2025 Parkinson's Disease Therapeutics Conference

October 16, 2025

New York City

THE MICHAEL J. FOX FOUNDATION
FOR PARKINSON'S RESEARCH

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Welcome

Welcome to the 17th annual Parkinson's Disease Therapeutics Conference. At The Michael J. Fox Foundation (MJFF), we know that collaboration is the key to accelerating breakthroughs. Bringing together researchers, clinicians and thought leaders in the Parkinson's community creates the space to share ideas, tackle challenges and drive progress toward precision medicine.

The Parkinson's research landscape is advancing at an unprecedented pace. Our ever-growing access to high-quality datasets — especially through the Parkinson's Progression Markers Initiative (PPMI) — is helping us uncover the genetic, cellular and clinical drivers of Parkinson's, while giving new insight into the patient experience. Combined with emerging funding opportunities, these discoveries are positioning the field to move faster than ever toward treatments that can slow or stop the disease.

Today, you'll hear from colleagues around the world about the latest findings shaping the future of Parkinson's research. Their work provides a glimpse into the breakthroughs we aim to achieve in the years ahead.

MJFF remains committed to supporting your research with the resources, tools and connections you need. We encourage you to engage deeply with your peers and the Foundation team, leaving this conference inspired, equipped and ready to advance the next wave of Parkinson's discoveries.

Sincerely,

Sohini Chowdhury
Chief Program Officer

About The Michael J. Fox Foundation for Parkinson's Research

As the world's largest nonprofit funder of Parkinson's research, The Michael J. Fox Foundation is dedicated to accelerating a cure for Parkinson's disease and improved therapies for those living with the condition today. The Foundation pursues its goals through an aggressively funded, highly targeted research program coupled with active global engagement of scientists, Parkinson's patients, business leaders, clinical trial participants, donors and volunteers. In addition to funding $2.5 billion in research to date, the Foundation has fundamentally altered the trajectory of progress toward a cure. Operating at the hub of worldwide Parkinson's research, the Foundation forges groundbreaking collaborations with industry leaders, academic scientists and government research funders; creates a robust open-access data set and biosample library to speed scientific breakthroughs and treatment with its landmark clinical study, PPMI; increases the flow of participants into Parkinson's disease clinical trials with its online tool, Fox Trial Finder; promotes Parkinson's awareness through high-profile advocacy, events and outreach; and coordinates the grassroots involvement of thousands of Team Fox members around the world. For more information, visit us at **michaeljfox.org**, **Facebook**, **Instagram** and **LinkedIn**.

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The Michael J. Fox Foundation for Parkinson's Research

The Michael J. Fox Foundation for Parkinson's Research
2025 Parkinson's Disease Therapeutics Conference
October 16, 2025
New York, NY

Conference Program

All presentations are followed by Q&A.

7:45 – 8:30 a.m.	**Arrivals and Breakfast**
8:30 – 8:40	**MJFF Welcome and Housekeeping** **SOHINI CHOWDHURY**, The Michael J. Fox Foundation
8:40 – 9:00	**Keynote Remarks** **SAMANTHA BUDD HAEBERLEIN, PhD**, Enigma Biomedical Group

Session 1: Therapies Directed Against Endolysosmal Dysfunction

9:00 – 9:10	**Session Introduction from Session Chair** **ANASTASIA HENRY, PhD**, Denali Therapeutics
9:10 – 10:00	**Company Fast Fire Presentations**
9:10 – 9:20	**Ultrapotent CNS-selective LRRK2 Inhibition to Address On-target Peripheral Toxicities** **NICHOLAS HERTZ, PhD**, Montara Therapeutics
9:20 – 9:30	**Targeting Endolysosomal Dysfunction to Treat Neurodegenerative Diseases** **JOANNA WOLAK, MSc, PhD**, Endlyz Therapeutics
9:30 – 9:40	**Development of a Potent, Selective and Brain-penetrant TRPML1 Agonist for the Treatment of Parkinson's Disease** **VALERIE CULLEN, PhD**, Lysoway Therapeutics

9:40 – 9:50	**VQ-101 Demonstrates Sustained Activation of Lysosomal Glucocerebrosidase (GCase) in Healthy Volunteers and Patients with GBA1-associated Parkinson's Disease** **DANIEL YSSELSTEIN, PhD**, Vanqua Bio
10:00 – 10:40	**Panel Discussion** *Moderator:* **ANASTASIA HENRY, PhD**, Denali Therapeutics *Panelists:* **VALERIE CULLEN, PhD**, Lysoway Therapeutics **NICHOLAS HERTZ, PhD**, Montara Therapeutics **JOANNA WOLAK, MSC, PhD**, Endlyz Therapeutics **DANIEL YSSELSTEIN, PhD**, Vanqua Bio
10:40 – 11:25	**Networking Break / Poster Viewing**

Session 2: Therapies Directed Against Immune Dysfunction

11:30 – 11:40	**Session Introduction from Session Chair** **MATTHEW FELL, PhD**, Merck
11:40 a.m. – 12:20 p.m.	**Company Fast Fire Presentations**
11:40 – 11:50	**LBT-3627 — A Precision Immune Rebalancing Approach to Treat Parkinson's Disease** **SCOTT SHANDLER, PhD, MBA**, Longevity Biotech
11:50 a.m.– 12:00 p.m.	**Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of VTX3232, a CNS-penetrant NRLP3 Inhibitor, in Participants with Early-stage Parkinson's Disease** **REBECCA CREAN, PhD**, Ventyx Biosciences
12:00 – 12:10	**Sortilin Inhibition Elevates Progranulin and Holds Therapeutic Potential in Parkinson's Disease** **LOUISE KLEM, PhD**, Vesper Biosciences
12:15 – 12:45	**Panel Discussion** *Moderator:* **MATTHEW FELL, PhD**, Merck *Panelists:* **REBECCA CREAN, PhD**, Ventyx Biosciences **LOUISE KLEM, PhD**, Vesper Biosciences **SCOTT SHANDLER, PhD, MBA**, Longevity Biotech
12:45 – 1:45	**Lunch / Networking Break / Poster Viewing**

Session 3: Biomarker Advances To Support Clinical Development

2:00 – 2:10	**Session Introduction from Session Chair** **TANYA SIMUNI, MD, FAAN**, Northwestern University
2:10 – 2:30	**A New Strategy for Dopamine Imaging Analytics to Accelerate PD Therapeutic Trials** **KENNETH MAREK, MD**, Institute for Neurodegenerative Disorders
2:30 – 2:50	**PET Imaging of Alpha-synuclein with 18F-FD4** **ROGER GUNN, PhD**, Xing Imaging **CONG LIU, PhD**, Shanghai Institute of Organic Chemistry
2:50 – 3:10	**Digital Droplet SAA** **TUOMAS KNOWLES, PhD**, University Of Cambridge
3:10 – 3:30	**Multi-modal Modeling of Neuronal Alpha-synuclein Disease Progression Using PPMI Data** **PIET AARDEN, MSc**, Novartis Pharma AG **MARI NIEMI, PhD**, Novartis Pharma AG
3:30 – 3:40	**Closing Remarks from Session Chair and Audience Questions** **TANYA SIMUNI, MD, FAAN**, Northwestern University
3:40 – 4:05	**Networking Break / Poster Viewing**

Closing Session: Hot Topics In Parkinson's Disease Therapeutic Development

4:10 – 4:50	**Panel Discussion** **Assessing the Value of Novel Therapies in Parkinson's: A Multi-Stakeholder Perspective** *Moderator:* **CATHERINE KOPIL, PhD**, The Michael J. Fox Foundation *Panelists:* **BILLY DUNN, MD**, The Michael J. Fox Foundation **FRED GOLDSTEIN, MS**, Accountable Health **GENNARO PAGANO, MD, PhD**, Roche **BRYAN TYSINGER, PhD**, University of Southern California
4:50 – 5:00	**Video Presentation** **"Everything Needs a Starting Point" — Patients Speak on What the First Disease-modifying Parkinson's Treatment Would Mean to Them**
5:00 – 5:05	**Closing Remarks** **SOHINI CHOWDHURY**, The Michael J. Fox Foundation
5:05	**Cocktail Hour / Poster Viewing**

Poster Session

An Overview of the Global Parkinson's Genetics Program (GP2)

CORNELIS BLAUWENDRAAT, PhD, Coalition for Aligning Science

Development of USP30 Inhibitors to Restore Mitophagy in Parkinson's Disease

SPRING BEHROUZ, PhD, Vincere Biosciences

Evaluation of the Pharmacodynamic Effects of BIIB122/DNL151 in Participants with LRRK2 Mutation-driven Parkinson's Disease (BEACON Study)

