REAGAN-UDALL FOUNDATION FOR THE FDA

Qualifying Biomarkers to Support Rare Disease Regulatory Pathways
Case example: Heparan sulfate in neuronopathic lysosomal storage diseases

Hybrid Public Meeting
February 21, 2024; 10AM - 4PM (eastern time)

Speakers

Nidal Boulos, PhD, CCRP
Director, Clinical Outcomes Research, Regenxbio

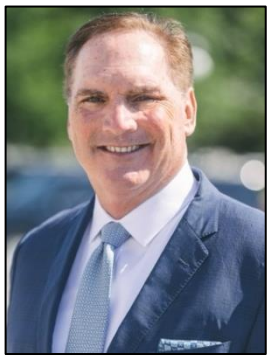
Dr. Nidal Boulos is the Director for Clinical Outcomes Research at Regenxbio with the primary responsibility of managing outcomes that support translational medicine and biomarkers. She has 20 years of research experience focused on translational and clinical research in a variety of indications including several rare diseases. Her current work includes supporting efforts to link outcomes from preclinical to clinical studies, developing increased evidence to support the role of biomarkers and defining the relationship between biomarkers and neurodevelopmental and daily activity measures.

John Crowley, JD, MBA
Executive Chairman, Amicus Therapeutics, Inc. / Incoming President & CEO, Biotechnology Innovation Organization

John F. Crowley is the Executive Chairman and founding CEO of Amicus Therapeutics, a global biotechnology company focused on the development of treatments for rare genetic diseases. He is the incoming President & CEO of the Biotechnology Innovation Organization (BIO). Crowley's involvement with biotechnology stems from the 1998 diagnosis of two of his children with Pompe disease—a severe and often fatal neuromuscular disorder. In his drive to find a cure, he became an entrepreneur as the Co-founder, President and CEO of Novazyme Pharmaceuticals, which he credits as ultimately saving his children's lives.

The 2010 major motion picture, Extraordinary Measures, is inspired by the Crowley family journey. Crowley served as a commissioned officer in the U.S. Navy Reserve from 2005-2016 and is a combat veteran of the Global War on Terrorism, with service in Afghanistan. He graduated with a bachelor's degree in Foreign Service from Georgetown University and earned a law degree from the University of Notre Dame Law School and a master's degree in Business Administration from the Harvard Business School. He was awarded a Doctor of Laws Degree from Notre Dame, where he delivered the Commencement Address to the Class of 2020. The Crowley family received the 2011 Family Exemplar Award from Notre Dame. Crowley is the former National Chairman of the Make-A-Wish Foundation of America and is a Henry Crown Fellow at the Aspen Institute. In 2023, he was inducted as a member of the Horatio Alger Association.

Mark Dant
Founder and Volunteer Executive Director, Ryan Foundation

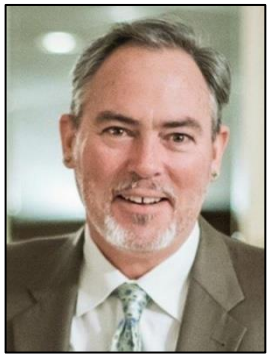


Mark Dant is the Founder and Volunteer Executive Director of the Ryan Foundation. Mark is also the former Board Chair of the of the Washington, DC based EveryLife Foundation for Rare Diseases and the former President and CEO of the National MPS Society. Dant and his family founded the Ryan Foundation in 1992 shortly after their only child, Ryan, was diagnosed with MPS I. Since inception, the Ryan Foundation has funded millions in research and provided the critical funding that led to the development of Aldurazyme, the first and to date only drug FDA-approved to treat MPS I. The Dant family's journey has been documented on CBS 60 Minutes, the Today Show, CNN, Biography Magazine, Readers Digest in thirteen languages around the world, Golf Digest, the LA Times and numerous newspapers and news outlets globally. He and his family have been key advocates speaking to the FDA and in 2009 successfully championed the US House of Representatives to pass the Ryan Dant Health Care Opportunity Act. A police officer for 32 years, he retired as an Assistant Chief of Police with the Carrollton Texas Police Department in 2016 and spends his time now volunteering for the Ryan Foundation and numerous other rare disease nonprofits to help empower the patient advocate through the understanding that all of us have the power to turn action to hope and hope to reality.

