emphasis on assay validation, assay performance monitoring, and hit validation. The purpose is to develop a statistically valid assay that truly assesses the modulation of the target of interest, and to deliver to the medicinal chemists compounds that have been evaluated to ensure that they are true-positive hits for further evaluation as medicinal chemistry candidates. Along the way I’ll direct you to assay methods and other resources. I will also briefly discuss sourcing compound libraries.
Amy Ripka, PhD, Lucy Therapeutics

Amy Ripka, PhD, has garnered more than 18 years of drug discovery and medicinal chemistry expertise ranging from big pharma to CROs. At Bristol-Myers Squibb, she was part of the teams that discovered and developed Asunaprevir and Daclatasvir, for the treatment of Hepatitis C. Later as Head of Chemistry at EnVivo/FORUM, Amy directly led the discovery and development of their PDE10 inhibitor into a Phase 1 Trial. She has also worked on compounds for GPCRs, kinases, ion channels, phosphatases, ADCs, and HDACs, some of which have also entered clinical trials.

Dr. Ripka has extensive biotech experience in multiple therapeutic areas including cardiovascular, oncology, pain and CNS having worked at several notable Boston biotechs including Infinity, HydraBiosciences, FoldRx and EnVivo/FORUM. Amy was on the Executive Team at two large life science CROs, Sai Life Sciences in India and WuXiAppTec in China. Her role was to advise and guide clients from academic labs and nascent biotechs/foundations through the preclinical drug discovery process. This included the development of chemical matter, SAR analysis, DMPK triaging as well as screening tree strategies, patenting of chemical matter as well as IND planning and engagement of VC and Foundation partnering contacts.

Most recently, Dr. Ripka founded Lucy Therapeutics, a Boston-based biotech focused on improving mitochondrial function both directly and indirectly for the treatment of neuronal impairment and neurodegenerative diseases. She chaired the prestigious Medicinal Chemistry Gordon Conference in 2012 and has been a member of the MEDI Executive Committee at the American Chemical Society since 2012. She has also been on the SABs of several national and international meetings (Frontiers in Medicinal Chemistry, National Medicinal Chemistry Symposium) and is currently on the SAB of the venture capital group Q Biomed.

Ask Your Chemist Which Chemical Series Is Right for You

Amy Ripka

Lucy Therapeutics, Boston, MA, USA

The choice of which chemical series to focus on for a CNS discovery program and how to know when to pursue or abandon it is a difficult one. My talk will develop several areas of thought in this area including the following: hit finding in the lab and in the literature, compound design for PK vs. PD target requirements, use of in silico parameters and filters as well as common misconceptions and pitfalls in the design of compounds for brain penetration, dosing route and exposure.
SESSION II: From Lead to Clinical Candidate

Chair: D. Martin Watterson, PhD—Northwestern University

Secondary Pharmacology in Lead Compound Development and Risk Reduction in CNS Disease Drug Discovery
D. Martin Watterson, PhD—Northwestern University

PK/PD in Preclinical Development
Isabel Gonzalez, PhD—Drug Discovery and Development Consultants Ltd

Predictive Disease Models for CNS Drug Development
Birgit Hutter-Paier, PhD—QPS

YOUNG INVESTIGATOR SCHOLARSHIP POSTER SESSION
Secondary Pharmacology in Lead Compound Development and Risk Reduction in CNS Disease Drug Discovery

D. Martin Watterson
Northwestern University, Chicago, IL, USA

A major goal in new drug development is to minimize risk and reduce the high cost of late stage failure, especially for early stage deliverables from small biotechs and translational science campaigns in academia. Small biotechs and academia may be societal innovation engines, but innovation is definitive high risk in a regulated industry. The challenge can be directly addressed by pushing risk reduction into earlier stages of the drug discovery and development process. A major trend, for example, is to address key pharmacogenetic liabilities and ADMET risks while the discovery campaign is still under the control of the medicinal chemistry team. The approach places an early and primary focus on drug discovery, and limits ligand optimization to only those aspects for reaching early stage Go or No Go decisions. A collateral effect is decreased synthetic chemistry costs due to focus on higher value chemistries and prioritization of chemical space exploration in the recursive medicinal chemistry refinement process. This workshop has previously recommended the early integration of what is sometimes called “secondary pharmacology” in a progressive manner, especially for novel therapeutic candidates for which there is no prior clinical art. This presentation will provide an overview and discuss selected examples of how the approach can potentially reduce risk, enhance value and facilitate more rapid entry into early stage first-in-human evaluations.

There is an increasing engagement of the secondary pharmacology approach during lead compound refinement and optimization by some pharmacuetic industry groups, although the approach is still not universally accepted. More recently, the approach has been addressed by Food and Drug Administration (FDA) scientists, thereby adding a regulatory perspective in support of the approach. The approach is based on increased leveraging of additional pharmacological screens as a campaign progresses. Initially, there is use of simpler in vitro screens. Selected in vivo screens are usually employed as the campaign moves towards best-in-class refined leads. The goal is selection of de-risked candidates for preclinical IND-enabling development. Secondary pharmacology screens employ standard operating procedures (SOPs) that can enhance future investigational new drug (IND) application packages. The SOPs are non-GxP, but mimic many of the key aspects of GxP operations. The increasing demand for such qualified assays with appropriate internal controls is now facilitated by the availability of a diverse array of lab service companies (e.g., contract research organizations, CROs) at costs competitive with internal set up, qualification and maintenance.

Overall, the portfolio of experimental outcomes from secondary pharmacology screens can profoundly impact the design of IND-enabling GLP preclinical safety pharmacology and toxicology studies and can enhance first-in-human IND applications. Further, a prevailing perspective is that dose-dependent clinical adverse drug reactions can be minimized when preclinical drug discovery and development campaigns employ secondary pharmacology analyses that complement the GxP analyses required for IND status.
Isabel Gonzalez, PhD, Drug Discovery and Development Consultants Ltd

Isabel Gonzalez, PhD, is a Director at Drug Discovery and Development Consultants Ltd, founded in 2018 by a team of consultants experienced in providing expert advice and support across all aspects of small molecule drug discovery and early development. Isabel has over 30 years of research experience, resulting in more than 50 publications.

