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Endpoint Considerations to Facilitate Drug Development for Niemann-Pick Type C (NPC)

Virtual Public Workshop

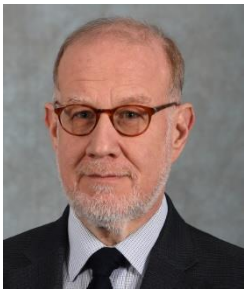
January 24-25, 2021

Speaker Biographies

Day 2: Potential Innovative Endpoints and Strategies to Support NPC Product Development

January 25, 2022

Opening Remarks



Peter Stein is the Director of CDER's Office of New Drugs (OND). OND is responsible for the regulatory oversight of investigational studies during drug development and decisions regarding marketing approval for new (innovator or non-generic) drugs, including decisions related to changes to already marketed products. OND provides guidance to regulated industry on a wide variety of clinical, scientific, and regulatory matters.

A nationally recognized leader in pharmaceutical research and development, Dr. Stein joined CDER in 2016 as the OND Deputy Director. Before coming to FDA, he served as Vice President for late-stage development, diabetes, and endocrinology at Merck Research Laboratories. He also served as Vice President, head of metabolism development at Janssen. He has more than 30 years of academic, clinical, and industry experience.

Dr. Stein holds a bachelor's degree in history from the University of Rochester in New York and a medical degree from University of Pennsylvania. He trained at Yale University and Yale-New Haven Hospital in internal medicine and in endocrinology and metabolism.

Session 4 Participants

Michelle Campbell is the Senior Clinical Analyst for Stakeholder Engagement and Clinical Outcomes in the Office of Neuroscience, Office of New Drugs (OND) in FDA's Center for Drug Evaluation and Research. Previously, Dr. Campbell was a reviewer on the Clinical Outcome Assessments (COA) Staff and Scientific Coordinator of the COA Qualification Program in OND. Dr. Campbell's focus is in patient-focused drug development and the use of patient experience data in the regulatory setting. Prior to joining FDA, Dr. Campbell spent more than 10 years conducting research in the academic-clinical setting, including five years in a neurology and developmental medicine department. Dr. Campbell earned her BA in Biology from the College of Notre Dame, her MS in Health Science from Towson University and her PhD in Pharmaceutical Health Services Research from the University of Maryland School of Pharmacy.

Ray Dorsey is the David M. Levy Professor of Neurology at the University of Rochester Medical Center. His vision is that anyone anywhere can participate in research and receive care. His research has been published in leading journals and has been featured in multiple news outlets. In 2020, Ray and his colleagues wrote *Ending Parkinson's Disease*, a book that provides a prescription for ending the world's fastest growing brain disease. Ray previously directed the movement disorders division and neurology telemedicine at Johns Hopkins and worked as a consultant for McKinsey & Company. In 2015, the White House recognized him as a "Champion for Change" for Parkinson's disease.

Harry Koujaian is the father of Alec, age 23, who has NPC and daughter Hayley, who passed away from NPC in April 2020. He and his wife are very involved in the NPC community in the quest to get regulatory approvals for some of the currently available treatments with the ultimate goal of finding a cure for NPC. His son Alec often presents at FDA sessions regarding his life living with NPC – both challenges and triumphs.

Greg Licholai teaches at the Yale School of Management and is Co-Director of the Center for Digital Health. He also co-teaches Innovating Health Care at Harvard Business School. He is Chief Medical and Information Officer at PRA Health Sciences, a leading pharmaceutical service, healthcare data and contract research provider. Previously, he was President of the rare disease division of Moderna Therapeutics, President and Chief Medical Officer at Castle Creek Pharmaceuticals and was a partner at McKinsey & Co. where he ran the healthcare data service line. He was also an executive at Proteostasis, Amicus Therapeutics and Medtronic Neurological as well as venture investor for Domain Associates. He was co-founder of Immunome Therapeutics. Greg has degrees from Harvard Business School, Yale School of Medicine, Columbia University and Boston College. He trained at the Brigham and Women's, Children's, and Massachusetts General Hospitals. He serves on multiple company and non-profit boards including the Digital Medicine Society (DiMe) and advisor on the Clinical Trials Transformation Initiative (CTTI), a public private partnership co-founded by Duke University and the Food and Drug Administration (FDA). He writes about innovation in healthcare for Forbes.