Patricia Dickson, MD
Professor, Washington University School of Medicine, St. Louis

Dr. Patricia Dickson is the Centennial Professor of Pediatrics and Chief of the Division of Genetics and Genomic Medicine at Washington University School of Medicine in St. Louis. Dr. Dickson earned her undergraduate degree in Classics from the University of Chicago and her medical degree from Columbia University College of Physicians and Surgeons. She completed an internship and residency at Harbor-UCLA Medical Center and trained in clinical and biochemical genetics atthe UCLA Intercampus Medical Genetics Training Program. Dr. Dickson has studied the pathogenesis and novel therapy development for central nervous system disease due to the genetic disease mucopolysaccharidosis (MPS) in animal models and clinical trials for more than 20 years. She has been the principal investigator of 15 federal grants, including an Orphan Products Development Grant from the FDA and a National Institutes of Health (NIH) Bench-to-Bedside award. She has served on multiple advisory boards for the design of clinical studies of brain-directed therapies for MPS disorders. Her honors include the NIH National Research Service Award Fellowship and the Richard B. Weitzman Memorial Award for Meritorious Research. She is a diplomate of the American Board of Pediatrics and the American Board of Medical Genetics and Genomics. She has been elected to the American Society for Clinical Investigation.

Matthew Ellinwood, DVM, PhD
Chief Scientific Officer, National MPS Society



Dr. Matthew Ellinwood, trained in molecular biology, reproductive physiology, innate antiviral immunity, and comparative medical genetics beginning at Colorado State University (DVM and PhD), with a subsequent residency in veterinary medical genetics (Univ of Pennsylvania) and post-doctoral training in comparative medicine (Univ of Pennsylvania) and gene therapy (Univ of Nantes). He has over two decades of research experience with mucopolysaccharidosis and mucolipidosis disorders. He now serves as the Chief Scientific Officer with the National MPS Society, where he guides the Society's research and science efforts, promoting clinical progress for the MPS and ML disorders. His current work at the Society comes after a long tenure on the Society's Scientific Advisory Board (2004-2020). He is a Professor Emeritus at Iowa State University, where he researched canine models of MPS I and IIIB, including natural history and interventional preclinical studies. He is experienced with preclinical studies of hematopoietic stem cell transplantation, intravenous enzyme therapy, intracisternal enzyme therapy, intraventricular enzyme therapy, systemic intravenous AAV-based gene therapy, and intraparenchymal CNS directed AAV-based therapy. He has worked on a variety of genetic diseases including preclinical models of: SCID; MPSs I, IIIB, IIID, VI, and VII; ML II alpha/beta; congenital glaucoma; and retinitis pigmentosa.

Cherie Fathy, MD, MPH
Medical Officer, Office of Therapeutic Products, Center for Biologics Evaluation and Research, FDA

Dr. Cherie Fathy is a medical officer in the Office of Therapeutic Products in the Center for Biologics Evaluation and Research (CBER). She earned her medical degree at the Vanderbilt University School of Medicine and graduated as a member of the Alpha Omega Alpha honors society. She also completed a master's degree in Public Health with a concentration in Epidemiology while at Vanderbilt. She completed her ophthalmology residency at the top-ranked Wills Eye Hospital, where she served as an editor for the best-selling reference book, The Wills Eye Manual, which is used by doctors around the world for treating eye diseases. She further subspecialized in cornea, external disease, and refractive surgery at the Wilmer Eye Institute at The Johns Hopkins Hospital. Dr. Fathy is committed to constantly improving how we care for patients. She has served as an Advocacy Ambassador in Washington, DC, where she has advocated for patients' access to care and affordable medications. She serves on the editorial board for the American Academy of Ophthalmology's Young Ophthalmologists Info section. Dr. Fathy has been recognized by the American Medical Association with the Excellence in Medicine Award for her leadership and dedication to her patients, the American Society of Cataract and Refractive Surgeons for her research and leadership in the field of ophthalmology and was named one of the "Top 40 under 40" ophthalmologists by Ophthalmology Management.