She combines a 12 year experience in University research laboratories with over 20 years of experience in the pharmaceutical industry, in three different multinational companies (Parke-Davis/Pfizer, Novartis and GSK) and the biotechnology company Proximagen (now part of BenevolentAI), where she was Head of Biology for the last 9 years. She specializes in the areas of neurodegeneration, pain and inflammation. She has been a successful project leader for a number of programs focused on Alzheimer’s Disease.

Dr. Gonzalez is a Graduate of the Universidad Complutense, Madrid (Spain) where she studied biology and completed a PhD in Animal Physiology.

PK/PD in Preclinical Development

Isabel Gonzalez

Drug Discovery and Development Consultants Ltd, UK

A good understanding of the pharmacokinetics (PK) and pharmacodynamics (PD) of any compound aimed at clinical therapeutic use is essential in drug discovery. Pharmacodynamics is the effect that drugs have on the body; while pharmacokinetics is the study of the way in which drugs move through the body during absorption, distribution, metabolism and excretion (ADME), or the effect that the body has on the drug. The combination of PK and PD assessment will inform the route of administration, the dose, the dosing frequency, the magnitude of the effect at the site of action and ultimately the safety margins of the molecule, to provide the optimal clinical effect. The early assessment of PK profiles is essential in any drug discovery screening cascade, in order to determine the required concentration of drug to elicit a meaningful biological effect at the appropriate receptor (potentially in the brain) without affecting other targets either in the CNS or the periphery that could confound the beneficial effect or provoke unwanted side-effects (the therapeutic range). Drug discovery projects that utilise robust pharmacodynamic readouts early on are much more efficient at selecting successful drugs. In a complex therapeutic area such as Alzheimer’s Disease, the possibility of establishing pharmacodynamic models requires thinking out of the box such as not necessarily utilizing efficacy models of cognition. Examples will be discussed, highlighting the challenges and successes across different drug targets.
Birgit Hutter-Paier, PhD, QPS

Birgit Hutter-Paier, PhD, is the Senior Director and Head of Neuropharmacology at QPS Austria. She has extensive experience in neuroscience life science research and development, covering drug discovery and project management and directing multiple diverse, concurrent projects ranging from early preclinical stages to pharmacology. She has created state-of-the-art labs as well as a behavioral pharmacology testing facility.

Dr. Hutter-Paier established and managed the preclinical research group, with whom she develops transgenic and non-transgenic mouse models, mainly in Alzheimer’s and Parkinson’s as well as in rare disease research.

Dr. Hutter-Paier is working as a consultant to several Biotech companies, supervising PhD and master students and author/co-author of many peer reviewed scientific publications.

Predictive Disease Models for CNS Drug Development

Birgit Hutter-Paier

QPS, Grambach, Austria

Today’s drug development process is often challenged by a poor translation of preclinical results into clinics. To overcome this hurdle, preclinical efficacy tests need to be thoroughly planned and performed after the selected compound was tested in depth in in vitro models.

For the development of new drugs two different drug discovery approaches are commonly applied: The so-called phenotype-based approach using phenotypic screening systems or/and the target-based approach developing compounds against defined disease-related targets and there are good arguments for both approaches. For preclinical analysis of newly developed compounds rodent animal models are often used to validate positive in vitro results. Here it will therefore be discussed, for which analyses the use of animal models is appropriate. Additionally, it will be talked over how the most appropriate animal model for your compound can be selected. Some of the discussed parameters include the comparability of symptoms between patients and animal models, animals’ phenotypes and the measurability by in vivo and ex vivo methods, disease targets and pathways and the need of validation of ‘mode of action’ in more than one model. Afterwards the design of the most efficient proof-of-concept study including related parameters is reviewed and finally, best practice tips how to initiate a study will be summarized e.g. how to handle all things around your compound and other requirements for a successful study are given.

This presentation from the perspective of a CRO should give a good insight into planning and performing preclinical efficacy in vitro and in vivo studies and help taking the appropriate steps at the right time during this part of the drug discovery process.
SESSION III: Accelerating Therapies into Clinical Trials

Chair: Edward Spack, PhD—MedaRed, Inc.

Requirements for an IND
Edward Spack, PhD—MedaRed, Inc.

The Role of Fluid Biomarkers in Clinical Trials
Robert Fox, MD—Cleveland Clinic

The Role of PET Biomarkers in Clinical Trials
Adam Fleisher, MD—Avid Radiopharmaceuticals

Using Wearable, Sensor, and Behavior Signals to Develop Digital Biomarkers for Neurodegenerative Diseases
Ernesto Ramirez, PhD—Evidation Health

Designing Early Stage Clinical Trials for Neurodegenerative Diseases
Suzanne Hendrix, PhD—Pentara Corporation

Selecting the Right Subjects for Clinical Trials in Neurodegenerative Diseases
Richard Margolin, MD—CNS Research Solutions LLC
Edward Spack, PhD, MedaRed, Inc.

Edward (Ted) Spack, PhD, has over 25 years of biotech translational experience, including preclinical development of drug candidates for multiple sclerosis, nosocomial infection, and biodefense. At SRI International, Dr. Spack directed the PharmaSTART program (a consortium of SRI, Stanford, UC Berkeley, UC San Diego, and UC San Francisco), drafting preclinical development blueprints that led to several major grants and new biotech companies. He has consulted with the NIH translational core services committee and several NIH institutes on preclinical development and serves on several study sections, including the NIA Alzheimer’s Disease Drug Development review panel, the NIH Small Business Review on Drug Discovery for Aging, Neuropsychiatric and Neurological Disorders, and the Falk Trust Catalyst and Transformational Award programs. As Managing Director of an innovative partnership between the National Multiple Sclerosis Society and EMD Serono he supported innovative early stage MS drug discovery and development projects in academic labs and biotech companies. Through the California Life Sciences Institute (CLSI) FAST program and the SRI Innovation program he mentors SF Bay area and international academic and industry teams in biotech company formation and pitch decks.