JILLIAN KLUSS, PhD, Denali Therapeutics

Patient Engagement Services for Industry and Study Partners

MAGGIE KUHL, The Michael J. Fox Foundation

Structure-guided Design of FD4—a PET Tracer of Alpha-synuclein Fibril

CONG LIU, PhD, Shanghai Institute of Organic Chemistry

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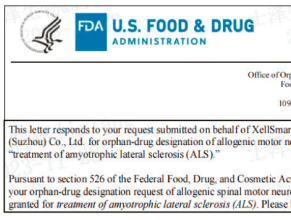
XellSmart Pipeline	Cell therapy	Indication	R&D	CMC	Pre-Clinical	FIH clinical study	IND	Phase I/II	Phase III Pivotal Study	BLA
GMP XS-411 Clinical midbrain Dopaminergic neural progenitor cell product	Allogeneic Off-the-shelf	PD				China's first case		China NMPA approved Phase I US FDA approved Phase I		2031
GMP XS-228 Clinical spinal-cord motor neural progenitor cell product	Allogeneic Off-the-shelf	SCI Spinal-cord injury				World's first case		China NMPA approved Phase I US FDA approved Phase I		2028
		ALS						China NMPA approved Phase I US FDA approved Phase I FDA Orphan Drug Designation		2030



U.S. FOOD & DRUG ADMINISTRATION

Office of Orphan Products Development
Food and Drug Administration
WO32- 5295
10903 New Hampshire Avenue
Silver Spring, MD 20993

This letter responds to your request submitted on behalf of XellSmart Bio-Pharmaceutical (Suzhou) Co., Ltd. for orphan-drug designation of allogenic motor neuron precursor cell for "treatment of amyotrophic lateral sclerosis (ALS)."

Pursuant to section 526 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360bb), your orphan-drug designation request of allogenic spinal motor neuron precursor cell is granted for *treatment of amyotrophic lateral sclerosis (ALS)*. Please be advised that it is the

In 2023, XellSmart received orphan drug designation from the US FDA for its iPSC-derived therapy XS-228.

XellSmart is seeking funding and partnerships to conduct FDA-approved Phase I/II trials for PD/SCI/ALS in the US. We welcome opportunities to license our global or territorial rights and other collaboration.

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For funding and BD cooperation, please contact: BD@xellsmart.com

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*Data on File - GE HealthCare Pharmaceutical Diagnostics Patient Impact letters entitled: Dec 2023

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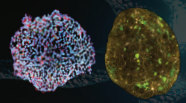
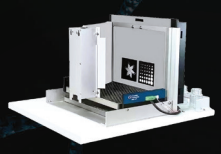


iPSC & Organoid

Mouse

Marmoset

3 Translational Biomarkers



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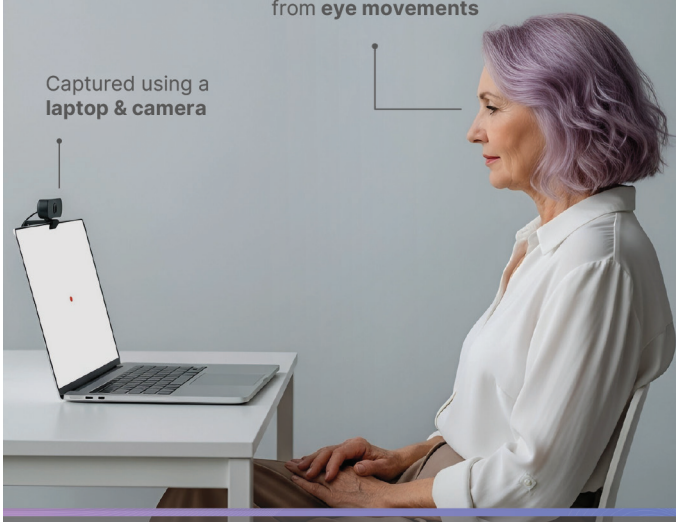

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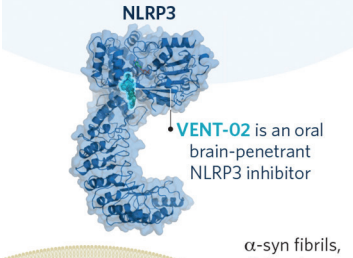
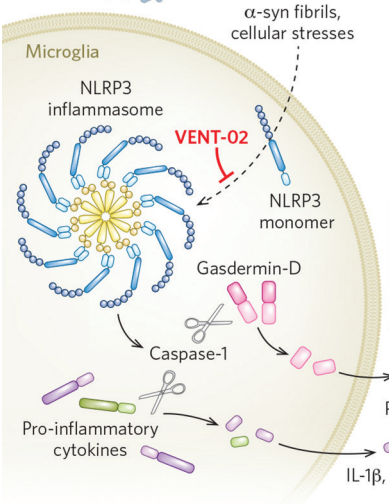


NLRP3 is a key component of the innate immune system.

Misfolded alpha-synuclein activates microglia and induces NLRP3-mediated inflammation via the release of IL-1β and IL-18 and pyroptosis.

NLRP3 inhibition interrupts the pathogenic cycle of inflammation and neurodegeneration.



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Please contact
Ventus Therapeutics for additional questions:
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Abstracts

Samantha Budd Haeberlein, PhD
Chief Medical Officer
Enigma Biomedical Group

Samantha Budd Haeberlein, PhD is a seasoned biopharmaceutical executive, researcher and drug developer, with a rich and productive career encompassing more than twenty years of international experience in the discovery and development of therapeutics and biomarkers for neurodegenerative diseases. Currently, Dr. Budd Haeberlein is chief medical officer of Enigma Biomedical Group, where she steers the development of multiple products to combat neurodegenerative diseases. Before joining Enigma, she was at AstraZeneca, holding senior research and development leadership roles across the United States, Canada, and Sweden, where she built global neuroscience programs and deepened expertise in translational medicine. She then moved to Biogen as senior vice president and head of neurodegeneration development, overseeing the portfolio that yielded Aduhelm and Leqembi the first new treatments approved for Alzheimer's disease since 2005 and the first therapies that target the fundamental pathophysiology of the disease. Dr. Budd Haeberlein earned her PhD and BSc in biochemistry from the University of Dundee, grounding her scientific rigor in molecular neuroscience. She also currently serves as a member of the Board of Directors of AlzPath, a venture partner to the Life Sciences Investment Team at ICG, and as a member of the Board of Trustees of The Boston Home, a nonprofit caring for adults with progressive neurological disease.

Session 1

Therapies Directed Against Endolysosmal Dysfunction

SESSION CHAIR

Anastasia Henry, PhD
Senior Director and Staff Scientist
Denali Therapeutics

Anastasia (Stacy) Henry, PhD, is a senior director and staff scientist at Denali Therapeutics, where she leads a team within the pathway biology group. Dr. Henry's research focuses on understanding how lysosomal dysfunction and disrupted neuronal homeostasis contribute to Parkinson's disease and other neurodegenerative disorders. Her group has been investigating the mechanisms by which disease-associated proteins affect lysosomal function and translating this insight into biomarker identification and interpretation, enabling the development of novel therapeutic approaches to treat Parkinson′s disease

and neuronopathic lysosomal storage disorders. Dr. Henry has served as the project leader for Denali's DNL310 program, a blood-brain-barrier-penetrant enzyme replacement therapy for MPS II disease and leads biology efforts supporting the LRRK2 kinase inhibitor program, both of which are now in late-stage clinical studies. She earned her PhD from the University of California, San Francisco, under the mentorship of Mark von Zastrow, MD, PhD, and completed her postdoctoral training at Pfizer in the lab of Warren Hirst, PhD.

Session 1

Therapies Directed Against Endolysosmal Dysfunction

Nicholas T. Hertz, PhD
Founder and CEO
Montara Therapeutics

Nicholas T. Hertz, PhD, is the Founder and CEO of Montara Therapeutics, a seed-stage biotech, developing therapies for brain diseases with its proprietary BrainOnly™ platform, originally developed in the Shokat Lab at the University of California, San Francisco (UCSF). He earned a BS in biochemistry from the University of California, Los Angeles, and a PhD in chemistry and chemical biology from UCSF, where he discovered the first PINK1-activating molecules and co-founded Mitokinin Inc. Following postdoctoral work at Stanford University, he served as chief scientific officer of Mitokinin, advancing PINK1 activators toward clinical development and leading the company's acquisition by AbbVie in 2023, in a deal valued up to $655 million. At Montara, Dr. Hertz emphasizes rigorous, mechanism-driven science and capital-efficient company building. He has authored over 20 publications in leading journals, including *Cell*, *Neuron*, and *Nature*, and is an inventor on more than 20 issued or pending patents. A father of three and an avid surfer, he finds creativity in both science and nature.

