Improving Qualitative Aspects of FSHD Clinical Trials

18 November 2023, Banff, AB, Canada

FSHD CANADA FOUNDATION
Curing the #1 Form of Muscular Dystrophy

PROJECT MERCURY
CANADA WORKING GROUP

Speeding safe and effective therapies to people affected by FSHD everywhere is the mission of Project Mercury. Key to achieving this is ensuring that promising therapies that enter clinical trials do not fail due to lack of patient engagement and retention, or lack of quantity or quality execution of trials by sites and investigators. These are not uncommon issues in rare disease drug development and our remit is to mitigate these possibilities as much as possible in FSHD.

The improvement of qualitative aspects of clinical trials is critical to addressing these issues. The Global Task Force of Project Mercury chose the FSHD Canada Foundation and the Canada Working Group to spearhead this work. We convened a one-day meeting in Banff of global experts in clinical trial management and access to scope and initiate the process. The key aims of this meeting were to:

1. Provide recommendations to the Global Task Force to solve the immediate challenges in current FSHD clinical trial protocols focused on operational issues involving speed of site onboarding, site capacity, and patient accessibility. This should focus on the next two years (2024-2025).
2. Provide the Global Task Force an implementable plan to "reimagine" data-informed, patient-friendly trial designs that broadens or "recategorizes" inclusion criteria (pediatrics, non-ambulatory, age, or functional metrics), implements innovative trial designs to enhance patient experience while easing site capacity and patient accessibility issues (validated remote assessments, validated biomarkers eliminating necessity of biopsies/MRI), along with other innovative initiatives. The goal is to identify feasible work (e.g. proof of concept or pilot programs) that can be initiated immediately (2024-2025).

I am pleased to report that the group accomplished these aims. While there is much work ahead to convert the ideas and recommendations that came out of the meeting into action, we now have a roadmap to follow. A brief overview of the roadmap is included in this recap and it will be advanced into an action plan by the Global Task Force at their meeting on December 9, 2023, in Boston, MA, USA.

Neil Camarta, Director, FSHD Canada Foundation
Lead of the Project Mercury Canada Working Group

AIM: Provide recommendations to the Global Task Force to solve the immediate challenges in current FSHD clinical trial protocols focused on operational issues involving speed of site onboarding, site capacity, and patient accessibility. This should focus on the next two years (2024-2025).

Recommendations and Approaches:

1. Recommendation: Provide cost guidance to support sites in budget development. Many sites, especially those with less experience in conducting multiple trials simultaneously struggle to forecast and manage budgets.

   Approach: Create budget templates and instruction (via pre-recorded videos) that site managers can use. This will be incorporated into a 'FSHD Resources Hub' that sites can access via the web. We will start with source documents and training/videos will be provided by Lawrence Korngut. Example of such a hub - https://dmdhub.org/the-dmd-hub-toolkit/

2. **Recommendation:** Expedite the timelines of imaging vendors. Trial sponsors expressed unanimous concerns over extensive imaging timelines and requirements hampering trial start-up.

   Approach: Patient advocacy groups (FSHD Canada Foundation, FSHD Society, etc.) spearhead engagement of vendors to determine viable methods to address these issues. This includes outreach to current and prospective imaging vendors; potential for a proof-of-concept project to bring in and validate additional vendors to the FSHD space.

3. **Recommendation:** Work with site staff (coordinators, evaluators) to better understand operational needs/gaps in this area and how to address and provide tools to enable site staff globally to interact, share best practices, opportunities for professional development, etc.

   Approach: Use peer-to-peer relationships and existing networks (e.g. NMD4C and CTRN networks) and establish a web-enabled platform that will support a healthy, vibrant and effective community. The idea here is that the 'wisdom of the crowd' will unleash new ideas and solutions across sites.