Maria Fuller, PhD
Professor, Genetics and Molecular Pathology, University of Adelaide

Dr. Maria Fuller is a Clinical Scientist specializing in biochemical genetics and leads the National Referral Laboratory within the state-wide public pathology service in South Australia (SA Pathology). The laboratory provides a clinical diagnostic laboratory service for inherited metabolic disorders and for a subset of these conditions, the lysosomal disorders, the laboratory is the national provider for the Australian population. Dr. Fuller is a Fellow of the Faculty of Science (Royal College of Pathologists of Australia), and she contributes to the National Pathology Accreditation standards for laboratory testing by serving as a specialist assessor for the governing body, NATA. Maria has a conjoint academic appointment with the University of Adelaide where she is a research leader at the Robinson Research Institute and enjoys supervising post-graduate students. She was awarded the 2022 Roman Lecture by the Australasian Association for Clinical Biochemistry and Laboratory Medicine in recognition of her contribution to the field as well as her teaching and mentoring role. Her laboratory has contributed 120 articles and book chapters to the scientific and medical literature, and she has a long-standing interest in improving the efficiency and accuracy of the laboratory diagnosis of lysosomal disorders, as well as trying to understand mechanisms underlying their pathology.

Carole Ho, MD
Chief Medical Officer & Head of Department, Denali Therapeutics, Inc.

Dr. 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 her leadership, Denali has advanced ten candidate therapeutics into clinical development since Denali's founding in 2015 across therapeutic areas including in Lysosomal Storage Disease, Parkinson's disease, Alzheimer's disease, ALS, FTD, and Autoimmune disease.
Prior to Denali, Dr. Ho most recently served as Vice President of Genentech in 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 with 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 rheumatoid arthritis, lupus, and multiple sclerosis. At Genentech, in collaboration with Banner Health, her 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.

Dr. Ho completed her residency in Neurology at Harvard Medical School/Massachusetts General Hospital/Brigham and Women's Hospital, where she also served as Chief Resident. She obtained her medical degree from Cornell University and bachelor's degree in Biochemical Sciences from Harvard College. Prior to her Industry career, she was on faculty in the Department of Neurology at Stanford University. Dr. Ho currently serves on the board of directors of Beam Therapeutics, NGM Therapeutics, and Target ALS.

Gavin Imperato, MD, PhD
Chief of General Medicine Branch 4, Office of Therapeutic Products, Center for Biologics Evaluation and Research, FDA

Dr. Gavin Imperato is Chief of General Medicine Branch 4, Office of Therapeutic Products, Center for Biologics Evaluation and Research (CBER) at FDA, where he supports development programs for gene, cell, xenotransplant, and plasma-derived therapies across multiple therapeutic areas. He is trained in internal medicine and clinical immunology and has research experience in the development of novel small molecule, device, and biological therapies. Prior to joining FDA, he was the Hearst Foundation Scholar at the Feinstein Institutes for Medical Research, and assistant professor of medicine at the Hofstra Northwell School of Medicine.

Simon Jones, MBChB
Consultant, Paediatric Inherited Metabolic Diseases, St. Mary's Hospital

Professor Simon Jones is a consultant in paediatric inherited metabolic diseases at the Willink Unit in Genomic Medicine, St. Mary's Hospital in Manchester, UK.

His major research interest is therapies for lysosomal storage diseases (LSDs).

He received his medical training at the Edinburgh University Medical School, Edinburgh, UK, with a BSc in Neurosciences. He moved to London and trained in Paediatrics at Guy's and St. Thomas' Hospital, London, UK. He has been working at the Willink Biochemical Genetics Unit in Manchester, UK since September 2005. Since 2008, he has been a consultant in paediatric inherited metabolic diseases at the Willink Unit and is now the clinical lead for the LSD service. The Willink Unit is now part of the Manchester Centre for Genomic Medicine at St. Mary's Hospital, Manchester, UK. He is also the medical director of the NIHR Manchester Children's clinical research facility and an honorary MAHSC Professor in paediatrics and translational medicine.

Prof. Jones has been actively involved in many phase I-IV international multicentre trials of novel therapies for LSDs. He is currently the principal investigator in a number of LSD trials, including several first in human gene therapy trials. He is the author of over 120 peer-reviewed papers and 5 book chapters.