Abstract

Ultrapotent CNS-selective LRRK2 Inhibition to Address On-target Peripheral Toxicities

Therapeutic inhibition of LRRK2 is a compelling approach for Parkinson's disease, but development has been limited by poor central nervous system (CNS) exposure and dose-limiting lung and kidney toxicities. Montara Theraputics' BrainOnly™ platform addresses this by pairing CNS-penetrant, FKBP12-dependent LRRK2 chimeras with a novel peripheral blocker, MT1110. In pre-clinical models, chimeras achieve single-digit picomolar potency in cell-based assays with >10,000-fold attenuation in the presence of peripheral blocker MT1110. Co-dosing blocks peripheral LRRK2 inhibition, enhances brain exposure and preserves central activity, decoupling CNS from peripheral pharmacology. Validated across multiple scaffolds, this strategy offers a broadly applicable path to best-in-class, brain-selective LRRK2 therapeutics with disease-modifying potential in Parkinson's disease and other neurological disorders.

Session 1

Therapies Directed Against Endolysosmal Dysfunction

Joanna Wolak, MSc, PhD
Co-founder and CEO
Endlyz Therapeutics

Joanna WolaKm, MSc,PhD, is an entrepreneurial biotech executive with a background in research and development, early-stage biotech investment and company creation with 20+ years of experience in academia, large pharma and venture capital. She was a senior member of the neuroscience group at Eli Lilly where she led central nervous system drug discovery programs and research platforms related to disease modification in neurodegenerative diseases. In 2020, Dr. WolaKck joined SV Health Investors as a venture partner within the Dementia Discovery Fund where she co-founded Endlyz. She has led Endlyz since 2021 and is the company CEO.

Abstract

Targeting Endolysosomal Dysfunction to Treat Neurodegenerative Diseases

Endlyz Therapeutics is a biotechnology company pioneering disease-modifying therapies to restore lysosomal function and neuronal health in Parkinson's disease and other neurodegenerative diseases. Endlyz is targeting lysosomal transporters ATP13A2 and ATP10B, which are critical for maintaining lysosomal homeostasis and have first-in-class potential. The company is developing several diverse series of structurally-enabled central nervous system-penetrant ATP13A2 potentiators with a focus on clinical translation. Endlyz has consolidated key Parkinson's disease and lysosomal biology thought-leaders and powerhouse institutions as scientific co-founders. Founded and incubated by the Dementia Discovery Fund, Endlyz is backed by Oxford Science Enterprises , AbbVie Ventures, Parkinson's UK and the Centre for Drug Design and Discovery. Endlyz is currently expanding its investor syndicate.

Session 1

Therapies Directed Against Endolysosmal Dysfunction

Valerie Cullen, PhD
Senior Vice President, Research & Translation
Lysoway Therapeutics

Valerie Cullen, PhD, is a neuropharmacologist with special interest in the discovery, translation, and development of first-in-class approaches to treat neurodegenerative and neuromuscular diseases. Currently she serves as senior vice president, research and translational science at Lysoway Therapeutics, developing small molecule agonists of lysosomal ion channels. Previously, as senior vice president, head of research at Expansion Therapeutics, she was responsible for multiple programs in Alzheimer's disease, myotonic dystrophy and amyotrophic lateral sclerosis (ALS). As vice president and program lead at Lysosomal Therapeutics, Inc., she led the GCase program from discovery into clinical testing in Parkinson's disease and directly contributed to numerous regulatory filings. Earlier in her career, she conducted pre-clinical research and translation at Generian Pharmaceuticals, Aldeyra Theraeputics, NeuroPhage Pharmaceuticals and Link Medicine. Dr. Cullen earned her PhD and BSc (First Class Hons) in pharmacology at University College Dublin, Ireland and completed neuroscience fellowships at King's College, London and Harvard Medical School. She is the recipient of the Zeneca Prize and the *Annals of Neurology* prize for Highest Clinical Impact and has served as grant reviewer for the ALS Association.

Abstract

Development of a Potent, Selective and Brain-penetrant TRPML1 Agonist for the Treatment of Parkinson's Disease

Study Rationale: The autophagy-lysosome pathway (ALP) is critical for degradation of intracellular macromolecules, aggregated proteins and damaged organelles; it also regulates lysosomal exocytosis, plasma membrane repair, phagocytosis, immune modulation, antioxidant defense and overall cellular resilience. The lysosomal ion channel TRPML1 acts as the master regulator of the ALP, orchestrating both rapid and sustained responses to cellular stress and maintaining proteins, lipids, and organelles homeostasis.

Hypothesis: Pharmacological activation of TRPML1 represents a uniquely powerful approach to counteract multiple disease-driving mechanisms in Parkinson's disease (PD), by systematically restoring homeostasis in neurons, glia and other cell types, and rebalancing intra- and extracellular protein/lipid pools.

Study Design: Lysoway Therapeutics has developed a selective, highly potent brain-penetrant TRPML1 agonist that has completed good laboratory practice toxicology studies and is advancing to first-in-human

clinical testing in 2026. In preclinical PD models, the agonist improved protein and lipid homeostasis, reduced neuroinflammation, restored neurotransmitter levels, protected against neuronal loss, and improved motor function.

Impact on Diagnosis/Treatment of Parkinson's disease: Successful clinical development could deliver a novel, first-in-class disease-modifying therapy for PD patients.

Next Steps for Development: First-in-human studies will evaluate safety, tolerability, pharmacokinetics and pharmacodynamics in healthy volunteers, guiding dose-selection and biomarker strategy for subsequent Phase IIb studies in patients with PD.

Session 1

Therapies Directed Against Endolysosmal Dysfunction

Daniel Ysselstein, PhD
Vice President of Discovery and Translational Biology
Vanqua Bio

Daniel Ysselstein, PhD, is the vice president of discovery and translational biology at Vanqua Bio, a neurodegeneration-focused biotech company located in Chicago Illinois. Prior to joining Vanqua, Dr. Ysselstein worked at Northwestern University with Vanqua co-founder Dimitri Krainc, MD, PhD. His work focused on using induced pluripotent stem cell-derived models to expand our understanding of disease mechanisms of Parkinson's disease and frontotemporal dementia. Prior to his post-doctoral research, Dr. Ysselstein received his PhD from Purdue University where he studied the interaction between alpha-synuclein and lipid membrane and worked to identify molecules that modulate this interaction and inhibit alpha-synuclein membrane-induced aggregation.

Abstract

VQ-101 Demonstrates Sustained Activation of Lysosomal Glucocerebrosidase (GCase) in Healthy Volunteers and Patients with GBA1-associated Parkinson's Disease

Study Rationale: Study Rationale: The objective of this study was to evaluate the safety/tolerability, pharmacokinetic (PK) and pharmacodynamics of VQ-101 in healthy volunteers and individuals with *GBA1*-associated Parkinson's disease (GBA-PD). Mutations in the *GBA1* gene, which encodes for GCase, result in an approximately 30% reduction, on average, in GCase activity in the lysosome. VQ-101 is a fully central nervous system (CNS) penetrant small molecule allosteric activator of lysosomal GCase. In patient-derived dopaminergic neurons with a *GBA1* mutation, VQ-101 displayed a concentration-dependent activation of GCase, with 50% GCase activation resulting in a significant reduction in misfolded alpha-synuclein (aSyn) accumulation.

Hypothesis: We believe that activation of GCase to levels that restore the activity deficit associated with a *GBA1* mutation and block accumulation of misfolded aSyn is a promising therapeutic strategy to slow progression of disease in people with GBA-PD.

Study Design: VQ-101 was evaluated in single and multiple ascending doses up to 14 days in healthy volunteers and up to 28 days in participants with GBA-PD. GCase activation by VQ-101 was assessed in fresh blood samples using an analytically validated live-cell GCase assay at the start of dosing and at several time points during the dosing period.

Results: VQ-101 demonstrated a favorable safety and tolerability profile, full CNS penetrance, and a PK profile supporting once daily dosing. Dose dependent activation of lysosomal GCase greater than 50% was observed in HVs and individuals with GBA-PD receiving 150 mg or more of VQ-101. This activation was sustained through the course of dosing.

Next Steps for Development: An open label extension evaluating VQ-101 for up to 3 months in individuals with PD, with and without *GBA1* mutations, is ongoing. PD-associated biomarkers, including sphingolipids, are being explored in cerebrospinal fluid and plasma to further demonstrate GCase pathway engagement.