Additional recommendations that need further review to create an approach:

- Regionally coordinated protocol approval
- Site feasibility database (for sites outside of the major FSHD site networks)
- Create shared evaluator training certification and advocate for acceptance across studies
- Simplify contracting via one Master Services Agreement (MSA) for all sites in a network
- Clinical trial best practices in FSHD opinion paper
- Patient advocacy with European Medicines Agency Clinical Trials Information System (CTIS)

AIM: Provide an implementable plan to "reimagine" data-informed, patient-friendly trial designs that broadens or "recategorizes" inclusion criteria (pediatrics, non-ambulatory, age, or functional metrics), implements innovative trial designs to enhance patient experience while easing site capacity and patient accessibility issues (validated remote assessments, validated biomarkers eliminating necessity of biopsies/MRI), along with other innovative initiatives. The goal is to identify feasible work (e.g. proof of concept or pilot programs) that can be initiated immediately (2024-2025).

Recommendations and Approaches

1. **Recommendation**: Create a current state of progress towards decentralizing FSHD trials
   Approach: Inventory potential endpoints for FSHD trials, identify gaps/next steps. This will help determine what parts of a FSHD trial are feasible for things like remote assessments, measures, etc.
2. **Recommendation:** Educate FSHD sites and investigators on how to decentralize FSHD studies and trials.
   Approach: Draft a guidance document with what you need to know, regulations, etc. Recommend visits/processes that can be moved outside the main site (e.g. consent, questionnaires, labs, telehealth).
3. **Recommendation:** Advance the ability to conduct Reachable Workspace (RWS) assessment from the clinic to the home. RWS is the primary assessment in current FSHD trial protocols and this will help alleviate burden (time and space) at the clinic and make it easier for more patients to engage in trials remotely.
   Approach: Conduct a pilot/proof-of-concept of the 2D RWS 'Kinetigram' from Bioniks (https://www.bioniks.net/kinetigram). The Kinetigram™ is a cloud-based platform for analysis of 3D human body motion. Current release (Version 2) of the FDA-registered and CE-marked Kinetigram™ includes evaluation of upper extremity joint function in adults. The upper extremity module incorporates controlled audio-visually guided data acquisition that allows for geographically distributed clinical sites to collect kinematic motion data easily and securely. We will look to conduct this pilot at an FSHD clinical research center in Alberta (Dr. Lawrence Korngut and the Calgary Neuromuscular Program at the Cumming School of Medicine).
4. **Recommendation:** Explore the use of positron emission topography (PET) scanning as a biomarker.
   Approach: The FSHD Society is assembling a project to test PET at UC Davis in Irvine, California.
5. **Recommendation:** Establish widely agreed upon consensus for a FSHD disease progression model. Not only will this impact trial designs but is critical to providing payers with data they need to inform their health technology assessments and reimbursement decisions.
   Approach: The Project Mercury Canada Working Group is assembling a project to lead this highly collaborative work.

Exploratory Group Members

Amanda Hill joined the FSHD Society in July 2022 after having been involved as a volunteer Chapter Director, writer, and fundraiser for over four years. As the Society's Director of Research and Patient Engagement, Amanda brings deep professional expertise in biomedical research, including in clinical studies and clinical trials administration, scientific engagement and communication, and project management. Prior to joining the FSHD Society, she worked at the University of Colorado Anschutz Medical Campus for 12 years in the fields of cancer and Down syndrome as a research scientist, development manager, and program director. In 2016, Amanda's husband was diagnosed with FSHD, spurring her personal and now professional drive to serve and empower the FSHD community and advance research towards treatments and a cure. Amanda earned her BA in Molecular Biology from Scripps College in Claremont, CA, and her MBA in Bioinnovation and Entrepreneurship from the University of Colorado Denver in Denver, CO.

