FSHD BONUS PRIZE:
Qualifying Submission Guidelines
July 31, 2024
Version 1.0

NOTE TO APPLICANTS:
This document outlines the Qualifying Submission format and judging criteria for **XPRIZE FSHD Bonus Prize ONLY**.

Teams interested in competing in $101M XPRIZE Healthspan competition should consult the Qualifying Submissions Document here. Teams competing in BOTH XPRIZE Healthspan and FSHD Bonus must submit TWO Qualifying Submissions applications, one submission to each of the two prize tracks, as the competition stages, patient populations, and Judging Panels differ.

FSHD BONUS PRIZE QUALIFYING SUBMISSION

XPRIZE FSHD Bonus Prize will take place over 7 years with 1 Milestone along the way: the Qualifying Submission (detailed in this document). Please see the XPRIZE Healthspan Competition Guidelines for an overview of the FSHD Bonus Prize.

XPRIZE FSHD Bonus Qualifying Submission (QS) is the formal opportunity for prospective teams to demonstrate their ability to proceed to Finals. The FSHD Qualifying Submission is the means by which teams are initially assessed by XPRIZE Judges for their ability to ultimately succeed and deliver an effective solution to improve muscle function in persons with genetically confirmed FSHD.

The FSHD Bonus Qualifying Submission is a declaration of the skills, experience, clinical and laboratory facilities, and attributes of teams as well as an outline of the proposed therapeutic solution and plans for advancement in the competition. XPRIZE does not expect that the Qualifying Submission will be a full representation of the final tested therapeutic. XPRIZE expects and anticipates that the Qualifying Submission will provide:

- background and rationale on the therapeutic or combination of therapeutics
- documented proof that the intervention has been regarded as safe by a regulatory body or is under consideration by an appropriate safety and regulatory body
- evidence supporting use of the therapeutic on relevant endpoints or biomarkers
- an assessment of safety and potential risks and benefits to human subjects
- supporting information demonstrating skills and experience of the team
- evidence of the quality of the clinical center that will be engaged for testing
- appropriate regulatory approval or evidence that regulatory approval will be obtained
- detailed Finals proposal
- statement describing sources and scope of funding and state of intellectual property for their proposed solution

In summary, the Qualifying Submission will describe the teams' therapeutic solution, supporting evidence, strengths of team and clinical center, and proposals for Finals clinical testing. FSHD Bonus Qualifying Submissions should take a risk-based approach to answering the questions herein. XPRIZE does not require all answers or clinical studies to be complete now, but does expect teams to demonstrate the ability to fully address all criteria in the prize timeframe.

PART I: OVERVIEW INFORMATION

Section I. Key Dates

Posted Date
July 31, 2024

Open Date (Earliest Submission Date)
August 14, 2024

FSHD Bonus Qualifying Submission Due Date(s)
December 20, 2024

Due Date	Review Dates		
FSHD Qualifying Submission	**XPRIZE Internal Administrative Review**	**FSHD Judges Review & Notifications**	**FSHD Milestone 1 Award Ceremony**
December 20, 2024	January 2025	March 2025	2nd Quarter 2025 (exact dates pending)

- All FSHD Bonus Qualifying Submissions are due by 7:00 PM Pacific Standard Time.
- Competitors are encouraged to apply early to allow adequate time to make any corrections to errors found in the FSHD Bonus Qualifying Submission by the due date.
- No late applications will be accepted for consideration of an award at Milestone 1.

Required FSHD Bonus Qualifying Submission Instructions
It is critical that applicants follow the instructions. Conformance to all requirements is required and will be strictly enforced. Competitors must read and follow all FSHD Bonus Qualifying Submission instructions in this Guidance document. FSHD Bonus Qualifying Submission applications that do not comply with these instructions may not be accepted for review.

Budget to Conduct Research
It is the competitor's sole responsibility to raise sufficient funds and develop full research budgets that reflect the actual needs of the proposed project. Milestone awards (~$250,000 awarded to 8 teams) may not be sufficient to cover costs required to develop and test therapeutics in human studies. Submission of detailed budgets are not required, but evidence that sufficient funding is secured by the teams will be requested to ensure competitors are able to proceed through Finals.