Session 2

Therapies Directed Against Immune Dysfunction

SESSION CHAIR

Matthew Fell, PhD

Former Executive Director, Neuroscience Discovery

Merck

Matthew Fell, PhD, is responsible for leading a team of scientists focused on the discovery of neuroimmune based therapies for neurodegenerative diseases. At Merck, he co-led teams that have discovered and advanced multiple molecules into clinical trials for Alzheimer′s disease, amyotrophic lateral sclerosis and Parkinson's disease including MK-1468 (a LRRK2 kinase inhibitor). Dr. Fell received his BSc inbBiomedical sciences/pharmacology and a PhD in neuropsychopharmacology from the University of Bradford in theU.K. As a post-doctoral fellow on the psychiatric disorders team at Eli Lilly and Company, Dr. Fell's research focused on the therapeutic potential of group II metabotropic glutamate receptors in schizophrenia.

Session 2

Therapies Directed Against Immune Dysfunction

Scott Shandler, PhD, MBA
Chief Executive Officer
Longevity Biotech, Inc.

Scott Shandler, PhD, MBA, is the co-founder of Longevity Biotech. Prior to founding Longevity, Dr. Shandler was a venture capitalist at BioAdvance, an early-stage investment fund where he was responsible for reviewing and supporting therapeutics, diagnostic and biomarker opportunities. During his career he has been involved in numerous fundraising rounds for early-stage biotech companies (>$50M) as well as supporting various in-licensing deals (>$800M). Previously, Dr. Shandler worked for Accenture's Pharmaceutical and Medical Products group, Merck Research Labs, and PolyMedix.

Dr. Shandler received a PhD in biochemistry and molecular biophysics from the University of Pennsylvania, an MBA in health care management from The Wharton School, a certificate of bioinformatics from Stanford University, and a BA in computer science from Brandeis University. He has published in leading peer-reviewed journals, is an inventor on multiple patents and has served as principal investigator on federal and private programs alike.

Abstract

LBT-3627: A Precision Immune Rebalancing Approach to Treat Parkinson's Disease

Longevity Biotech is conducting a first-in-human Phase Ia/Ib clinical trial to evaluate the safety, tolerability, pharmacokinetics and exploratory efficacy of LBT-3627, a novel immunoregulatory peptide that selectively activates the VPAC2 receptor. This two-part study will enroll both healthy volunteers and individuals with early-stage Parkinson's disease.

LBT-3627 is designed to rebalance the immune system through the VPAC2 receptor, which is the primary vasoactive intestinal peptide pathway involved in immune regulation. In multiple Parkinson's disease preclinical models, treatment with LBT-3627 demonstrated meaningful central nervous system (CNS) benefits as well as robust immunoregulatory effects, including normalization of immune responses in both animal studies and ex vivo human assays.

The trial incorporates a broad set of exploratory endpoints assessed at baseline, during treatment, and throughout a washout period. These include immune functional assays, immune cell phenotyping, peripheral alpha-synuclein analysis, and a panel of exploratory biomarkers to guide precision patient enrichment and tracking in the next clinical phase of clinical development. Clinical assessments, including the Unified Parkinson's Disease Rating Scale and the Brief Smell Identification Test, will also be evaluated.

Importantly, the trial is designed to validate findings from a prior Phase 0 study in Parkinson's patients while providing the first comprehensive evaluation of whether LBT-3627 safely restores immune balance and provide preliminary evidence of clinical efficacy in Parkinson's disease patients.

Session 2

Therapies Directed Against Immune Dysfunction

Rebecca Crean, PhD
Chief Executive Officer
Ventyx Biosciences

Rebecca Crean, PhD, is executive director, clinical development at Ventyx Biosciences, a clinical-stage biopharmaceutical company focused on developing innovative medicines for patients with neurodegenerative, autoimmune, and inflammatory diseases, where she leads clinical strategy and execution for central nervous system programs. She brings deep expertise in neurotherapeutics and translational research with a focus on advancing treatments for complex neurological and inflammatory conditions. Prior to joining Ventyx, Dr. Crean served as executive director at Ionis Pharmaceuticals, leading the clinical development of antisense oligonucleotide therapy programs for rare, neurological disorders. Earlier, she led the translational research program at The Scripps Research Institute, investigating the impact of neurological disease on brain function. Dr. Crean earned a PhD in clinical psychology and completed her post-doctoral training in neuropsychology at the Naval Medical Center, San Diego.

Abstract

Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of VTX3232, a CNS-penetrant NRLP3 Inhibitor, in Participants with Early-stage Parkinson's Disease

Study Rationale: Neuroinflammation mediated by the innate immune system has been shown to play a critical role in the pathogenesis of Parkinson's disease. NLRP3, a key regulator of the innate immune system, is activated by pathologic alpha-synuclein, resulting in inflammation in the brain and cell death. VTX3232 is a potent, brain-penetrant, oral inhibitor of NLRP3. In Phase I studies in healthy adults, VTX3232 was well-tolerated and achieved predicted therapeutic drug concentrations in both plasma and cerebrospinal fluid (CSF; the fluid surrounding the brain) at doses ≥12 mg. At these doses, VTX3232 was associated with reduced NLRP3-mediated inflammation.

Hypothesis: The long-term goal of the VTX3232 program is to test whether blocking NLRP3-mediated inflammation impacts the progression of Parkinson's disease. In the current study, the key objectives were to evaluate the safety, drug levels in the blood and central nervous system, and biological activity of VTX3232 in participants with early-stage Parkinson's disease.

Study Design: An open-label trial was conducted in approximately 10 participants with early-stage Parkinson's disease. Study participants received a 40 mg oral dose of VTX3232 once daily for 28 days. Safety and tolerability of VTX3232 were assessed as the primary endpoint. VTX3232 concentrations were determined in plasma and CSF and the effect of VTX3232 on NLRP3-related biomarkers of inflammation was assessed. Lastly, exploratory endpoints included an assessment of Parkinson's disease symptoms before and after treatment with VTX3232.

Impact on Diagnosis/Treatment of Parkinson's disease: In this safety and biomarker study, once-daily administration of VTX3232 was well-tolerated for 28 days in participants with Parkinson's disease. Drug concentrations of VTX3232 in the central nervous system were well above levels that block the majority of NLRP3 activity. Furthermore, in the study participants, VTX3232 was associated with robust inhibition of biomarkers of the innate immune system. Thus, this clinical trial of VTX3232 represents an important milestone in advancing our understanding of the potential of NLRP3 inhibition as a disease-modifying treatment for Parkinson's disease and related neurodegenerative disorders.

Next Steps for Development: The next phase of development is to assess whether inhibition of inflammation by VTX3232 impacts the clinical progression of Parkinson's disease. To this end, planning is underway for a placebo-controlled clinical efficacy trial in patients with early-stage Parkinson's disease.

Session 2

Therapies Directed Against Immune Dysfunction

Louise Klem, PhD
Lead Research Scientist
Vesper Biosciences

Louise Klem, PhD, is Lead Research Scientist at Vesper Bio, where she leads the team of Research Scientists and acts as the Head of Preclinical Research, driving the early-stage efforts to develop novel therapies to treat central nervous system diseases. She is co-principal investigator on the Michael J. Fox Foundation (MJFF)-funded project assessing the therapeutic potential of sortilin inhibition in Parkinson's disease. She holds a PhD in neuropharmacology and combines expertise in rodent behavior research, translational neuroscience and cross-functional project management.

Abstract

Sortilin Inhibition Elevates Progranulin and Holds Therapeutic Potential in Parkinson's Disease

Background: Sortilin is a multifunctional sorting receptor that regulates inflammation and neuronal viability. It forms a complex with the P75 neurotrophin receptor that binds pro-neurotrophins and facilitates apoptosis. Components of this complex are upregulated during conditions of insidious cell health, shifting the balance from survival to death. This complex is expressed on dopaminergic neurons of the substantia nigra and is implicated in dopaminergic neuron loss in Parkinson's disease (PD). Separately, sortilin regulates progranulin levels, a protein with potent neurotrophic and anti-inflammatory effects. Progranulin deficiency is causative or worsens neuroinflammation and degeneration in different neurodegenerative diseases. Reduced progranulin levels correlate with worsened disease severity in patients with Parkinson's disease, and progranulin elevation attenuates inflammation, apoptosis, and motor phenotypes in rodent models. Together, these mechanisms support that sortilin inhibition holds therapeutic potential in Parkinson's disease both by directly attenuating the complex-driven neurodegeneration and by elevating progranulin-driven neuroprotection and anti-inflammation.