Craig Lipset is Former Head of Clinical Innovation at Pfizer, and Co-Founder of the Decentralized Trials & Research Alliance (DTRA). Craig is also the founder of Clinical Innovation Partners, providing advisory and board leadership with pharma, tech, and venture capital to bring vision and driving action at the intersection of research, digital solutions, and patient engagement. Craig was the Head of Clinical Innovation and Venture Partner at Pfizer, on the founding Operations Committee for TransCelerate Biopharma, and on the founding management teams for two successful startup ventures. Craig is Adjunct Assistant Professor in Health Informatics at Rutgers University, and Adjunct Instructor in the Center for Health + Technology at University of Rochester. He serves on the Board of Directors for the Foundation for Sarcoidosis Research and the MedStar Health Research Institute, as well as on the Editorial Board for Therapeutic Innovation & Regulatory Science. Craig has been listed among the PharmaVOICE most inspiring people in the life sciences (Red Jacket hall-of-fame), Pharmaceutical Executive's Emerging Leaders, CenterWatch Top 20 Innovators in Clinical Trials, and the AlleyWatch Who's Who in eHealth.

Dillon Chen is the Medical Lead for Arrowhead Pharmaceutical's FSHD program. He is a board-certified child neurologist with more than 20 years of clinical medicine and neuroscience research experience. Dillon has published extensively in clinical and basic neuroscience journals and currently serves as a faculty member in the Department of Neurosciences at UC San Diego and as an attending physician in Child Neurology at Rady Children's Hospital-San Diego. As a physician-scientist and a child neurologist who sees children with devastating neurological diseases, Dillon hopes to become a part of the solution, whether it be on the research, clinical, or health system front, to help these patients.

Homira Osman is Vice President, Research and Public Policy at Muscular Dystrophy Canada. She is trained as an audiologist-scientist and knowledge translation specialist. Homira holds an Honours B.Sc. in Neuroscience and Population Health from the University of Toronto. She earned a clinical doctorate and a PhD in neuroscience from the University of Washington (Seattle), followed by a post-doctoral fellowship at the Hospital for Sick Children in Toronto. At MDC, Homira works closely with persons with lived experience, physicians, allied healthcare professionals, researchers, academic, community and industry partners to engage, learn and share in knowledge generation, synthesis, and mobilization and ensures that evidence turns into action. As Vice President of Research and Public Policy, Homira delivers strategic and operational leadership for all elements of MDC's research portfolio, knowledge translation, clinical relationships, and advocacy work. Homira is also an investigator at the Neuromuscular Disease Network for Canada (NMD4C), serves on the Canadian Institutes of Health Research Community of Practice in Peer Review Steering Committee and is a member of the pan-Canadian Disability Coalition.

Jamshid Arjomand is Chief Science Officer for the FSHD Society. He is a neuroscientist with more than 15 years of pharmaceutical and biotechnology experience in chronic pain, neurodegeneration, neuromuscular disorders, and human stem cell disease modeling. Prior to joining the Society, he came from Genea Biocells, a San Diego-based biotechnology company where he served for five years as Vice President of Business Development. At Genea, he managed the scientific direction and collaborative efforts necessary to expand the company's drug discovery efforts, internal R&D capabilities, and revenue streams. Genea's pipeline included FSHD for which their lead asset, GBC0905, received orphan drug designation by the FDA in May 2018. From 2005 to 2013, Arjomand served as Director of Basic Research at CHDI Foundation. There he designed and managed a complex portfolio of academic, clinical and industry driven projects, primarily related to biomarker discovery, stem cell development, and target discovery and validation efforts for Huntington disease.

Jay Han is an associate professor in the Department of Physical Medicine and Rehabilitation at the University of California, Davis School of Medicine. He is the associate director of the National Institute on Disability and Rehabilitation Research (NIDRR)-funded UC Davis Rehabilitation Research Training Center (RRTC) in Neuromuscular Diseases, and the director of the Neuromuscular Medicine Fellowship, one of only a few in the U.S. His research interests focus on the development of functional outcome measures in patients with neuromuscular disorders and research in electrodiagnosis/electromyograms (EMGs). He is a fellow of the American Academy of Physical Medicine and Rehabilitation and the American Association of Neuromuscular and Electrodiagnostic Medicine. Han is the author of numerous publications and a recipient of the Outstanding Faculty Teaching Award from the UC Davis Department of Physical Medicine and Rehabilitation.

