The 4th DRUG DISCOVERY FOR NEURODEGENERATION CONFERENCE

February 1-2, 2010 • Houston, TX

Presented by the Alzheimer's Drug Discovery Foundation

www.alzdiscovery.org
# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABOUT ADDF</td>
<td>2</td>
</tr>
<tr>
<td>WELCOME</td>
<td>3</td>
</tr>
<tr>
<td>PROGRAM</td>
<td>4</td>
</tr>
<tr>
<td>SUPPORTERS, EXHIBITORS, PARTNERS</td>
<td>5</td>
</tr>
<tr>
<td>ADDF YOUNG INVESTIGATOR AWARDS AND SCHOLARSHIPS</td>
<td>10</td>
</tr>
<tr>
<td>CHAIRS, SPEAKERS, PANELISTS – BIOS AND PRESENTATIONS</td>
<td>11</td>
</tr>
<tr>
<td>Heather Behanna, PhD, Astellas Research Institute of America</td>
<td>17</td>
</tr>
<tr>
<td>Louis Berneman, EdD, Texelerate</td>
<td>30</td>
</tr>
<tr>
<td>Neil Buckholtz, PhD, National Institute on Aging (NIA)</td>
<td>41</td>
</tr>
<tr>
<td>Joy Cavagnaro, PhD, Access BIO</td>
<td>25</td>
</tr>
<tr>
<td>Laura Chico, MS, PhD, LKC Pharma Services</td>
<td>16</td>
</tr>
<tr>
<td>Timothy Coetzee, PhD, Fast Forward LLC</td>
<td>45</td>
</tr>
<tr>
<td>Mark Creswell, PhD, IDSC Biotech Network</td>
<td>39</td>
</tr>
<tr>
<td>Kathleen Denis, PhD, Rockefeller University</td>
<td>28</td>
</tr>
<tr>
<td>Howard Fillit, MD, Alzheimer’s Drug Discovery Foundation</td>
<td>12</td>
</tr>
<tr>
<td>Marcie Glicksman, PhD, Harvard NeuroDiscovery Center</td>
<td>19</td>
</tr>
<tr>
<td>Taleen Hanania, PhD, PsychoGenics, Inc.</td>
<td>24</td>
</tr>
<tr>
<td>Frank Longo, MD, PhD, Stanford University</td>
<td>35</td>
</tr>
<tr>
<td>William Matthew, PhD, National Institute of Neurological Disorders and Stroke (NINDS)</td>
<td>42</td>
</tr>
<tr>
<td>Lisa Minor, PhD, Johnson &amp; Johnson</td>
<td>20</td>
</tr>
<tr>
<td>Colleen Niswender, PhD, Vanderbilt University</td>
<td>36</td>
</tr>
<tr>
<td>Gary Olson, PhD, Provid Pharmaceuticals, Inc.</td>
<td>37</td>
</tr>
<tr>
<td>Euan Ramsey, PhD, Centre for Drug Research and Development</td>
<td>43</td>
</tr>
<tr>
<td>Lorenzo Refolo, PhD, National Institute on Aging</td>
<td>40</td>
</tr>
<tr>
<td>Susan P. Rohrer, PhD, Merck Research Laboratories</td>
<td>32</td>
</tr>
<tr>
<td>Lee Rubin, PhD, Harvard University</td>
<td>13</td>
</tr>
<tr>
<td>Colin G. Sandercock, Perkins Coie LLP</td>
<td>29</td>
</tr>
<tr>
<td>Todd Sherer, PhD, Michael J. Fox Foundation for Parkinson’s Research</td>
<td>34</td>
</tr>
<tr>
<td>Edward Spack, PhD, Fast Forward LLC</td>
<td>26</td>
</tr>
<tr>
<td>Karen L. Steinmetz, PhD, DABT, SRI International</td>
<td>21</td>
</tr>
<tr>
<td>John S. Swartley, PhD, University of Pennsylvania</td>
<td>31</td>
</tr>
<tr>
<td>Leticia M. Toledo-Sherman, PhD, CHDI Foundation</td>
<td>45</td>
</tr>
<tr>
<td>D. Martin Watterson, PhD, Northwestern University</td>
<td>15</td>
</tr>
<tr>
<td>Nancy Wehner, PhD, Nancy Wehner Non-Clinical Consulting Services</td>
<td>23</td>
</tr>
</tbody>
</table>
ABOUT ADDF

Mission

The Alzheimer’s Drug Discovery Foundation’s (ADDF) sole mission is to rapidly accelerate the discovery and development of drugs to prevent, treat and cure Alzheimer’s disease, related dementias and cognitive aging.

ADDF was established in 2004 to expand upon programs initiated by the Institute for the Study of Aging (ISOA) Inc., a private foundation founded by the Estée Lauder family in 1998. In addition to operating as a traditional philanthropic foundation, we use a sophisticated venture philanthropy investment model to bridge the global funding gap between basic research and later-stage development, recycling any return on investment to support new research.

ADDF has an impressive track record of selecting and supporting excellent Alzheimer’s disease (AD) drug discovery research. Our scientists have created entirely new classes of drugs in development for AD, screened millions of compounds, identified hundreds of leads, executed tens of patents and licenses, and have advanced compounds into clinical trials. To date, we have awarded over $37M for more than 270 research programs and conferences worldwide.

Our Annual Conferences

ADDF organizes two international scientific conferences yearly as part of our ongoing efforts to increase researchers’ knowledge about Alzheimer’s disease and the drug discovery process. The conferences promote networking to catalyze the exchange of ideas and foster alliances that accelerate the development of new treatments for AD.

Our Annual International Conference for Alzheimer’s Drug Discovery, held in October, focuses on the discovery and development of drugs targeting Alzheimer’s disease and related dementias. The Drug Discovery for Neurodegeneration conference, held in February, is designed to educate scientists on the process of translating basic neuroscience research into innovative therapies. ADDF also plans smaller “catalyst conferences” that center around a relevant topic in the field of neurodegeneration.

www.alzdiscovery.org
On behalf of the Alzheimer's Drug Discovery Foundation (ADDF), I am pleased to welcome you to the 4th Drug Discovery for Neurodegeneration Conference!

We hope this meeting will advance the development of new drugs for neurodegenerative diseases by educating scientists on the principles of drug discovery. This conference will also give participants knowledge and relevant resources about this field of scientific investigation and address the associated barriers and challenges, including issues such as target validation, lead discovery, pre-clinical proof-of-concept and HTS.

I would like to extend my personal thanks to the conference advisors, chairs and speakers for investing their time and energy into bringing today’s event to fruition. Their dedication and commitment will make this meeting a great success.

Please do not forget to fill out the evaluation form and provide us with your input on this conference’s format, content and presentations. Your responses will help us determine whether the conference achieved its objectives and provide us with valuable feedback to develop meetings that better address the emerging needs of our drug discovery and neurodegenerative disease community.

Thank you for joining us and, once more, welcome to the 4th Drug Discovery for Neurodegeneration Conference!

Howard Fillit, MD
Executive Director
Alzheimer’s Drug Discovery Foundation

This activity has been planned and implemented in accordance with the Essential Areas and policies of the Accreditation Council for Continuing Medical Education through the joint sponsorship of PESI, LLC and Alzheimer’s Drug Discovery Foundation (PESI, LLC is accredited by the ACCME to provide continuing medical education for physicians).

Funding for this conference was made possible in part by Cooperative Agreement 2U13AG031125 from the National Institute on Aging and the National Institute of Neurological Disorders and Stroke. In addition, we are most grateful for the generous support of our sponsors: The Michael J. Fox Foundation for Parkinson’s Research, JSW Life Sciences, the CHDI Foundation, Fast Forward LLC and the Alzheimer’s Foundation of America. Our thanks go to our exhibitors: Apredica, IDCS Biotech Network, Power 3 Medical Products and SRI International. We are also grateful to our media partners: the Alzheimer Research Forum (ARF), Karger, the New York Academy of Sciences, PD Online Research, Bentham Publishers, ALS-TDI, Prize4Life, the Association for Frontotemporal Dementias, the Children’s Tumor Foundation, the Centre for Drug Research and Development, Faster Cures, the Parkinson’s Disease Foundation and Pharma Connections.

The conference presentations will be recorded and the resulting videocast will be made available on ADDF’s website (www.alzdiscovery.org). Recordings from the 2008 and 2009 editions are available on the website as well.

A conference summary and session abstracts will also be published in BMC Neurology.
**PROGRAM**

**FEBRUARY 1, 2010**

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
</tr>
</thead>
<tbody>
<tr>
<td>7:45 – 8:30</td>
<td>Registration &amp; Continental Breakfast</td>
</tr>
<tr>
<td>8:30 – 8:40</td>
<td><strong>Overview of Drug Discovery for Neurodegenerative Disease</strong> - Howard Fillit, MD, Alzheimer’s Drug Discovery Foundation</td>
</tr>
<tr>
<td>8:40 – 9:00</td>
<td><strong>Stem Cells to Accelerate Drug Discovery for Neurodegenerative Disease</strong> - Lee Rubin, PhD, Harvard University</td>
</tr>
</tbody>
</table>

**I. BASICS OF MEDICINAL CHEMISTRY**  
Chair: D. Martin Watterson, PhD, Northwestern University

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
</tr>
</thead>
<tbody>
<tr>
<td>9:00 – 9:20</td>
<td><strong>Overview: Medicinal Chemistry Rules of Thumb, Myths and Realities in CNS Drug Discovery</strong> - D. Martin Watterson, PhD, Northwestern University</td>
</tr>
<tr>
<td>9:20 – 9:30</td>
<td>Q&amp;A</td>
</tr>
<tr>
<td>9:30 – 10:00</td>
<td><strong>Designing Small Molecules with Increased Potential for CNS Penetration</strong> - Laura Chico, MS, PhD, LKC Pharma Services</td>
</tr>
<tr>
<td>10:00 – 10:10</td>
<td>Q&amp;A</td>
</tr>
<tr>
<td>10:10 – 10:40</td>
<td><strong>Synthetic Chemistry Essentials for Biologists</strong> - Heather Behanna, PhD, Astellas Research Institute of America</td>
</tr>
<tr>
<td>10:40 – 10:50</td>
<td>Q&amp;A</td>
</tr>
<tr>
<td>10:50 – 11:05</td>
<td>BREAK</td>
</tr>
</tbody>
</table>