Objectives: Vesper Bio has developed novel small molecule sortilin inhibitors for oral administration and is investigating the therapeutic potential in different neurodegenerative diseases, including Parkinson's disease.

Methods: Lead candidate for Parkinson's disease, VES002, has been thoroughly characterized in a variety of assays. Measures included target affinity, pharmacokinetics, pharmacodynamics, and impact on sortilin protein. VES002 and VES001, the clinical candidate for frontotemporal dementia, have been tested in a viral alpha-synuclein overexpression mouse model of PD (AAV-A53T-aSyn).

Results: The compounds show high affinity for sortilin, do not impact total or cell surface levels of sortilin and show satisfactory pharmacokinetic and pharmacodynamic profiles for oral delivery. Furthermore, VES001 has been shown to elevate central progranulin levels 2- to 2.5-fold. Some data from the AAV-A53T-aSyn mouse model will be available for presentation at the MJFF conference.

Conclusion: Orally delivered sortilin inhibitors hold promise as a novel therapeutic approach to attenuate neuroinflammation and neurodegeneration for different neurodegenerative diseases, including PD.

Session 3

Biomarker Advances to Support Clinical Development

SESSION CHAIR

Tanya Simuni, MD, FAAN

Arthur C. Nielsen Jr. Professor of Neurology
Director, Parkinson's Disease and Movement Disorders Center
Northwestern University

Tanya Simuni, MD, FAAN, leads a comprehensive movement disorders center at Northwestern University Feinberg School of Medicine that is recognized by the Parkinson's Foundation, the Huntington Disease Society of America and the Wilson's Foundation as a Center of Excellence and serves as a training model in the region.

She is an internationally recognized expert in design and implementation of Parkinson's disease (PD) clinical trials focused on disease modification. Dr. Simuni is the lead author of the new biological definition and staging framework of Neuronal synuclein disease (NSD). She serves on the leadership team of the Michael J. Fox Foundation-sponsored Parkinson's Progression Marker Initiative (PPMI) study —the largest PD biomarker initiative — where she also serves as the principal investigator for the first platform trial to test therapeutics in biologically defined prodromal population (P2P). She serves on several steering committees for the PD international clinical trials, several committees of the Parkinson Study Group, and the Parkinson Foundation. Dr. Simuni is the site primary investigator for the Network for Excellence in Neuroscience Clinical Trials (NEXT). She has more than 150 publications in peer-reviewed scientific journals, and she has lectured nationally and internationally on PD and other movement disorders. In addition to her research career, Dr. Simuni is highly committed to education of the next generation of physicians and patient advocacy.

Dr. Simuni is an active member of the American Academy of Neurology, the American Neurological Association, the Movement Disorders Society, and the Parkinson's Study Group.

Session 3

Biomarker Advances to Support Clinical Development

Kenneth Marek, MD
Distinguished Scientist
The Institute for Neurodegenerative Disorders

Kenneth Marek, MD, is president and senior scientist at the Institute for Neurodegenerative Disorders. Dr. Marek's major research interests include identification of biomarkers for early detection, assessment of disease progression and development of new treatments for neurodegenerative disorders including Neuronal synuclein disease (Parkinson's disease and dementia with Lewy bodies), Alzheimer disease and related neurodegenerative disorders. His specific interest has been in in vivo neuroreceptor imaging biomarkers. He has authored numerous neurology and neuroscience publications on these topics. Dr. Marek has and continues to be the principal investigator of several ongoing multi-center international studies, including the Parkinson's Progression Marker Initiative (PPMI) and the Parkinson Associated Risk Syndrome (PARS) study.

Dr. Marek serves as a special scientific advisor to The Michael J. Fox Foundation. He has served in leadership roles in several organizations focused on neurodegenerative disorders and has been the recipient of numerous grants to support his work in Parkinson's disease, Alzheimer's disease and Huntington's disease, including the Robert A. Pritzker Prize for Leadership in Parkinson's Research. He also was a co-founder of Molecular NeuroImaging, LLC and Xing Imaging LLC, companies providing discovery and clinical neuroimaging research services.

Abstract

A New Strategy for Dopamine Imaging Analytics to Accelerate PD Therapeutic Trials

Dopamine imaging is a key biomarker for Parkinson's Disase (PD) and other synucleinopathies, and a core biomarker in the Neuronal synuclein disease (NDS) biologic definition and staging platform. Robust data acquired over decades have demonstrated that dopamine imaging is an effective tool to enrich clinical studies for PD pathology. Dopamine imaging has also been widely used as a marker of longitudinal change in clinical studies, but data have been less consistent largely due to the variance in the imaging outcome measure.

Recently advances optimizing dopamine imaging analysis have been developed to enhance the power of dopamine imaging to detect longitudinal change. An automated analysis workflow was implemented in MIAKAT v5.0, whereby each image was normalized to template space via a linear combination of the 17 template images. Specific binding ratio (SBR) values were calculated via 3D atlas definitions of striatal regions, with occipital lobe and cerebral white matter reference regions. The workflow was applied to over 7,700 images from the Parkinson's Progression Markers Initiative (PPMI) dataset.

The MIAKAT PPMI DaTscan (DAT) data will be presented and compared to the legacy PPMI DAT data. In addition, dopamine imaging data acquired with both dopamine transporter tracers and vesicular monoamine tracers were harmonized using a newly developed centamine scale. The centamine scales enable multiple tracer outcomes to be quantified on a common quantitative scale to both measure both cross-sectional imaging data and longitudinal change in a study utilizing multiple dopaminergic tracers.

The improved power of dopamine imaging using an optimized analysis pipeline and the potential for quantification of multiple tracers using the centamine scale offers the opportunity to acquire more valuable imaging data that will accelerate clinical therapeutic development.

Session 3

Biomarker Advances to Support Clinical Development

Roger Gunn, PhD

Chief Science Officer

Xing Imaging

Roger Gunn, PhD, is an international expert in imaging and drug development. He has discovered, developed and translated imaging techniques to measure biological processes for drug development and they are now central to biomarker strategies of pharmaceutical companies. In his current role as chief science officer at Xing Imaging, he is heading the research and development of new biomarkers and analytics and leading the design, analysis and delivery of clinical imaging trials for pharmaceutical companies. He is also Emeritus Professor of Molecular Neuroimaging at Imperial College and founder of the analytics software company MIAKAT Ltd. Dr. Gunn has published over 200 peer reviewed papers in the field of imaging, neuroscience and drug development with an H-index of 75 and has delivered over 80 invited lectures. His career has involved positions on research councils, consultancy to pharmaceutical companies and the training and mentoring of PhD students and clinical research fellows.

Cong Liu, PhD

Professor

Shanghai Institute of Organic Chemistry

The research of Cong Liu, PhD, focuses on protein phase separation and pathological aggregation of amyloid proteins in neurodegenerative diseases with systematical achievements during his independent research career since 2013. In brief, by combining cutting-edge chemical and biological approaches, Dr. Liu revealed the structural basis of protein pathological aggregation in neurodegenerative diseases; demonstrated the regulation mechanism of protein aggregation by disease-related chemical modification; explained at the atomic level how small molecules bind to pathological amyloid fibril; and developed new strategies of small molecules modulating protein phase separation for therapeutic application. Dr. Liu has published over 100 SCI papers, the majority of which focus on alpha-synuclein. As corresponding or co-corresponding author, he has published over 70 papers in various journals including *Cell*, *Science*, and *The Proceedings of the National Academy of Sciences of the United States*, *Nature Structural & Molecular Biology*, *Nature Chemical Biology*, *Journal of the American Chemical Society*, *Cell Research*, *Nature Communications*, and *Angewandte Chemie International Edition*, *Molecular Cell*, *Developmental Cell*, and *Science Advances*.

Abstract

PET Imaging of Alpha-synuclein with 18F-FD4

Study Rationale: Alpha-synuclein is central to Parkinson's disease (PD) and accumulates over time in the brain of patients. The ability to measure brain levels of alpha-synuclein would have important consequences for further understanding of the disease and the development of treatments. A new PET tracer, 18F-FD4, which has the potential to measure levels of alpha-synuclein in the human brain will be presented.

Hypothesis: Is 18F-FD4 a suitable PET imaging biomarker to measure a-synuclein deposition in PD?

Study Design: Alpha-synuclein is the key misfolded protein that accumulates in the brain of patients with PD. Data will be presented from the discovery and development program of the putative alpha-synuclein tracer, 18F-FD4. This will include in vitro, pre-clinical and initial human data along with plans for future clinical studies.