Dr. Edward Spack received his doctoral degree from The Johns Hopkins University and his postdoctoral fellowship in cellular immunology at Stanford University.

Requirements for an IND
Edward Spack
MedaRed, Inc., San Francisco, CA, USA

The purpose of this presentation is to provide an overview of the preclinical activities required to prepare a drug candidate for clinical testing. Understanding this path and planning the proper studies at the earliest stages of drug lead optimization increases the probability of success. In the United States, permission to initiate a clinical trial requires submission of an Investigational New Drug (IND) application to the Food & Drug Administration (FDA). Each IND includes information on three broad areas:

1.) animal pharmacology and toxicology studies;
2.) chemistry and manufacturing processes; and
3.) clinical protocol and investigator information.

This talk will outline the preclinical activities for a monoclonal antibody and a small molecule to highlight similarities and differences in the development paths of these two drug candidate classes. Several useful tools and resources will be discussed, including FDA Guidance for Industry publications and other regulatory information. Preparing for an IND is not simply a matter of following a recipe or coloring within the lines- there are strategic considerations that should be part of the earliest planning for a drug candidate. A Target Product Profile (TPP) provides a good guideline for drug optimization and testing, defining optimal and minimal characteristics that will help the development team begin with the end in mind and build toward an acceptable goal. Coordinating parallel and dependent activities requires careful project management and “preventative worrying”.

In summary, this talk will provide an overview of the transition from drug discovery to clinical testing, a challenging stage of drug development where good ideas too often falter.
SESSION III: Accelerating Therapies into Clinical Trials

Robert Fox, MD, Cleveland Clinic

Robert Fox, MD, is Staff Neurologist at the Mellen Center for Multiple Sclerosis, Vice-Chair for Research of the Neurological Institute, Cleveland Clinic, and Professor of Medicine (Neurology) at Cleveland Clinic Lerner College of Medicine.

Dr. Fox’s current research interests focus clinical trials in multiple sclerosis, innovative MRI techniques to evaluate tissue recovery after injury and the effects of MS treatments, as well as MS patient decision-making and tolerance to risk.

He has published over 200 peer-reviewed papers, book chapters, and books. He serves as an advisor for many clinical trials, including the principal investigator of the NIH-funded SPRINT-MS phase II trial of ibudilast in progressive MS.

Fluid Biomarkers in Clinical Trials

Robert Fox

Cleveland Clinic, Cleveland, OH, USA

The ideal clinical trial fluid biomarker will measure the effect of the therapeutic intervention on a mechanistically relevant biologic pathway which has clinical relevance to the disease. That biomarker should be easily obtainable, biologically stable, and reliably measured. This goal is difficult to attain when the biologic pathway is unknown and there are few (if any) effective therapies to validate its clinical relevance. Nonetheless, significant progress has been made in fluid biomarker development. Measuring at the earliest point in the pathologic process allows evaluation of target engagement by the therapy. A drawback of this approach is the potential for the target to be irrelevant to the disease mechanism: even if the biomarker shows benefit, it may not help the disease. Alternatively, a biomarker could measure a downstream effect of disease injury. Neurofilaments are structural proteins within neurons and axons that spill into the CSF (and eventually the blood) following almost any CNS injury. Neurofilaments are biologically stable in both the body and after sampling (i.e. frozen plasma). Since neurofilaments are a general measure of CNS injury, they are attractive to use when the underlying biologic pathway is not clearly established. However, sensitive and reliable assays to measure neurofilaments have been more difficult to develop than previously recognized.

Biomarkers can be employed in other ways in clinical trials. Biomarkers can confirm the diagnosis and identify sub-types of a disease, both of which help create more homogenous patient populations. Biomarkers can identify diseases at a very early stage, when it may be more responsive to therapeutic intervention. Finally, biomarkers can identify patients with specific biologic pathway disruptions, which can help target treatments that utilize a specific mechanism of action.
Adam Fleisher, MD, is the Chief Medical Officer at Avid Radiopharmaceuticals (a wholly owned subsidiary of Eli Lilly and Co). Prior positions at Eli Lilly included Clinical Research Physician leading early and late phase global Alzheimer’s trials, and Director of Global Medical Affairs, Alzheimer’s team. From 2008-2014 he was the Director of Imaging at the Banner Alzheimer’s Institute where he managed the imaging center and cyclotron facility, the computational imaging laboratory, was a site investigator for dementia clinical trials, and cared for patients in the Stead Family memory clinic. He previously held an academic appointment as Associate Professor, Department of Neurosciences, at the University of California, San Diego (UCSD), where he served as the Medical Director of the Alzheimer’s Disease Cooperative Study from 2003-2013.

He received his medical degree from the University of Rochester School of Medicine, New York, and completed general neurology residency training at Johns Hopkins Hospital in Baltimore, Maryland. He completed a clinical and research dementia fellowship at UCSD, as well as a Master’s degree of advanced studies in clinical research administration. Dr. Fleisher has over 100 peer review publications in the field of Alzheimer’s and other neurodegenerative disorders with a focus on MRI and PET imaging, as well as clinical trials in Alzheimer’s disease.