**II. IN-VITRO TESTING: EARLY PHASES OF DRUG DISCOVERY**  
Chair: Marcie Glicksman, PhD, Harvard NeuroDiscovery Center

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
</tr>
</thead>
<tbody>
<tr>
<td>11:05 – 11:10</td>
<td>Session Overview – Marcie Glicksman, PhD, Harvard NeuroDiscovery Center</td>
</tr>
<tr>
<td>11:10 – 11:35</td>
<td><strong>Developing Relevant High-Throughput Assays for the Identification of Potential Drug Candidates</strong> - Marcie Glicksman, PhD, Harvard NeuroDiscovery Center</td>
</tr>
<tr>
<td>11:35 – 11:45</td>
<td>Q&amp;A</td>
</tr>
<tr>
<td>11:45 am – 12:10 pm</td>
<td><strong>Role of In Vitro Models in Drug Discovery for Neurodegenerative Disease</strong> - Lisa Minor, PhD, Johnson &amp; Johnson</td>
</tr>
<tr>
<td>12:10 – 12:20</td>
<td>Q&amp;A</td>
</tr>
<tr>
<td>12:20 – 1:20</td>
<td>LUNCH</td>
</tr>
<tr>
<td>1:35 – 1:45</td>
<td>Q&amp;A</td>
</tr>
</tbody>
</table>

**III. PRE-CLINICAL PROOF-OF-CONCEPT & DEVELOPMENT**  
Chair: Edward Spack, PhD, Fast Forward LLC

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
</tr>
</thead>
<tbody>
<tr>
<td>1:45 – 1:50</td>
<td>Session Overview – Edward Spack, PhD, Fast Forward LLC</td>
</tr>
<tr>
<td>1:50 – 2:15</td>
<td><strong>Requirements for a Lead Compound to Become a Clinical Candidate</strong> - Nancy Wehner, PhD, Nancy Wehner Non-Clinical Consulting Services</td>
</tr>
<tr>
<td>2:15 – 2:25</td>
<td>Q&amp;A</td>
</tr>
<tr>
<td>2:25 – 2:50</td>
<td><strong>Behavioral Testing in Neurodegenerative Disease</strong> - Taleen Hanania, PhD, PsychoGenics, Inc.</td>
</tr>
<tr>
<td>2:50 – 3:00</td>
<td>Q&amp;A</td>
</tr>
<tr>
<td>3:00 – 3:15</td>
<td>BREAK</td>
</tr>
<tr>
<td>3:15 – 3:40</td>
<td><strong>Regulatory Requirements &amp; Strategy</strong> - Joy Cavagnaro, PhD, Access BIO</td>
</tr>
<tr>
<td>3:40 – 3:50</td>
<td>Q&amp;A</td>
</tr>
<tr>
<td>3:50 – 4:00</td>
<td><strong>The Basics of Pre-Clinical Development</strong> - Edward Spack, PhD, Fast Forward LLC</td>
</tr>
<tr>
<td>4:00 – 4:10</td>
<td>Q&amp;A</td>
</tr>
<tr>
<td>4:10 – 4:20</td>
<td><strong>Closing Remarks</strong> - Howard Fillit, MD, Alzheimer’s Drug Discovery Foundation</td>
</tr>
<tr>
<td>4:20 – 6:30</td>
<td>NETWORKING RECEPTION</td>
</tr>
</tbody>
</table>
### IV. ISSUES IN TECHNOLOGY TRANSFER: INTERACTIONS AND INTELLECTUAL PROPERTY

**Chair: Kathleen Denis, PhD, Rockefeller University**

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
</tr>
</thead>
<tbody>
<tr>
<td>8:35 – 8:40</td>
<td>Session Overview – Kathleen Denis, PhD, Rockefeller University</td>
</tr>
<tr>
<td>8:40 – 9:10</td>
<td><strong>Working Effectively with Your TTO: Roles and Responsibilities</strong> - Kathleen Denis, PhD, Rockefeller University</td>
</tr>
<tr>
<td>9:10 – 9:20</td>
<td>Q&amp;A</td>
</tr>
<tr>
<td>9:20 – 9:50</td>
<td><strong>Intellectual Property 101: A Primer For Investigators</strong> - Colin G. Sandecock, Perkins Coie LLP</td>
</tr>
<tr>
<td>9:50 – 10:00</td>
<td>Q&amp;A</td>
</tr>
<tr>
<td>10:00 – 10:30</td>
<td><strong>Creating Relationships with Industry: Consulting, Research, MTA’s &amp; Patent Licensing</strong> - Louis Berneman, EdD, Texelerate</td>
</tr>
<tr>
<td>10:30 – 10:40</td>
<td>Q&amp;A</td>
</tr>
<tr>
<td>10:40 – 10:55</td>
<td>BREAK</td>
</tr>
<tr>
<td>10:55 – 11:25</td>
<td><strong>Should You start a Biotechnology Company?</strong> - John S. Swartley, PhD, University of Pennsylvania</td>
</tr>
<tr>
<td>11:25 – 11:35</td>
<td>Q&amp;A</td>
</tr>
<tr>
<td>11:35 am – 12:00 pm</td>
<td><strong>What Companies Look for in a Licensing Partner</strong> - Susan P. Rohrer, PhD, Merck Research Laboratories</td>
</tr>
<tr>
<td>12:00 – 12:10</td>
<td>Q&amp;A</td>
</tr>
<tr>
<td>12:10 – 1:00</td>
<td>LUNCH</td>
</tr>
</tbody>
</table>

### V. CASE STUDIES

**Chair: Todd Sherer, PhD, Michael J. Fox Foundation for Parkinson’s Research**

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
</tr>
</thead>
<tbody>
<tr>
<td>1:00 – 1:10</td>
<td>Session Overview – Todd Sherer, PhD, Michael J. Fox Foundation for Parkinson’s Research</td>
</tr>
<tr>
<td>1:10 – 2:10</td>
<td><strong>Track 1: Target Validation to Lead Optimization AD Case Study</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Moderator and Presenter:</strong> Frank Longo, MD, PhD, Stanford University</td>
</tr>
<tr>
<td></td>
<td>Panel Members: D. Martin Watterson, PhD</td>
</tr>
<tr>
<td></td>
<td>Marcie Glicksman, PhD</td>
</tr>
<tr>
<td></td>
<td>Howard Fillit, MD</td>
</tr>
</tbody>
</table>

### VI. RESOURCES AND SERVICES FOR ADVANCING DRUG DISCOVERY

**Chair: Lorenzo Refolo, PhD, National Institute on Aging**

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
</tr>
</thead>
<tbody>
<tr>
<td>2:10 – 2:15</td>
<td>Session Overview – Lorenzo Refolo, PhD, NIA</td>
</tr>
<tr>
<td>2:15 – 2:40</td>
<td><strong>How to Outsource Early Drug Discovery</strong> – Mark Creswell, PhD, IDSC Biotech Network</td>
</tr>
<tr>
<td>2:40 – 2:50</td>
<td>Q&amp;A</td>
</tr>
<tr>
<td>2:50 – 3:15</td>
<td><strong>Resources at the National Institute of Health</strong> – William Matthew, PhD, National Institute on Neurological Disorders and Stroke; Neil Buckholtz, PhD, National Institute on Aging</td>
</tr>
<tr>
<td>3:15 – 3:25</td>
<td>Q&amp;A</td>
</tr>
<tr>
<td>3:25 – 3:50</td>
<td><strong>Types of Academic Drug Discovery Programs</strong> – Euan Ramsey, PhD, Centre for Drug Research and Development</td>
</tr>
<tr>
<td>3:50 – 4:00</td>
<td>Q&amp;A</td>
</tr>
<tr>
<td>4:00 – 4:30</td>
<td><strong>Foundation Resources: Venture Philanthropy</strong> – Howard Fillit, PhD, Alzheimer’s Drug Discovery Foundation; <strong>Other Philanthropic Approaches</strong> – Timothy Coetzee, PhD, Fast Forward LLC; <strong>Funding and other challenges for rare diseases</strong> – Leticia M. Toledo-Sherman, PhD, CHDI Foundation</td>
</tr>
<tr>
<td>4:30 – 4:40</td>
<td>Q&amp;A</td>
</tr>
<tr>
<td>4:40 – 4:50</td>
<td><strong>Closing Remarks</strong> – Howard Fillit, MD, Alzheimer’s Drug Discovery Foundation</td>
</tr>
</tbody>
</table>
SPONSORS, EXHIBITORS AND MEDIA PARTNERS

Funding for this conference was made possible in part by Cooperative Agreement 2U13AG031125 from the National Institute on Aging and the National Institute of Neurological Disorders and Stroke.

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.

GENERAL MEETING SPONSORS

BRONZE:

[Logos of sponsors]

[Logos of sponsors]
Congratulations to all the winners of the 2010 Outstanding Young Investigator Awards and the ADDF Young Investigator Scholarships! These highly prestigious Awards and Scholarships recognize the early achievements of talented young investigators and seek to encourage the career development of the next generation of research scientists.

ADDf OUTSTANDING YOUNG INVESTIGATOR AWARDS

The 2010 ADDF Outstanding Young Investigator Awards are presented to:

- **Rocco Gogliotti, BS**, Northwestern University/Children's Memorial Hospital
- **Jungsu Kim, PhD**, Washington University
- **Lamin Han Mbye, PhD**, Harvard Medical School/Massachusetts General Hospital
- **Rebecca Rosen, PhD**, Emory University
- **Kim Wilkinson, PhD**, Harvard NeuroDiscovery Center

ADDf YOUNG INVESTIGATOR SCHOLARSHIPS

The winners of the 2009 ADDF Young Investigator Scholarships are:

- **Sabah Ansar, PhD**, University of Kansas
- **Karthik Arumugam, MPharm**, Manipal University
- **Bhavani Shankara Bagepally, MBBS, PhD**, NIMH India
- **Joshua Bagley, University of California, San Francisco**
- **Irina Epifantseva, MS**, LA Biomedical Research Institute - UCLA Medical Center
- **Amos Fatokun, PhD**, Johns Hopkins University School of Medicine
- **Ruchi Gupta, PhD**, Rockefeller University
- **Rima Hajjo, PhD (c)**, UNC-Chapel Hill
- **Malik Hellal, PhD**, Harvard NeuroDiscovery Center
- **Kristen Henkins, UCLA**
- **Ali Jawaid, MD**, Baylor College of Medicine
- **Neeraj Kapoor, PhD**, Rockefeller University
- **Hyun Jin Kim, Case Western Reserve University**
- **Lakshmi Devasena Kuravi, PhD**, University of Illinois at Chicago
- **Huiyuan Li, PhD**, University of California at Los Angeles
- **Anil Mantha, PhD**, University of Texas Medical Branch at Galveston
- **Suneet Mehrotra, PhD**, Loyola University Medical Center
- **Abhishek Mukherjee, Harvard NeuroDiscovery Centre**
- **John Panos, MA**, Western Michigan University
- **Dariusz Pytel, PhD**, University of Pennsylvania and Harvard NeuroDiscovery Center
- **Sadashiv Shiva, Ph.D., Centre for Medicinal Plants Research**
- **Kelvin (Kaihua) Sun, PhD**, Cornell University
- **Debjani Tripathy, PhD**, Texas Tech University Health Science Center
- **Lawren VandeVrede, University of Illinois at Chicago-COM**
We don’t just fund research.
We fund results.

