PROJECT MERCURY

The Global Initiative to Speed the Delivery of Therapies for FSHD

Global Task Force

Preliminary Phase 1 Guidance Document

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Status of this document:

This document is the first of eventually two documents provided by the Global Task Force (GTF) of Project Mercury in 2023. The guidance represents the views of the GTF at the time of publication. It is not legally binding. This first document, Preliminary Phase 1 Guidance, includes background on the launch and scope of Project Mercury and considers the discussions and conclusions within the inaugural meeting of the GTF, held 11 May 2023 in Leiden, NL, as well as written comments received from members following the meeting. The second document, Final Phase 1 Guidance, will build on the preliminary document by adding the specific work packages to be completed to support the initiative's aims, and the resources, organisations and roles that form implementation of the work packages. The Final Phase 1 Guidance document is slated for publication by the Fall of 2023.

All guidance documents can be downloaded from the Project Mercury website at projectmercuryFSHD.org

** New/additional members have been added to the Global Task Force since the inaugural meeting in Leiden and will be included in the second iteration of this Guidance Document.*

Table of Contents

1. Executive Summary

With dozens of biopharmaceutical companies currently in active research and development of therapies in Facioscapulohumeral Muscular Dystrophy, the prospect of effective, approved therapies for people affected by FSHD around the world has never been more promising.

Three serious challenges must be solved if these therapies are ever to reach patients everywhere:

Challenge 1: Insufficient FSHD clinical trial readiness. Promising therapies in clinical trials fail to get to market almost 95% of the time. Some fail due to lack of efficacy, but many other reasons include lack of qualified patient involvement in clinical trials and not enough trial sites capable of conducting the trials.

Challenge 2: Patients may never be able to access approved therapies. Even if a therapy for FSHD gains regulatory approval, it does not a guarantee that patients everywhere around the world will be able to get it. Once a therapy is granted regulatory approval, payers in many countries may not cover the costs or will seriously delay their decision to do so.

Challenge 3: The global collaboration required to solve the first two challenges does not currently exist. Success requires specialised resources and active, focused collaboration on a global scale that does not currently exist. No single organisation can succeed at doing this on their own.

Solving these challenges is the remit of Project Mercury, the new global initiative to speed the delivery of therapies for FSHD. The project's four objectives are to:

1. Grow a global cohort of thousands of patients, starting with 10,000 patients in patient registry databases across nine countries who have completed a core dataset, who have engaged with educational materials from their registry or local patient advocacy organisation (PAO), and who are willing and able to participate in clinical research.

2. Grow and enhance the existing clinical trial site infrastructure, starting by doubling the number of qualified clinical sites within current site networks across nine countries (see Section 4.2 for list of countries) and ensure all can meet or exceed clinical trial industry sponsor timelines for study start-up.
3. Remove the barriers to patient access to approved therapies and enable by significantly improving average times from first global approval to local reimbursement in nine countries.
4. Establish the structure and operating framework for stakeholders who are needed to lead and manage the work involved in the first three objectives. Patient-centricity is the foundation for success, but it will require the combined, focused efforts and commitment of researchers, clinicians, biopharma companies and many other stakeholders working together to get the work done.

Success in Project Mercury means:

- Patients worldwide affected by FSHD will access approved therapies faster.
- Patient advocates will have access to resources and expertise to have their voices heard by biopharma, governments, and payers.
- Biopharma companies will improve success in their clinical trials with greater participation by qualified patients and a robust, highly capable trial site infrastructure.
- Researchers will have greater access to needed resources.
- Clinicians will have better tools to care for their FSHD patients.
- Biopharma companies, regulators and payers will have the evidence they need to approve and provide patient's access to, and reimbursement of, FSHD therapies.

This Preliminary Guidance document spells out the strategies that the Global Task Force of Project Mercury has laid out for the next three years (referred to as "Phase 1"). It will be followed by an updated Guidance document that will include the specific resources, organisations, and timelines for Project Mercury's stakeholders to complete Phase 1 strategies.

The stakes could not be higher.

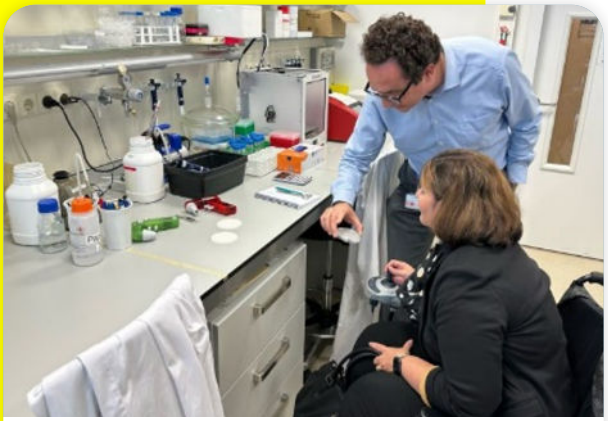
The challenges could not be greater.

The solution could not be clearer.

Introducing Project Mercury — the Global Initiative to Speed the Delivery of Therapies for FSHD.

2. A Patient-Centric Description of Facioscapulohumeral Muscular Dystrophy (FSHD) Reveals the Urgent Need to Speed Delivery of Therapies

> *"Every day I live with the knowledge that I face inevitable muscle and function loss with complete uncertainty about the timing of disease progression. I feel like I have no control over my life, and while I try to retain as much independence as possible, I am always having to adapt my life to accommodate the change in my abilities. As well as the physical impacts of muscle loss and weakness, the invisible aspects of the disease present challenges that many underestimate, including chronic pain, fatigue, and poor mental health.*
>
> — Emma Weatherley, FSHD patient and advocate, Australia



Emma visiting the FSHD lab of Prof Silvere van der Maarelat Leiden University Medical Center

Often characterized in medical literature as a 'slowly progressive disease', this description does not adequately represent the lived experience of people affected by FSHD. Regardless of how or what stage in life it robs them of their well-being and independence, their hope for stopping, slowing, or reversing it is urgent. It is a highly variable disease and those with early onset FSHD tend to progress rapidly. Even those not affected by FSHD live with the knowledge that the disease could be triggered in their body at any point in time and they could continue to decline throughout their life. Beyond muscle loss and weakness, people with FSHD live with pain, fatigue and mental health challenges that are often understated and misunderstood. These impacts are further extended due to FSHD being experienced in multiple generations, limiting the availability and capacity of informal supports usually in place to assist people with disabilities in family circles.

Hope is on the horizon. Numerous FSHD therapies are in clinical trials today, and all indications point to continued growth of the research pipeline. The possibility of approved therapies for FSHD being available is greater now than at any time in history.

Unfortunately, there are specific challenges that if not addressed, will slow, or prevent these therapies from ever reaching the people who need them. Strategies to overcome these hurdles have been identified and are detailed in this document. These strategies are designed to prevent two unthinkable scenarios:

- Promising and effective FSHD therapies fail during clinical trials, never reaching the patients.
- FSHD therapies are successful in clinical trials and receive regulatory approval but patient access to them in many countries is then significantly delayed or denied altogether.

Both scenarios have already happened in neuromuscular diseases like Spinal Muscular Atrophy (SMA) and Duchenne Muscular Dystrophy (DMD). They are avoidable in FSHD, but it requires coordinated efforts, focused collaboration, resource commitments, and sharing across multiple stakeholders at multinational scale that until now, does not exist.

Hope is on the horizon but the time and call to act is now.

Our FSHD community deserves a life without the burden of FSHD. They are waiting.

3. About Project Mercury — the Global Initiative to Speed Delivery of Therapies for FSHD

3.1 History and Background

The prospect of effective therapies available to the hundreds of thousands of people globally affected by FSHD has never been brighter. Dozens of biopharma companies currently have active research and development programs in FSHD, and the number of therapies in human clinical trials is growing rapidly. Yet, there are real and present challenges standing in the way of realizing a future with approved therapies that current and future patients can access.