Heather Lau, MD, MS
Executive Director, Global Clinical Development, Ultragenyx

Dr. Heather Lau is a renowned physician-scientist and neuro-geneticist with a bio-psycho-social approach to medical care focused on the holistic care of the patient rather than specific aspects of a disease. As Executive Director of Global Clinical Development at Ultragenyx Pharmaceutical, she leads teams in developing therapies for pediatric patients with rare genetic diseases.

Dr. Lau joined industry in 2021 after 10 years in academia where she was the Director of the Lysosomal Storage Disorders Program and the Associate director of Neurogenetics at NYU School of Medicine. She studied biology as an undergraduate at Cornell University and holds a masters in biochemistry and molecular biology from New York Medical College. She obtained her medical degree from the University of Rochester. She later trained in pediatrics at Montefiore Medical Center; and trained in neurology and neurogenetics at NYU School of Medicine. During her time at NYU, she ran an undiagnosed disease clinic to aid in the diagnosis and management of suspected inherited neurodegenerative diseases for both adult and pediatric patients. During her clinical tenure, she coordinated multidisciplinary care for her patients with neuronopathic and non-neuronopathic lysosomal storage disorders, including managing one of the largest Gaucher cohorts in the country. She has extensive experience in management of

intravenous infusions of lysosomal enzyme replacement therapies. Her clinical research ranged phase I through IV clinical trials investigating a range of modalities including small molecule (chaperones and substrate reduction inhibitors), protein (enzyme)-based and both systemic and CNS directed gene therapy for a variety of lysosomal disorders. She was also involved in natural history studies of rare diseases to help with endpoint development and oversaw post-marketing disease monitoring programs and registries.

In addition to her clinical research and patient care, Dr. Lau collaborates with patient foundations to foster disease awareness and early diagnosis. She has worked closely with her colleagues in pastoral care and palliative care to address end of life issues for her patients. She continues her academic career as adjunct assistant professor at Yale University in the Department of Internal Medicine.

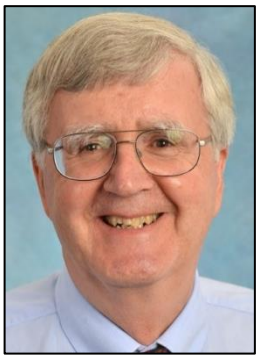
Peter Marks, MD, PhD
Director, Center for Biologics Evaluation and Research, FDA

Dr. Marks serves as the Director of the Center for Biologics Evaluation and Research (CBER) at the Food and Drug Administration. The center is responsible for assuring the safety and effectiveness of biological products, including vaccines, allergenic products, blood, and blood products, and cellular, tissue, and gene therapies. Marks and center staff have committed themselves to facilitating the development of biological products and providing oversight throughout the product life cycle.

Dr. Marks received his graduate degree in cell and molecular biology and his medical degree at New York University. Following this, he completed an Internal Medicine residency and Hematology/Medical Oncology fellowship at Brigham and Women's Hospital in Boston, where he subsequently joined the attending staff as a clinician-scientist and eventually served as Clinical Director of Hematology.

He then moved on to work for several years in the pharmaceutical industry on the clinical development of hematology and oncology products prior to returning to academic medicine at Yale University where he led the Adult Leukemia Service and served as Chief Clinical Officer of Smilow Cancer Hospital. He joined the FDA in 2012 as Deputy Center Director for CBER and became Center Director in 2016. Dr. Marks is board certified in internal medicine, hematology, and medical oncology, and is a Fellow of the American College of Physicians. In 2022, he became a Member of the National Academy of Medicine, one of the highest honors in the fields of health, science, and medicine.

Joseph Muenzer, MD, PhD
Professor, Pediatric Genetics and Metabolism, Univ. of North Carolina at Chapel Hill



Dr. Joseph Muenzer is the Bryson Distinguished Professor in Pediatric Genetics and a Professor in the Department of Pediatrics and Department of Genetics at the University of North Carolina at Chapel Hill, where he has practiced since 1993. He received a medical degree (1976) and doctoral degree in Biochemistry (1979) from Case Western Reserve University in Cleveland, OH. He completed a residency in pediatrics at the University of Wisconsin Hospitals, Madison, and a genetic/endocrine fellowship at the National Institute of Child Health and Human Development, NIH, in Bethesda, MD. Dr. Muenzer is the Director for the recently created Joseph Muenzer MPS Research and Treatment Center at the University of North Carolina at Chapel Hill.