David Lynch is a graduate of Yale University, majoring in Molecular Biophysics and Biochemistry, and obtained his MD and PhD at the Johns Hopkins University School of Medicine, graduating in 1988. His PhD thesis was on processing of endogenous opioid peptides. He completed internship and neurology residency at the University of Pennsylvania, followed by a fellowship in molecular pharmacology, neurogenetics and movement disorders at the same institution. He was appointed to the faculty in 1995 as an Assistant Professor in Neurology and Pediatrics. He was promoted and received tenure in 2004 and promoted to Full Professor in 2010. He has published over 250 scientific papers, mainly on NMDA receptors, antiNMDA receptor encephalitis, and Friedreich

Ataxia, with greater than 23,000 citations. He has been continuously funded by the NIH since 1994 for basic science, clinical science and translational projects.

Anindita (Annie) Saha is the Assistant Director for the Digital Health Center of Excellence (DHCoE) at the Food and Drug Administration (FDA) Center for Devices and Radiological Health (CDRH). Ms. Saha is leading the development of partnerships, regulatory science, strategic planning, and operations for the newly formed DHCoE to empower digital health stakeholders in advancing healthcare. Additionally, Annie helped incubate and continues to support CDRH's patient science and engagement efforts to advance the science and adoption of patient input as evidence, including patient preference information (PPI), clinical outcome assessments (COAs) including patient-reported outcomes (PROs), and patient-generated health data (PGHD). These efforts include researching the use of digital health technologies to capture the patient perspective. Previously, Annie was the Director of Partnerships to Advance Innovation and Regulatory Science (PAIRS) where she oversaw a broad program portfolio, supporting a number of strategic partnership and regulatory science programs for CDRH. This included relationships with the Medical Device Innovation Consortium and other public-private partnerships, Network of Experts, Critical Path, and technology transfer. Ms. Saha began her FDA career as a researcher in the CDRH's Office of Science and Engineering Laboratories in the Division of Imaging and Applied Mathematics in the area of imaging display technologies before working to coordinate Critical Path and Regulatory Science activities for the Center. Ms. Saha has a Bachelor of Science in Bioengineering and Minor in History from the University of Pittsburgh. She was a student researcher at the McGowan Institute for Regenerative Medicine working in tissue engineering and wound healing.

Session 5 Participants

Patricia Dickson is the Centennial Professor of Pediatrics at Washington University School of Medicine. She also is Professor of Genetics and Chief of the Division of Genetics and Genomic Medicine in the Department of Pediatrics. Dr. Dickson earned an undergraduate degree from the University of Chicago in 1995 and her medical degree in 1999 from Columbia University College of Physicians and Surgeons. She completed an internship and residency at Harbor-UCLA Medical Center, a Los Angeles County hospital affiliated with UCLA and the Los Angeles Biomedical Research Institute. She is a member and past president of the Scientific Advisory Board of the National MPS Society. Dr. Dickson is a member of the American Society for Clinical Investigation.

Carole Ho is the Chief Medical Officer and Head of Development at Denali Therapeutics, Inc. Carole has built an integrated development organization that is responsible for advancing therapeutic candidates from IND enabling toxicology through Phase 1 to Phase 3 testing. Under Carole's leadership, Denali has advanced more than five programs into clinical development since Denali's founding in 2015 across therapeutic areas including Rare Disease, Parkinson's disease, Alzheimer's disease, and ALS.

Carole previously served as Vice President of Genentech Early Clinical Development and was responsible for delivery of pivotal trial-ready drug candidates in Neurology, Ophthalmology, Immunology,

and Infectious Disease. During her 8-year tenure at Genentech, Carole held roles with leadership responsibility across multiple early- and late-stage clinical programs including Rituxan® for Wegener's granulomatosis and microscopic polyangiitis and ocrelizumab for Multiple Sclerosis. At Genentech, in collaboration with Banner Health, Carole's team led the initiation of the world's first prevention trial in Alzheimer's disease in participants at risk for dementia due to a genetic mutation.

Carole completed her residency in Neurology at Harvard Medical School at the Massachusetts General Hospital / Brigham and Women's Hospital, where she also served as Chief Resident. She obtained her M.D. from Cornell University and S.B. in Biochemical Sciences from Harvard College. Prior to her Industry career, Carole was on Faculty in the Department of Neurology at Stanford University. Carole currently serves on the Board of Directors of Beam Therapeutics, NGM Therapeutics, and Target ALS.