Impact on Diagnosis/Treatment of Parkinson's disease: The ability to measure brain levels of alpha-synuclein would be transformative for both diagnosis and the development of treatments because it is one of the earliest hallmarks of the disease and accumulates over time. This means that imaging could be used to identify patients early and to monitor their progression in the presence and absence of novel therapies.

Next Steps for Development: Plans for future clinical validation studies will be presented. Successful outcomes from these studies would lead to the establishment of a radiochemistry network to enable larger scale studies that would look at further characterizing the imaging tracer in a larger cohort of subjects with PD cross-sectionally and longitudinally, laying the groundwork for its effective use in clinical trials of new potential treatments.

Session 3

Biomarker Advances to Support Clinical Development

Tuomas Knowles, PhD
Professor of Physical Chemistry
University of Cambridge

Tuomas Knowles, PhD, is the 1920 Professor of Physical Chemistry at the University of Cambridge and the co-director of the Cambridge Centre for Misfolding Diseases. He studied biology at the University of Geneva and physics at ETH Zürich, and obtained his PhD working at the Cavendish Laboratory and the Nanoscience Centre in Cambridge. Dr. Knowles joined the faculty of the Department of Chemistry at Cambridge University in 2010. He then successively held a university readership between 2013 and 2015 and a professorship between 2015 and 2023 in the Department of Chemistry. In 2023 he was elected to the 1920 Chair of Physical Chemistry at Cambridge. Dr. Knowles is the recipient of multiple international prizes, including the Sackler Prize for Biophysics and the Corday-Morgan Prize from the Royal Society of Chemistry.

Abstract

Digital Seed Amplification Assays

Study Rationale: Pathological aggregation of alpha-synuclein is a defining feature of Parkinson's disease (PD). Seed amplification assays (SAAs) have emerged as powerful tools to detect misfolded alpha-synuclein in biofluids including cerebrospinal fluid (CSF), offering a potential molecular biomarker for PD. Our project aims to advance this approach using a digital seed amplification platform that enhances sensitivity and quantification. This technology enables detection of minute quantities of aggregates at the single seed level, providing a novel platform for PD biomarker development.

Hypothesis: We hypothesize that digital seed amplification of CSF can help to enhance sensitivity of conventional seed amplification assays and can provide a route towards quantifying the aggregate load in patient samples.

Study Design: We use a microfluidic-based digital seed amplification platform to partition CSF samples into thousands of nanoliter reactions, enabling precise quantification of alpha-synuclein seeding activity. Early results show promise for detecting and quantifying PD-related seeding activity in patient samples.

Impact on Diagnosis/Treatment of Parkinson's disease: This project could establish a quantitative, scalable biomarker for PD diagnosis, supporting earlier and more accurate detection of disease onset. Such a tool would also facilitate patient stratification and enable better monitoring of disease-modifying therapies in clinical trials.

Next Steps for Development: We will validate the assay in larger, longitudinal cohorts to assess its predictive and diagnostic performance, optimize assay standardization, and explore integration with other molecular and digital biomarkers.

Session 3

Biomarker Advances to Support Clinical Development

Mari Niemi, PhD

Senior Expert Data Science
Novartis Pharma AG

Mari Niemi, PhD, is a senior expert in data science at Novartis Biomedical Research, where she specializes in harnessing human molecular data to accelerate early target and drug discovery in neurodegeneration. Her work bridges cutting-edge data science with translational research, with an emphasis on developing new innovative approaches for target and biomarker discovery. Dr. Nemi serves as the early-research co-lead for The Michael J. Fox Foundation–Novartis collaboration, guiding a team of drug discovery data scientists in integrating molecular and multimodal data to uncover disease signatures and progression markers. Prior to joining Novartis, her research focused on understanding the genetic contributions to rare and common diseases. She has co-authored several papers on neurodevelopmental disorders and infectious diseases in peer reviewed journals and served as analysis team lead in a global consortium. Dr. Nemi holds a BSc in biomedical science, an MSc in molecular genetics from Imperial College London and a PhD in computational genetics from the University of Cambridge.

Piet Aarden, MSc

Associate Director Data Science
Novartis Pharma AG

Piet Aarden, MSc, is associate director of data science at Novartis, where he serves as the late-stage development co-lead for The Michael J. Fox Foundation–Novartis collaboration. He leads a multidisciplinary team of statistical methodologists and data scientists focused on advancing disease understanding in Neuronal synuclein disease. Since joining Novartis, Mr. Aarden has specialized in multi-modal disease progression analysis, integrating diverse data sources to uncover insights into neurological disorders. He holds a master of science in mechanical engineering with a specialization in control engineering from Delft University of Technology.

Abstract

Multi-modal Modeling of Neuronal Alpha-synuclein Disease Progression Using PPMI Data

Study Rationale: Neuronal synuclein disease (NSD) begins years before it clinically manifests; early disease trajectory is therefore not fully represented by clinical or biomarker assessments at diagnosis. Analyzing NSD progression is further complicated by the variability in age of onset and progression across multiple domains. There is a critical need for robust, data-driven frameworks to characterize disease evolution and inform clinical trial design.

Hypothesis: We hypothesize that a novel, multimodal modeling approach will enable comprehensive and individualized characterization of NSD progression. Integrating clinical, imaging and biomarker data may facilitate earlier detection of changes across domains and help clarify sources of heterogeneity in disease trajectories.

Study Design: Within the MJFF–Novartis research collaboration, we utilized data from the Parkinson's Progression Markers Initiative (PPMI), selecting individuals with NSD confirmed by cerebrospinal fluid alpha-synuclein seed amplification assay. We developed a statistical modeling framework that incorporates individual participant trajectories to generate multi-modal progression curves for diverse outcome measures. The model currently integrates clinical assessments and neuroimaging outcomes, with plans to further incorporate molecular biomarkers after evaluation of the cross-sectional proteomic, transcriptomic and metabolomic signatures of NSD. This approach supports a multidimensional characterization of disease onset and progression.

Impact on Diagnosis/Treatment of NSD: The resulting progression curves delineate the evolution and variable rates of progression across domains. This framework enables quantification of progression speed relative to expected trajectories for each disease phase and individual. Furthermore, integration of molecular data, including proteomics, facilitates identification of factors distinguishing slow and fast progressors, with the long-term goal of informing clinical and biomarker strategies in future trials.

Next Steps for Development: Future work will focus on identifying molecular characteristics that differentiate rate of progression among individuals with NSD, and biomarkers differentiating individuals who progress differently in certain clinical or subclinical domains. Additionally, we aim to use the clinical framework to expand the NSD-ISS by establishing data-driven cutoffs for multi-modal outcomes, further enhancing disease staging and stratification.

Closing Session

Hot Topics in Parkinson's Disease Therapeutic Development

Catherine Kopil, PhD

SVP and Head of Clinical Research

The Michael J. Fox Foundation

Catherine (Katie) Kopil, PhD, is the Senior Vice President and Head of Clinical Research at The Michael J. Fox Foundation where she focuses on building the Foundation's capacity as an unprecedented stakeholder in Parkinson's drug development – a nimble, patient-focused problem-solver whose efforts are demonstrably accelerating progress toward treatment breakthroughs. She leads a team investing in solutions to de-risk clinical development for Parkinson's and related disorders. Katie and her team support field-enabling efforts including seminal natural history studies like the Parkinson's Progression Markers Initiative, alignment on regulatory acceptable endpoints for clinical trials and integrating patient perspectives throughout R&D.

Prior to joining the Foundation, Katie completed doctoral and postdoctoral training in Neuroscience and Bioengineering respectively at the University of Pennsylvania. Her research focused on brain injury that occurs during acute trauma such as cardiac arrest and concussion. Katie also helped speed clinical research as a clinical trial coordinator at Memorial Sloan-Kettering Cancer Center in NYC, which is where her dual passions for science and serving patients first intersected.

Katie graduated from Princeton University with a BA in Psychology and holds a PhD in Neuroscience from the University of Pennsylvania.

Billy Dunn, MD

Senior Advisor

Michael J. Fox Foundation

Billy Dunn, MD, was the founding director of the Office of Neuroscience, Center for Drug Evaluation and Research, at the U.S. Food and Drug Administration, a position he held since the founding of the office in 2019 through February 2023. He was responsible for the regulatory oversight of all research conducted to support neuroscience drug development, including the regulation and review of investigational new drug applications and marketing applications for drug and biologic products. From 2005 to 2019, he held positions of increasing seniority in the Division of Neurology Products, Center for Drug Evaluation and Research, including his role as director of that division. Dunn is a trained neurologist and vascular neurologist with experience in basic research, clinical research, and clinical care. He earned his BA from the University of Virginia and his MD from the F. Edward Hébert School of Medicine in Bethesda, Maryland.