In April of 2022, two members of the World FSHD Alliance, the FSHD Canada Foundation and the FSHD Society, began a formal initiative to discover and validate key problems that need to be addressed to ensure rapid development, regulatory approval, and patient access to FSHD therapies globally. Their work involved discovery meetings with biopharmaceutical companies, FSHD researchers, various experts, and other neuromuscular disease advocacy organisations who have been addressing these same issues (in SMA and DMD specifically). The key insights gleaned from this process and specific requirements for success revealed:

1. All stakeholders in the FSHD ecosystem play important roles. This includes patients, advocates, biopharma companies, clinical researchers, healthcare providers, and various experts, including those that understand how to build disease-level health economics and outcomes evidence. Any void in stakeholder representation results in negative impact to achieving desired objectives.
2. Rallying effective and focused collaboration amongst all these stakeholders, providing them incentives to work together, and generating sustainable resources and facilitating the sharing of these resources among them are critical, but is no small feat.

Armed with this knowledge, three action steps were completed:

1. A value-sharing network approach coupled with a platform operating model in which the work can occur and be managed was developed. This was tested in Canada between the FSHD Canada Foundation and the FSHD Society and proved successful.
2. A naming process was undertaken for the global initiative to provide it identity and create a 'place' where collaborators could come together and build a recognizable 'brand' to generate ongoing awareness and support. The name had to be synonymous with intentionality of effort, goal-orientation, and urgency to produce positive outcomes that are hallmarks of the initiative. Hence, 'Project' captured the intentionality and goal orientation, and 'Mercury', the Roman god of speed, represented the urgency. Project Mercury captures the essence of this global initiative to speed delivery of therapies for FSHD.
3. A short-term advisory group was convened in Chicago, IL in September of 2022 to further assess, validate, and provide overall guidance to expanding and refining Project Mercury. The group comprised experts and contributors representing all stakeholder groups, and global perspectives from North America, Europe, and the UK. They refined the aims and strategies and helped identify the risks and challenges to consider for taking the initiative global.

3.2 The 3 Challenges That Must Be Solved

The Chicago advisory group provided specificity and clarity across three specific challenges Project Mercury should focus on:

Challenge 1: Insufficient FSHD clinical trial readiness. The current global clinical trial networks are not sufficient to support a growing, robust clinical trial pipeline that calls for multiple, simultaneous clinical trials around the world. Additionally, the FSHD patient and clinician communities' preparedness and willingness to participate in clinical trials should not be overestimated or taken for granted. Establishing the

education and engagement tools necessary for them to navigate their decision-making journey is foundational to overall success. It is widely reported that the success rate of rare disease clinical trials resulting in an approved drug on the market is only about 6%[1]. More than 30% of these failures are not related to the safety or performance of the therapy but instead are due to insufficient numbers of qualified patients to participate and remain in the trials and/or lack of medical sites with capacity and capability to conduct the trials[23].

Challenge 2: Ensuring patient access. Even when a therapy for FSHD gains regulatory approval, it does not guarantee that patients everywhere will be able to get it. This has happened already in SMA and DMD and in numerous countries. Regulators like the Food and Drug Administration (FDA) and the European Medicines Agency (EMA) assess and approve or disapprove a therapy for issues of safety, tolerability, efficacy, and consistent, quality manufacturing. But these regulators do not determine the price, affordability, reimbursement schemes or patient access to these medicines. These decisions belong to payers — whether they be government health payers or private insurers. Once a therapy for FSHD is granted regulatory approval, these payers will determine if the benefits of the therapy outweigh the cost. This cost-benefit analysis, often referred to as a health technology assessment, or HTA, requires mountains of quality, data-driven evidence and takes time, often many years in some countries after a therapy receives regulatory approval. The hard lessons learned in SMA and DMD can and should be avoided in FSHD.

Challenge 3: Global sustainability in solving the first two challenges. The advisory group was unanimous in their agreement that success in solving the first two challenges requires resources and active, focused collaboration on a global scale. No single organisation can succeed at doing all of this on their own. While some of the resources needed to execute the work already exist, this level of collaboration, cooperation and resource commitment does not currently exist in the FSHD ecosystem and Project Mercury's operational framework can support it and incorporate incentives for the stakeholders needed to participate. Additionally, this operating framework requires effective program and project management around the world and ongoing sustainability efforts to resource and support the program which the FSHD Society can provide. Lastly, and importantly, oversight of Project Mercury must be patient-centered and global in its perspectives.

3.3 Vision and Values

The Chicago advisory group established the vision and values that must underpin the program:

Vision

The vision for Project Mercury starts and ends with the patient.

What does success look like?

Better patient understsanding…
driving better clinical research…
leading to better clinical trial experiences…
to provide an arsenal of effective therapies…
which patients everywhere can access

Values

Value 1. Patients hold the keys. Only by deeply understanding and addressing the needs and experiences of patients can we unlock successful therapies that ultimately improve their lives. Thus, Project Mercury is led by patients.

Value 2. Collaboration liberates progress. Stakeholders globally have already made significant inroads toward these goals, and their work is celebrated. Now, building on those efforts by enabling the sharing of knowledge and resources and by advancing a unified global vision, we can achieve together the remarkable feats needed.

3.4 Oversight and Project Management

Oversight — Global and Country/Region Levels

Based on the Chicago advisory group's recommendations, a Global Task Force, or GTF, has been formed and now provides oversight of Project Mercury. The GTF focuses on the micro and macro levels in support of Project Mercury. At the micro level, the GTF provides advice, support, and guidance to Project Mercury Country Working Groups, or CWGs, to identify optimal strategies and pathways that address and accomplish the primary aims. At the macro level, the GTF identifies strategies best executed at the global level and establishes global projects to execute them; identifies opportunities for sharing of resources and outputs of the CWGs to scale Project Mercury globally; and further embeds global perspective into Project Mercury's structure and governance. The GTF also identifies and engages additional expertise as needed and determines where and when CWGs will be formed for implementation of Project Mercury.

Membership

Membership in the GTF comprises Voting and Non-Voting Members. While achieving consensus is always the goal, the Voting Members have exclusive decision-making and voting rights when needed.

Voting Members

- A Chair (always filled by a FSHD patient advocacy group leader; Phase 1 will be led by FSHD Society CEO; position rotates every 2 years)
  - » Supported by a Secretariat
- Country Working Group Leads (local FSHD advocacy group leaders)