Daniel Ory graduated from Harvard Medical School and trained at MIT before joining the faculty at Washington University in 1995. Over the next two decades his laboratory made fundamental contributions to our understanding of cholesterol biology and Niemann-Pick type C (NPC). Dr. Ory's use of metabolomics for biomarker discovery led to development of new diagnostic markers for NPC, as well as other lysosomal storage disorders. Clinical assays based on these biomarkers have become the worldwide standard for diagnosis of NPC and culminated in a newborn screen that is being piloted in New York. Working closely with the Therapeutics for Rare and Neglected Diseases Program at NIH, Dr. Ory co-led development of the Phase 1/2a trial of intrathecal cyclodextrin. Dr. Ory is internationally recognized for this research, has served on numerous Scientific Advisory Boards, including those of the National Niemann-Pick Disease Foundation and the Ara Parseghian Medical Research Foundation, and was elected to the ASCI, AAP, and as a AAAS fellow. Dr. Ory is currently Chief Medical Officer at Casma Therapeutics, a biotechnology company developing drugs that activate autophagy to treat disease.

Jie (Jack) Wang is the team leader for Rare Diseases and Inborn Errors of Metabolism review team in the Division of Translational and Precision Medicine, Office of Clinical Pharmacology (OCP) at the FDA. Dr. Wang also serves as vice chair for review of the Biologics Oversight Board in OCP, steering committee member of OCP's Rare Disease Scientific Interest Group, and member of Immunogenicity Working Group in CDER. He has contributed to drafting multiple policy briefs and guidances in OCP. Dr. Wang first joined the FDA in 2011 and has served as a reviewer and team leader for clinical pharmacology review teams responsible for evaluating IND, NDA and BLA for drugs and biologics in therapeutic areas including dermatology, dentistry, urology, obstetrics, gynecology, gastroenterology, and inborn errors of metabolism. Dr. Wang received his BS in Pharmacy from Beijing Medical University, MS in Pharmaceutical Sciences from Peking University, and PhD in Pharmaceutics from The Ohio State University. Dr. Wang has authored/co-authored 30 peer-reviewed journal articles and 40 abstracts in the areas of pharmacokinetics, pharmacodynamics, biopharmaceutics, immunogenicity, gene therapy and nanomedicine.

Session 6 Participants

Debbie Kaflowitz lives in New Providence, New Jersey, with her husband. She taught for 33 years, three in Brookline, MA, and 30 in Summit, NJ. She retired earlier than she expected to take care of their only child, Rachael, who became very ill her junior year in high school. Debbie and her husband searched for 12 years to find the correct diagnosis. Rachael was finally diagnosed with Niemann-Pick type C, at age 26. Sadly, Rachael passed away on October 25, 2018, at age 33. Now Debbie spends her time helping the NPC community and tutoring children from Syria and Afghanistan.

Janet Maynard as the Director of the Office of Rare Diseases, Pediatrics, Urologic and Reproductive Medicine (ORPURM) oversees the development, review, and regulation of applications for drugs and biologic products reviewed within the divisions in ORPURM: The Division of Pediatrics and Maternal Health (DPMH), the Division of Rare Diseases and Medical Genetics (DRDMG), the Division of Urology, Obstetrics and Gynecology (DUOG), and the Division of Pharmacology-Toxicology for Rare Diseases, Pediatrics, Urologic and Reproductive Medicine/Specialty Medicine (DPT-RPURM/SM). Prior to serving as Director, she was the Deputy Director of ORPURM.

Prior to ORPURM, Dr. Maynard was the Director of the Office of Orphan Products Development (OOPD) and oversaw the legislatively mandated designation and grant programs intended to promote the development of products for rare diseases including, orphan drug, rare pediatric disease, and humanitarian use device designation programs, as well as clinical trial, natural history study, and pediatric device consortia grant programs.

Prior to OOPD, she worked in the Center for Drug Evaluation and Research (CDER), where she was a clinical team leader in the Division of Anesthesia, Analgesia, and Addiction Products (DAAAP). Dr. Maynard has been with FDA since 2011, when she joined FDA's Division of Pulmonary, Allergy, and Rheumatology Products (DPARP) as a Medical Officer, before becoming a clinical team leader in DPARP.