Current funding opportunities

**Rapid Response Innovation Awards**
Fast funding for great ideas with no deadline

**Target Validation**
Next deadline: June 1, 2010
Funding to demonstrate whether modulating a novel biological target has an impact in a relevant model of Parkinson’s

**Therapeutics Development Initiative**
Next deadline: June 1, 2010
Industry-exclusive support for pre-clinical Parkinson’s therapeutic development

Instant communication to move your work forward

Become a member, reap the benefits
- Pose questions and answers
- Find collaborators
- Get your work noticed
- Connect with funders

Membership is free. Participation is priceless.
Sign up at [www.pdonlineresearch.org](http://www.pdonlineresearch.org)

---

**FasterCures**
The Center for Accelerating Medical Solutions

FasterCures is an organization committed to saving lives by saving time in the research, discovery, and development of new treatments for deadly and debilitating diseases.

It is a nonprofit think tank and catalyst for action that works across sectors and diseases to transform the medical research enterprise. FasterCures, a center of the Milken Institute, is nonpartisan and independent of interest groups.

Get involved:

[FasterCures.org](http://FasterCures.org)
[SMARTBRIEF](http://SMARTBRIEF)
[FasterCuresBlog](http://FasterCuresBlog)

---

The 4th Drug Discovery for Neurodegeneration Conference, Houston, TX
CNS & Neurological Disorders
Drug Targets

Impact Factor: 4.69
www.bentham.org/cnsnddt

Leading review journal in Neuroscience

- Publishing Peer Reviewed Articles Rapidly
- Available in Print & Online
- Abstracted in MEDLINE, BIOSIS, Chemical Abstracts and more...
- FREE Online Trials for Institutions
- FREE Sample Issues Available on Website

www.bentham.org/cnsnddt

Central Nervous System Agents
in Medicinal Chemistry

Impact Factor: 3.57
www.bentham.org/cnramc

Current Neurovascular Research
Eliciting Neurological and Vascular Disease Mechanisms for Basic and Clinical Discovery

www.bentham.org/cnr

Recent Patents on CNS Drug Discovery

www.bentham.org/rpcn

To Attendees of 4th Drug Discovery for Neurodegeneration Conference
Valid until March 15th, 2010
To apply, refer discount code “DDNC10” and email at: marketing@bentham.org

20% Subscription Discount

Publishers of Quality Research
CHAIR, SPEAKER, PANELIST BIOS AND ABSTRACTS
Howard Fillit, MD, Alzheimer’s Drug Discovery Foundation

Dr. Fillit, a geriatrician and neuroscientist, is the founding Executive Director of the Institute for the Study of Aging, Inc. as well as its affiliated public charity the Alzheimer’s Drug Discovery Foundation, both of which are dedicated to funding drug discovery for Alzheimer’s disease. Dr. Fillit was formally the Corporate Medical Director for Medicare at NYLCare Health Plans (now a division of Aetna, Inc.), where he was responsible for over 125,000 Medicare members in eight regional markets. He has also had a distinguished academic career at The Rockefeller University and The Mount Sinai Medical Center (NY), where he is currently a clinical professor of geriatrics and medicine and a professor of neurobiology.

Dr. Fillit has received many awards and honors, including the Rita Hayworth Award for Lifetime Achievement from the Alzheimer’s Association. He is a fellow of the American Geriatrics Society, the American College of Physicians, the Gerontological Society of America, and the New York Academy of Medicine. Dr. Fillit is the author or co-author of more than 250 publications, including the leading international Textbook of Geriatric Medicine and Gerontology. He served as a consultant to a variety of individuals, managed care organizations, health care systems, and pharmaceutical and biotechnology companies.

An Overview of Drug Discovery for Neurodegenerative Disease

The scope of discovery, development and delivery of a drug for neurodegenerative disease is often under-appreciated by those who have not been directly involved in pre-clinical research or clinical development. Success in this field requires an extremely broad and coordinated multidisciplinary effort. Impediments to success can arise from a large number of sources. A discussion of these challenges within a context of current targets for treating neurodegenerative diseases will be presented.
Lee Rubin, PhD, Harvard University

Dr. Rubin received his Ph.D. in Neuroscience from The Rockefeller University and completed postdoctoral fellowships in Pharmacology from Harvard Medical School and in Neurobiology from Stanford University School of Medicine. He was then an Assistant and Associate Professor at Rockefeller University. Subsequently, he joined Athena Neurosciences (now Elan Pharmaceuticals) as head of their blood-brain barrier (BBB) and multiple sclerosis groups, ultimately initiating a project to discover an antibody that blocks lymphocyte trafficking across the BBB. This work successfully identified an anti-integrin antibody, now known as Tysabri, which has been approved for treatment of multiple sclerosis and more recently, for Crohn’s disease. After leaving Athena, he became Professor of Anatomy and Developmental Biology at University College London and Director of the Eisai London Laboratory of Neurodegenerative Disease. In 1998, he returned to Boston as Chief Scientific Officer of Ontogeny, Inc (now Curis, Inc) a biotechnology company in Cambridge, MA, founded by Dr. Douglas Melton, a well-known stem cell and developmental biologist. Dr. Rubin’s work there centered on the hedgehog (Hh) pathway and its involvement in cancer and neurodegenerative disease. Potent small molecule Hh antagonists were identified and partnered with Genentech for clinical development. Two INDs were submitted, and one phase II study is currently underway for an orally available Hh antagonist used to treat solid tumors. In 2006, Dr. Rubin moved to the Harvard University Stem Cell Institute as Director of Translational Medicine and is a member of the new Department of Stem Cell and Regenerative Biology. Much of his effort there is devoted to identifying therapeutics for orphan neural disorders such as Spinal Muscular Atrophy, ALS, HD and MS using new kinds of stem cell-based screens. He also directs a group that carries out a broad set of stem cell differentiation assays with numerous other members of the Harvard Stem Cell Institute.

Stem Cells and Drug Discovery for Neurodegenerative Disease

Experiments designed to understand the pathological basis of disease and to discover effective therapeutics often rely on having suitable cell culture systems. In the last few years, many academic and pharmaceutical scientists have decided that a stem cell-based approach may be utilized productively to create just these types of systems. A characteristic of many of the well-known neurodegenerative diseases is that they tend to affect some types of neurons more than others, and it has been relatively difficult to understand how these diseases acquire this selectivity. For example, motor neurons, but not spinal cord interneurons, die in the genetic forms of both Amyotrophic Lateral Sclerosis and Spinal Muscular Atrophy. Even in a more widespread degenerative disease, such as Alzheimer’s Disease, there are some neuronal types, such as forebrain cholinergic neurons, that are much more affected than others, such as those in the cerebellum. Stem-like cells (induced pluripotent stem cells) can now be derived from individuals –even from many individuals -- that have particular neurodegenerative diseases. In principle, these cells can then be re-differentiated into the sensitive and insensitive neuronal populations. Those cells can then be used to further insight concerning the cellular and molecular changes that accompany the disease. They also can be used to configure screens to find drug candidates that slow the rate of development of the disease in the cells that are most affected by it. I will describe methods to produce various kinds of neurons from ES cells and to use them to establish predictive cell culture disease models.
The goal of this session is to review fundamentals of medicinal chemistry relevant to drug discovery for CNS disorders. Although the focus is on small molecule drugs, due to the extensive state of knowledge, many of the fundamental concepts are also relevant to peptide and protein therapeutics. The attendee should leave the session with a practical, working familiarity with contemporary approaches and key issues that should be considered by interdisciplinary teams as they take hits to lead compounds, and lead compounds to candidate therapeutics.

Medicinal Chemistry Rules of Thumb, Myths and Realities in CNS Drug Discovery
D. Martin Watterson, PhD, Northwestern University

Designing Small Molecules with Increased Potential for CNS Penetration
Laura Chico, MS, PhD, LKC Pharma Services

Synthetic Chemistry Essentials for Biologists
Heather Behanna, PhD, Astellas Research Institute of America
D. Martin Watterson, PhD, Northwestern University

Dr. Watterson holds the John G. Searle Endowed Chair in Molecular Biology and Biochemistry at Northwestern University and is Professor of Molecular Pharmacology and Biological Chemistry at the Northwestern University Feinberg School of Medicine in Chicago. He has published extensively in the areas of drug discovery, signal transduction, structural biology, pharmacology and medicinal chemistry, and has developed diagnostics and novel small molecule therapeutic candidates licensed to industry. Dr. Watterson has worked successfully with major pharmaceutical and biotech companies in diverse areas of drug discovery, participated actively in bringing new drug candidates to clinical development, served on the Board of Directors for technology companies, and assisted colleagues and various government agencies with science and technology development. Related to the latter advisory and administrative experience, he founded the Drug Discovery Program at Northwestern University’s Feinberg School of Medicine in 1995, which later became a university-wide Center. The Center investigators have a productive record of successfully shepherding novel compounds from initial synthesis through the discovery and development steps necessary to reduce risk, thereby allowing unique compounds with firm intellectual property positions to be taken by industry into product development. In 2008, the 31 Center investigators filed 41 invention disclosures and had research funding income greater than $105,000,000. Dr. Watterson’s doctoral training in chemical sciences was at Emory University, followed by postdoctoral training in bioorganic chemistry at Duke University Medical Center where he was supported by a National Research Service Award from the National Institutes of Health. Dr. Watterson held faculty positions at The Rockefeller University, where he was an Andrew Mellon Fellow, and at Vanderbilt University Medical Center, where he was Professor of Pharmacology and Howard Hughes Investigator, before moving to Northwestern University. At Northwestern, he has served as a Department Chair, Drug Discovery Program Director, and Co-Director of a University Center.

Medicinal Chemistry Rules of Thumb, Myths and Realities in CNS Drug Discovery

This presentation will provide an introduction to the drug discovery and drug development continuum from the perspective of medicinal chemistry goals, and scientific background to concepts that will be covered in more detail by the two main lectures in this session.
Laura Chico, PhD, LKC Pharma Services

Dr. Chico is the founder and President of LKC Pharma Services, a privately held scientific consulting firm, and holds a faculty position at Northwestern University Feinberg School of Medicine. Dr. Chico has worked successfully with teams of chemists and biologists in the improvement of efficiencies for early stage small molecule drug discovery processes, participated in bringing novel small molecule drugs into late stage drug development for CNS disorders and facilitated the discovery of new classes of small molecule drug candidates for cancer therapeutics. Dr. Chico’s experience also includes conducting investigations of signal transduction pathways contributing to therapeutic resistance to cancer therapies and working with bioinformatics and information technology professionals to leverage public data repositories for the discovery of novel diagnostic tools. LKC Pharma Services uses its proprietary computational algorithms and diverse experience at the interface of pharmacological and chemical sciences to facilitate client Go/NoGo decisions or project proritizations in drug discovery and early stage product development, rendering significant time and cost savings in the short term and major risk reduction at later stages. Dr. Chico received her Ph.D. at Northwestern University in the areas of computational biology and pharmacological sciences. While at Northwestern University, Dr. Chico was the recipient of a National Institutes of Health traineeship and the only student to complete a novel combined training program in engineering and life sciences. Her prior accomplishments in the biotechnology and life sciences industries include successful project management experience in a production environment and advancing software deliverables from concept to deployment.