Dr. Muenzer is involved in the diagnosis, management, and treatment of patients with inborn errors of metabolism, especially the mucopolysaccharidoses (MPS) and newborn screening for MPS I and MPS II. He is board certified in Pediatrics and in Clinical Biochemical/Molecular Genetics. He has been actively involved in developing new treatments for MPS disorders his entire professional career. He has created a mouse model for Hunter syndrome (MPS II) that has been widely used to develop new treatment for MPS II. He has been a principal investigator (PI) for IV enzyme replacement clinical trials (ERT) for both MPS I and MPS II resulting in FDA approval. His recent clinical research has focused on the development of new treatments for brain disease in MPS. Dr. Muenzer was the PI for Phase I/II and Phase II/III intrathecal enzyme replacement clinical trials for severe MPS II and now the post-trial access PI. He has been the principal investigator for >20 MPS clinical trials/observational studies. Dr. Muenzer is currently the PI for a Phase I/II gene editing clinical trial for MPS II and a Phase I/II and phase II/III IV ERT clinical trials to treat brain disease in MPS II.

Edward Neilan, MD, PhD
Chief Medical & Scientific Officer, National Organization of Rare Diseases

Dr. Edward Neilan is the Chief Medical and Scientific Officer of the National Organization for Rare Disorders (NORD®). Dr. Neilan is a physician-scientist and rare disease expert, and he joined NORD in 2021 to lead its medical and research programs.

Dr. Neilan seeks to encourage and enable institutions and companies to develop innovative approaches and new treatments to help rare disease patients. He is an expert in clinical trial design and drug development, has contributed data that helped support the FDA and global regulatory approvals of five new rare disease therapies, and has authored or co-authored multiple clinical trial protocols and safety and regulatory reports to global health authorities.

Prior to joining NORD, Dr. Neilan worked at Sanofi Genzyme, a major biopharma company, where he led global medical affairs strategy and execution for the rare neurological diseases portfolio and contributed medical expertise to clinical development efforts across multiple programs. Prior to that, he served as the President of the Medical Staff at Boston Children's Hospital. As a staff physician, clinical geneticist, and the Director of Quality Improvement in the metabolism program at Boston Children's, Dr. Neilan directly cared for and studied patients with many genetic diseases.
After completing BS and MS degrees in Biology at Yale University, Dr. Neilan earned his medical and doctoral degrees at Stanford University. He completed residency and fellowship training at Harvard Medical School, where he subsequently served as a faculty member for more than 12 years. Dr. Neilan is triple board-certified in pediatrics, clinical genetics, and clinical biochemical genetics. He is a fellow of both the American Academy of Pediatrics and the American College of Medical Genetics and Genomics.

Cara O'Neill, MD
Chief Scientific Officer & Co-Founder, Cure Sanfilippo Foundation

Dr. Cara O'Neill is the Chief Science Officer at Cure Sanfilippo Foundation, an organization she co-founded following the diagnosis of her daughter, Eliza, with Sanfilippo syndrome in 2013. Her professional background as an academic pediatrician and personal caregiver experience allows her to bridge gaps between scientists, clinicians, industry, and families. She collaborates extensively with stakeholders throughout the rare disease space to advance patient-centered research, trial design and advocacy initiatives which has led to publications on caregiver treatment priorities and the first consensus clinical care guidelines for Sanfilippo syndrome. She also serves as an external advisor to the Lysosomal Disease Network and as a member of the FDA's Patient Engagement Collaborative.

James Wilson, MD, PhD
Rose H. Weiss Professor and Director, Orphan Disease Center
Professor of Medicine and Pediatrics
Director, Gene Therapy Program, Perelman School of Medicine, University of Pennsylvania

Dr. James M. Wilson is a Professor in the Perelman School of Medicine at the University of Pennsylvania where he has led an effort to develop the field of gene therapy. Dr. Wilson began his work in gene therapy during his graduate studies at the University of Michigan nearly 40 years ago. He then moved to Boston to do a residency in Internal Medicine at the Massachusetts General Hospital and continued his work in gene therapy at MIT. Dr. Wilson has been at the nexus of this emerging therapeutic area from its inception. He created the first and largest academic-based program in gene therapy after being recruited to Penn in 1993. He initially focused on the clinical translation of existing gene transfer

technologies but soon redirected his efforts to the development of second and third generation gene transfer platforms.