Prize Purse, and Milestone Awards, and Testing Information
Please see Competition Guidelines for details on XPRIZE FSHD Bonus Prize concept, Prize Purses (Milestone Award and Grand Prize), and requirements for testing.

Section II. Qualifying Submission Content and Page Limits

Contents and Page Limits:

- **Summary:** **1 page**
- **Team:** **2 pages**
- **Environment & Clinical Center(s):** **2 pages**
- **Technical Application:** **5 pages**
  Recommended Subheadings:
  1. Scientific Rationale & Impact
  2. Preliminary Data
  3. Innovation (for Therapeutic Solution)
  4. Approach
     - Study Design
     - Ethical Issues
     - Data Management & Statistical Analyses
     - Sample Size Justification
- **Study Timeline:** **1 page**
- **Scale & Accessibility** **1 page**

Appendices for Judge Considerations: *no page limits*

- References
- Human Subjects
- Safety & Biohazards (if applicable)
- Trial Resourcing Plan
- Regulatory materials and informed consent documents (if available), or assurance that such materials will be prepared

Formatting:
Adherence to spacing, font size, type density, and text color requirements is necessary to ensure readability and fairness

- Margins: Must be 0.5 inch (1.27cm) or larger
- Font size: Must be 11 points or larger. Smaller text in figures, graphs, diagrams and charts is acceptable, as long as it is legible.
- Font type: Sans serif font (Arial, Helvetica, or Calibri preferred)
- Text color: Though not required, black or other high-contrast text colors are recommended.
- No specified citation formatting; the use of "et al." in place of listing all authors of a publication is acceptable.

PART 2. FSHD BONUS QUALIFYING SUBMISSIONS ANNOUNCEMENT

Section I. FSHD Bonus Qualifying Submissions Description

Purpose & Objectives

This request for FSHD Bonus Qualifying Submissions invites competitor applications that propose early-stage translational studies of therapeutics that may target disease-related muscle wasting and strength loss impacting quality of life in and improve healthspan in middle-aged and older adults with genetically confirmed FSHD.

The studies should assess therapeutics that, alone or in combination, can be tested for use in adults aged 50-80 years with genetically confirmed FSHD by the competing teams. US-based competitors considering submission of an Investigational New Drug (IND) may wish to refer to https://www.fda.gov/drugs/types-applications/investigational-new-drug-ind-application. Teams will have approximately ~4-years (2025-2029) Finals period to obtain regulatory approval, recruit subjects, and conduct clinical studies of up to one year.

Teams should detail their experience, rationale, and relevant research and development related to their therapeutic to date. Preliminary evidence generated by the team is not mandatory but strongly recommended to demonstrate proof of principle, and the track record of testing by the team or clinical center will provide confidence that the team will be able to deliver in subsequent competition stages. Information in Part 3 of this Qualifying Submission details the recommended information teams should include in their application to allow Milestone 1 judging of the:

- Team
- Environment & clinical center
- Scientific rationale & preliminary data
- Finals study design and approach
- Timeline
- Scale & accessibility
- Safety, human subjects protections, regulatory approvals, and resourcing plans

Competitors are strongly encouraged to contact XPRIZE Healthspan staff prior to submitting their FSHD Bonus Qualifying Submissions to discuss whether the proposed work would be within the intended scope.

Section II. Research Types

Qualifying Research Types

Secondary research, preclinical studies in animal models, clinical observations in patient populations, and *in silico* research are acceptable supporting evidence for Qualifying Submissions. However, to advance through Finals, clinical trials per defined criteria in the Competition Guidelines are required.

Finals Timeline
The Finals clinical studies must be complete with analysis reports and data submitted to XPRIZE for Finals judging by February 2030. The Team's anticipated timelines for Finals will be evaluated by judges to ensure readiness and likelihood of success. A timeline document should be included in the application.