The Role of PET Biomarkers in Clinical Trials
Adam Fleisher
Avid Radiopharmaceuticals, Philadelphia, PA, USA

Positron Emission Tomography has played an important role in clinical therapeutic trials in Alzheimer’s disease. As an endpoint measure PET imaging currently serves to identify levels of key pathologies associated with clinical disease progression, including both fibrillary amyloid plaques and tau paired helical filaments. These imaging biomarkers may allow for tracking of disease modifying therapy effects on AD pathology and have potential to function as surrogates for clinical endpoints to expedite future therapy development. In addition, PET biomarkers of AD pathology are now being used to identify appropriate clinical trial populations, ensuring that clinical trial participants meet biomarker confirmed diagnostic criteria, and have the pathologies of interest for specific therapies. These tools may also facilitate selection of patients at specific stages of disease that are most likely to benefit from the therapy being investigated in a given trial, contributing to clinical trial designs that increase likelihood of trial success. Future PET tracers that identify neuroinflammation and other key pathological states are also in development. Examples of PET tracers used in these ways to facilitate and expedite clinical trials in AD will be presented.
Ernesto Ramirez, PhD, is a Senior Data Scientist at Evidation Health, a new kind of health and measurement company that provides the world’s most innovative healthcare ecosystem players the technology and expertise they need to understand how everyday behavior and health interact.

As part of the multi-disciplinary data science team at Evidation, Dr. Ramirez’s role involves hands-on work with projects that are exploring digital biomarker development and the unique health-related signals present within large-scale longitudinal patient-generated data, primarily for clients in the biopharma space. He is also responsible for driving numerous internal and client-supported projects through ongoing collaborations with experts from industry, academic, and non-profit institutions.

Dr. Ramirez received his PhD in Public Health from the Joint Doctoral Program at San Diego State University and the University of California, San Diego.

Using Wearable, Sensor, and Behavior Signals to Develop Digital Biomarkers for Neurodegenerative Diseases

Ernesto Ramirez

Evidation Health, San Matteo, CA, USA

The lived experience of patients with neurodegenerative is difficult to measure, making it challenging to effectively address current treatments and develop new treatments to meet unmet needs. To date, reliable, scalable and objective measures remain elusive—existing approaches potentially miss behavioral or contextual factors that may be contributing to or showcasing the individual’s disease trajectory.

Digital biomarkers have the potential to revolutionize clinical trials and post-approval efficacy evaluations. In recent years, wearables and other digital devices have gained popularity with consumers, generating continuous “real life” data (e.g., Fitbit steps, smartphone geolocation, voice recordings, etc.) that, when correlated with traditional clinical information, deepens our ability to contextualize and objectively measure health. This presentation will introduce novel approaches to digital biomarker and novel endpoint development. It will highlight the work Evidation Health has done to explore potential digital biomarkers for neurodegenerative diseases and cognitive impairment.
Suzanne Hendrix, PhD, has worked for the past 26 years as a biostatistician focusing on clinical trial research in many different indications. She has extensive experience designing clinical trials, writing statistical analysis plans, running analyses, writing statistical reports, interacting with the FDA and preparing manuscripts for publication. She is experienced at communicating statistical concepts in an understandable way, and has helped develop software for graphically understanding large complex datasets.

For the past 14 years, Dr. Hendrix has specialized in statistical issues in Alzheimer’s disease such as identifying appropriate outcomes, addressing measurement issues, demonstrating disease modification and optimizing clinical trial design and analysis. She has been on multiple advisory boards and expert panels addressing current issues in Alzheimer’s disease, and has interacted with the division of Neurology products at the FDA and with the EMA through scientific advice regarding these issues. She is currently president and owner of Pentara, a company that provides data management and statistical consultation to the pharmaceutical industry, academic groups and non-profit groups, primarily supporting clinical trial design and optimization in Alzheimer’s disease. She has researched methods for discerning disease modification of treatments, and has proposed novel approaches to this problem. Dr. Hendrix is an active researcher in the Alzheimer’s disease field with over 100 publications and presentations.

Designing Early Stage Clinical Trials for Neurodegenerative Diseases

Suzanne Hendrix
Pentara Corporation Salt Lake City, UT, USA

Alzheimer’s clinical development is very challenging due to the inherent complexity of the disease, the highly heterogeneous patient population, the requirement of co-primary endpoints and the relatively slow progression, particularly in early disease stages. Careful study design can substantially improve the power of a study by reducing error with averaged values, selecting well timed visits, appropriate covariates in the model and careful outcome selection. These approaches can have as much impact as doubling the sample size of a study, reducing the chance of a false negative result.
Richard Margolin, MD, CNS Research Solutions LLC

Richard Margolin, MD, is the Founder and Principal Consultant at CNS Research Solutions LLC. CNSRS provides clinical development guidance to biotechnology companies advancing novel therapeutics to address serious CNS disorders, especially neurodegenerative diseases. The consultancy supports firms active from early Discovery through later clinical development; its expertise incudes biomarkers and translational medicine, as well as early and late stage trial design. Prior to founding CNSRS in 2018, Dr. Margolin was Executive Director, Clinical Neuroscience, and Interim Alzheimer’s Disease Clinical Head in the Internal Medicine Research Unit at Pfizer. He has a career-long focus on neurodegenerative diseases and has broad drug development experience, including leadership roles in CRO, large pharma and small biotech company settings. Following research and clinical training in nuclear medicine at the NIH and psychiatry at Vanderbilt University, he built and directed Vanderbilt’s Division of Geriatric Psychiatry and later the University of Southern California’s Consultation-Liaison Psychiatry Division. Dr. Margolin transitioned to industry R&D in 2005 as VP and Global Head, CNS, i3 Research, a leading global therapeutic CRO. Subsequently, he held positions in early clinical development/translational medicine at Schering-Plough/Merck and biomarkers at Janssen Alzheimer Immunotherapy (Johnson & Johnson). Later, he was VP, Clinical Development at CereSpir, a small biotech company developing neuroinflammation-targeting treatments for AD. Dr. Margolin received an AB degree from Harvard College and an MD degree from the University of California, Irvine. He has authored or co-authored approximately 60 scientific publications and spoken widely on challenges and opportunities in CNS discovery and clinical development.