Designing Small Molecules with Increased Potential for CNS Penetration

Establishing effective drug concentrations in the brain represents a major challenge in the development of novel central nervous system (CNS) therapeutics. The magnitude of poor CNS bioavailability is exemplified by estimates that 98% of small molecule drugs poorly penetrate the blood-brain barrier (BBB). Further, cytochrome P450 (CYP)-mediated metabolism limits brain uptake by reducing systemic drug bioavailability and pharmacodynamics. The biological processes underlying the in vivo fate of a small molecule drug are significantly influenced by the drug’s physical characteristics, called molecular properties. Molecular properties represent the traits that help make a chemical a drug. Statistical analyses of molecular properties have been helpful in identifying trends associated with oral bioavailability, yet CNS focused drug discovery requires a more stringent set of parameters and considerations. This presentation will define and highlight strategies for designing compounds with a higher potential for CNS penetration using discrete case studies.
Heather Behanna, PhD, Astellas Research Institute of America

Dr. Behanna is a Senior Scientist at the Astellas Research Institute of America (ARIA). ARIA is involved in early stage drug discovery in the fields of transplantation and CNS disorders. She received her PhD in organic chemistry from the Dept of Chemistry at Northwestern University, and did postdoctoral training at the Feinberg School of Medicine in pharmaceutical chemistry. Her past research has included novel compound discovery chemistry as well as developing a synthetic scheme for large scale production of clinical grade material under FDA regulated conditions.

---

**Synthetic Chemistry Essentials for Biologists**

There are a number of different approaches used in small molecule drug discovery for finding initial compounds ("hits") as starting points for medicinal chemistry refinement. However, there is little variance at the subsequent refinement steps in the approaches used for medicinal chemistry refinement of hits into lead compounds, and further refinement of lead compounds into candidates for clinical development. Therefore, a set of general principles has evolved regardless of the planned disease indication or use of the resultant drugs. These general chemical principles are involved not only in choosing which hit to refine for development, but are also in play in the construction and modification of libraries. These chemical principles will be defined to help understand how to have the strongest chance for success in a drug discovery campaign. Different strategies and rationale for finding hits and the requirements that make a hit viable for further development will also be discussed. The presentation will be oriented for a biology audience and provide an overview of the chemist’s toolbox for medicinal chemistry refinements.
A key component of the development of new therapeutic agents is the identification of molecules that can serve as initial lead structures on which drug discovery programs can be built. High-throughput screening of large collections of drug-like molecules for modulatory activity in disease-relevant assays is an important means to discovering these lead molecules. This session will first address strategies for the development of assays that are suitable for high-throughput screening and then strategies for secondary assays to validate the primary screening results. Most drug development efforts fail due to toxicity and ADME (absorption, distribution, metabolism and excretion) properties. This session will end with a presentation on technology used for in vitro toxicity and ADME testing.
Marcie Glicksman is Co-Director of Laboratory for Drug Discovery in Neurodegeneration (LDDN) as part of the Harvard NeuroDiscovery Center. Dr. Glicksman has extensive experience in assay development, high throughput screening, chemical databases, animal pharmacology and preclinical development. Her bachelor’s degree is from Brown University and Ph.D. from Washington University. Before joining LDDN in 2004, she had been in industry for thirteen years. Previously, she was at the start-up company, Descartes Therapeutics focused on imaging techniques.

Before this, she was Director of Leads Discovery at Cubist. Before this, she was at DuPont-Merck and at Cephalon, Inc. She led the assay development and screening program for a cell-based protease project, and numerous G-protein coupled receptors, many of which were continued when Bristol Myers Squibb bought DuPont Pharmaceuticals. At Cephalon, she was co-inventor of CEP1347, a neuroprotective agent directed at a novel kinase, currently in Phase III clinical trials. She was a board member of the non-profit drug discovery organization Society for Biomolecular Sciences and served as the Chairman for two years and continues to be active in the organization.

Developing Relevant High-Throughput Assays for the Identification of Potential Drug Candidates

There are two critical steps in the development of an assay for high throughput screening (HTS). First is the selection of the assay type that must closely model the science known about the target. This target can be an isolated enzyme or can be endogenously expressed or stably expressed in a relevant cell. Second is the optimization of the selected assay so that the small molecules that are identified are likely to be the ones of interest and with potential artifacts minimized. Included will be examples to illustrate different types of assays and the metrics and validation process for the purpose of HTS.
Lisa Minor, PhD, Johnson & Johnson

Dr. Lisa Minor joined Johnson and Johnson directly following her postdoctoral studies at Medical College of Pennsylvania. During her 21 years at Johnson and Johnson she was involved in target identification, assay development and screening, and secondary pharmacology. She has been responsible for developing biochemical and cell based assays for target identification, high throughput screening and lead optimization and has been instrumental in developing new technologies for cell-based assays. Included are assays to measure the translocation of G protein coupled receptors from the membrane to the cytoplasm using cell-based image analysis as well as developing an HTS mRNA detection assay using branched DNA and has recently been involved in exploring the use of label free tools for cell based assays. Dr. Minor is a past Board member of the Society for Biomolecular Sciences.

Secondary Screening in Drug Discovery

So, you have completed your screen and have identified “hits”. Now what? This presentation will shed light on this subject by detailing secondary screening assay strategies that can be used to characterize hits generated from a high throughput screening campaign. Potential assay types for different target classes will be discussed as well as the ultimate aim of secondary screening.
Karen L. Steinmetz, PhD, DABT, SRI International

Dr. Karen Steinmetz has over 25 years experience in the fields of toxicology, safety and preclinical development applicable a wide variety of pharmaceutical products. She has served as Principal Investigator on several NIH preclinical testing contracts including those with the National Institutes on Aging, of Diabetes & Digestive & Kidney Diseases, and of Child Health and Human Development. She has also served as the preclinical representative on industrial project teams. Dr. Steinmetz received her B.S. from the University of California-Davis, Masters Degree from California State University-San Jose, and Ph.D. from Indiana University-Indianapolis. Her industrial background includes overseeing preclinical development activities and IND preparation for several San Francisco Bay Area biotechnology pharmaceutical companies. Dr. Steinmetz is currently the Director of the Mammalian Toxicology Program at SRI International.

Early-Stage ADME and Toxicity Testing: What, Why & How

Preclinical Development represents activities within a continuum linking discoveries in the lab to initiation of human clinical trials by acquiring unbiased evidence for new drug entities intended for use in humans. Preclinical studies are designed to identify a lead candidate from several ‘Hits,’ develop the best process for drug manufacturing, select the best formulation composition, identify potential safety liabilities, and ultimately support the intended clinical trial design. Since these parameters tend to vary between drugs and drug classes, the specific details for each preclinical development package is tailored to fit a specific application. The first step for most drugs is a general understanding of the intended clinical use including the patient profile, route, frequency, and duration of drug administration, as well as some thought on how the drug will be manufactured. Some of this information is available by knowing the disease target as well as from the efficacy screens using in vitro and in vivo models of the disease. Hits identified in the efficacy models may be tested using in vitro assays and small in vivo screens for their drug-like properties, potential indicators of toxicity, and absorption, distribution, metabolism, and excretion (ADME) properties. Before in vitro testing begins, the drug’s physiochemical properties are determined, particularly solubility. ADME profiling may include microsomal metabolic stability, membrane permeability, enzyme inhibition and induction, enzyme identification and metabolite profiling, and plasma protein binding. Toxicity assays may include ‘mini’ Ames, hERG (iKr), and various endpoints in cultured cells to assess potential liabilities for genotoxicity, cardiotoxicity, and general toxicity, respectively. Finally, small in vivo screens assess both pharmacokinetic and toxicity parameters in the whole animal. The goal of these early assessments is to rank-order Hits for their drug-like properties and potential safety liabilities. Medicinal chemists also use this information to evaluate the impact of structural modifications or substitutions and to understand structure-activity relationships as they work to enhance a drug series. Hits having the desired ADME and toxicity profiles are moved further along the Preclinical Development continuum to enter more complex pharmacokinetic and safety studies.
Preclinical development, the phase of drug development between discovery and clinical trial, is often referred to as the “Valley of Death”. Several factors contribute to this barren landscape. Many promising leads fail due to problems of formulation, delivery, bioavailability, scalable manufacturing, or safety. Investigators seeking to navigate past these hazards also encounter challenges in funding, resources, and expertise. This session offers an overview of the steps involved in optimization of a lead compound and in vivo efficacy and safety studies that determine dosing strategies. Presentations will include examples of go/no-go stage decision points, funding resources, and outsourcing options to complete the journey of discovery to an Investigational New Drug (IND) application for clinical trial.

Session Overview – Edward Spack, PhD, Fast Forward LLC

Requirements for a Lead Compound to Become a Clinical Candidate
Nancy G. Wehner, PhD, Nancy Wehner Non-Clinical Consulting Services

Drug Screening in Neurodegenerative Disease
Taleen Hanania, PhD, PsychoGenics, Inc.

Regulatory Requirements and Strategy
Joy Cavagnaro, PhD, Access BIO

The Basics of Pre-Clinical Development
Edward G. Spack, PhD, Fast Forward LLC
Nancy G. Wehner, PhD, Nancy Wehner Non-Clinical Consulting Services

Dr. Wehner received her PhD degree in Immunology from the University of Minnesota (Minneapolis, MN) in 1987. Her post-doctoral fellowship was at the same institution in the Department of Chemistry. Dr. Wehner began her career in medical diagnostics research with Sanofi Diagnostics Pasteur where she specialized in assay development for autoimmune disease diagnosis. Following a move to California, she joined Anergen where she was head of Bioanalytical Assays (clinical and nonclinical support services), Quality Control, and Pharmacology & Toxicology. While there, she was responsible for the development of monoclonal antibodies, complex biologics and vaccines for the treatment of autoimmune diseases.

Dr. Wehner moved to Elan Pharmaceuticals, South San Francisco, CA where she held the position of Vice President of Nonclinical Safety Evaluation and was responsible for pharmacology and toxicology programs in support of the development of biologic and small molecule drug products in the areas of autoimmunity and neurology. Dr. Wehner is currently working as an independent consultant doing business as Nancy Wehner Nonclinical Consulting Services.