His laboratory discovered a family of viruses from primates called adeno-associated viruses (AAV) that could be engineered to be very effective gene transfer vehicles. These so called "vectors" have become the technology platform of choice and have set the stage for the recent resurgence of the field of gene therapy. Dr. Wilson has also been active in facilitating the commercial development of these new gene therapy platforms through the establishment of several biotechnology companies. He is currently leading a national dialogue on the challenges of commercializing these potentially lifesaving treatments due to the disruptive nature they will have on traditional business models. Throughout his career, the focus of Dr. Wilson's research has been rare inherited diseases, ranging from cystic fibrosis to dyslipidemias to a variety of neurologic disorders.

Eric Zanelli, PhD
Co-Founder, Allievex

Dr. Eric Zanelli co-founded the Allievex Corporation and was its Head of Research for the last five years. He was responsible for all nonclinical and translational medicine aspects of the projects; he was the principal analyst and writer for most of the documents submitted to the FDA. Prior to the founding of Allievex, Dr. Zanelli served as Senior Scientific Advisor at CoLucid Pharmaceuticals, Inc. (NASDAQ: CLCD), where he focused on the development of lasmiditan for the acute treatment of migraine headaches. He has also served in senior scientific management roles at Peptimmune Inc., Praecis Pharmaceuticals, Inc. and Cardion AG. Additionally, Eric was the Scientific Founder of Déclion Holdings LLC, a biopharmaceutical company focused on the discovery and development of innovative treatments for neurodegenerative diseases. He is the co-author of 51 peer-reviewed scientific articles and a co-inventor or sole inventor of 12 families of granted or pending patent applications.

Prior to his industry roles, Eric was a Senior Investigator at the Leiden University Medical Center, Leiden, The Netherlands, from 1996 to 2000 and a Postdoctoral Fellow in the Department of Immunology at the Mayo Clinic, Rochester MN, from 1992 to 1996. His research focused on the epidemiology of autoimmune diseases, with particular interest in the role of the Human Leukocyte Antigen (HLA) genes in the predisposition and severity of Rheumatoid Arthritis. Eric was a pioneer in establishing the influence of certain HLA alleles and haplotypes in the disease progression in patients suffering from Rheumatoid Arthritis. He has also served as a mentor to several students who have received their PhD degrees under his guidance.

Eric graduated with a doctoral degree in Immunology from the University of Luminy, now part of the Aix-Marseille University, in France. His dissertation was about the characterization of autoantibodies against thyroid peroxidase in patients suffering from autoimmune thyroiditis.

Moderator

Susan C. Winckler, RPh, Esq.
Chief Executive Officer, Reagan-Udall Foundation for the Food and Drug Administration

Susan C. Winckler, RPh, Esq., is CEO of the Reagan-Udall Foundation for the Food and Drug Administration. The Foundation is the non-profit organization created by Congress to advance the mission of the FDA. Prior to accepting the Foundation post in May of 2020, Ms. Winckler served as President of Leavitt Partners Solutions. As President and Chief Risk Management Officer for the Leavitt Partners family of businesses, Ms. Winckler advised corporate executives on policy and business matters. As CEO of the Food & Drug Law Institute, she provided attorneys, regulators, industry leaders, and consumers with a neutral forum to address domestic and global issues. As FDA Chief of Staff from 2007-2009, Ms. Winckler managed the Commissioner's office; served as his/her senior staff adviser; analyzed policies; and represented FDA before myriad government and external stakeholders. She simultaneously led FDA's Offices of Legislation, External Relations, Public Affairs, and Executive Secretariat. As APhA Vice President Policy/Communications and Staff Counsel, she served as the association's lead spokesperson and senior liaison to Congress, the executive branch, state associations, and allied groups. Ms. Winckler earned a bachelor's degree from the University of Iowa College of Pharmacy and her juris doctorate *magna cum laude* from Georgetown University Law Center. She is an APhA Fellow, an elected member and Chair of the United States Pharmacopeial Convention (USP) Board of Trustees (2015-2020, 2020-2025), a member of the Purgo Scientific, LLC board, and a member of the Virginia Commonwealth University School of Pharmacy National Advisory Council.