Dr. Maynard received her medical degree from Vanderbilt University and completed a residency in internal medicine at Duke Hospital. Subsequently, she completed a fellowship in rheumatology at Johns Hopkins Hospital. During her fellowship, she completed a Master of Health Science at the Johns Hopkins Bloomberg School of Public Health in the Graduate Training Program in Clinical Investigation.

Jennifer Rodriguez Pippins as a Clinical Advisor in the Office of New Drug Policy (ONDP) within the Office of New Drugs, advances strategic new drug policy priorities. She leads the development of policy-related guidance, provides internal training on policy-related matters, and advises OND and CDER stakeholders on clinical and regulatory policy issues.

Prior to ONDP, she served as an acting Associate Director for Clinical Programs in the Office of Medical Products and Tobacco (OMPT) within the Office of the Commissioner. She provided clinical expertise to inform OMPT's cross-center initiatives, including work on youth tobacco cessation and orphan product development.

Prior to OMPT, Dr. Pippins was the Deputy Division Director for Safety in the Division of Metabolism and Endocrinology Products (DMEP) within the Office of New Drugs. As Deputy Director for Safety, she oversaw the division's work on Risk Evaluation and Management Strategies (REMS) both pre- and post-approval, the

evaluation of emerging safety signals, the approval of safety labeling changes, and the issuing of Drug Safety Communications.

Prior to DMEP, Dr. Pippins was a Medical Officer in the Division of Pulmonary, Allergy, and Rheumatology Products (DPARP) which she joined in 2009 upon first arriving at FDA.

Dr. Pippins received her medical degree from Harvard Medical School and completed residency at the Harvard Combined Med/Peds Program. Subsequently, she completed a General Internal Medicine Research Fellowship at Brigham and Women's Hospital. During her fellowship, she completed a Master of Public Health degree with a concentration in Clinical Effectiveness at the Harvard School of Public Health.

Forbes D. Porter received his degrees from Washington University in St. Louis and subsequently trained in Pediatrics and Genetics at St. Louis Children's Hospital. He is board certified in Pediatrics and Clinical Genetics. Dr. Porter came to the NIH in 1993 as a postdoctoral fellow in Dr. Heiner Westphal's laboratory and subsequently formed his own research laboratory in the Heritable Disorders Branch of NICHD. Dr. Porter's research at the NIH has been focused on understanding pathophysiological processes underlying human genetic disorders in order to develop and test therapeutic interventions.

Dr. Porter served as the Program Head for the Program on Pediatric Developmental Endocrinology and Genetics from 2011 through 2015. Dr. Porter has been the Director of the NICHD Molecular Genomics Core and NICHD Clinical Director since 2010. He has also served as the NCATS Clinical Director since 2015. Dr. Porter serves on multiple medical/scientific advisory boards corresponding to the rare disorders studied by his section. Dr. Porter was elected to the Association of American Physicians in 2019.

Sean K. Recke is a STEM teacher at Salisbury Middle School. He and his wife Amy have three children: Josh, Katie, and Adam. Adam was diagnosed with NPC at age six and is now 22 years old. Adam is taking Zavesca and has been part of the NPC natural history study since the age of six. Adam has had 143 lumbar punctures and was the first patient in the IV Trial of adrabatadex.

Steve Romano is a seasoned pharmaceutical executive with deep leadership experience in research and development, regulatory and medical affairs, corporate strategy and portfolio management. He has led organizations and product development teams in a wide range of therapeutic and disease areas, successfully bringing innovative medicines to patients. He is a strong business partner, valued for his strategic thinking, succinct advice and sound judgment.

Dr. Romano has served as EVP, Chief Scientific Officer of Mallinckrodt Pharmaceuticals since 2015. He is responsible for Science & Technology and has been instrumental in building a premier organization comprising centers of excellence in R&D, Medical Affairs, Pharmacovigilance & Drug Safety, Regulatory Affairs, Health Economics & Outcomes Research (HEOR), Development Operations, and Device Engineering. Current areas of therapeutic focus include hepatology, burns and other areas of critical care, and immunology. As an Executive Committee member, he is instrumental in implementing Mallinckrodt's

strategic vision to establish a pipeline of innovative pharmaceutical products spanning all phases of drug development.

