Duke | MARGOLIS CENTER *for* Health Policy

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

Virtual Public Workshop
January 24-25, 2021

Speaker Biographies

Day 1: Introduction and Overview of Endpoints for Niemann-Pick Type C (NPC) Clinical Trials
January 24, 2022

Opening Remarks

Patrizia Cavazzoni is the Director at the Center for Drug Evaluation and Research (CDER) at the Food and Drug Administration (FDA). Dr. Cavazzoni received her medical degree at McGill University and completed a residency in Psychiatry and a fellowship in mood disorders at the University of Ottawa. She subsequently joined the faculty of medicine at the University of Ottawa as an assistant professor, where she was engaged in clinical work, teaching, and research on genetic predictors of mood disorders, authoring numerous peer-reviewed scientific publications. Following this, Dr. Cavazzoni worked in the pharmaceutical industry for several years, and held senior leadership positions in clinical development, regulatory affairs and safety surveillance. Dr. Cavazzoni is certified by the American Board of Neurology and Psychiatry, a Fellow of the Canadian Royal College of Physician and Surgeons, a member of the Canadian College of Neuropsychopharmacology and recipient of the American College of Psychiatrists' Laughlin Fellowship.

Session 1 Participants

Elizabeth Berry-Kravis is a Professor of Pediatrics and Neurological Sciences at Rush University Medical Center in Chicago. She established the Fragile X Clinic and Research Program in 1991, through which she has provided care to over 700 patients with fragile X syndrome (FXS). She has studied medical issues, epilepsy and psychopharmacology in FXS, and has been a leader in translational research in FXS for 20 years, including development of clinical outcome measures and biomarkers, natural history studies, newborn screening, and particularly clinical trials of new targeted treatments in FXS, for which she has been PI or Co-PI of 25 trials, both industry and investigator sponsored. Her laboratory studies the cellular role of fragile X mental retardation protein (FMRP), relationship between FMRP and clinical function, and optimization of genetic testing methods. More recently she has expanded clinical and translational work to other neurodevelopmental disorders in addition to FXS, including autism spectrum disorders and single gene models of ASD, including Phelan McDermid syndrome, Rett syndrome, and Angelman syndrome. She also is working on translational research in rare neurogenetic disorders including Niemann-Pick type C, Battens disease, pantothenate kinase-associated neurodegeneration, and creatine transporter deficiency. She is on Advisory and/or Review Boards for the FRAXA Research Foundation, National Fragile X Foundation, Phelan McDermid Syndrome Foundation, International Rett Syndrome Foundation, Angelman Syndrome Foundation, Foundation for Angelman Syndrome Therapeutics, Combined Brain, N=1 Collaborative and the GATHER Foundation. She has received the NFXF Jarrett Cole Clinical Award,

FRAXA Champion Award, NFXF William and Enid Rosen Research Award, March of Dimes Jonas Salk Research Award, American Academy of Neurology Sidney Carter Award in Child Neurology, John Merck Fund Sparkplug Award and the inaugural Martha Bridge Dencla Award from the Child Neurology Society for work in cognitive disorders of children. She has been working on translation of targeted treatment with adrabetadex in NPC for 8 years, has been PI of a multi-patient multi-site expanded access program that has provided treatment to over 60 patients. She was Co-PI of the phase 2/3 adrabetadex trial and has been a co-Investigator on biomarker studies in NPC, and site PI for the Orphazyme arimoclomol EAP.

Ebony Dashiell-Aje is currently the Senior Director and Head of Patient Engagement and Outcomes Research in Regulatory Affairs at BioMarin. Dr. Dashiell-Aje is a leading expert in patient-centered outcome tool development, including clinical outcome assessment (COA) design and implementation; digital health technology tool development and optimization; and related study endpoint issues in regulatory science, with an emphasis in rare disease drug development. As a health outcomes researcher and methodologist, Dr. Dashiell-Aje is driven by her passion for public health and promoting patient-focused medical product development. Dr. Dashiell-Aje has notably contributed her research expertise in academic, consulting, and regulatory environments to arrive at evidence-based solutions, to shape health policy.