Non-Voting Members

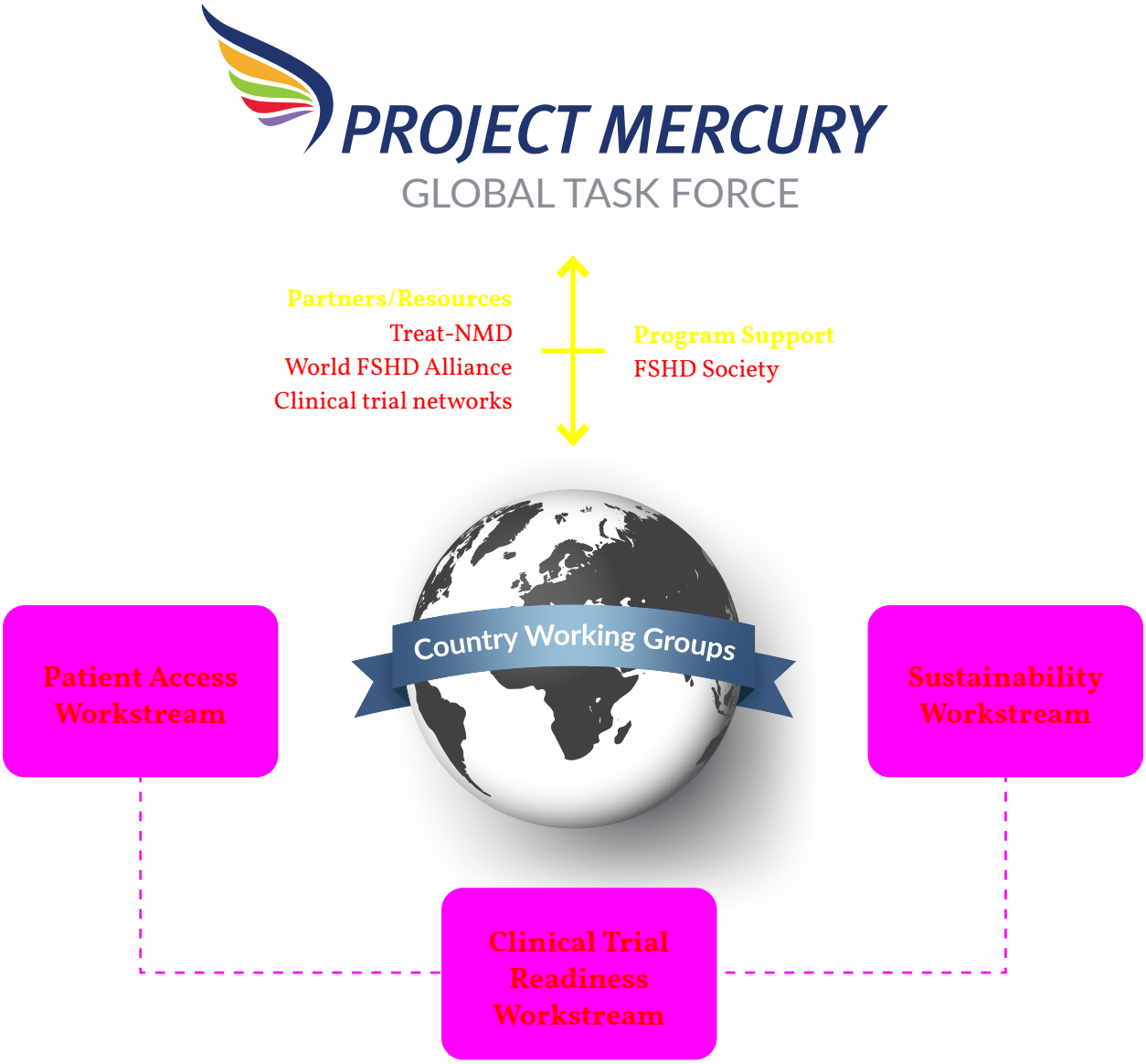
- Global patient access/health technology assessments subject matter expert
- Global health economics subject matter expert
- Biopharma company representatives
- TREAT-NMD (representing global FSHD patient registry network and clinician education programming)
- Clinical research Key Opinion Leaders
- Clinical care Key Opinion Leaders
- Non-MD clinician (physiotherapy, nurse, etc.)
- FSHD patient education subject matter expert (provided by FSHD Society)
- FSHD patient-centered research subject matter expert (provided by FSHD Society)
- Global Business Development/Partnerships Manager (oversees public and private funding to support Project Mercury; provided by FSHD Society)

The GTF will also periodically include independent subject matter experts (SME) and contractors when needed. The GTF will also encourage participation from regulatory/health technology assessment representatives.

All Members agree to the GTF Member Charter, included in Appendix.

Project Management

Foundational to Project Mercury's success is enabling focused, intentional, and beneficial collaboration among all stakeholders. Our **operating framework** is designed to facilitate this — supporting connections between organisations interacting and sharing resources. This alleviates risks to each organisation, optimises resource investments for all and ensures maximum efficiencies in time and execution. Through the sharing of resources, it also provides the necessary benefits for stakeholders to participate.



Each country/region has a CWG. CWG's have a lead - a representative from a World Alliance Member (FSHD advocacy group). CWGs have bespoke needs based on their capabilities and resources to manage the three workstreams. Collaboration between CWG's with guidance and other resources provided by the GTF ensures optimal execution and efficiencies. The lead of each CWG also serves on the GTF. Various partners, tools and resources are available to all as needed.

The FSHD Society provides overall program support, including project management and managing business development and strategic partnerships. In this role, the FSHD Society reports to the GTF.

This model has been tested successfully in Canada and is now the established method for Project Mercury to facilitate its work everywhere.

3.5 Sustaining Project Mercury

Ensuring adequate resources and engaged partners is foundational to success in Project Mercury. Thus, multiple avenues to generate funding and strategic partnerships is essential and is being done at the local (country/region) and global levels. The GTF identifies the resources needed and is responsible for oversight and dissemination of those resources. Four goals were identified and will be the basis of the work in this aim:

GOAL ONE: Ensure the launch & work of global/in-country initiatives of Project Mercury from 2023-26. Identify & secure partnerships & grants to underwrite start-up funding for global work packages. Identify work packages, implementation costs, & secure funding for in-country work.

GOAL TWO: Ensure ongoing in-country work of Project Mercury by building & implementing an in-country, fit-for-purpose sustainability structure operational by 2026. Landscape analysis of each country's existing structures & potential. Develop fit-for-purpose strategy for project implementation & revenue generation. Implement strategy & adjust/add as necessary.

GOAL THREE: Ensure ongoing work of Project Mercury beyond 2026 while providing resources for additional countries to participate.

GOAL FOUR: Ensure global costs are minimized and resources not wasted.

Global Sustainability

The FSHD Society leads business development and partnering efforts on behalf of Project Mercury by provisioning their Chief Business Officer to serve as Project Mercury Global Business Manager (GBM) and negotiating and finalizing formal agreements in support of Project Mercury. This work entails:

1. Generating revenues through public-private partnerships, such as government grants. Through researching available opportunities in countries where Project Mercury is operating, we will uncover grant funding that is focused on various aspects of the program.
2. Generating revenues and resources through biopharma industry partnerships. Industry has a lot to benefit from the work in Project Mercury, so not only do they supply their subject matter expertise through representation on the Global Task Force, but they also sponsor Project Mercury and contribute funding and in-kind support of various programs and projects.
3. Generating in-kind resources and support from various organisations through established agreements.

Local Sustainability (country/region)

The FSHD Society provides advice, support and consultation to the patient advocacy groups that lead the working groups in their respective regions. CWGs are responsible for generating patient engagement, fundraising, educational and networking events for patients and families.

A case study for local sustainability is the Project Mercury work to-date in Canada. The FSHD Canada Foundation leads the country working group in Canada. The FSHD Society has been providing them consultation, patient education materials and templates, fundraising systems and consulting and volunteer leadership training. To-date, three regional volunteer chapters have been established across Canada, and over $100,000 CAD has been raised. The FSHD Canada Foundation uses these proceeds to help fund various activities in support of Project Mercury.

4. Project Mercury Global Task Force Guidance

4.1 Phased Implementation of Project Mercury

Achieving success in accelerating the development of therapies and then ensuring FSHD patients everywhere can access approved therapies is a monumental task on a global scale. In implementing Project Mercury's work, it is necessary to takes a phased approach as there aren't enough available resources to address every country or region's unique needs simultaneously. This phased approach not only will allow for maximum and efficient use of resources, but as Project Mercury expands into other regions, existing resources and learnings can be applied, making implementation in new regions faster and more cost-effective.

4.2 Phase 1 Timeline and Geographic Targets

Phase 1 Timeline:

The first phase ('Phase 1') of Project Mercury began with the concept development in Canada, which started in June of 2022. The remainder of Phase 1 (including Canada and the geographic regions specified below) launched at the convening of the Global Task Force meeting in May of 2023 and will continue through the end of 2026.