Selecting the Right Subjects for Clinical Trials in Neurodegenerative Diseases

Richard Margolin

CNS Research Solutions LLC, Cambridge, MA, USA

Optimal conduct of clinical trials for promising neurodegenerative disease treatments is essential to the appropriate evaluation of such agents and thus to their clinical availability if shown to be beneficial. Trials performed during clinical development range from initial small-scale human studies in healthy volunteers to large, long and very expensive multinational pivotal trials designed to achieve global marketing approval. Selection of appropriate subjects is one of the most critical elements of trial conduct. This presentation will consider key subject selection factors for Phase 1-3 studies such as diagnostic certainty, medical comorbidities, the handling of genetic information, ability to provide informed consent and participate in often complex study procedures, and the role of a caregiver/informant. The importance of gender balance and racial/ethnic diversity in study samples will also be addressed. Trials for Alzheimer’s disease will be the main context for discussion, and considerations for some other conditions will also be briefly communicated.
DAY 3: Welcome and Opening Remarks

Betsy Mills, PhD, Alzheimer’s Drug Discovery Foundation

Betsy Mills, PhD, is a member of the ADDF’s Aging and Alzheimer’s Prevention program. She critically evaluates the scientific evidence regarding prospective therapies to promote brain health and/or prevent Alzheimer’s disease, and contributes to CognitiveVitality.org.

Dr. Mills came to the ADDF from the University of Michigan, where she served as the grant writing manager for a clinical laboratory specializing in neuroautoimmune diseases. She also completed a Postdoctoral fellowship at the University of Michigan, where she worked to uncover genes that could promote retina regeneration. She earned her doctorate in neuroscience at Johns Hopkins University School of Medicine, where she studied the role of glial cells in the optic nerve, and their contribution to neurodegeneration in glaucoma.

She obtained her bachelor’s degree in biology from the College of the Holy Cross. Dr. Mills has a strong passion for community outreach and has served as program presenter with the Michigan Great Lakes Chapter of the Alzheimer’s Association to promote dementia awareness.
Therapeutic Strategies from the Plasma Proteome for Age-related Disorders

Steven Braithwaite, PhD, Alkahest

Steven Braithwaite, PhD, is Chief Scientific Officer of Alkahest, developing therapeutic products for patients with age related health conditions. He also holds the position of Adjunct Associate Professor of Neurology at Rutgers University.

He founded MentiNova Inc and previously led research at Circuit Therapeutics, drug discovery at Signum Biosciences, headed the cellular neurodegeneration group at Wyeth Research/Pfizer, and was a program leader at AGY Therapeutics. In these roles he has led research and development programs through multiple therapeutic modalities across a diverse range of indications in the field of neuroscience.

Dr. Braithwaite is a graduate of the University of Cambridge, UK, received his PhD from the University of Bristol, UK and performed postdoctoral work at Stanford University. He has published extensively in the fields of basic neuroscience research, Alzheimer’s and Parkinson’s diseases.

Therapeutic Strategies from the Plasma Proteome for Age-related Disorders

Steven P. Braithwaite

Alkahest, San Carlos, CA, USA

Age-related disorders are the result of a range of genetic and environmental factors accumulating and converging to give complex pathophysiological changes. Due to the multifactorial nature of these diseases there are often multiple mechanisms affected in multiple organs of the body. Intriguing data from parabiosis and related experiments have given the enticing possibility that components of plasma can drive communication between different organs, modulating function and having the potential to reverse age-related deficits via diverse molecular and cellular mechanisms. Capitalizing on these foundations a strategy to develop therapeutics which can act in a multimodal manner has been embarked upon.

Human plasma, and fractions thereof, have been characterized for the ability to enhance function in mouse models of aging and age-related disorders. With a particular focus on cognitive functions, beneficial properties of viable plasma-derived therapeutics have been identified. Advancing our understanding of these potential therapeutics has uncovered that they can modulate multiple relevant biological mechanisms including enhancing neuronal activity, reducing neuroinflammation and enhancing neurogenesis. Our studies have demonstrated that proteins in plasma can drive these beneficial effects and that, as we age, there are significant age-dependent changes in the plasma proteome. These aging associated protein drivers of both beneficial and detrimental functions, termed chronokines, provide the molecular underpinnings of the observed activities.

Together these studies provide a novel and attractive approach to treat disorders of aging through capitalizing on the plasma proteome with strong scientific rationale. Studies with plasma fractions and targeting individual proteins within the plasma proteome are currently in clinical testing for a range of age-related disorders.
SESSION IV: Strategies for Challenging CNS Targets—Case Study Examples

Chair: Kurt Brunden, PhD—University of Pennsylvania

Case Study on Stem Cells
Marcie Glicksman, PhD—Orig3n Inc.

Designing Combination Therapies Trials for ALS and Alzheimer’s Disease
Kent Leslie, MS—Amylyx Pharmaceuticals

NLRP3 Inflammasome Inhibitors to Arrest Neuroinflammation in CNS Diseases
David Miller, PhD—Inflazome

The Intersection of the Brain, Immune, and Vascular Systems
Katerina Akassoglou, PhD—Gladstone Institutes, University of California San Francisco

Lessons Learned in Drug Development from an Academic and Small Biotech Perspective
Frank Longo, MD, PhD—Stanford University & PharmatrophiX

YOUNG INVESTIGATOR SCHOLARSHIP POSTER SESSION
Kurt Brunden, PhD, University of Pennsylvania

Kurt Brunden, PhD, is Director of Drug Discovery and a Research Professor in the Center for Neurodegenerative Disease Research (CNDR) at the University of Pennsylvania, where he oversees drug discovery programs in the areas of Alzheimer’s disease (AD), frontotemporal lobar degeneration and Parkinson’s disease.

Prior to joining CNDR in 2007, Dr. Brunden was an executive in the biotechnology sector, where he served as VP of Research at Gliatech, Inc. and later as Sr. VP of Drug Discovery at Athersys, Inc. In these positions, he initiated and managed drug discovery programs in AD, cognitive enhancement, schizophrenia, inflammation, metabolic disease and cancer. Prior to his time in industry, Dr. Brunden was an NIH-funded faculty member within the Biochemistry Department at the University of Mississippi Medical Center, with a research focus on the regulation of myelination.