Josie Godfrey serves on the Global Task Force of Project Mercury where she leads our patient access workstream. Josie is Director at JG Zebra Consulting. She has worked in rare diseases and innovative therapies for over 12 years. She currently runs a consultancy business specialising in strategic market access, policy, and stakeholder engagement. She is the Strategic Director for Duchenne UK's Project HERCULES, an award-winning Global collaboration developing evidence and tools to support HTAs for new treatments for Duchenne Muscular Dystrophy. Josie is also co-founder and joint CEO of Realise Advocacy, which supports patient involvement in drug development and access processes. She previously led work at NICE to establish the Highly Specialised Technologies programme.

Ken Harvey is Head of Clinical Operations at Epic Biosciences where he oversees all clinical operations activities in support of their clinical trials. He has a background working directly with patients in hospitals as well as research-focused clinics, but for the last 20 years he has led cross-functional teams, in Global multicenter trials, in all phases of drug development. For the last decade he has been focused primarily on building infrastructure and capabilities for startup Biotechs to work with rare and ultra-rare diseases. In the past he has helped launched first-in-human therapeutics for companies like Genentech, Audentes, Cytokinetics and Kezar Life Sciences. Ken really believes in the potential of AAV therapies and the novel application of CRISPR-based technology. Ken received an International Executive MBA in Business and Finance from the International School of Management (ISM) in Paris, France.

Ken Kahtava is Chief Business Officer for the FSHD Society and Project Mercury's global partnerships lead. He joined the Society in January 2022 after working with them as a consultant, focused on business development strategies to support clinical research programs. Ken has held senior leadership roles in non-profit/research advocacy and various private industries for more than thirty years. He worked with the Society's CEO, Mark Stone, when they were both with the Polycystic Kidney Disease (PKD) Foundation. Ken led business development strategy and industry partnerships to support therapeutic development from 2007 to 2012, resulting in the first-ever approved drug for ADPKD. Thereafter, Ken worked as a consultant to the rare disease units of pharmaceutical and biotech organisations to effectively partner with research-focused advocacy organisations to accelerate treatments to patients. Throughout his career, Ken has also been heavily involved in architecting health IT applications designed to improve patient education, participation in clinical research and healthcare provider engagement.

Lawrence Korngut Dr. Korngut is a neuromuscular neurologist at the Calgary Neuromuscular Program where he diagnoses and treats neuromuscular conditions and performs electromyographic (EMG) studies, he served as Director of the program from 2017 through 2021. He is an Associate Professor at the University of Calgary Cumming School of Medicine in the Department of Clinical Neurosciences, and a full member of the Hotchkiss Brain Institute. His research program focuses on collecting real world health data to improve health outcomes of patients with neuromuscular disease (ie. ALS). He has published over 62 peer-review articles and is a regular speaker at international conferences. Dr. Korngut led the growth of the Calgary ALS & Motor Neuron Disease Clinic from 2010 through 2021 further establishing the clinic as a premier provider of multidisciplinary ALS care worldwide. He led the development of the University of Calgary Neuromuscular Clinical Trial Program since 2009 having conducted over 80 clinical trials of new therapies for conditions including ALS providing access to promising new experimental therapies for patients across Alberta and Western Canada. Dr. Korngut led the formation and continued Calgary-based operations of the Canadian Neuromuscular Disease Registry (CNDR) that has recruited over 6000 neuromuscular patients across 48 Canadian clinics and has resulted in over 230 data releases supporting clinical trial recruitment and advocacy for improved access to emerging therapies. The CNDR is a highly respected source of data supporting clinical research for patients across Canada.