Phase 1 geographic areas:

Australia, Brazil, Canada, France, Germany, Italy, Netherlands, Spain, United Kingdom (currently England but plan is to expand to other sites in the UK) and the United States.

The GTF acknowledges that this work will eventually extend beyond the Phase 1 geographies. We anticipate ongoing efforts during phase one with organisations in other countries depending on availability of resources.

4.3 Phase 1 Aims and Targeted Outcomes

4.3.1 Clinical Trial Readiness Aim 1: Grow Global Cohort of Clinical Trial Ready Patients

> *Even if it might not help me, it will help others someday.*
>
> — In the FSHD Society survey, 70 percent of FSHD patients responding agreed with this sentiment

4.3.1.1 Targeted Outcome(s) and Challenges to Success

Targeted Outcome:

10,000 patients in phase 1 country registries who have completed a core dataset, who have engaged with educational materials from their registry or local patient advocacy organisation (PAO), and who are willing and able to participate in clinical research.

Challenges to Achieving Target Outcome:

- Many patients have not had genetic confirmation of their diagnosis.
- Many patients do not receive optimal symptomatic treatment.
- Getting genetic confirmation can be time-consuming and expensive. It is also a difficult issue within families, and there is a shortage of genetic counselors.
- Need to change clinician behavior so that they systematically counsel newly diagnosed patients to join advocacy groups and enroll in registries and other studies.
- Large numbers of people with an FSHD diagnosis "go into denial" and do not want to think about anything having to do with FSHD.
- Genetic diagnosis' can be expensive.

4.3.1.2 Recommended Strategies and Measurements

Strategies:

1. Create globally accessible education program templates for both patients and clinicians covering the following topics. Templates will be coordinated and created at the global level through a sub-committee made up of Global Task Force members, leveraging existing resources and work across countries, and dispersed to all patient advocacy organisations in phase 1 countries for local adaptation and translation by country working groups.
    a. The importance of signing up with and regularly providing updates to registries.
    b. What it means to take part in a clinical trial and how to get involved (for physicians, this education will tie into expansion of clinical trial infrastructure in Aim 2).
    c. How to prepare for upcoming treatment approvals.
    d. (For physicians) How to recognise, diagnose, provide care for FSHD patients, and how to connect FSHD patients to local support and resources.

    Measurements:

    i. # of patients in registries and % with annual engagement/data updates.
    ii. # of educational templates distributed to local orgs (patient advocacy groups, clinical trial sites).
    iii. Estimated engagement with educational materials (e.g., website hits, click-through rates, etc.)
    iv. # of physicians completing masterclass.
2. Update the recommended FSHD registry dataset, ensuring fit-for-purpose for the following uses. The updated recommendation should include prioritized tiers of data collection that registries can adapt based on their individualized purpose, scope, and abilities. It should also include guidance and plans for appropriate interoperability and data sharing. This work will be coordinated at the global

level by TREAT-NMD, and resources provided to phase I country working groups to implement the new recommendations. Objectives of dataset update:

a. Continuing to broaden our understanding of disease progression and the patient experience.

b. Clinical trial feasibility and matching.

c. Ensure data items collected are relevant and important to direct users including patients, registries, and clinicians.

d. Ensure data supports Health Technology Assessments (HTA) and payor decision about treatment access when a drug comes to market.

e. Ensure that data is of use to future post-marketing studies.

Measurements:

i. Review feedback on current TREAT-NMD dataset.

ii. Creation of expanded TREAT-NMD core FSHD dataset with itemized, well-defined data items (reviewed by KOLs).

iii. # of registries in TREAT-NMD network targeted for piloting new dataset.

iv. Later: # of registries in TREAT-NMD network using new dataset.

v. Later: % of data items answered/unanswered by registries using new dataset.

vi. Flexibility and Speed of Reporting of dataset for key users and research without restrictive / limiting processes and accessibility.

4.3.2 Clinical Trial Readiness Aim 1: Expand and Optimise Global Clinical Trial Infrastructure

> *"Whenever you are trying to advance care for a rare disease like FSHD, qualifying high caliber centers of excellence can be a catalyst for advancing innovation."*
>
> — Mel Hayes, Chief Operating Officer, Fulcrum Therapeutics.

Due to small patient populations in rare diseases like FSHD, clinical trials are multicenter and often multi-national, to enable adequate patient recruitment. This presents challenges in finding and establishing qualified sites that can run the trial due to various issues - ethical review, harmonization of protocol, standards of care, services agreements, and cultural diversity - among them. It is widely reported that more than 85% of all clinical trials experience delays due to site selection and activation.

Optimising the global clinical trial capacity and infrastructure is a major aim of Project Mercury, especially with the reality that there are already multiple trials running simultaneously, trial sponsors are already reporting delays in getting their trials running, and more trials are on the way.

4.3.2.1 Targeted Outcome(s) and Challenges to Success

Targeted Outcome:

Double the number of qualified clinical sites within the existing site networks of the Clinical Trial Research Network (CTRN), the European Trial Network and sites in Australia in phase 1 countries and ensure all can meet or exceed sponsor timelines for study start-up.

Challenges to Achieving the Targeted Outcome

- Specialised equipment (e.g., specific MRI machines) and training (e.g., administration of clinical assessments) is needed for FSHD clinical trials.
- Identifying and engaging new physicians that are motivated to set up and run a clinical trial site.
- Labor shortages make it difficult to find and retain talented trial staff.
- It can take a long time for a new site to be fully ready to run a clinical trial.

4.3.2.2 Recommended Strategies and Measurements

Strategies:

1. The GTF will convene an appropriate forum to share lessons learned from Fulcrum Therapeutics, Avidity Biosciences, and previous biopharma companies who have run clinical trials in FSHD, with the goal of ensuring Project Mercury GTF's work and guidance in this area is correct and complete.
2. Improve clinical trial site creation, selection, and start-up processes by:
    a. Create and implement a uniform legal template/guidance/master clinical trial agreement across sites and networks globally to simplify site contracting. This work will happen at the global level.
    b. Assemble roadmaps to trial approval at each site. Roadmaps will be created or collected by country working groups and will be coordinated at the global level.
    c. Support stand-alone research sites that are multi-disciplinary (i.e., physio, RWS, access to specialised MRI) which can significantly decrease start up timelines by using central ethics/Institutional Review Boards (IRBs). These types of sites have less bureaucracy regarding contracts, budgets, committees, etc.

d. Create and share a checklist to define what is needed to become a clinical trial site. This work will happen at the global level.

e. Create and share standard operating procedures (SOPs) for new site creation. This work will happen at the global level.

3. CWGs will identify new sites and assist with their onboarding using the materials produced in #2 above.

Measurements:

i. # of clinical trial sites.

ii. # (%) under a master services agreement.