He obtained his BS degree (magna cum laude) from Western Michigan University, with dual majors of Biology and Health Chemistry, and his PhD in Biochemistry from Purdue University, with a post-doctoral fellowship at the Mayo Clinic. Dr. Brunden has over 100 scientific publications, and multiple issued and pending U.S. and PCT patents.
Marcie Glicksman, PhD, Orig3n, Inc.

Marcie Glicksman, PhD, is the Chief Scientific Officer at Orig3n, Inc., a biotechnology company that has established the world’s largest uniformly consented HLA-matched cell repository to be used for cell therapy and to better understand the cellular and molecular foundations of disease.

Dr. Glicksman has been in the field of drug discovery for more than 20 years. Previously, Dr. Glicksman was Co-Director of the Laboratory for Drug Discovery in Neurodegeneration (LDDN) at Harvard Medical School and Brigham and Women’s Hospital. LDDN was focused on accelerating the identification of new therapeutics. While at LDDN, she helped spin out 8 new companies. Previously, she was at the company, Descartes Therapeutics focused on pain therapeutics and Cubist focused on novel antibiotics. Prior to these positions, she was at DuPont-Merck and at Cephalon, Inc. She has led multiple advanced programs for neurodegenerative diseases including co-inventor of CEP1347, a kinase inhibitor that has been in Phase III clinical trials. She has also been part of the team to prepare an IND for a drug for neuropathic pain that has completed Phase II clinical trials. She was elected (2005-2009) to the Board of Directors and served as Chairman of the Board for the Society for Biomolecular Sciences (now Society for Laboratory Automation and Screening).

Dr. Glicksman is on the science advisory board for the Alzheimer’s Drug Discovery Foundation (ADDF) and the California Institute for Regenerative Medicine (CIRM), and reviews grants for NIH, Department of Defense, SBIR, the Michael J Fox, Alzheimer’s Association, and Rett Foundation. Dr. Glicksman co-founded the Academic Drug Discovery Consortium to build a collaborative network for the academic drug discovery community. She co-designed and developed an annual drug discovery course supported by NIH.

Dr. Glicksman received a bachelor’s degree from Brown University and a PhD degree in Neuroscience from Washington University. Dr. Glicksman has over 80 publications and 16 issued patents.

Case Study on Stem Cells

Marcie Glicksman

Orig3n Inc., Boston, MA, USA

Neurodegenerative diseases are challenging from a drug discovery perspective with no validated targets. Access to human disease cells had been limited until the discovery of the possibility of reprogramming adult human cells to form induced pluripotent stem cells (iPSCs). iPSCs can differentiate to any cell in the body and serve multiple roles in the drug discovery process. Patient-derived iPSCs have a huge potential for understanding disease mechanisms and serving as disease models for identifying new therapeutics. They also have the potential to serve as cell therapeutics since their role in adult organs is to repair and restore function in cases of injury and disease. I will talk about these topics and provide case studies on how stem cells can be used most effectively for drug discovery.
SESSION IV: Strategies for Challenging CNS Targets—Case Study Examples

Kent Leslie, MS, Amylyx Pharmaceuticals

Kent Leslie, MSc, joined Amylyx Pharmaceuticals in 2015 and serves as its Chief Scientific Officer. He oversees the design and conduct of all preclinical scientific studies and academic collaborations, as well as seeking new therapies and applications.

Mr. Leslie received his MSc in Biotechnology from Brown University while completing research in the lab of Dr. Richard Bennett.

Prior to receiving his Master’s degree, he received Bachelor’s degrees in Biology and Economics from Brown University.

Designing Combination Therapies Trials for ALS and Alzheimer’s Disease

Kent Leslie

Amylyx Pharmaceuticals, Cambridge, MA, USA

Amylyx has developed a novel therapeutic, AMX0035, for the treatment of neurodegenerative disease. AMX0035 is a proprietary combination of two small molecule compounds, Sodium Phenylbutyrate (PB) and Tauroursodeoxycholic Acid (TUDCA), designed to promote neuronal viability through simultaneous inhibition of proteostatic and bioenergetic stresses. PB and TUDCA have been evaluated separately in in vitro and in vivo models of Alzheimer’s disease (AD), and clinical trials in amyotrophic lateral sclerosis (ALS) and Huntington’s disease. Amylyx identified a synergy between these two compounds when administered together in a particular range of ratios across multiple preclinical models.

Amylyx is currently conducting a 6-month, parallel-group, randomized, double-blind, placebo-controlled study of people with late mild cognitive impairment (MCI) or early to moderate dementia due to AD. The study will evaluate safety, tolerability, and biomarkers of molecular target engagement, AD pathology, neurodegeneration and neurophysiology that indicate AMX0035 target engagement and neurobiological effects over 24 weeks. Participants in the active treatment arm will receive 3g of PB and 1g TUDCA administered orally twice daily.

Participants will be evaluated at baseline and at week 24 with multi-sequence structural and functional MRI to assess changes in regional brain volumes (T1), functional connectivity (BOLD) and cerebrovascular pathology (FLAIR, SWI). Lumbar punctures will be performed at baseline and 24 weeks for selected CSF biomarkers including: amyloid-β1-42, tau, neurofilament light chain (NfL), and markers of mitochondrial redox, HDAC activity, neuronal injury, and neuroinflammation. Patients will be evaluated at weeks 1, 6, 12, 18, and 24 for safety, tolerability, and changes in symptoms, as measured with the ADAS-Cog 13, ADCS-ADL, and NPI.