Fred Goldstein, MS

President and Founder
Accountable Health, LLC

Fred Goldstein, MS, is the president and founder of Accountable Health, LLC, an international population health consulting firm, and host of *Unscripted — The AMCP Podcast for the Academy of Managed Care Pharmacy*. His extensive career includes roles as a hospital CEO, vice president and general manager of an HMO, and founder of Specialty Disease Management Services (SDM). Notably, at SDM he developed the first Medicaid disease management programs for several chronic illnesses. His policy work includes contributing to the inclusion of the Medicare Annual Wellness Visit in the Affordable Care Act and testifying before several state legislative committees on population health and disease management. Mr. Goldstein is an Instructor at the John D. Bower School of Population Health at the University of Mississippi Medical Center and serves on the editorial board of *Population Health Management*.

Gennaro Pagano, MD, PhD

Group Leader and Expert Medical Director in Neuroscience and Rare Disease
Roche

Gennaro Pagano, MD, PhD, is a physician-neuroscientist and pharmaceutical medical director with over 15 years of translational research in academia and drug development. He is leading the early clinical development of small and large molecules, gene therapies, and potential disease-modifying therapies for Parkinson's disease at Roche Pharma Research and Early Development (pRED). He served as chair of the Parkinson's Progression Markers Initiative Partner Scientific Advisory Board from 2020 to 2021 and industry co-director of Critical Path for Parkinson's Disease from 2023 to 2025. Dr. Pagano is also an honorary clinical associate professor at the University of Exeter Medical School, London.

Dr. Pagano obtained an MD at the University of Naples Federico II, a master in epidemiology (MSc) at the University of Milan, a PhD in clinical neuroscience at King's College London, and postdoctoral training in PET imaging with focus on genetics, preclinical and prodromal Parkinson's disease at Imperial College London. He also completed fellowships in movement disorders and neuroimaging at Mount Sinai Medical Center in New York and Cedars Sinai Medical Center in Los Angeles.

Bryan Tysinger, PhD

Associate Professor
The University of Southern California

Bryan Tysinger, PhD is an associate professor (research) at the University of Southern California (USC) Sol Price School of Public Policy and director of health policy simulation at the USC Schaeffer Center. His research models health and economic outcomes over the life course to identify policy solutions that improve early-life trajectories, support mid-life course corrections, and promote healthy aging. He leads development of the Future Elderly Model, Future Adult Model, and the U.S. Cost of Dementia Model, large-scale microsimulation platforms used to evaluate health and policy interventions in the U.S. and internationally. His current work examines Alzheimer's disease, Parkinson's disease and obesity, focusing on their long-term impacts on health, longevity and economic well-being. Dr. Tysinger earned a BS in applied mathematics from Harvey Mudd College and both MA and PhD degrees in policy analysis from the RAND School of Public Policy.

Poster Session

An Overview of the Global Parkinson's Genetics Program (GP2)

Cornelis Blauwendraat, PhD
Chief Data Strategy Officer
Coalition for Aligning Science

Cornelis Blauwendraat, PhD, is the chief data strategy officer of the Coalition for Aligning Science (CAS), where he provides strategic guidance on the organization's data strategy and ensures that data assets are used effectively to achieve CAS's goals across the initiatives under the Coalition's management. He also serves as one of the leads for the Global Parkinson's Genetics Program (GP2) which is a resource initiative of Aligning Science Across Parkinson's (ASAP), aiming to dramatically expand our understanding of the genetic basis of PD and to make that knowledge globally relevant. Previously, Dr. Blauwendraat was a Stadtman Investigator at the National Institutes of Health National Institute on Aging at the Bethesda campus. While there, his lab worked on dissecting the genetic basis of neurodegenerative disorders including Alzheimer's disease and Parkinson's disease using large omics datasets with the goal of understanding disease mechanisms and identifying potential future therapeutic targets. Dr. Blauwendraat received his MSc in biomedical sciences from VU University, Netherlands and his PhD in neuroscience from University of Tübingen, Germany. Both his MSc and PhD were focused on dissecting the complex genetic architecture across neurodegenerative diseases.

Abstract

While genetics is known to play a crucial role in Parkinson's disease (PD), our understanding remains incomplete. A significant barrier to progress has been the lack of diversity in genetic studies, with over 90% of participants in large-scale analyses being of European ancestry. This lack of genetic diversity limits our ability to: 1) Discover novel risk loci that may be rare or absent in European populations; 2) Understand how genetic risk varies across different ancestral backgrounds; and 3) Develop effective therapies and prevention strategies for all populations.

To address this critical gap, the Global Parkinson's Genetics Program (GP2) was established in 2020 as a foundational program of the Aligning Science Across Parkinson's (ASAP) initiative.

The overall goal of GP2 is to comprehensively understand the genetic architecture of Parkinson's disease by genotyping over 250,000 volunteers from diverse ancestries across the globe, making the data broadly accessible to the research community.

GP2 is now at a point where major data production enables rapid discovery. Even at this early stage of large data, GP2 is already making transformative discoveries, identifying more than 70 new risk loci/genes, and mapping out the global spectrum of genetic risk variants across each population. This work is just the beginning of realizing our vision: a world where the genetic underpinnings of PD are understood for every individual, enabling the development of personalized treatments and preventative strategies.

Development of USP30 Inhibitors to Restore Mitophagy in Parkinson's Disease

Spring Behrouz, PhD
Chief Executive Officer
Vincere Biosciences

Spring Behrouz, PhD, is the co-founder and CEO of Vincere Biosciences, where she leads the development of therapeutics that enhance mitochondrial quality control to slow or halt Parkinson's disease progression. She also serves as co-founder and CEO of NeuroInitiative, a computational biology company with patented simulation platforms that accelerate drug discovery.

Dr. Behrouz's research has long centered on converging biological pathways in Parkinson's disease, from her doctoral work at Michigan State University on the selective vulnerability of dopaminergic neurons to her postdoctoral studies at the Mayo Clinic on LRRK2-mediated pathogenesis. She has overseen ambitious discovery and development programs, recruited top scientific talent, and earned recognition including *Jacksonville Business Journal*'s 40 Under 40, One Spark's top science award, and speaking platforms such as TEDx and the March for Science. These efforts are aimed to yield significant benefits for patients with Parkinson's disease and other age-related diseases.

Abstract

Study Rationale: Mitochondrial dysfunction and impaired mitophagy are core drivers of Parkinson's disease. USP30, a mitochondrial deubiquitinase, suppresses mitophagy by counteracting the PINK1/parkin pathway. Genetic or pharmacological inhibition of USP30 enhances the clearance of damaged mitochondria, reduces oxidative stress, and confers neuroprotection in preclinical models. Targeting USP30 therefore represents a promising disease-modifying strategy.

Hypothesis: Selective inhibition of USP30 will restore mitochondrial quality control, enhance clearance of damaged mitochondria, ultimately slowing or halting Parkinson's disease progression

Study Design: Vincere has developed central nervous system (CNS)-penetrant, orally bioavailable USP30 inhibitors optimized for potency, selectivity, and brain exposure. Preclinical studies assess their ability to protect neurons from mitochondrial stress, enhance mitophagy in genetically engineered Mito-QC reporter mice, and improve outcomes across age groups. Safety, tolerability, and pharmacokinetic studies are underway to support regulatory approval and first-in-human trials.

Impact on Diagnosis/Treatment of Parkinson's disease: This program has the potential to deliver the first disease-modifying therapy that directly targets mitophagy, addressing a root cause of Parkinson's disease.

Next Steps for Development: Following successful Investigational New Drug application-enabling studies, Vincere will initiate first-in-human clinical trials supported by translational biomarkers of mitophagy activation, advancing toward a novel therapeutic option for Parkinson's patients.

Poster Session

Evaluation of the Pharmacodynamic Effects of BIIB122/DNL151 in Participants with LRRK2 Mutation-driven Parkinson's Disease (BEACON Study)

Jillian Kluss, PhD
Senior Scientist
Denali Therapeutics

Jillian Kluss, PhD, received her PhD in cell biology at the National Institute on Aging, where she developed readouts of endogenous kinase activity of LRRK2 across various tissues, and identified novel cellular pathways that are modulated by chronic LRRK2 inhibition *in vivo*. Currently, she serves as the biomarker lead for Denali's Parkinson's Disease portfolio, developing the biomarker strategy at both pre-clinical and clinical program stages, including the Phase IIb (LUMA) and Phase IIa (BEACON) studies investigating the safety, pharmacodynamic effects and clinical efficacy of the selective, investigational LRRK2 small molecule inhibitor BIIB122/DNL151.