Lise Kjems is the chief medical officer at Cyclo Therapeutics. She brings more than 20 years of experience in life sciences, academia, biotech and large pharmaceutical industry and, more recently, as Vice President, Head of Clinical Development at Albireo Pharmaceutical, where she led their phase 3 program in progressive familial intrahepatic cholestasis (PFIC) to successful completion and approval by the FDA and EMA and was responsible for the clinical portfolio and co-lead the R&D team. Prior Albireo Pharma, she led and contributed to several pre-IND to late-stage development programs in Cardiometabolic, Diabetes, Rare Diseases, Special Lipid Metabolism, Inflammation, Endocrinology and Oncology. She has been part of building out translational medicine and drug evaluation organizations, and brings extensive global experience in the end-to-end drug process. Lise has an M.D. and a Ph.D. from the University of Copenhagen.

Naomi Knoble is a reviewer in the Division of Clinical Outcome Assessment (DCOA), Office of New Drugs (OND), Center for Drug Evaluation Research (CDER), with the US Food and Drug Administration (FDA) focused on reviewing pediatric rare disease programs. Dr. Knoble is a clinical outcome assessment measurement expert and psychologist specializing in pediatric neuropsychology. She has a MEd in Couples and Family Therapy, MS and PhD in Counseling Psychology from the University of Oregon. Her clinical training included Autism and neurodevelopmental disorders with the Oregon Health & Science University (OHSU) and pediatric neuropsychology with the University of Minnesota Medical School including rare diseases (i.e., MPS disorders), pediatric oncology, organ transplantation, fetal alcohol spectrum disorder, and other neurodevelopmental conditions. Prior to joining FDA, Dr. Knoble was a research scientist and global healthcare consultant specializing in patient-centered outcomes and measurement. She has served as principal investigator of multiple global research studies in COA endpoint development and post-marketing evidence generation across a wide range of indications. She serves as FDA's liaison to C-Path's newly launched Rare Disease Clinical Outcome Assessment Consortium. Dr. Knoble's current regulatory research focuses on score development and interpretation for neurodevelopmental tests for children with disabilities.

Philip Marella is a founding trustee of Dana's Angels Research Trust, a 501(c)(3) public charity directed toward funding medical research, medical education, or medical or hospital care for the treatment or cure of Niemann-Pick type C disease (NPC) or other similar genetic diseases. Phil and his wife Andrea live in Greenwich, Connecticut. Two of their four children, Dana and Andrew, were diagnosed with NPC. Sadly, Dana passed away at the age of 19 in 2013, but Andrew at age 22 is doing much better because of experimental medications DART has help to bring forward for patients.

Professionally, Phil is President of Green Light Worldwide Media, Inc., a content management and development company founded in 2000. Phil has almost 30 years of experience with Fortune 100, early stage development, and start-up companies in media and finance. Before joining Green Light, Phil was the Executive Vice President of Business Affairs and General Counsel for Microcast, Inc., at the time the world's largest capacity video streaming provider in the World. Prior to Microcast, Mr. Marella was the Senior Vice President, Legal and Business Affairs for Worldvision Enterprises, Inc., the global marketing and distribution subsidiary of Spelling Entertainment. Phil has a law degree from Fordham University School of Law and a Bachelor of Science degree with Special Attainments in Commerce from Washington and Lee University.

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.

Session 2 Participants

Kiera Berggren is a research speech-language pathologist (SLP) in the Department of Neurology at Virginia Commonwealth University and a current doctoral student at James Madison University. Prior to working as an SLP, she had trained as a chemist and worked as a research technician in several different labs. She started her second career as an SLP in rehabilitation for individuals with acquired neurological injuries such as stroke and traumatic brain injury. She quickly discovered a passion for working with people with neurodegenerative diseases and currently provides swallow, communication, and cognitive support to patients and families in multidisciplinary clinics for ALS and the MDA. Marrying her current career and her research background has allowed her to also be active in research in several neuromuscular diseases including myotonic dystrophy, FSHD, ALS, and others where she has been looking at orofacial strength, swallow function, and changes in speech. Her doctoral studies are focused on quantification of swallow function in neuromuscular disease.