Mark Stone is the Chair of the Project Mercury Global Task Force and CEO of FSHD Society. He has served as an executive leader of research-focused patient advocacy nonprofit organisations since 2004. Prior to joining the FSHD Society, he was the chief executive officer of NephCure Kidney Global. During his tenure at NephCure, Stone launched the NephCure Accelerating Cures Institute (NACI), a drug discovery initiative anchored by a clinical trial network comprising more than thirty-five sites, which seeks to expedite potential treatments for nephrotic syndrome. Stone was CEO of NephCure Kidney Global from 2014 until the launch of NACI. Prior to his work there, Stone served CFIDS Association of America, the largest private funder of research for chronic fatigue syndrome as chief development officer, and the American Association of Physicians of Indian Origin as CEO. From 2004-2011, he was executive vice president and COO of the Polycystic Kidney Disease (PKD) Foundation. Stone has also served as the deputy director of a global relief and development organisation and as a pastor within the Nazarene Church.

Mel Hayes is EVP, Patient Experience at Fulcrum Therapeutics. He joined Fulcrum in September 2021 as Chief Commercial Officer and was subsequently appointed to the role of Chief Operating Officer in June 2022. In a recent restructuring Mel has been appointed Executive Vice President, Patient Experience. In this new role Mel is responsible for developing an external facing integrated enterprise model that leverages the intersection of Patient Affairs, Advocacy, Access, Policy, and Communication to support the pipeline in both SCD and FSHD. Mel brings more than 30 years of experience in asset development and management of commercialization strategies in a range of therapeutic areas including many rare, specialty and primary care diseases. Prior to Fulcrum, Mel served as Global Head Commercial, Vice President, Rare Blood Disorders at Sanofi-Genzyme, where he led the commercial organization for hemophilia and complement assets. His previous roles also include U.S. Vice President, Hemophilia and Global Head, Hematology Rare Blood Disorders at Bioverativ (acquired by Sanofi-Genzyme) and Global Vice President, Head of Global Marketing and Launch Excellence at Shire and Global Vice President, Hemophilia at Baxalta (acquired by Shire). He also spent 10 years at Bayer and nine years at Bristol Myers Squibb in progressive leadership roles where he was responsible for launching products in diabetes, cardiovascular disease, neurology, rheumatology, multiple sclerosis, and Parkinson's disease globally.

Neil Camarta is Lead of the Canada Working Group and is a chemical engineer and a member of the Canadian Academy of Engineering. Neil joined Shell Canada Ltd in 1975 and led the development and delivery of world-class energy projects in Canada and abroad. Neil is currently a director of Western Hydrogen and Enlighten Innovations, two cleantech start-ups he founded which are focused on commercializing green fuel technologies and grid-scale battery systems. Neil co-founded the FSHD Canada Foundation and Solve FSHD.

Nicholas Johnson is an associate professor, division chief of neuromuscular, and vice chair of research in the department of neurology at Virginia Commonwealth University with a focus in inherited neuromuscular disorders. He received his undergraduate degree in molecular and cellular biology and psychology at the University of Arizona. He then obtained his medical degree at the University of Arizona. He completed his neurology residency and combined fellowship in neuromuscular medicine and experimental therapeutics at the University of Rochester. His laboratory is focused on identifying the pathogenesis of myotonic dystrophy, the limb girdle muscular dystrophies, and facioscapulohumeral muscular dystrophy and identifying appropriate clinical endpoints for these conditions.

Nicol Voermans is Chair of the FSHD European Trial Network, located at Radbound University Medical Centre, The Netherlands. Nicol's main research interest is inherited myopathies, in particular congenital myopathies, fascioscapulohumeral muscular dystrophy, and the neuromuscular features of inherited connective tissue disorders. Recently, she has focused on the wide spectrum of RYR1-related myopathies, including those presenting in adulthood. She has started a congenital myopathy biobank to facilitate future research and has joined the international consortium for gene discovery and clinical research for congenital muscle diseases.

Stefania Risso is Senior Director, CNS & Neuromuscular Diseases at Arrowhead Pharmaceuticals. She is an experienced leader and scientist, successful in developing and managing scientific and business strategies for multiple projects within Arrowhead and her previous positions in biotechnology and pharmaceutical industries; with extensive experience in building innovative pipelines and successfully managing multiple projects from target validation to clinical development.

For more information about Project Mercury, please go to www.ProjectMercuryFSHD.org