Requirements for a Lead Compound to Become a Clinical Candidate

Lead compounds are usually selected during the screening and validation processes for primarily pharmacological attributes that make them potentially useful for a targeted indication. These compounds still require significant optimization to become an acceptable clinical candidate – they are a starting point, not an end. Lead Optimization is a process for improving efficacy and ADME properties while identifying and, where possible, minimizing toxicities. Fast and efficient optimization with early attrition of poor candidates should be the goal. This talk will look at the process of lead optimization including 1) traditional assays and methodologies for optimization, 2) new technologies being applied to optimization, 3) toxicology considerations during optimization, and 4) process tools (e.g. flow schemes) to help guide optimization.
Taleen Hanania, PhD, PscyhoGenics, Inc.

Taleen Hanania received her Ph.D. in Pharmacology at the University of Texas Medical Branch, Galveston. She completed her post doctoral training and was a faculty member of the Department of Pharmacology at the University of Colorado Health Sciences Center in Denver. Dr. Hanania has extensive neuropharmacology and behavioral pharmacology experience in various neuropsychiatric areas and has been instrumental in establishing and validating many of PsychoGenics' behavioral tests. Currently she is Senior Director of Pharmacology at Psychogenics Inc where she leads a team specialized in behavioral phenotyping new lines of mice and rats and also drug screening novel therapeutic compounds in rodent models of psychiatric and neurodegenerative disorders.

Drug Screening in Neurodegenerative Disorders

Much research is devoted to the understanding of the pathology underlying neurodegenerative diseases. Due to the advances of molecular biology and genetics, the rodent models of ALS, Huntington’s Disease (HD), Spinal Muscular Atrophy (SMA), Parkinson’s Disease (PD), Alzheimer’s Disease (AD) for example are now widely available. However, behavioral phenotyping and drug screening studies in these models, has yielded in many cases inconsistent results across the different laboratories. Some of these discrepancies can arise from the lack of standardized testing conditions, in addition to intrinsic differences between the models. We will discuss issues concerning animals sources, breeding, genetic background and the proper controls. We have developed several standardized testing batteries, amenable to drug screening in several mouse models. We will show examples of Huntington’s Disease, SMA and ALS.
Joy Cavagnaro, PhD, Access BIO

Joy Cavagnaro, PhD, DABT, RAC, Fellow ATS, RAPS FELLOW is the President and Founder of Access BIO a consultancy specializing in science-based regulatory strategies and development services to facilitate biomedical research, emerging technologies and product development. Dr. Cavagnaro’s career spans academia, the CRO and biotechnology industries and government (FDA/CBER). She has served in leadership positions in SOT, RAPS, and DIA and is Past Chair and Founder of BioSafe, an expert preclinical science committee within BIO. Dr. Cavagnaro serves on a number of SAB’s and consults and lectures internationally. She contributed to and edited “Preclinical Safety Evaluation of Biopharmaceuticals: A Science-based Approach to Facilitating Clinical Trials” John Wiley and Sons, NJ which was published in 2008.

Regulatory Requirements and Strategy

A key responsibility of preclinical development scientists is to continually strive to enhance the design of programs in order to improve their predictive value. Unfortunately toxicology programs have more often been designed to satisfy a discipline and meet regulatory requirements rather than provide answers to questions to support clinical decision-making. In 1987 Professor Gerhard Zbinden challenged toxicologists to “refrain from following the beaten track of routine toxicity testing.” Emerging technologies created the opportunities for novel approaches to toxicology testing including use of animal models of disease.

Although the principles of preclinical safety evaluation are similar between conventional pharmaceuticals and biopharmaceuticals the differences between them lies in the way that these principles are put into practice. The practice has more commonly been referred to as the “case-by-case” approach and has embraced a practical and informed search to improve the predictive value of preclinical safety evaluation for extrapolation to humans and define potential mechanisms of toxicity. Strategically, the implementation of “case-by-case” has been focused on designing studies to answer specific questions for development programs based upon specific product attributes and intended use. Implementation of this approach has enabled the safe introduction of hundreds of biopharmaceuticals into clinical trials. Importantly, the path for ensuring successful clinical development programs based upon science-driven toxicology is critically dependent on maintaining effective dialogues.
Edward G. Spack, PhD, Fast Forward LLC

Edward Spack, PhD received his doctoral degree from The Johns Hopkins University and his postdoctoral fellowship in cellular immunology at Stanford University. He worked in Bay area biotech companies for 14 years developing therapies for autoimmunity, cancer, and infectious disease spanning discovery and preclinical development through Phase III trial support. At SRI International, Dr. Spack directed the PharmaSTART program, a consortium of SRI, Stanford, UC Berkeley, UC San Diego, and UC San Francisco chartered to support translational development. His responsibilities included designing preclinical development plans for academic researchers, foundations, NIH programs, and start-up companies. He consulted with the NIH translational core services committee and several individual NIH institutes on preclinical development and served as an advisor on the NIH Regional Centers of Excellence for Biodefense and Emerging Infectious Diseases Produce Development Working Group. As Sr. Director of Business Development for SRI’s Bioscience Division, Dr. Spack was responsible for alliance management, in-licensing, and out-licensing of drug candidates. He has served on scientific advisory boards, grant review boards, or national board of directors for several foundations, and is currently a managing director at Fast Forward LLC, supporting a translational development program advancing therapeutics for the prevention/reversal of neurodegeneration in multiple sclerosis in partnership with EMD Serono.

The Basics of Pre-Clinical Development

Preclinical development is more than a checklist of requirements for an Investigational New Drug (IND) application. There are many strategic decisions required as a drug candidate passes from discovery and optimization to clinical trial, and these decisions can have profound effects on the outcome of a program. To guide these decisions, it is important to begin with the end in mind. A target product profile, anticipating the parameters on the label of an approved drug, can provide a clearly defined goal to the drug development team. This profile is not a formal regulatory requirement; rather, it is a prospective tool that evolves over the development lifetime of a drug. The IND application on the other hand is an FDA-proscribed document, reviewing the rationale and supporting data, safety testing, manufacturing process, and characterization of the drug while also outlining the planned clinical protocol. In addition to the safety testing reviewed in previous presentations, preclinical activities include establishment of a scalable, reproducible manufacturing process. This can include changes in chemical synthesis and purification strategies to improve reproducibility, efficiency, and cost, as well as new formulations and stability testing to improve shelf life and delivery. Documentation of these parameters is included in the Chemistry, Manufacturing, and Control (CMC) section of the IND. Preclinical development requires coordination amongst a diverse set of skill sets and temperaments. Project management is an essential role that anticipates challenges and facilitates hand-offs between team members. Drug development is a team sport, and though it often feels like playing basketball on ice skates, as with any sport there are rules that must be followed and strategies that can increase the odds of success.
Session IV

Issues in Technology Transfer: Interactions and Intellectual Property

Chair — Kathleen A. Denis, PhD, Rockefeller University

This session will focus on the interactions among academic researchers, their technology transfer office and industry partners. An introduction will discuss the various roles and responsibilities of all of the parties involved and hope to begin to demystify academic – industry relations. The basics of patents will be presented with an emphasis on what they can and cannot successfully cover, as well as what a researcher needs to do to maximize the chances of a positive outcome. A variety of agreements used in academic – industry relationships will be discussed in the next talk, with an emphasis on the importance of creating a good relationship amongst all parties. Following will be an honest appraisal of the good, the bad and the ugly of new company formation in the biotech industry, and the session will close with a view from large pharma as to what it is looking for in a licensing partner.

Session Overview – Kathleen A. Denis, PhD, Rockefeller University

Working Effectively with Your TTO: Roles and Responsibilities
Kathleen A. Denis, PhD, Rockefeller University

Intellectual Property 101: A Primer for Investigators
Colin G. Sandercock, Perkins Coie LLP

Creating Relationships with Industry: Consulting, Research, MTA's and Patent Licensing
Louis P. Berneman, EdD, Texelerate

Should You Start a Biotechnology Company?
John S. Swartley, PhD, University of Pennsylvania

What Companies Look for in a Licensing Partner
Susan P. Rohrer, PhD, Merck Research Laboratories
Kathleen A. Denis, PhD, Rockefeller University

Kathleen A. Denis, PhD, is the Associate Vice President of Technology Transfer at The Rockefeller University, a premier biomedical research institution located in New York City. She is a Past President of the Licensing Executives Society USA/Canada (LES), and has served on the Board of Directors of the Association of University Technology Managers (AUTM) and the Pennsylvania Biotechnology Association. She is a Certified Licensing Professional. Specializing in the management of intellectual assets in the life sciences, she has worked with academic institutions and industry clients to manage intellectual property portfolios, evaluate new technologies, market and license technologies and start new technology-based businesses. Dr. Denis is active in numerous professional organizations and speaks frequently about early stage technology evaluation, formation of start-up companies, conflict of interest and other issues of academic technology transfer.

Dr. Denis holds a Ph.D. in immunology from the University of Pennsylvania, an M.A. in Human Genetics from University of Texas Medical Branch at Galveston and an undergraduate degree in genetics from Cornell University.

Working Effectively with Your TTO: Roles and Responsibilities

Technology transfer refers to the numerous interactions between universities and industry. It can mean the publication of research, the delivery of seminars, consultancy, or the transfer of the skills and knowledge that a student brings to his or her future employers. Formally, however, the term denotes the management of intellectual property from research that is sponsored by a company but carried out at a university, and the licensing of university intellectual property to both established and start-up companies.

Technology Transfer Offices (TTO’s) have been established at almost all research universities over the past 25 years. Their role is to promote and support the research enterprise at the university by creating relationships with the private sector to develop, protect, transfer and commercialize research results for the public benefit. This session will examine the legal and university policy underpinnings of technology transfer, the various tasks performed by the TTO, and how researchers can productively interact with their TTO.
Colin G. Sandercock, Perkins Coie LLP

Colin G. Sandercock is a partner in the Patent litigation group of Perkins Coie LLP, co-chair of our Life Sciences Group, and practices in the area of life sciences, including licensing, patent and trademarks, and intellectual property. Colin was recently named in The Best Lawyers in America in the field of biotechnology law. Since 1984, Colin has counseled clients in life science matters including district court litigation, interferences, licensing and the management of domestic and foreign patent portfolios. His technical experience includes biotechnologies, pharmaceutical chemistry, organic and inorganic chemistry, medical devices, and chemical and biochemical engineering. Colin has served as an adjunct professor of law at George Washington University Law School, lecturing on the licensing of intellectual property rights. Colin served on the AAA Patent Advisory Committee for patent disputes, and previously chaired the Electronic Records ad hoc Subcommittee of the AIPLA Interference Committee. He also chaired the Annual Electronic Records Conferences in London in 1999, 2000, 2002 and 2004. He has served as legal counsel to CENSA (Collaborative Electronic Notebook Systems Association) and frequently lectures on the topics of electronic record keeping for use in research, litigation and interferences.