Diana Bohm is a speech-language pathologist with over 15 years of hospital-based experience specializing in assessment and treatment of pediatric feeding and swallowing disorders. She currently works at Northwestern Medicine Central DuPage Hospital located in the Chicago-land area where she provides assessment and treatment services to pediatric patients and their families as part of a multidisciplinary Feeding Clinic offered in collaboration with Ann & Robert H. Lurie Children's Hospital. Other responsibilities include inpatient treatment in the NICU, PICU, conduction of videoflouroscopic swallow studies and participation in clinical research studies. She has provided continuing education via pediatric feeding/swallowing presentations in the Midwest, co-authored a feeding chapter in the CALM Baby Method book, and she was recently awarded the Tom Williams Award for Clinical Excellence (2021). Areas of specialized expertise include infants/children with oropharyngeal dysphagia, feeding aversions and NG or G-tube dependence.

Barbara Lazarus is the mother of two sons with adult-onset NPC who were diagnosed four years ago. She resides in Connecticut along with her husband and sons. Barbara is a Speech-Language Pathologist by training with a background in rehabilitative medicine and the educational setting and has worked primarily with the early pediatric population. She is currently semi-retired, continuing to work part-time in diagnostics and providing supervision within a private practice.

Beth Solomon is the Lead Senior Speech Language Pathologist of the Speech Language Pathology Section of the Rehabilitation Medicine Department at the NIH Clinical Center. She earned her undergraduate degrees at the University of Massachusetts in Communication Disorders and Elementary Education and her Master's degree in Speech Language Pathology at Columbia University in New York. She did her fellowship training at the Memorial Sloan Kettering Cancer Center in New York and subsequently earned her Certificate of Clinical Competency from the American Speech Language and Hearing Association.

Her clinical practice and primary areas of interests include the assessment and management of oral motor and swallowing of medically complex infants and children, rehabilitation of speech and swallowing in head and neck cancer, treatment of voice disorders and craniofacial anomalies.

She is currently involved in a host of research protocols investigating phenotypic expressions of Niemen Pick Disease, Neurofibromatosis Type I, Smith Lemli Opitz Syndrome, and Smith Mavens Syndrome, Neonatal Onset Multisystem Inflammatory Disease and Kennedy's Disease. Additionally, she is investigating other speech and swallowing treatment outcomes in myositis disease and aphasia. Beth currently is collaborating with many of the NIH institutes including National Institutes of Child Health and Development, National Cancer Institutes, National Institute of Neurological Diseases and Stroke and National Institutes of Arthritis and Musculoskeletal and Skin Diseases.

Ms. Solomon has been recognized as an Infant and Toddler Specialist by the Governor's Office for Children, Youth and Families in the State of Maryland. She has been appointed the Speech Language Pathology Liaison to the Public Health Service and United States Surgeon General's Office for five consecutive terms of office. She received the National Institutes of Health Directors Award in 1998 for her clinical practice and research in head and neck cancer and in 2005 for teaching, training and leadership in developing, implementing and evaluating a tracheostomy care project to improve patient care and staff competencies.

Dina Zand received both her undergraduate and medical degrees from Northwestern University. She completed a residency in Pediatrics at St. Louis Children's Hospital (SLCH) and was on faculty at SLCH as a pediatric hospitalist prior to completion of fellowship training in Clinical Genetics at the Children's Hospital of Philadelphia. Prior to joining the FDA in the Division of Rare Disease and Medical Genetics, she was an Assistant Professor at Children's National Medical Center in the Division of Genetics and Metabolism.