Dr. Romano's leadership experience has included professional societies, most notably the International Society of CNS Trials and Methodology (ISCTM), of which he was a founding member and a past president, and the National Pharmaceutical Council (NPC), where he currently serves as Chair of the Board of Directors for 2021-2022. Dr. Romano is also a non-executive Board member of Silence Therapeutics, a leading RNA therapeutics company, and a non-executive Board member of Evolution Research Group LLC, an independently held clinical research site company.

Prior to Mallinckrodt, Dr. Romano served as Senior Vice President, Head of Global Medicines Development at Pfizer, Inc., where he was responsible for overseeing development of Pfizer's Global Innovative Pharmaceuticals portfolio in the areas of inflammation, immunology, cardiovascular, metabolic, neuroscience, pain, renal and rare diseases. As a member of Pfizer's Portfolio Strategy and Investment (PSI) Committee, which governs pipeline investments and strategic R&D priorities, he ensured the company was investing and focusing its scientific resources in the areas with the most potential.

Dr. Romano has been a board-certified psychiatrist since 1990, and after completing his residency and fellowship at New York Hospital-Cornell Medical Center, he continued as a faculty member of the medical school for six additional years. He received his Doctor of Medicine from the University of Missouri-Columbia in 1985 and earned a Bachelor of Arts in Biology and English Literature from Washington University in St. Louis in 1981.

Moderators

Mark McClellan is the Robert J. Margolis, M.D., Professor of Business, Medicine and Policy and Director of the Duke-Margolis Center for Health Policy. Dr. McClellan is a doctor and an economist who has addressed a wide range of strategies and policy reforms to improve health care, including payment reform to promote better outcomes and lower costs, methods for development and use of real-world evidence, and strategies for more effective biomedical innovation. Before coming to Duke, he served as a Senior Fellow in Economic Studies at the Brookings Institution, where he was Director of the Health Care Innovation and Value Initiatives and led the Richard Merkin Initiative on Payment Reform and Clinical Leadership. He also has a highly distinguished record in public service and academic research. An independent director on the boards of Johnson & Johnson, Cigna, Alignment Healthcare, and PrognomIQ, Dr. McClellan co-chairs the Guiding Committee for the Health Care Payment Learning and Action Network and serves as an advisor for Arsenal Capital Partners, Blackstone Life Sciences, and MITRE.

Christina Silcox is the Digital Health Policy Fellow at the Duke-Margolis Center for Health Policy, working on policy solutions to advance innovation in health and health care and improve regulation, reimbursement, and long-term evaluation of medical products, with a focus on digital health. Dr. Silcox's portfolio includes multiple areas in digital health policy and real-world evidence, with a focus on medical devices. Currently, she is concentrating on challenges to regulating and adopting artificial intelligence-enabled software as a medical device, using mHealth to collect real-world data, and characterizing real-world data quality and relevancy. Her projects have included the use of patient-generated health data in medical device evaluations, the exploration of value-based payments for medical devices, and the convening the National Evaluation System for health Technology (NEST) Planning Board.

Before she joined Duke-Margolis, Dr. Silcox was a senior fellow at the National Center for Health Research, focused on federal regulation of and policies for medical products. She earned a M.S. from the Massachusetts Institute of Technology (MIT) in Electrical Engineering and a Ph.D. in Medical Engineering and Medical Physics from the Harvard-MIT Division of Health Sciences and Technology (HST).

Jeffrey Siegel is the director of the Office of Drug Evaluation Sciences (ODES) in the Office of New Drugs (OND), CDER, FDA. ODES oversees Clinical Outcome Assessments, Biomarker Qualification, Research and Bioinformatics in OND. Dr Siegel has over 20 years of experience in research, regulatory, and clinical drug development. Jeff received his B.A. from Columbia University and M.D. from Yale University. He trained in internal medicine at University Hospitals of Cleveland. Then he did a fellowship in Immunology and Signal Transduction at NIH. He served at FDA from 1996-2010 as a medical officer and then Medical Team Leader. In 2010, he left FDA for industry and worked at Genentech/Roche as global lead for Rheumatology and Rare Diseases and subsequently at Gilead Sciences as Translational Medicine lead in Clinical Research/Inflammation before rejoining FDA in February, 2021.