**Intellectual Property 101: A Primer for Investigators**

This presentation will cover basic patent law issues that researchers will encounter, including (i) the common forms of protecting IP in the biotech industry (e.g., patents, trade secrets and material transfer agreements), (ii) how to protect inventions from conception though patenting, (iii) tips for making and keeping records of invention, and (iv) inventorship and ownership. The presentation also will address some of the common pitfalls for patents involving academic researchers and practical suggestions for avoiding them.
Louis P. Berneman, EdD, Texelerate

Louis P. Berneman is an experienced intellectual property licensing and business development executive. He has founded and financed intellectual property-based entrepreneurial ventures, built and managed university technology transfer programs, and has been involved in patenting and licensing since 1982 as both a licensee and licensor. Since September 2005, Lou has been the Principal of Texelerate, a consultancy specializing in monetizing intellectual property. From 1995-2005, Lou was Managing Director of the Center for Technology Transfer (CTT) at the University of Pennsylvania. Under his leadership, CTT assessed more than 3,000 technology disclosures, filed more than 1500 patents, completed more than 600 commercialization agreements including negotiating a number of substantial corporate research collaborations and creating about 80 new start up ventures, and generated more than $100 million in license income. From 1989-1995, Berneman was Director, Licensing and Business Development at Virginia's Center for Innovative Technology patenting and licensing on behalf of the eight public research universities in Virginia. Berneman is a Past President of the Association of University Technology Managers (AUTM) and a former Vice President and Trustee of the Licensing Executives Society (LES USA & Canada). He has served as a member of the Board of the Pennsylvania Biotechnology Association, Greater Philadelphia Venture Group and the LES Foundation. Dr. Berneman is the 2005 recipient of the LES Barnes Mentoring Award, the 2003 recipient of an Award of Excellence from the Association of University Research Parks, and 2002 service award from the Pennsylvania Biotechnology Association. Berneman currently serves as an advisor and member of the Advisory Board of the Paul Capital Partners Royalty Healthcare Fund. Dr. Berneman holds a baccalaureate degree in history from the Pennsylvania State University, a teaching credential from University of California at Santa Barbara, and masters and doctoral degrees in education from Teachers College, Columbia University.

Creating Relationships with Industry: MTAs, Consulting, Research, and Patent Licensing

In recent years, an increasing number of academic institutions have created increasingly effective Technology Transfer Offices (TTOs). However, conflicting roles, values, drivers, and agendas as the bases of numerous challenges is establishing and maintaining productive relationships between academic institutions and companies. In an open innovation environment (and economy), institutions will be increasingly looked to for basic research discoveries that offer commercial potential. Despite differences and challenges, institutions and companies can collaborate to achieve mutual and respective interests.
John S. Swartley, PhD, University of Pennsylvania

John S. Swartley, MBA, PhD, is Senior Director of New Ventures at the Center for Technology Transfer at the University of Pennsylvania, where he leads a team that fosters the formation of new ventures based on Penn technologies and faculty expertise. Prior to joining Penn in 2007, Dr. Swartley served as Senior Vice President and Partner of BCM Technologies (BCMT), the venture capital investment subsidiary of Baylor College of Medicine. Dr. Swartley joined BCMT in 2003 from the Yale University Office of Cooperative Research where he served as Associate Director of the Medical Campus. Dr. Swartley has participated in the formation and oversight of more than two dozen university spin-out companies that have collectively raised nearly one billion dollars of investment capital. He holds a B.S. in Biology from Bates College, an MBA from the Goizueta School of Business at Emory University, and a Ph.D. in Microbial & Molecular Genetics from Emory University.

Should You Start a Biotechnology Company?

The most recent issue of the Licensing and Activity Survey from the Association of University Technology Managers stated that 553 new start-up companies were launched from academic institutions in 2006. The same report states that over 5,700 new companies have been formed based on university technologies since 1980. These start-ups range from companies that simply take a license to university technologies, new ventures that are founded and incubated within the academic institution itself, and everything in between. Companies spun out of academia exhibit an increasingly important economic impact, locally, nationally and globally, and are one of the main drivers of numerous high tech industries, including the biotechnology industry.

This session will examine the criteria and rationale for forming new companies based on discoveries made in academia, followed by an exploration of the process of new venture formation from the scientific founders’ perspective. Issues relating to founder expectations, specific roles and responsibilities, potential outcomes, and likely challenges will be covered.
Susan P. Rohrer, PhD, Merck Research Laboratories

Susan Rohrer obtained her undergraduate degree in biology at the University of Michigan and her graduate degree in biochemistry at the University of Notre Dame. She joined the Merck Research Laboratories in 1987 to work on the biochemical isolation of the receptor for Merck’s antiparasitic agent known as ivermectin. She subsequently contributed to the development of small molecule analogues of somatostatin as potential agents for the treatment of diabetes and diabetic retinopathy and to the identification of selective estrogen receptor modulators for use as safer alternatives to currently available hormone replacement therapies.

Susan joined External Scientific Affairs as liaison for Neuroscience Licensing in September 2004. She chairs Merck’s Neuroscience Review and Licensing Committee and is responsible for identifying external licensing opportunities aligned with priorities and needs of the Neuroscience Franchise. Her recent major licensing deals include Neuromed (NMED-160 patent license and research collaboration), Gladstone Institute of Neurological Disease (patent license and research collaboration covering ApoE mechanisms involved in neurodegenerative diseases), Addex mGluR5 (patent license covering mGluR5 PAMs for schizophrenia) and Addex mGluR4 (patent license and research collaboration covering mGluR4 PAMs for Parkinson’s disease).

What Companies Look for in a Licensing Partner

Companies like Merck are looking for Licensing Partners interested in bringing new medicines to patients around the world by addressing major unmet medical needs and developing superior and clinically differentiated therapies. Merck identifies the best licensing opportunities by leveraging its strong internal research capability and collaborates openly with partners on the development of small molecule therapeutics, vaccines, biologics and enabling technologies. Ideal licensing partners bring strengths and capabilities which complement Merck’s internal capabilities. The importance of patent coverage on molecules and targets, pharmacokinetic and metabolic profiling, and biomarker strategies for assessing target engagement will be discussed. Recent neuroscience licensing deals will be highlighted in order to illustrate what Merck looks for in a Licensing Partner.
Session V

Ask the Experts: Drug Discovery for Neurodegenerative Disease

*Chair — Todd Sherer, PhD, Michael J. Fox Foundation for Parkinson’s Research*

This session will consist of parallel breakouts focused on different aspects of the drug development pipeline. Within each track, a disease-specific case study will be used to illustrate individual aspects of the drug development process.

Track 1 will focus on Target Validation and Optimization using a case study from Alzheimer’s disease.

Track 2 will cover the pre-clinical to IND enabling process with an example from Parkinson’s disease.

Track 3 will focus on specific aspects relevant to the development of a biologic therapy using a case study from MS.

Each parallel session will include a presentation of the disease-specific case study followed by a panel discussion of the relevant issues. The goal of this session is to provide meeting attendees with tangible examples from relevant neurodegenerative diseases for addressing critical roadblocks in the drug development pipeline.

**Breakout Session Overview – Todd Sherer, PhD**

<table>
<thead>
<tr>
<th>Track 1: Target Validation to Lead Optimization</th>
<th>Track 2: Pre-Clinical to IND Enabling</th>
<th>Track 3: Rational Design &amp; Development</th>
</tr>
</thead>
<tbody>
<tr>
<td>AD Case Study</td>
<td>PD Case Study</td>
<td>MS Case Study</td>
</tr>
</tbody>
</table>

**Moderator and Presenter:**
- Track 1: Frank Longo, MD, PhD
  Stanford University
- Track 2: Colleen Niswender, PhD
  Vanderbilt University
- Track 3: Gary Olson, PhD
  Provid Pharmaceuticals, Inc.

**Panel Members:**
- Track 1: D. Martin Watterson, PhD, Northwestern University
  Marcie Glicksman, PhD, Harvard NeuroDiscovery Center
  Howard Fillit, MD, Alzheimer’s Drug Discovery Foundation
- Track 2: Taleen Hanania, PhD, Psychogenics, Inc.
  Lorenzo Refolo, PhD, National Institute on Aging
  Todd Sherer, PhD, Michael J. Fox Foundation for Parkinson Research
- Track 3: Nancy Wehner, PhD, Nancy Wehner Non-Clinical Consulting Services
  Edward Spack, PhD, Fast Forward LLC
  Timothy Coetzee, PhD, Fast Forward LLC
Dr. Todd Sherer joined the Foundation as Associate Director, Research Programs, in April 2004, and was promoted to Vice President, Research Programs, in June 2006. Dr. Sherer earned his undergraduate degree in psychology from Duke University and his PhD in Neuroscience from the University of Virginia. His thesis work focused on neurotrophins and cell death pathways in neurodegenerative disease. Dr. Sherer then became a postdoctoral fellow at the Emory University laboratory of Timothy J. Greenamyre. During this fellowship, Dr. Sherer concentrated on understanding the role of environmental factors in Parkinson’s disease, as well as on the development of PD model systems. As a result of this work, Dr. Sherer was awarded a Postdoctoral Fellowship from The Michael J. Fox Foundation for Parkinson’s Research. Dr. Sherer is the author of over 20 research articles in the field of neurodegeneration with a focus on Parkinson’s disease.
Frank M. Longo, MD, PhD, Stanford University

Dr. Longo received his MD in 1981 and PhD in Neurosciences in 1983 from the University of California, San Diego. Following an internship in medicine at NYU/VA, he trained as a resident in neurology and fellow in neurobiology at University of California, San Francisco. While at UCSF he created the Neurogenetics Clinic which was the first West Coast site in the U.S. to offer DNA testing for families with Huntington’s disease. He also led the creation of a national referral center for deep brain stimulation for Parkinson’s disease and contributed to the development of programs in dementia, epilepsy and other areas. At UCSF, Dr. Longo became professor and vice chair of the Department of Neurology and in 2001 he was recruited to become chair of the Department of Neurology at the University of North Carolina, Chapel Hill. While at UNC, Dr. Longo launched or expanded programs for Alzheimer’s disease and other dementias, stroke, epilepsy, sleep disorders, multiple sclerosis and Parkinson’s disease.

In January 2006, Dr. Longo became chair of the Department of Neurology and Neurological Sciences at Stanford where he is focused on building and expanding multidisciplinary programs in neurology and neuroscience. In 2006 he was named a Stanford Fellow. Dr. Longo’s research team focuses on elucidating novel mechanisms that prevent neural degeneration and promote regeneration. He and his colleagues have pioneered the development of small, drug-like, molecules that target neurotrophin receptors to delay onset of or slow progression of Alzheimer’s and other neurodegenerative disorders.