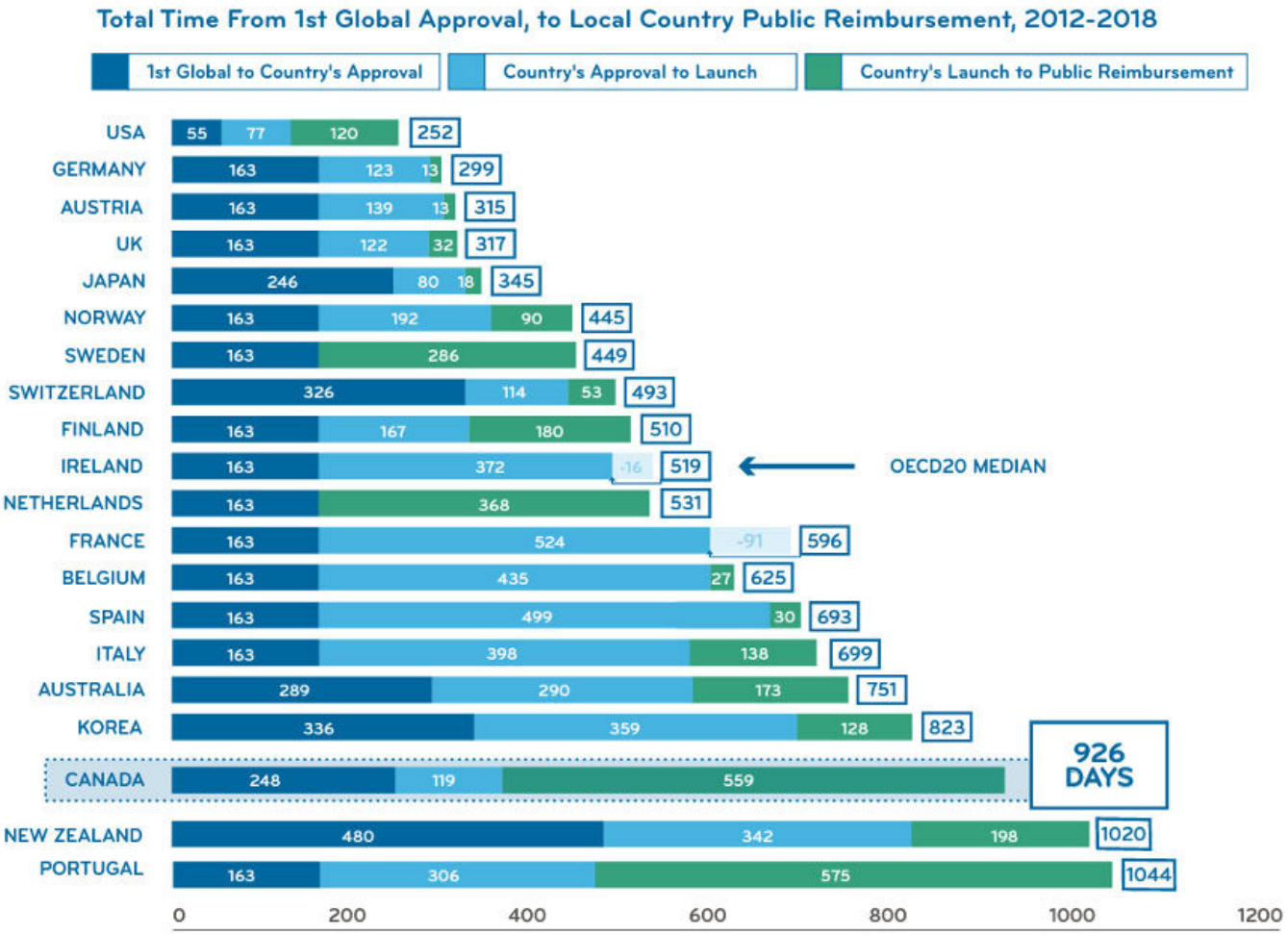
iii. Average time from sponsor contact to first enrollment (for those under the MSA).

4.3.3 Patient Access Aim: Remove barriers that slow or delay patient access to approved therapiess

"The prospect of delays or denials in accessing approved FSHD therapies is nightmarish. But it happens too often in rare diseases and has already happened in SMA and DMD here in Canada and elsewhere around the world. As approved therapies for FSHD are now within sight, as a patient and advocate, I will do everything I can to make sure patients everywhere can access them.

— Neil Camarta, FSHD patient and co-founder of FSHD Canada Foundation

Many countries experience significant delays in patient access to approved therapies:



Data from IQVIA, International Access to Medicines 2019. Analysis by Innovative Medicines Canada, February 2020. New Active Substances approved in individual countries between 2011-2016, and launched or publicly-reimbursed between 2011-2018. Measure of "Most", "Median", and "Fewest" country selected based on number of reimbursements for consistency (with their respective number of launches). NAS = new active substances. "At best" or Best-case = 20% of public plan beneficiaries. "Country-wide" = 80% or public plan beneficiaries. Special Review Status = expedited review pathway in respective country. Orphan = FDA or EMA designated.

4.3.3.1 Targeted Outcome(s) and Challenges to Success

Targeted Outcome

Beat average times from first global approval to local reimbursement in each country.

Challenges to Achieving the Targeted Outcome

The GTF acknowledges that achieving this outcome will likely extend beyond the timelines of Phase 1 but given the importance of this work, the strategies will be deployed during phase 1.

Challenges:

1. The availability of robust clinical data and readiness of healthcare professionals and patient representatives to work together to develop a consensus disease model will be a determining factor in the success of this workstream.
2. The availability of suitable measures of disease progression and Health Related Quality of Life (HR-QoL) will be determined in phase 1. The availability of financial resources to address any gaps in these will be a further determining factor in the success of this workstream.

4.3.3.2 Recommended Strategies and Measurements

Strategies:

1. Create and publish a widely agreed-upon FSHD disease model suitable for HTA and payor decision making. This work will happen at the global level.
    a. We will work with clinicians and patients to develop a disease model that provides sufficient clarity to inform access and reimbursement decisions in different countries. This will require pooling available clinical data to test and improve existing disease models.

b. An initial meeting with clinicians based in the Netherlands has been set up to explore current availability of disease models with well-defined health states and evidence on patient transitions between these health states.

c. Explore options for accessing clinical data with TREAT-NMD.

d. Select external contractor to develop a clinical model using data analysis and patient, family, and HCP input to inform the most significant aspects of different health states and likely transition rates.

e. Publish model through peer-reviewed publication and clinical conference presentations.

f. Create educational materials on FSHD targeted for payer engagement.

2. Perform and publish FSHD economic/cost model studies in all phase 1 countries. This work will happen at the country level.

a. Complete US, Canada and UK HEOR studies and publish results and Australia (pending available resources).

b. Review any remaining evidence gaps .

c. Develop EU HEOR study for participating countries.

d. Publish results in individual and collective manuscripts and at HEOR and HTA related conferences.

e. Develop a core disease level economic model based on the clinical disease model. Work with a modelling expert to deliver this.

3. Perform and publish a review of HR-QoL measures for FSHD, including a recommendation for the development and/or use of HR-QoL tools in future clinical trials and HTA and payor decision making.

a. Commission independent review of current HR-QoL measures in FSHD building on work already undertaken. This will include engagement with patients and families to inform our understanding of what is most important to people affected by FSHD.

b. Publish a review highlighting any areas of "good fit" with current measures and any areas where current measures are not adequate.

Measurements:

1. Publication of a widely accepted disease model developed with patient and clinical involvement.
2. Publication of UK, Canada and US HEOR studies and agreement on remaining gaps.
3. Commissioning of disease level economic model.
4. Publication of independent review of HRQoL measures.
5. Time to approval by reimbursement authorities in key countries is faster than average. (Note — this measurement may not be done in the timeframe of Phase 1).

4.3.4 Sustainability Aim: Ensure Resources are Available for Clinical Trial Readiness and Patient Access Strategies

4.3.4.1 Targeted Outcome(s) and Challenges to Sustainability

Targeted Outcome

All resources acquired to supported prioritized strategies in Phase 1 Clinical Trial Readiness and Patient Access aims.

Challenges to Sustainability

The GTF acknowledges that resource constraints can and likely will influence our ability to implement the recommended Phase 1 strategies itemized in this guidance document. This reality will be considered by the Voting Members of the GTF as they prioritize the work based on these constraints.