This early phase trial is designed to evince target engagement, neurobiological effects, safety and tolerability of AMX0035 with multiple objective endpoints including, standard clinical assessments and both established and novel biomarkers associated with neurocognitive impairment. Data will help determine whether to advance AMX0035 to a larger study to establish efficacy and safety and inform choices in study design, patient characteristics and outcome measures.
SESSION IV: Strategies for Challenging CNS Targets—Case Study Examples

David Miller, PhD, Inflazome

David Miller, PhD, completed his BSc and PhD in heterocyclic chemistry at Hull University before going on to post-doc with Professor Chris Moody (Loughborough University) and then Professor Andreas Pfaltz (Max-Planck-Institut für Kohlenforschung, Mülheim an der Ruhr, Germany). His first industrial position was at Organon Laboratories in Newhouse, Scotland where he spent over 5 years becoming a chemistry and project team leader working on schizophrenia, pain and depression programs. In 2002, David moved to Cambridge with Amedis Pharmaceuticals, then Paradigm Therapeutics which was later acquired by the Takeda Pharmaceutical Company. At Takeda, David was a parallel project leader, leading the team that delivered a clinical candidate for a challenging CNS target. He became Associate Director, Medicinal Chemistry, also having responsibility for analytical chemistry and DMPK.

Dr. Miller is now Head of Medicinal Chemistry at Inflazome, a company developing targeted therapies for inflammatory diseases.

NLRP3 Inflammasome Inhibitors to Arrest Neuroinflammation in CNS Diseases

David Miller

Inflazome, Dublin, Ireland

New leads in drug discovery come from many different origins, from modification of endogenous ligands to natural products and high throughput screening of libraries of synthetic compounds. Here we describe a new program from Inflazome based on a known molecule of unknown mechanism of action. CP-456,773 (also known as CRID3 and MCC950) is a sulfonylurea that was discovered by Pfizer around 20 years ago. It was shown clinically to decrease levels of IL-1B, although how it worked was unknown. A few years later, Tschopp and colleagues discovered the NLRP3 inflammasome, and demonstrated it is a ‘danger sensor’ found in our innate immune cells and drives production of IL-1B and subsequent inflammation. Since then there have been more than 5000 publications that support NLRP3 as a core driver of chronic inflammation and in the CNS of neurodegeneration and cognitive decline. Working in areas of novel chemical space, Inflazome has been able to identify candidate drugs that engage with NLRP3 in the CNS in various disease models. The first of these new compounds is scheduled to enter clinical trials in 2019.
Katerina Akassoglou, PhD, is a Senior Investigator at the Gladstone Institutes, and a Professor in the Department of Neurology at UCSF. She has discovered new mechanisms that control the communication between the brain, immune and vascular systems and developed a new immunotherapy approach for suppressing neurodegeneration. She has pioneered studies that uncovered new roles for the blood clotting factor fibrinogen in CNS autoimmunity, trauma, and neurodegeneration.

Dr. Akassoglou has published over 85 papers in peer-reviewed journals, she is a named inventor on 7 issued patents and 9 patent applications and she is active in several national and international organizations, editorial boards, and funding agencies. Her laboratory had a long-standing funding from the NIH, the National Multiple Sclerosis Society, the American Heart Association, and the Conrad N. Hilton Foundation, and the Department of Defense. Dr. Akassoglou was awarded by the White House the Presidential Early Career Award for Scientists and Engineers, the Abel Award from ASPET, the Dana Foundation Award in Brain and Immunoimaging, a EUREKA award from NINDS, The Marilyn Hilton Award for Innovation in Multiple Sclerosis Research, the NINDS R35 Research Program Award, and the Barancik Prize for Innovation for MS research by NMSS.

The Intersection of the Brain, Immune, and Vascular Systems

Katerina Akassoglou

Gladstone Institutes, University of California San Francisco, San Francisco, CA, USA

The neurovascular interface fundamentally changes during disease due to increased blood-brain barrier (BBB) permeability and influx of blood proteins in the CNS parenchyma. The blood coagulation protein fibrinogen is deposited in the brain in a wide range of neurological diseases and traumatic injuries with BBB disruption. In my laboratory we uncovered pleiotropic roles for fibrinogen in neuroinflammation, neurodegeneration, and inhibition of repair. Furthermore, we developed novel methods for imaging BBB disruption and fibrinogen at the neurovascular interface with high-resolution in vivo two-photon microscopy and 3D volume imaging of cleared brains from patients with AD. We developed fibrin-targeting immunotherapy to selectively target proinflammatory functions of fibrin without interference with effects on clotting. Fibrin-targeting immunotherapy inhibits autoimmunity- and amyloid-driven neurotoxicity in animal models of multiple sclerosis and Alzheimer’s disease, suggesting selective fibrin targeting might be beneficial for suppressing vascular-driven neurodegeneration. These findings could be a common thread for the understanding of the etiology, mechanisms of progression, and the development of new treatments for several neurologic diseases with cerebrovascular alterations and deposition of fibrin in the CNS.
Lessons Learned in Drug Development from an Academic and Small Biotech Perspective

Frank Longo

Stanford School of Medicine, Menlo Park, CA, USA

Important drug candidates with significant novel clinical potential continue to emerge from translational programs in universities as well as the continuous emergence of small biotech companies. In both settings, there are key important lessons to learn in terms of reaching value inflection points, avoiding common pitfalls and obtaining funding. We will review the rationale, challenges and alternatives for academic-based faculty spinning a biotechnology company out of an academic program. Key areas of focus will include the following: approaches for creating technology elements that pharma partners seek (including quality and execution of intellectual property, target rationale/validation/engagement, quality and translational value of preclinical work, availability of relevant biomarkers, clinical trial plans and/or data); the basics of starting or partnering with a company; following university and conflict-of-interest policies; options for funding; elements of the virtual company model; working with CROs; large pharma partnership models and goals; and exit strategy options.
SESSION V: Building the Infrastructure to Commercialize Science into Products

Chair: Frank Longo, MD, PhD—Stanford School of Medicine & PharmatrophiX

Working with Your Tech Transfer Office to Commercialize Technologies
Lukasz Kowalik, PhD—University of California, Los Angeles, Technology Development Group

How to Pitch an Idea to Investors with Total Confidence
Shobha Parthasarathi, PhD—Harrington Discovery Institute

The View from Here - A Corporate Venture Capital Perspective
Rana Al-Hallaq, PhD—Pfizer Inc.
SESSION V: Building the Infrastructure to Commercialize Science into Products

Lukasz Kowalik, PhD, University of California, Los Angeles, Technology Development Group

Lukasz Kowalik, PhD, is a Business Development Officer at the UCLA Technology Development Group. At UCLA, Dr. Kowalik manages close to 300 technologies in the Central Nervous System, Infectious Disease and Regenerative Medicine spaces, working closely with faculty, startup founders, VCs and large companies to commercialize UCLA inventions. He dedicated his career to enabling innovation in academia and business. His personal innovation philosophy is to create productive interfaces between different disciplines, units and industries. He previously worked at Merck KGaA, Darmstadt, Germany, where he was an Innovation Facilitator and Head of the Innovation Think Tank. Prior to that he was a Technology and Business Development Consultant at Now Labs in San Francisco.