Alzheimer’s Disease Case Study: Academic Development and Commercial Licensing of First-In-Class p75 Neurotrophin Receptor Small Molecule Ligands

In this Alzheimer’s disease Case Study Session, we will review the pathway taken, in an academic setting, starting at novel target validation and proceeding through small molecule screening, lead characterization, preclinical studies and industry licensing. Our group conducted a series of studies indicating that the p75 neurotrophin receptor regulates fundamental signaling mechanisms relevant to synaptic dysfunction and degenerative signaling mechanisms occurring in Alzheimer’s disease. Nerve growth factor (NGF) is a ligand for p75 which as a protein has limited potential for CNS therapeutics, and moreover, in a number of contexts promotes death through p75 signaling. We hypothesized that small molecule ligands of p75 might be created that would preferentially activate p75-induced survival signaling and counteract degenerative signaling. We used knowledge derived from our peptide mapping studies pointing to domain features in the loop 1 region of NGF to design pharmacophores which were used to screen in silico small molecule libraries with the goal of finding the first non-peptide, small molecule p75 receptor ligands. Resulting hits were characterized for their p75 binding and signaling properties. Selected compounds were further characterized in in vitro Alzheimer’s disease-relevant models. Compounds demonstrating the ability to inhibit Aβ-induced degeneration were submitted for ADMET evaluation. A lead and backup compound were applied in a number of mouse-based preclinical studies and found to demonstrate morphological and behavioral efficacy in a number of models. P75 ligands have been licensed to Elan for clinical development in Alzheimer’s disease. We will discuss issues of in silico screening, lead characterization, ADMET and preclinical studies in an academic setting. Experiences with grant funding and options for moving academic-derived technology into the commercial sector will also be discussed.
Colleen Niswender, PhD, Vanderbilt University

Colleen Niswender obtained her Ph.D. in pharmacology in the lab of Dr. Ronald Emeson at Vanderbilt, studying the regulation of RNA editing in the mammalian central nervous system and characterization of molecular determinants regulating RNA editing events within the AMPA subtype glutamate receptor, GluR2, and the G protein-coupled 5HT 2C serotonin receptor. She then pursued postdoctoral studies with Dr. G. Stanley McKnight at the University of Washington, focusing on the study of Protein Kinase A signal transduction using recombinant mouse lines and genetically engineering mutations within the PKA enzyme. She joined the Vanderbilt Program in Drug Discovery in 2004 and has focused on the development of high throughput-compatible assays to search for ligands specific for G protein-coupled receptors (GPCRs) of the muscarinic and metabotropic glutamate receptor families. Currently, she directs the Molecular Pharmacology group within the Vanderbilt Program in Drug Discovery and is particularly interested in the concepts of functional selectivity and context-dependent pharmacology of allosteric modulators. She is also the biology project team leader for a Linked Efforts to Accelerate Parkinson’s Solutions (LEAPS) program dedicated to the development of small molecule modulators of metabotropic glutamate receptor 4 for symptomatic and disease-modifying treatment of Parkinson’s disease.

The Development of Positive Allosteric Modulators of mGluR4 for the Treatment of Parkinson’s Disease


Vanderbilt Program in Drug Discovery, Departments of Pharmacology and Chemistry, Vanderbilt Institute for Chemical Biology, Vanderbilt University, Nashville, TN 37212.

Parkinson’s disease (PD) is a debilitating movement disorder caused by the degeneration of dopaminergic neurons in the substantia nigra pars compacta of the basal ganglia. Improved understanding of basal ganglia circuitry has opened new and nondopaminergic strategies for PD treatment. Metabotropic glutamate receptor 4 (mGluR4) is expressed presynaptically at the striatopallidal synapse within the indirect pathway of the basal ganglia. Activation of mGluR4 decreases the release of the inhibitory neurotransmitter GABA at this location, restoring balance within the basal ganglia motor circuit in animal models of PD. Studies from multiple laboratories have now clearly shown that mGluR4 activation has antiparkinsonian, as well as neuroprotective, effects in rodent PD models, suggesting that this receptor represents a novel target for symptomatic and disease-modifying PD therapy. We are taking the approach of selectively activating mGluR4 using positive allosteric modulators (PAMs) of mGluR4 function. These compounds act by increasing the activity of the endogenous neurotransmitter glutamate at mGluR4. Using functional high-throughput screening, we have identified multiple novel chemical scaffolds that can potentiate mGluR4 activity in vitro. Within the Vanderbilt Program in Drug Discovery, we have initiated a chemical optimization program to improve the potency, efficacy, and pharmacokinetic properties of these compounds. We have characterized many diverse chemotypes and have improved upon the in vitro pharmacological as well as pharmacokinetic parameters of numerous leads. We have now developed brain-penetrant mGluR4 PAMs that are serving as excellent tools for the rigorous evaluation of the utility of mGluR4 PAMs in PD. The activity of these compounds is being assessed in multiple PD models such as haloperidol-induced catalepsy, reserpine-induced akinesia, and full and partial 6-hydroxydopamine lesions. These ligands will also expand our ability to explore the potential of mGluR4 in additional neurological and psychiatric disorders such as anxiety, schizophrenia, and addiction. Supported by grants from the NIH and MJFF.
Rational Design & Development—MS Case Study

PV-267, an MHC Class II DR2 inhibitor for MS

Christopher Self, Hong Chen, Charles Cook, Thomas Forsthuber (University of Texas San Antonio), Lora Hamuro, Neil Hayward (Daiaimed, LLC), Bernard Mailiere (CEA-Saclay), William May, Nallaganchu Rao, Barbara Sluboski, Guangtao Zhang, and Gary L. Olson, (Provid Pharmaceuticals Inc.)

The discovery and preclinical development of PV-267, a potential therapeutic for the treatment of multiple sclerosis (MS), will be described. PV-267 is a novel, specific inhibitor of antigen binding to the MHC class II molecule HLA-DR2 that is associated with MS in over 60% of patients. PV-267 is a small molecule peptide mimetic antagonist (MW ca. 750) that binds at low nanomolar concentration to DR2, preventing antigen binding. The compound is stabilized toward cathepsin degradative enzymes found in antigen presenting cells and is also fully stable in plasma. The efficacy of PV-267 was demonstrated in EAE models in DR2 transgenic mice. Exploratory pharmacokinetics, toxicology, formulation, and synthesis studies have been completed and support the selection of PV-267 for development. The work has been partially supported by an NIH SBIR grant (1R43 NS048731-01) and by Fast Forward, LLC.
Session VI

Resources and Services for Advancing Drug Discovery

Chair — Lorenzo Refolo, PhD, National Institute on Aging

This session will focus on descriptions of the resources available through a variety of mechanisms within academia, the National Institutes of Health (NIH), foundations and commercial vendors. Speakers will focus on resources for assay development, target identification, drug discovery, drug development, pre-clinical toxicology evaluation and other components needed for the translation of pre-clinical drug candidates into potential therapies tested in clinical trials. In particular, it will include specific descriptions of programs available to academic investigators through individual NIH Institutes, including the National Institute on Aging (NIA) and the National Institute of Neurological Disorders and Stroke (NINDS), as well as trans-NIH programs including the NIH Roadmap for Medical Research and the NIH Blueprint for Neuroscience Research.

Session Overview – Lorenzo Refolo, PhD, National Institute on Aging

Preclinical Outsourcing for Startup and Biotech Companies
Mark Creswell, PhD, IDSC Biotech Network

Resources at the National Institute of Health
William Matthew, PhD, National Institute of Neurological Disorders and Stroke
Neil Buckholtz, PhD, National Institute on Aging

Types of Academic Drug Discovery Programs
Euan Ramsey, PhD, Centre for Drug Research and Development

Foundation Resources:

Venture Philanthropy – Howard Fillit, MD, Alzheimer’s Drug Discovery Foundation

Other Philanthropic Approaches – Timothy Coetzee, PhD, Fast Forward LLC

Funding and other Challenges for Rare Diseases – Leticia M. Toledo-Sherman, PhD, CHDI Foundation
Mark W. Creswell, PhD, IDSC Biotech Network

Mark Creswell is the founder, President and CEO of IDSC. Mark’s 20 years Big Pharma experience began at Warner-Lambert's Ann Arbor, Michigan facility. While working in many therapeutic areas including cardiovascular, antibacterials, oncology, and CNS, Mark held many positions of increasing responsibility. In 1998, Mark accepted the responsibility of building and managing Warner-Lambert's Discovery Chemistry Outsourcing Program. He and his team pioneered the art of managing a successful outsourcing program that brought tremendous value to Warner-Lambert. Following the Pfizer acquisition of Warner-Lambert, Mark was instrumental in forming a centralized global sourcing team. Following the closure of the Pfizer Ann Arbor facility, Mark founded IDSC.

Preclinical Outsourcing for Startup and Biotech Companies

Designed for startup and virtual biotech companies, this presentation will review many aspects of outsourcing preclinical drug discovery and development services. Attendees should come away with practical information that may be implemented immediately. When outsourcing budgets are limited, as with many startup and biotech companies, it is important to make the correct decisions when placing and managing chemistry, biology, and toxicology work outside the company. Maximizing return on investment (ROI) is important and choosing the wrong partner can be devastating.

Over the last twelve years, preclinical outsourcing has gone through many stages of transformation. For example, big pharma has gone from outsourcing only development raw materials and API to outsourcing discovery intermediates, analogs, reference compounds, libraries, and metabolites as well as ADME, in vitro screening, and toxicology studies. In addition, big pharma has moved most of their discovery chemistry outsourcing overseas and are now beginning to look at integrated outsourcing approaches.

Startup and virtual biotech companies are faced with decisions like: Do I outsource on shore or off shore; do I use big-box CROs or boutique companies; how do I know if I am getting the highest ROI; how do I go about outsourcing chemistry, ADME, in vitro screening, in vivo efficacy, or toxicology studies? Many questions like these will be addressed in this presentation.
Lorenzo M. Refolo, PhD, National Institute on Aging

Dr. Lorenzo M. Refolo received a BSc. from the University of Connecticut, and was awarded a Ph.D. in Molecular Genetics from the Department of Molecular Genetics at the Rutgers University School of Medicine and Dentistry. Subsequently, Dr. Refolo trained as a post-doctoral fellow at Mt Sinai Medical Center in New York, investigating the molecular and cell biology of the Alzheimer’s Amyloid Precursor Protein. After concluding his post-doctoral training Dr. Refolo served as Transgenics Group Leader at Athena Neurosciences and later held faculty positions at the Mayo Clinic Jacksonville and New York University’s Nathan Kline Institute for Psychiatric Research. In 2001, Dr. Refolo was named the Scientific Director at the Institute for the Study of Aging, a private, disease-focused foundation with a mission to fund the discovery and clinical development of drugs for the treatment of Alzheimer’s disease. Since 2005, Dr. Refolo has been Program Director in the Neurodegeneration Cluster at NINDS where his major responsibility was the management of a portfolio of grants on ALS, Alzheimer’s and Parkinson’s diseases and Vascular Cognitive Impairment. In 2009, Dr. Refolo joined NIA, the Division of Neuroscience, Dementia Branch.
Neil S. Buckholtz, PhD, National Institute on Aging

Neil S. Buckholtz, Ph.D., is Chief of the Dementias of Aging Branch of the Neuroscience and Neuropsychology of Aging Program at the National Institute on Aging, National Institutes of Health (NIH), Bethesda, Maryland. This involves overall programmatic responsibility for development, coordination, and implementation of basic and clinical Alzheimer’s disease research. Specifically Dr. Buckholtz is the program administrator for the areas of diagnosis and treatment and management of Alzheimer’s disease. Dr. Buckholtz holds a doctorate in physiological psychology from the University of Wisconsin, Madison and was a faculty member at the Medical University of South Carolina, Department of Psychiatry, from 1970-1983, before coming to NIH.