4.3.4.2 Recommended Strategies and Measurements

1. Prepare a Phase 1 Business Development Plan to support work at the global and country/regional levels. The Global Business Manager (GBM) and GTF Chair and Secretariat will create first draft of the plan, with a target completion date of July 15, 2023, to include:
    a. a. Details of work packages needed to implement GTF recommended strategies in all aims:
        i. Description of work and deliverables for each work package including timelines and dependencies.
        ii. GTF members who will lead each work package and GTF members who will support; whether work is done at local or global level.
    b. Estimated resources needed to execute work packages:
        i. Determine available resources from GTF members.
        ii. Determine resources needed (gap analysis and risk assessment); potential sources to acquire resources and mitigations vs risks.
    c. Review plan with GTF Voting Members and prioritize strategies/work packages by August 15, 2023 (influenced by resources/gap analysis).
2. Incorporate Business Development Plan into Final Phase 1 Guidance Document by September 1, 2023, and circulate to entire GTF for input and final approval.

5. Special Sub-Group to Address Qualitative Aspects of Clinical Trial Readiness

> *"It's not just a hard day physically, but it's also a mental game. The surveys ask you tough questions like, can you lift a baby? Some of the questions are ridiculous, like, can you dig a six-foot hole? But these questions are hard to get through. Grading yourself is emotionally difficult, and you have to be mentally prepared to do it in front of a coordinator or your loved one. It is very long days when you factor in travel and getting to and from all the buildings. And it's a really close look at your progression. You're doing physical things to show where you are in this disease. Doing some of the assessments is difficult. The next day, you're sore.*
>
> — Colette Wheeler, FSHD patient

The GTF acknowledges that optimizing clinical trial readiness should include work in trial designs and protocols. By making clinical trials more accessible and patient-friendly, we can improve likelihood of patient participation and retention, accrual and ultimately trial success. Work in this area extends beyond the scope of Phase 1 (time and geographic constraints), and thus, the GTF recommends a special sub-group be formed to initiate and manage work in this area.

Specific aims of this sub-group are:

1. Provide recommendations to the GTF to solve the immediate challenges in current clinical trial protocols focused on the issues involving speed of site onboarding, site capacity, and patient accessibility.
2. 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.

6. Global Task Force Member Organisations and Individual Bios

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.

Amy Winnen is currently the Vice President, Head of Market Value, Access, and Policy including Patient Affairs at Fulcrum Therapeutics. She is responsible for building the global market and patient access capabilities for Fulcrum's first commercial product launches, including establishing the value story to facilitate patient access and reimbursement. Her responsibilities include patient advocacy and patient affairs. She has over twenty years of experience in the pharmaceutical industry primarily focused on new product launches in the orphan and rare disease space. When not helping to ensure patients have access to critical treatments, she can often be found with her horses. She is a nationally ranked equestrian in the disciplines of dressage and eventing. Ms. Winnen is also the co-chair of the National Adult Rider Program for the United States Eventing Association. She holds an MBA from the Simmons School of Management in Boston, Massachusetts and a Bachelor of Arts in Economics and Sociology from St. Lawrence University in Canton, New York. She facilitates the inclusion of the patient voice into the strategy and operations through her advocacy and patient affairs responsibilities. Amy has over twenty years of experience in the pharmaceutical industry primarily focused on strategic operations in the orphan oncology and rare disease space.

Andrew Graham has been a leader in FSHD advocacy for several years originally being Vice President of MD UK and in 2010 became a Board Trustee and Treasurer. In leading a fundraising initiative on FSH, Andrew recognised the importance of patient registries as part of the preparation for clinical trials and was instrumental in establishing the UK FSHD registry at the University of Newcastle Upon Tyne.

Annie Poll, MD is Research and Communications Lead for TREAT-NMD. Dr Poll trained in academic research laboratories in the UK studying the neuroscience underpinning motor control. At TREAT-NMD she is responsible for data analysis, scientific publications, and research communication for the team.

Emma Weatherley is the purpose driven Managing Director of FSHD Global Research, Ltd in Australia. After her diagnosis of FSHD in her early thirty's, Emma quickly formed connections to FSHD Global and within the FSHD community. She became a strong advocate for FSHD, Muscular Dystrophy and access and inclusion for people with disabilities. Emma joined the FSHD Global board in 2021 as Executive Director and has been working to revolutionise Australian diagnostics and build clinical trial readiness. Emma's background in risk, compliance, and assurance, combined with her lived experience of FSHD and strong connections with the FSHD community made her the perfect fit for the role of Managing Director.

Josie Godfrey, Director at JG Zebra Consulting, 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 which has developed evidence and tools to support access 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 and has held roles in the pharmaceutical industry, government and on the board of patient organisations.

June Kinoshita, Sr. Director of Research and Education, joined the FSHD Society in 2012 and served as its Executive Director until September of 2017. Previously, June co-founded and served as Executive Editor of the Alzheimer Research Forum, the pre-eminent Web community for researchers in neurodegenerative disorders. June has worked closely with a variety of foundations to develop initiatives for multiple sclerosis, schizophrenia, amyotrophic lateral sclerosis, Parkinson's disease, and other disorders. June served on the National Board of the BrightFocus Foundation. She is also an entrepreneur, having co-founded N-of-One, Inc., a pioneering targeted oncology company. June graduated from Harvard College, where she concentrated in physics, and began her career as a science journalist, working as a writer and editor for Scientific American, Science, The New York Times Magazine, and many other national publications.

Ken Kahtava is Chief Business Officer (CBO) for the FSHD Society. Ken has held senior leadership roles in non-profit/research advocacy and various private industries for more than thirty years. He led business development strategy and industry engagement to support therapeutic development at the PKD Foundation 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 engage non-profit research-focused advocacy organisations to accelerate treatments to patients. He has also been heavily involved in architecting health IT applications designed to improve patient education, participation in clinical research and clinician engagement.

Kristi Clark is Vice President Clinical Operations for Avidity Biosciences. As a senior strategic leader for clinical operations, Kristi develops and executes global clinical operations strategy across all development programs and ensures clinical study conduct and integrity are maintained to highest standards and best practices. Kristi has over 30 years of experience in global clinical operations, including green fielding an office in Czech Republic. Kristi has worked in the rare disease space since 2005 and co-founded Agility Clinical, Inc. in 2012, a rare disease focused clinical research organisation. Kristi has a son with a rare disorder and is passionate about ensuring that the patient is a true partner throughout the clinical trial process and educating the patient on how their voice is heard during participation in natural history, registries, and clinical trials.

Lawrence Korngut, MD, is a neurologist and clinical neurophysiologist at the Calgary Neuromuscular Clinic and is the Director of the Calgary ALS and Motor Neuron Disease Clinic. His research includes phase II and III clinical trials of new therapies for neuromuscular conditions. He is the National Principal Investigator of the Canadian Neuromuscular Disease Registry that now includes thirty-one participating clinics. He chairs the Canadian Neuromuscular Diseases Network (CAN-NMD) funded by the Canadian Institutes of Health Research and Muscular Dystrophy Canada. He also chairs the Advisory Group and member Executive Committee of the Canadian Clinical Trial Coordination Centre, an initiative of the Canadian Institutes of Health Research Strategy for Patient-Oriented Research.

Mark Stone is CEO of FSHD Society and has served as an executive leader of research-focused patient advocacy non-profit 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.

Marina Kolochavina, PharmD, PhD has biopharmaceutical expertise spanning more than 18 years, including trusted advisory, executive leadership and integrated lifecycle asset discovery, development, approval, access, and use of over 252 rare and orphan assets (72% in rare paediatrics) in 42 therapeutic classes, resulting in approximately $4.2bn in capital committed to alliances with biotechnology and pharmaceutical partners of all sizes.es.