Session 3 Participants

Emily Freilich is an Acting Associate Director of Therapeutic Review for the Division of Neurology 1 in the Office of New Drugs in FDA's Center for Drug Evaluation and Research. Dr. Freilich is a board-certified pediatric neurologist. Dr. Freilich graduated from Duke University with a Bachelor of Science degree in Biology and received her medical degree from Rutgers-New Jersey Medical School. She completed her pediatric residency and child neurology training at Children's National Health System in Washington, D.C. Prior to joining FDA, Dr. Freilich worked at Children's National Health System and the Pediatric Specialists of Virginia, where she was a general child neurologist with special interest in rare pediatric epilepsies and served as co-director of the Tuberous Sclerosis Clinic. Dr. Freilich was on the medical staff at Children's National and Inova Fairfax Hospitals and was an Assistant Professor of Pediatrics and Neurology at George Washington University School of Medicine, where she was involved in the education of medical students, pediatric residents, and neurology fellows. She joined the Division of Neurology Products at FDA in 2016, where she has worked as a clinical reviewer and team leader in the areas of epilepsy, migraine, neuromuscular, and rare neurologic disorders.

Eric Marsh received his Medical Degree at New York University School of Medicine, as well as PhD in physiology and neuroscience at NYU Sackler School of Biomedical Sciences. He then completed his Internship and pediatric residency at NYU. He moved to CHOP for a Child Neurology residency where he stayed for fellowship in clinical neurophysiology and also completed a post-doctoral fellowship, followed by being hired as faculty at Perelman School of medicine in the Departments of Neurology and Pediatrics. He is now an associate professor of neurology at University of Pennsylvania Perelman School of Medicine and CHOP, Clinical Director of Penn Orphan Disease Center, and Director of the CHOP Rett and Related disorders clinic.

Dr. Marsh has particular clinical interests in developmental epilepsies, neurodevelopmental disorders, and cortical malformations. His research has focused strongly on the impact of intraneuronal development and altered excitability on epilepsy, analyzing intracranial EEG recordings to better localize the epileptic zone and network, and performing natural history and electrophysiological biomarker studies. He has also been involved in a number of clinical trials for children with the DEEs, including Dravet, LGS, and Rett syndrome.

Sara McGlocklin is the mother of six-year-old Marian, who is fighting Niemann-Pick type C. Marian was the youngest patient to access an experimental medication in 2017, when she was 19 months old. Sara is the founder of Hope for Marian Foundation which is leading the Save Our Medicine and Don't Give Up On NPC campaigns alongside families and patients with NPC. Sara and other mothers came together early last year when faced with the news that the experimental medicine their children needed, and have used for many years, would be taken away. Their advocacy efforts brought national attention to the issue. Recently, this group, in collaboration with Representatives Lesko and Representative Sewell, organized a Capitol Hill briefing to educate Members of Congress about the urgent needs in the NPC community to save access to existing medications. Sara has also shared Marian's story on The Doctors TV show, The Dr. Oz show, Scary Mommy, Daily Mail, Redbook, ABCNews.com and Today.com. Sara is a licensed attorney in California specializing in child welfare and advocacy and worked for Children's Law Center of California for several years before taking time off from practicing law to focus on rare disease advocacy for Niemann Pick Type C. Sara lives with her husband and three children in Los Angeles County

Marc Patterson was born and educated in Australia, and trained in neurology, child neurology and neurometabolic disease at the University of Queensland in Australia, at Mayo Clinic, and at NINDS/NIH, the last mentioned under the guidance of Roscoe Brady, MD. He is currently Professor of Neurology, Pediatrics and Medical Genetics. He was Director of the Child Neurology Training program at Mayo 2008-2016), and Chair of the Division of Child and Adolescent Neurology (2008-2017) (Mayo Clinic administrative positions are term-limited). Dr Patterson had previously served as Professor and Director of Pediatric Neurology at Columbia University in New York (2001-2007). He has served as a member of the Neurology Topic Advisory Group for revision of the ICD-10 of the World Health Organization, the Committee on Adverse Effects of Vaccines for the Institute of Medicine, and leads the Education Core of the NIH-funded Lysosomal Disease Network.