Translational Research Initiatives for Neurodegeneration at the NIH

This presentation will be an overview of trans-NIH resources and programs available to academic investigators involved in drug discovery. We will also outline the translational research initiatives that NIA and NINDS have in place to support drug discovery and preclinical drug development for Alzheimer's disease and other major neurodegenerative disorders.
William Matthew, PhD, National Institute of Neurological Disorders and Stroke

William Matthew, Ph.D. is the Director of the Office of Translational Research at The National Institute of Neurological Disorders and Stroke (NINDS). Dr. Matthew holds a Ph.D. in biochemistry from the University of California, San Francisco. At the beginning of his career, Dr. Matthew helped pioneer the use of antibodies as tools for neuroscience research and as therapies for neurological disease. In the early 1980s, as a professor at Harvard Medical School, he was among the first to develop antibodies that modulate the function of neural proteins in animal models of neural injury. In 1990, Dr. Matthew moved to Duke University Medical Center to help establish the Neurobiology Department. With further refinements in immunologic methods, his lab was the first to create agonist antibodies capable of facilitating recovery functions of both neuronal and glial cells after injury. In 1998, Dr. Matthew became scientific director of The George and Jean Brumley Neonatal-Perinatal Research Institute within Duke’s Department of Pediatrics. The mission of the Institute was to apply principles of cellular and molecular developmental neurobiology to improve recovery from hypoxia in neonatal intensive care medicine. Throughout his academic career Dr. Matthew was active in graduate and undergraduate teaching; he was the director of graduate studies at both Harvard and Duke and a member of the executive committee of the M.D./Ph.D. Program at Duke.

In 2001, Dr. Matthew was recruited to Schwarz Pharma (Monheim, Germany) to lead CNS Business Development and to transition the company from a generic drug-based enterprise to a specialty pharmaceutical company. Dr. Matthew was integral to creating and building Schwarz Biosciences, an international research and development division. Prior to joining NINDS he was Vice President of R&D Partnering and Business Development at UCB, a biopharmaceutical company based in Brussels.

Translational Research Initiatives for Neurodegeneration at the NINDS

The translation of basic science into patient therapies is a critical mission of the National Institutes of Health. The Office of Translational Research (OTR), within NINDS, manages multiple initiatives in drug discovery and preclinical development of neurological therapeutics. These initiatives include: Exploratory Projects in Translational Research, Cooperative Agreement Program in Translational Research, Anti-Convulsant Screening Program, Small Business Program, Spinal Muscular Atrophy Project, Blueprint Neurotherapeutics, CounterACT and certain programs within the NIH Roadmap and RAID (Rapid Access to Interventional Development). An overview of OTR activities in drug discovery will be presented and the funding mechanisms available to these programs will be discussed.
**Euan Ramsey, PhD, Centre for Drug Research and Development (CDRD)**

Dr. Euan Ramsay holds the position of Grant Development Scientist at the Centre for Drug Research and Development (CDRD), based in Vancouver, British Columbia, Canada. CDRD guides and supports early-stage drug development from leading academic and health research institutions to increase the successful commercialization of new therapeutics. In his current position, Euan is responsible for sourcing projects with exceptional therapeutic and commercial potential, and securing funding partnerships for academic drug discovery and development. Prior to joining CDRD, Euan was a Senior Scientific Fellow in the Department of Advanced Therapeutics, at the British Columbia Cancer Agency where his research interests focused on the lipid nanoparticle delivery of anticancer drug combinations. Euan is the inventor on two patents, one of which describes a novel anticancer agent that has been developed in an academic setting and will enter Phase 1 clinical trials in 2010. In addition, he is an author on 20 papers and has written and contributed to grants that have secured funding in excess of $30 million. Euan has an undergraduate degree (B.Sc. Hons) in Pharmacy from Strathclyde University, Glasgow, Scotland (1992) and a Ph.D. in Non-Viral Gene Therapy from the Welsh School of Pharmacy, Cardiff University, Wales (1999).

---

**Academic Models of Drug Discovery Services**

The billions of dollars invested in academic research in the lifesciences sector have resulted in relatively few new medicines and therapies. Often this reflects a gap in the infrastructure, multidisciplinary expertise and specific funding necessary to develop academic innovations to the point where investors will commit the millions of dollars necessary to progress a drug through clinical trials to regulatory approval. This gap is often referred to as the "commercialization gap," and an increasing number of academic, not-for-profit and for-profit organizations are being established to bridge this gap and accelerate the translation of academic discoveries to the clinic.

This presentation will provide an introduction to the various models of drug discovery and development services available to the academic scientist. The Centre for Drug Research and Development (CDRD) will be used as a case study to compare and contrast these models and to provide an overview for their role in drug discovery and development for neurodegeneration.

The Centre for Drug Research and Development (CDRD) (www.cdrd.ca) guides and supports early-stage drug development from leading academic and health research institutions to increase the successful commercialization of new therapeutics. CDRD provides drug development expertise and infrastructure to enable researchers to develop promising drug candidates. CDRD’s commercial arm, Drug Development Inc (DDI), licenses technologies from affiliated institutions, advances projects by leveraging CDRD’s expertise and infrastructure, and establishes working collaborations with other biotech and life sciences companies.
Foundation Resources Panel

**Venture Philanthropy** - Howard Fillit, MD, Alzheimer’s Drug Discovery Foundation

**Other Philanthropic Approaches** - Timothy Coetzee, PhD, Fast Forward LLC

**Funding and other Challenges for Rare Diseases** - Leticia M. Toledo-Sherman, PhD, CHDI Foundation

---

**Howard Fillit, MD, Alzheimer’s Drug Discovery Foundation**

Dr. Fillit, a geriatrician and neuroscientist, is the founding Executive Director of the Institute for the Study of Aging, Inc. as well as its affiliated public charity the Alzheimer’s Drug Discovery Foundation, both of which are dedicated to funding drug discovery for Alzheimer's disease. Dr. Fillit was formally the Corporate Medical Director for Medicare at NYLCare Health Plans (now a division of Aetna, Inc.), where he was responsible for over 125,000 Medicare members in eight regional markets. He has also had a distinguished academic career at The Rockefeller University and The Mount Sinai Medical Center (NY), where he is currently a clinical professor of geriatrics and medicine and a professor of neurobiology. Dr. Fillit has received many awards and honors, including the Rita Hayworth Award for Lifetime Achievement from the Alzheimer's Association. He is a fellow of the American Geriatrics Society, the American College of Physicians, the Gerontological Society of America, and the New York Academy of Medicine. Dr. Fillit is the author or co-author of more than 250 publications, including the leading international Textbook of Geriatric Medicine and Gerontology. He served as a consultant to a variety of individuals, managed care organizations, health care systems, and pharmaceutical and biotechnology companies.

---

**Timothy Coetzee, PhD, Fast Forward LLC**

Dr. Timothy Coetzee is the President of Fast Forward, LLC, a venture philanthropy of the National Multiple Sclerosis Society. In this capacity, Dr. Coetzee is responsible for the Society’s strategic funding of biotechnology and pharmaceutical companies as well as partnerships with the financial and business communities. Prior to assuming his current position, Dr. Coetzee led the Society’s translational research initiatives on nervous system repair and protection in MS as well as the Society’s programs to recruit and train physicians and scientists in MS research. Dr. Coetzee received his PhD in molecular biology from Albany Medical College in 1993 and has since been involved in the field of multiple sclerosis research. He was a research fellow in the laboratory of Society grantee Dr. Brian Popko at the University of North Carolina at Chapel Hill, where he received an Advanced Postdoctoral Fellowship Award from the Society. After completing his training with Dr. Popko, Dr. Coetzee joined the faculty of the Department of Neuroscience at the University of Connecticut School of Medicine, where he conducted research that applied new technologies to understand how myelin is formed in the nervous system. He is the author of a number of research publications on the structure and function of myelin. Dr. Coetzee joined the National MS Society’s Home Office staff in the fall of 2000.
Leticia M. Toledo-Sherman, PhD, CHDI Foundation

Leticia Toledo-Sherman directs drug discovery projects at CHDI combining her expertise in the areas of medicinal and computational chemistry. Before joining CHDI in 2005, she was Executive Director of Chemistry at LymphoSign Inc., where she managed medicinal and computational chemistry as well as associated research relationships. Prior to LymphoSign Inc, Toledo-Sherman directed drug design and discovery activities at Protana Inc. (formerly MDS Proteomics). There, she led several successful discovery and lead optimization projects and managed the company's Chemical Proteomics program. The latter involved a multidisciplinary team working at multiple sites. Before Protana, Toledo-Sherman worked at Kinetix Pharmaceuticals Inc. (acquired by Amgen in December 2000), one of the earliest successful biotech companies to focus exclusively on targeted kinase inhibition. While at Kinetix, she designed and implemented a Computer-Aided Design and Virtual Screening platform that led to the discovery of several novel potent small molecule inhibitors of protein kinases. Toledo-Sherman holds a PhD in Organic Chemistry from SUNY Stony Brook. She did postdoctoral research at MIT and the Skaggs Institute of Chemical Biology at The Scripps Research Institute.
ADDENDUM

SPONSORS, EXHIBITORS AND MEDIA PARTNERS
(continued)

GENERAL MEETING SPONSOR

BRONZE:

biogen idec
Transforming Discovery Into Care®

Neil Buckholtz will replace D. Martin Watterson in Session V: Case Studies, Track 1, Target Validation to Lead Optimization - AD Case Study
A two-day global conference for research scientists to engage in discussion and cross fertilization of ideas focusing on Alzheimer’s drug discovery research.

The conference objectives are to:

1. discuss scientific progress on drug discovery programs aimed at treating Alzheimer’s disease and related dementias;

2. increase networking opportunities for scientists to share information and resources; and

3. publish a post-meeting report in a scientific journal.

The meeting attracts 150 participants from around the world.

Feeding the Pipeline:

**Novel Drug Discovery for Alzheimer’s Disease**

November 3, 2010 • Toulouse, France

A one-day meeting focusing on biotechnology companies in Europe conducting early-stage high risk research for Alzheimer’s disease and related dementias. This meeting is a pre-conference satellite in conjunction with the 3rd Clinical Trials on Alzheimer’s Disease.