Mel Hays is Chief Operating Officer of Fulcrum Therapeutics. Mr. Hayes has more than 25 years of Global and U.S. experience in all areas of product commercialization including marketing, sales, new product planning, pricing and reimbursement, advocacy, and patient engagement. Prior to Fulcrum, he served as Global Head Commercial, Vice President, Rare Blood Disorders at Sanofi-Genzyme where he led the global commercial organisation for haemophilia. He also served as U.S. Vice President Haemophilia and Global Head, Haematology Rare Blood Disorders at Bioverativ (acquired by Sanofi-Genzyme). Prior to Bioverativ, he served as Global Vice President, Head of Global Marketing and Launch Excellence at Shire and at Baxalta (acquired by Shire) as Global Vice President Haemophilia. Prior to Baxalta, Mr. Hayes spent 10 years and nine years at Bayer and Bristol Myers Squibb respectively in progressive commercial leadership roles where he was responsible for launching products in Diabetes, Cardiovascular Disease, Neurology, Rheumatology, Multiple Sclerosis and Parkinson's Disease.

Neil Camarta 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 commercialising green fuel technologies and grid-scale battery systems. Neil co-founded the FSHD Canada Foundation and Solve FSHD.

Nicole Voermans, MD, is a neuromuscular neurologist working at the Radboudumc in Nijmegen with more than 15 years of clinical and research experience. Her main fields of research are 1) FSHD: genotype - phenotype coupling, trial readiness, optimal symptomatic treatment and trial fitness, and clinical trials; and 2) Congenital myopathies: genotype - phenotype coupling, trial readiness, optimal symptomatic treatment and trial fitness, and clinical trials. In 2021, She has launched the FSHD European Trial Network, bringing together all researchers and clinicians involved with FSHD in Europe. She organized two ENMC workshops on FSHD in 2022 focusing on genetic diagnosis, clinical outcome measures, biomarkers, and imaging.

Olga Mitelman, MD, is Senior Vice President, Head of Medical Affairs for Fulcrum Therapeutics. Olga has over twenty years' experience in leadership roles in medical affairs at pharmaceutical and biotechnology companies. She has supported drug development in phases one through four at such diverse companies as Johnson & Johnson, Biogen, and Sarepta. She has

participated in several launches in the neurology and psychiatry space. She has led the medical affairs function at Fulcrum Therapeutics since September 2021.

Rajeshri Badiani started FSHD UK in July 2021 with the idea of bringing together key stakeholders to collaborate and coordinate in getting the UK ready for FSHD clinical trials. This idea has become a reality with FSHD UK having 6 Sites and a reach of 800 patients. The Core team is multi-stakeholder — with patients, clinicians, research scientists, physiotherapists, UK Registry and both MDUK and FSHD Society representatives. FSHD UK has built on-going engagement plans with key FSHD Pharmaceuticals as well as starting a new Patients@site engagement plan. Since 2022 the UK now has ReSolve, MOVE and two clinical trial sites with hopefully more on the way. Raj is a committee member of the FSHD World Alliance (since 2021) and is also the patient representative on the I-SOC for FSHD. She has recently become a patient representative of the TreatNMD TGDOC FSHD Sub-Group. Raj began her career in banking and rapidly left that to do an MSC in Information Management and there-after started a career in IT to lead business & IT projects, manage a large portfolio of projects and also spend time doing a few years of services management (the other arm of project management) for a global FMCG company.

Robert Matthezing is chair of FSHD Stichting in The Netherlands since 2021. He is owner of Corundum B.V., an IT and IP law consultancy. Prior to that he worked for more than 30 years in various patent attorney, senior counsel and associate general counsel roles at Shell Global in London and The Hague. Robert has an MSc Geochemistry from Utrecht University, LL.B from the University of Law in London, UK, and an LL.M Law and Technology from Tilburg University. He is a registered Dutch and European Patent Attorney and a Solicitor (Law of England and Wales).

Teresinha Evangelista, MD, has over 20 years' experience working as a Neurologist and later as a Consultant at the Neurosciences Department of the Hospital de Santa Maria in Lisbon. These roles have been completed in conjunction with research work as a member of the Neuromuscular Research Unit at the Institute of Molecular Medicine as well as has ab Invited Lecturer at the Faculty of Medicine at Lisbon University in addition to a range of other teaching and advisory posts. Her work currently focuses on clinical and research work on hereditary muscle diseases, FSHD and Congenital Myasthenic Syndromes. Simultaneously as a member of the Joint Actions for rare diseases (EUCERD Joint Action and RD-Action), developed a particular interest on Rare Diseases policies. As a result of the policy work become responsible for the concept and setting up of the neuromuscular ERN (EURO-NMD) that integrates sixty-one healthcare providers from across Europe.

7. Glossary of Terms

Project Mercury's work is innovative and often complex. Thus, explanation about some of the terms we often use is in order as many of them have different meanings depending on where and how they are used.

Access (also referred to as 'Patient Access')	It refers to the ability for individuals to access the medicines they need at acceptable prices. Unfortunately, in rare diseases like FSHD, medicines are often expensive and getting the government health payers and private health insurers to agree to cover the costs can be seriously delayed or even denied.
Advocacy Group/ Organisation	Non-profit organisations that focus on a single disease or a broader category of diseases. For example, in Canada, the FSHD Canada Foundation advocates specifically for FSHD and Muscular Dystrophy Canada advocates across all neuromuscular diseases.
Approved Therapies/ Medicines	Drugs and medical devices that have received approval from regulatory bodies like the Food and Drug Administration (FDA) in the United States, Health Canada in Canada, European Medicines Agency (EMA) in Europe, etc.
Biopharma Company/Industry	Companies that develop medicines, medical devices, and other therapies. There are many companies working in FSHD. Two examples are Fulcrum Therapeutics and Avidity Biosciences.
Clinical Research	Is intended to produce knowledge valuable for understanding FSHD, living with and treating it, and promoting the best possible health outcomes. Examples of clinical research include genetic studies that involves blood tests but no changes in medication; studies of family history that involves gathering insights from family members to learn about people's medical needs and history; surveys of patients and families to understand the burden and costs of living with FSHD; testing of new FSHD medications or devices (often referred to as clinical trials).

Clinical Trials	There are two types of clinical trials. An interventional clinical trial is a voluntary research study conducted in people and designed to answer specific questions about the safety or effectiveness of drugs, vaccines, medical devices, other therapies, or new ways of using existing treatments. Most interventional clinical trials are sponsored by biopharma companies. An example of an interventional study is the REACH trial sponsored by Fulcrum Therapeutics. Observational studies don't test potential treatments. Instead, researchers observe participants who have volunteered to participate on their current treatment plan and track health outcomes. An example of an observational study in FSHD is the MOVE study.
Clinician	A person qualified in the clinical practice of medicine, psychiatry, or psychology as distinguished from one specializing in laboratory or research techniques or in theory. Examples of clinicians are primary care doctors, pediatricians, neuromuscular disease specialists, psychiatrists and psychologists, and physical therapists.
Country Working Group (CWG)	A formal group of people and organisations in a country working to implement various programs of Project Mercury. Led by a FSHD-specific non-profit advocacy group (most often a member of the World FSHD Alliance), the group includes experts from various fields and volunteer patient engagement leaders. CWG's work with other CWG's and the Global Task Force to maximize and share resources to ensure efficiency so work and outputs that only need to be done once are not being duplicated elsewhere. This 'shared value' approach to the network of CWG's is critical to success in Project Mercury's vision to speed the delivery of therapies in FSHD.
Global Task Force (GTF)	Is the oversight body of Project Mercury. The GTF comprises two types of members. Voting Members are the leaders from each of the Country Working Groups. Non-Voting Members are comprised of biopharma company representatives, clinicians, researchers and research network representatives, patient registry managers, patient education experts, experts from patient access and clinical trial readiness and regulatory and payer representatives.