Dr. Kowalik holds a BA and MS in Chemistry from Trinity College, University of Cambridge, a PhD in Neuroscience from the Rockefeller University, and he completed his postdoctoral training in Chemical Biology at Stanford University.

Working with Your Tech Transfer Office to Commercialize Technologies

Lukasz Kowalik

University of California, Los Angeles, CA, USA

The talk will focus on explaining the basics of technology transfer, common pitfalls and misunderstanding, and suggesting best practices for working with your office.
SESSION V: Building the Infrastructure to Commercialize Science into Products

Shobha Parthasarathi, PhD, Harrington Discovery Institutes

Shobha Parthasarathi, PhD, is VP, Strategic Alliances and Business Development at Harrington Discovery Institute. She is responsible for leading, negotiating, executing transactions/agreements and managing alliances with corporate, academic and foundation partners. She is also involved in sourcing new technologies, conducting due diligence and managing Harrington Discovery Institute’s portfolio of investments in startups. Prior to joining Harrington Discovery Institute, Shobha was Senior Director, Technology and Business Development Group at the North Carolina Biotechnology Center where she evaluated emerging technologies for the development of therapeutics, diagnostics and medical devices, assessed and funded life sciences start-up companies and contributed to growth of biotechnology companies. Preceding NC Biotechnology Center, Shobha was a research scientist and manager at Millennium Pharmaceuticals (Takeda Oncology) in Cambridge, Massachusetts, where she conducted drug discovery research, evaluated technologies and developed in-house expertise for multiple therapeutic groups. She received her Ph.D. in molecular genetics and microbiology from Rutgers University/University of Medicine and Dentistry of New Jersey-Robert Wood Johnson Medical School.

How to Pitch an Idea to Investors with Total Confidence—Key Elements of a Successful Pitch to Investors

Shobha Parthasarathi

Harrington Discovery Institutes, Cleveland, OH, USA

Whether you are a rising or established scientist in academia or scientific founder/CEO of a startup company, chances are, you are seeking funding. You have just one chance to get it right. Pitching successfully to potential investors requires following well-established strategies and tips, and avoiding common pitfalls. While maintaining one’s individuality is important, there are some basic guidelines, which if followed, could dramatically improve your chances of getting funded. Learn to pitch like a pro. Examples and template pitch decks will be shared with attendees.
Rana Al-Hallaq, PhD, Pfizer

Rana Al-Hallaq, PhD is Senior Director, WWBD and Principal at Pfizer Ventures. She is responsible for identifying, evaluating, making and managing equity investments aligned with the future directions of Pfizer. She currently has responsibility for Pfizer’s investments in Actifony, Blade, Cortexyme, Imara, RefleXion Medical, and Therachon.

Prior to her current role, Dr. Al-Hallaq was a Transactionalist in Worldwide Business Development at Pfizer where she was responsible for negotiating and transacting licenses, acquisitions, and partnerships across therapeutic areas. She joined Pfizer in 2015 as an Early Candidate Clinical Lead where she advised early clinical programs in CNS to ensure alignment with business strategies. Prior to joining Pfizer, she held roles at Allergan (formerly Actavis, formerly Forest Laboratories), first in Clinical Development Psychiatry as scientific and operational lead on Phase 2 and Phase 3 studies investigating novel treatments for Major Depressive Disorder and schizophrenia, and later in Business Development where she assessed and executed on a number of acquisitions and licenses across therapeutic areas. She began her training as a research fellow at the National Institutes of Health.

Dr. Al-Hallaq received her BA in Biology from Hamilton College and holds a PhD in Neuroscience from Georgetown University Medical Center.

The View from Here - A Corporate Venture Capital Perspective

Rana Al-Hallaq

Pfizer, Cambridge, MA, USA

This presentation will provide an overview to financing discussions from the perspective of Corporate VC. I will highlight the key components of a strong pitch, what a successful interaction looks like, and common mistakes to avoid. The objective is to demystify the process and provide simple steps that would lay the foundation for a productive relationship.
**National Institutes of Health (NIH)**
NIH’s mission is to seek fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce illness and disability. The National Institute on Aging (NIA)—one of the 27 Institutes and Centers of the NIH -- has been at the forefront of the Nation’s research activities dedicated to understanding the nature of aging, supporting the health and well being of older adults, and extending healthy, active years of life for more people.

**Merck & Co.**
From developing new therapies that treat and prevent disease to helping people in need, we're committed to improving health and well-being around the world. Our vision is to make a difference in the lives of people globally through our innovative medicines, vaccines, biologic therapies, consumer care and animal health products. We aspire to be the best healthcare company in the world and are dedicated to providing leading innovations and solutions for tomorrow.

**National Multiple Sclerosis Society**
The National Multiple Sclerosis Society exists because there are people with MS. Our vision is a world free of MS. Everything we do is focused so that people affected by MS can live their best lives as we stop MS in its tracks, restore what has been lost and end MS forever. The Society is a gathering place for people with MS, their family and loved ones, healthcare providers, volunteers, donors, fundraisers, advocates, community leaders and all those that seek a world free of MS.