Abstract

Study Rationale: BIIB122/DNL151 is a central nervous system (CNS)-penetrant small molecule LRRK2 inhibitor co-developed by Biogen Inc. and Denali Therapeutics Inc. as a potential treatment for individuals with Parkinson's disease (PD). Dose-dependent reductions in whole-blood pS935 LRRK2, urine BMP(22:6/22:6) and cerebrospinal fluid (CSF) total LRRK2 have been observed in healthy participants and individuals with sporadic PD treated with BIIB122/DNL151.

Hypothesis: The BEACON study (NCT06602193), solely funded and conducted by Denali Therapeutics Inc, aims to characterize these target and pathway biomarker effects in addition to lysosomal and disease biomarkers in LRRK2-PD participants treated with BIIB122/DNL151 as well as to deeply characterize the biologic profile of individuals with LRRK2-driven PD.

Study Design: By leveraging biomarker data from our Phase I studies as well as from our Parkinson's Progression Marker Initiative study characterizing the lipid and metabolic profiles of genetic and sporadic PD, this Phase IIa, randomized study will evaluate pharmacodynamic biomarker effects in approximately 50 LRRK2-PD participants during the 12-week, double-blind, placebo-controlled period followed by an open label extension period (up to 96 weeks). Exploratory endpoints may include assessment of biomarkers of lysosomal function such as the measurement of lipids in the glycosphingolipid pathway. In addition, we aim to explore measurements of lysosomal enzymes, and biomarkers of neurodegeneration such as Tau and phospho-Tau species in CSF, plasma, and/or urine at baseline and post-dose timepoints. Furthermore, since a substantial portion of individuals with LRRK2-PD do not manifest alpha-synuclein pathology, assessment of alpha-synuclein aggregation via the seed amplification assay (SAA) will be employed to determine differential treatment responses based on SAA status.

Impact on Diagnosis/Treatment of Parkinson's disease: Data generated from this study will enable scientific insights into mechanisms and biomarkers of LRRK2-driven PD, deepen our understanding of the therapeutic mechanism of action of BIIB122/DNL151, and may reveal unique SAA+ vs. SAA- LRRK2-PD biomarker signatures.

Next Steps for Development: This study has the potential to advance our understanding of the safety, tolerability and pharmacodynamic effects of BIIB122/DNL151 in individuals with LRRK2-PD and may inform a Phase IIb or Phase III clinical trial in this population.

Poster Session

Patient Engagement Services for Industry and Study Partners

Maggie Kuhl
Vice President, Head of Patient Engagement
The Michael J. Fox Foundation

As vice president and head of patient engagement at The Michael J. Fox Foundation, Maggie Kuhl leads a team engaging community partners and gathering patient experience data toward patient-focused drug development, as well as practicing and piloting recruitment and retention methods to enable faster trials. Ms. Kuhl directs recruitment strategy for the Foundation's Parkinson's Progression Markers Initiative, a longitudinal observational study with remote screening and enrollment at 50 international sites for thousands of participants. Prior to joining the Foundation in 2013, Ms. Kuhl worked in communications at the National Institutes of Health.

Abstract

The Michael J. Fox Foundation's (MJFF) patient engagement team partners with sponsors to bring the voice of the Parkinson's community into every stage of research. The team builds bridges between the Parkinson's community and research sponsors, ensuring studies reflect the needs, experiences, and priorities of those affected to accelerate the science. We do this by gathering and leveraging partnerships and perspectives, developing resources and sharing learnings widely with stakeholders.

Our support includes:

Patient Insights: Compiled datasets and tailored input on patient preferences, needs, and experiences. We support sponsors with targeted insight reports, survey design consultation, and storytelling strategies grounded in community perspective.

People with Lived Experience (PWLE) Network: A diverse network of over 500 individuals representing a wide range of demographics, disease experiences, stages, and research backgrounds. Our infrastructure enables timely, targeted engagement of PWLE through interviews, panels, and advisory activities.

Trial Design and Materials Reviews: Early stage, practical feedback on study protocols, patient-facing materials, and recruitment strategies. Reviews aim to address feasibility, reduce burden, improve accessibility, and ensure the research reflects patient priorities and needs in the Parkinson's community.

Recruitment & Retention Strategy Support: We build research infrastructure through toolkits, site/vendor consultation, and partnerships with community-based organizations. Current efforts include testing novel recruitment and retention tactics including return of research information, piloting strategies for increased diversity and launching a community health worker training program focused on PD and research awareness.

Clinical Trial Matching (Fox Trial Finder): MJFF's matching tool filters by study type, location, and disease stage. We provide customizable study listings with patient-friendly language, site-level referral tracking, and access to over 3,000 research volunteers for targeted outreach.

Our poster showcases how these offerings can be leveraged individually or in combination to support trials, boost enrollment, and center the Parkinson's community in research. By engaging with MJFF's patient engagement team, sponsors gain a trusted partner committed to improving trial relevance, accessibility, and impact.

Structure-guided Design of FD4—a PET Tracer of Alpha-synuclein Fibril

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Cong Liu, PhD
Professor
Shanghai Institute of Organic Chemistry

The research of Cong Liu, PhD, focuses on protein phase separation and pathological aggregation of amyloid proteins in neurodegenerative diseases with systematical achievements during his independent research career since 2013. In brief, by combining cutting-edge chemical and biological approaches, Dr. Liu revealed the structural basis of protein pathological aggregation in neurodegenerative diseases; demonstrated the regulation mechanism of protein aggregation by disease-related chemical modification; explained at the atomic level how small molecules bind to pathological amyloid fibril; and developed new strategies of small molecules modulating protein phase separation for therapeutic application. Dr. Liu has published over 100 SCI papers, the majority of which focus on alpha-synuclein. As corresponding or co-corresponding author, he has published over 70 papers in various journals including *Cell*, *Science*, and *The Proceedings of the National Academy of Sciences of the United States*, *Nature Structural & Molecular Biology*, *Nature Chemical Biology*, Journal of the *American Chemical Society*, *Cell Research*, *Nature Communications*, and *Angewandte Chemie International Edition*, *Molecular Cell*, *Developmental Cell*, and *Science Advances*.

Abstract

Investigators: Cong Liu, Dan Li, Jian Wang, Chuantao Zuo, Li Tan, Jiang Bian, Roger Fan, Qing Liang

Study Rationale: Parkinson's disease (PD) and related synucleinopathies are characterized by the pathological aggregation of alpha-synuclein (aSsyn), which constitutes a central hallmark of disease progression. Non-invasive imaging of aSyn pathology is urgently needed to facilitate early diagnosis, patient stratification, and therapeutic monitoring. However, effective aSyn PET tracers — particularly those capable of reliably detecting pathology in PD — remain lacking. High-resolution cryogenic electron microscopy (cryo-EM) structures have delineated the precise binding modes of small molecules on α-syn fibril, defining the key structural determinants that are critical for guiding the rational design of novel PET tracers.

Informed by these insights, we employ a structure-guided design paradigm to generate a candidate PET tracer with enhanced binding specificity to α-syn pathology.

Hypothesis: The structure-guided design is anticipated to generate a candidate PET tracer (FD4) with superior affinity and specificity for pathological aSyn fibrils, thereby enabling precise in vivo imaging of aSyn pathology in PD.

Study Design: The lead compound was first identified through structure-based high-throughput screening and subsequently optimized via structure-guided design to generate the candidate tracer FD4. Its specificity for aSyn fibrils was rigorously validated using radioligand binding, autoradiography, and immunofluorescence assays. *In vivo* PET imaging in rodent and marmoset models further demonstrated the tracer's capability to visualize aSyn pathology *in vivo*. Finally, investigator-initiated clinical studies demonstrated that FD4 enables robust *in vivo* visualization of aSyn pathology in both PD and multiple system atrophy, underscoring its potential as a clinically applicable PET tracer.

Impact on Diagnosis/Treatment of Parkinson's disease: By enabling *in vivo* visualization of aSyn pathology, FD4 holds the potential to advance the diagnostic landscape of PD through earlier detection and more precise patient stratification. Moreover, FD4 may serve as a robust biomarker for monitoring therapeutic efficacy, thereby facilitating the development and evaluation of disease-modifying interventions.

Next Steps for Development: The next phase will focus on expanding investigator-initiated trials with larger, multicenter cohorts and longitudinal imaging, alongside comparative analyses with established biomarkers such as seed amplification assays. In parallel, Investigational New Drug applications will be pursued in both China and the U.S. to initiate comprehensive clinical studies.

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