He has served in a number of positions in the Child Neurology Society, American Academy of Neurology, American Board of Psychiatry and Neurology and American Neurological Association. Dr Patterson has served on the editorial board of Neurology, on the oversight committee of Annals of Neurology and is currently an Editor for the Journal of Inherited Metabolic Disease, and its sister Journal JIMD Reports. He became Editor-in Chief of the Journal of Child Neurology on January 1st, 2014, and subsequently Editor-in-Chief of its open-access sister journal, Child Neurology Open.

His research and practice have focused on rare diseases in children, including multiple sclerosis and neurometabolic disorders in general, with special interests in Niemann-Pick disease, type C (NPC), other lysosomal diseases (including glycoproteinoses), mitochondrial cytopathies and congenital disorders of glycosylation, areas in which he has published more than 240 peer-reviewed papers and book chapters. He has presented widely through the United States and internationally, both to professional and lay organizations. He serves on the scientific advisory boards of several rare disease foundations. Dr Patterson has received funding support from NIH, industry and private foundations.

Dawn Phillips is the Director of Clinical Outcomes Research at REGENXBIO Inc. Dr Phillips received her doctorate in Human Movement Science from UNC Chapel Hill with a focus on motor learning, motor control and principles of outcome measurement. She was a fellow in the Leadership Education in Neurodevelopmental Disabilities (LEND) program and completed a certificate in Core Public Health Concepts. Dr Phillips also has a MSc in Human Movement Science with a focus on Infant and Family Studies and a BSc in Physical Therapy. She has been working in in rare disease clinical research for 20 years with a focus on research design and endpoint development, qualitative research, concept elicitation and validation, site training, data analysis and regulatory submission and engagement. She also was an assistant professor at UNC Chapel Hill with a course instruction focus on evidence-based medicine and pediatric outcomes. Dr Phillips's work has appeared in multiple journals including *Molecular Genetics and Metabolism, Neuromuscular Disorders, Value in Health, Human Gene Therapy, and the Journal of Pediatric Rehabilitation Medicine.*

Kevin Weinfurt is Professor and Vice Chair of Research in the Department of Population Health Sciences at Duke University Medical Center and a faculty member of the Duke Clinical Research Institute. Dr. Weinfurt is also a Professor of Psychology and Neuroscience, Professor of Psychiatry and Behavioral Sciences, Professor of Biostatistics and Bioinformatics, and a Faculty Associate of the Trent Center for the Study of Medical Humanities and Bioethics. Dr. Weinfurt co-directs the Center for Health Measurement in the Duke University School of Medicine. Currently, Dr. Weinfurt is working part-time as a Special Governmental Employee with the U.S. Food and Drug Administration in the Office of Biostatistics, developing guidance for the Patient-Focused Drug Development initiative. Dr. Weinfurt received his PhD in psychology at Georgetown University and did graduate work in the history of science and philosophy of mind at Linacre College, Oxford.

Dr. Weinfurt conducts research on measuring patient-reported outcomes, research ethics, and the psychology of medical decision making. Currently, Dr. Weinfurt is co-PI of the coordinating center for the NIH Health Systems Research Collaboratory, dedicated to improving understanding of how to conduct pragmatic clinical trials. Within the NIH Collaboratory, he has led or co-led work on bioethics, patient-reported outcomes, and dissemination of lessons learned. He served on the Board of Directors for the International Society of Quality of Life Research and a member of the Patient-Centered Outcomes Research Institute's Clinical Trials Advisory Panel. As an educator, Dr. Weinfurt co-directs Duke's masters-level Clinical Research Training Program and has taught undergraduate and graduate courses in bioethics, health measurement, psychology, and research methods.

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.

Robyn Bent is the director of the Patient-Focused Drug Development (PFDD) Program in the Center for Drug Evaluation and Research (CDER). PFDD is an effort to systematically obtain patient input and facilitate the incorporation of meaningful patient input into drug development and regulatory decision making. Prior to joining FDA, Robyn held several positions at the National Institutes of Health. Captain Bent has extensive experience in clinical trial design, conduct, and oversight. Robyn earned her Bachelor of Science in Nursing from The Catholic University of America and her Master of Science degree from the George Washington University.