Patient Registry	Is an organized system that uses observational study methods to collect data (clinical and other) to evaluate specified outcomes for people affected by FSHD. There are many FSHD registries globally. Registry organizers receive information from multiple sources (patient-reported and clinician-reported chief among them), maintain the information over time, control access to the information and are responsible for keep patient information secure. For Project Mercury, registries are critically important to success in engaging patients and families in clinical research and clinical trial engagement.
Payer	In the health care industry are organisations — such as private health plan providers/insurers, Medicare and Medicaid in the United States, the National Health Service in the UK, and Canadian Medicare — just to name a few. These organisations set service rates, determine what drugs/therapies for which they cover the costs, collect payments, process claims, and pay healthcare provider claims. For Project Mercury, payers are a critical stakeholder in our patient access work.
Regulatory Agency	The drug regulatory authority — are agencies that develop and implement most of the legislation and regulations on pharmaceuticals in their respective country or region. Their main task is to ensure the quality, safety and efficacy of drugs, therapies and medical devices, and the accuracy of product information. Examples of these agencies are the Medicines & Healthcare products, Regulatory Agency (MHRA) in the UK, the European Medicines Agency (EMA), the U.S. Food and Drug Administration (FDA), and the Therapeutics Goods Administration (TGA) in Australia — to name a few. Biopharma companies submit their clinical trial data to these agencies when they are seeking approval of their drug, therapy, or medical device in that country/region.

Researcher	A health professional who works directly with patients or uses data from patients (often from patient registries), to do research on health and disease and to develop new treatments. These professionals work in a variety of places, including academic institutions, biopharma companies, government institutions and non-profit advocacy organisations.
Therapy/Therapies/ Treatments	The attempted remediation of a health problem, usually following a medical diagnosis. There are many different types — drugs, medical devices, physical therapy, mental health, and behavior therapy, and more. For Project Mercury, unless otherwise described, we use the term in reference to drugs and medical devices.

8. How to Contact Project Mercury

Website:

www.projectmercuryFSHD.org

For media and general enquiries:

Global Task Force Chair: Mark Stone
mark.stone@fshdsociety.org

For enquiries about partnering with Project Mercury:

Global Business Manager: Ken Kahtava
ken.kahtava@fshdsociety.org

Appendix

Global Task Force Member Charter

The Global Task Force (GTF) will provide advice, support, and guidance to the Country Working Groups of each country to identify optimal strategies and pathways that address and accomplish our primary goals. In addition, Members of the GTF will define Global Projects as needed to support the goals of Project Mercury. The preferred courses of action will reflect consideration of various FSHD community goals, issues, concerns, and find the appropriate balance among competing interests.

I. Global Task Force Goals

- Advise the Country Working Groups about key aspects of Project Mercury, provide a global perspective on key considerations, and be a sounding board for program projects and deliverables.
- Work towards consensus among GTF Members on the desired program goals, alternatives, phasing, and mitigation measures.
- Identify key resources amongst the GTF Members themselves that can be contributed toward Project Mercury's objectives. Note, this does not mean or imply financial support for this program from GTF Members.

II. Project Mercury Outcomes

The process will be considered a success if:

- The GTF establishes clear, consensus-based recommendations on the best strategies and pathways to include in Project Mercury's strategies and tactics (globally and locally via the Country Working Groups);
- The stakeholders in the FSHD global community are engaged in a meaningful way in evaluating the proposed project programs and initiatives and in reviewing and commenting on the project;
- The project schedule takes the least amount of time and makes the most effective use of project resources;
- Appropriate regulatory and government agency(s) are involved and understand the outputs of Project Mercury to avoid surprises that lead to delays.

III. Terms of GTF Membership

Members agree to volunteer through the process and contribute expertise and resources where feasible and relevant to the member.

A member's position on the GTF may be declared vacant if the member:

- Resigns from the GTF (this should be in writing to the GTF Chair)
- Fails to attend more than two meetings without prior notice
- In a case where a member's position is declared vacant, the Chair may appoint an alternative representative from the same interest group to fill the position (interest group to decide who they want as their representative).

IV. GTF Operating Guidelines

Convening of Meetings

- Meetings will be held at the time and place chosen by GTF Members during their meetings.
- At the inaugural GTF meeting, the GTF will determine meeting frequency for the remainder of 2023 and 2024.
- Members will be informed of meetings through email, depending on his/her preference, at least ten weeks prior to the meeting.

Communication

- Meetings will be posted in a special project section of the Project Mercury website (projectmercuryFSHD.org)
- Project documents and notices will be posted on the project website.
- Email: The Chair (or the Secretariat) should be copied on all Member correspondence. Members will be provided the contact details of the Chair and Secretariat.

Conduct of meetings

- Meetings will be open to all Members.
- Meetings will be facilitated virtually and/or in-person.

- The Chair will moderate meetings.
- We will comply with the Global Federation of Pharmaceutical Manufacturers and Associations' (IFPMA) EFPIA Code to ensure ethical and transparent interactions with the healthcare, patient, and biopharma community. See https://www.efpia.eu/relationships-code/the-efpia-code for more information.
- Informed alternates are acceptable and encouraged if the Member cannot attend.
- All meeting participants will be afforded opportunities for open discussion throughout the meeting and all members in attendance to voice their opinions.
- Meetings will end with a clear understanding of expectations and assignments for next steps.
- In-person meetings are expected to be no more than one full day in length (8 hours). Virtual meetings are expected to be no more than 3 hours in length. Extension of time in either case will require the consent of the majority of members attending that meeting.
- Secretariat will keep a record of meeting attendees, key issues raised, and actions required.
- The previous meeting record and a meeting agenda will be forwarded to Members at least one week before the next meeting. Any changes to the record of the past meetings shall be in writing and forwarded to the Secretariat prior to the next meeting.

Meeting Ground Rules

- Speak one at a time — refrain from interrupting others.
- Wait to be recognised by moderator before speaking.
- The Chair will call on people who have not yet spoken before calling on someone a second time for a given subject.
- Share the oxygen — ensure that all Members who wish to have an opportunity to speak are afforded a chance to do so.
- Maintain a respectful stance toward towards all participants.
- Listen to other points of view and try to understand other interests.
- Share information openly, promptly, and respectfully.

- If requested to do so, hold questions to the end of each presentation.
- Remain flexible and open-minded, and actively participate in meetings.

Roles and Responsibilities

The GTF is an advisory group to Project Mercury and the Country Working Groups.

GTF Voting Members and Non-Voting Members agree to:

- Provide specific expertise, including identifying emerging issues;
- Where feasible and relevant, provide resources to the project;
- Review project reports and comment promptly;
- Attend all meetings possible and prepare appropriately;
- Complete all necessary assignments prior to each meeting;
- Relay information to their constituents after each meeting and gather information/ feedback from their constituents as practicable before each meeting;
- Articulate and reflect the interests that Members bring to the table;
- Maintain a focus on solutions that benefit the entire program;
- Identify and participate in Global Projects together, pursuant to mutually agreeable terms that the participating Members of that project will specify in a written Statement of Work between them.

The Chair agrees to:

- Provide GTF Members the opportunity to collaborate with other agencies and groups on making recommendations for the project;
- Effectively manage the scope, schedule, and budget;
- Keep GTF Members, partners and the FSHD global community informed of Project Mercury progress;
- Provide documentation to support recommendations;
- Provide domain and other technical expertise;
- Brief decision makers and produce briefing materials and reports;

- Provide early notification of GTF meetings and provide ten business days to review and comment on reports and other documents;
- Manage planning for meetings.

V. Decision Making

The GTF is primarily advisory. In those areas where it has decision-making authority, only Voting Members will vote. Voting Members will strive to reach agreement by consensus at a level that indicates that all Members are willing to "live with" the proposed action. All Members will strive to work expeditiously and try to avoid revisiting decisions once made.

VI. Conflict Resolution

When an issue arises that cannot be easily resolved, Members agree to:

- Remember that controversial projects are unlikely to receive funding, so the intent of all parties is to resolve issues so the project can be funded.
- Determine if the issue should be resolved within or outside of the GTF and participate however is appropriate.
- Ensure the appropriate decision makers are at the table to resolve the issue.

Index/Citations

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