Competitors should feel free to contact XPRIZE Healthspan staff prior to submitting their Qualifying Submissions to discuss whether the proposed work would be within the intended scope.

PART 3. Application Review Information

Section I. Primary Review Criteria

Only the review criteria described below will be considered in the review process.

Overall Score
Judges will provide an overall impact score to reflect their assessment of the likelihood for the project to improve muscle function or exert a sustained meaningful change in the underlying biology of persons with genetically confirmed FSHD. Judges will consider the following criteria listed below.

Scored Judging Criteria
Judges will consider each of the criteria below in the determination of scientific merit and give a separate score for each. An application does not need to be strong in all categories to be judged likely to have major scientific impact and potential for success in Finals testing for the FSHD Bonus Prize. For example, a project that by its nature is not innovative may be essential to advance the field and deliver an effective therapeutic to persons with FSHD.

Team

- Are the Team Leaders or scientific director, collaborators, and other researchers well suited to testing the therapeutic?
- Does the team have appropriate experience and training in FSHD?
- If the team is collaborative, do the investigators have complementary and integrated expertise; are their leadership approach, governance and organizational structure appropriate for the competition or developing the therapeutic for persons with FSHD after the competition?
- With regard to the proposed team leadership, do the investigators leading the team and key personnel have the expertise, experience, and ability to organize, manage and implement the clinical trials required for Finals and meet timelines?
- Does the team have appropriate expertise in study coordination, data management and statistics?
- For teams that will use a multicenter trial, is the organizational structure appropriate and does the application identify a core of potential center investigators and staffing for a coordinating center?

Environment and Clinical Center(s)

- Will the environment in which the work will be done contribute to the probability of success?
- Are the staff support, equipment, and other physical resources available to the competing teams adequate for the proposed studies?
- Will testing of the proposed therapeutic benefit from unique features of the scientific environment, research populations, or collaborative arrangements?
- Are the laboratory/testing centers appropriate for clinical studies?
- Does the application adequately address the capability and ability to conduct the trial at the proposed site(s) or centers? Or are plans available to add or drop enrollment centers, as needed to obtain the appropriate number of persons with confirmed FSHD?
- If international site(s) is/are proposed, does the application adequately address the complexity of executing a clinical trial with international sites?
- If multiple clinical centers will be used, is there evidence of the ability of each individual site or center to: (1) enroll the proposed numbers; (2) adhere to the protocol; (3) collect and transmit data in an accurate and timely fashion?

Scientific Rationale, Impact, & Preliminary Data

- Is the prior research that serves as the key support for the proposed project rigorous?
- Are the scientific rationale for the proposed intervention well supported by preliminary data, clinical and/or preclinical studies, or information in the literature or knowledge of biological mechanisms?
- Is this clinical trial design appropriate for testing the proposed intervention?
- If the therapeutic is successful, how will clinical practice be improved?
- Is it possible to scale the therapeutic delivery beyond the 1-year clinical trial?
- Is there future commercial possibility in developing the therapeutic, beyond the timeframe of the FSHD Bonus Prize competition?
- Would the therapeutic be accessible to many persons, or are there considerable constraints due to therapeutic administration, stability, burden of use, financial demands?

Innovation

- Does the application challenge and seek to shift current research or clinical practice paradigms by utilizing novel theoretical concepts, approaches or methodologies, instrumentation, or interventions for FSHD?
- Are the concepts, approaches or methodologies, instrumentation, or interventions novel in a broad sense?
- Is a refinement, improvement, or new application of approaches, methodologies, instrumentation, or interventions for FSHD proposed?
- Does the design/research plan include innovative elements, as appropriate, that enhance its sensitivity, potential for information, or potential to advance scientific knowledge or clinical practice for persons with FSHD?

Approach

- Are the overall strategy, methodology, and analyses well-reasoned and appropriate to accomplish the specific aims of the project?
- Are the competing team's plans of proposed clinical studies rigorous and supported by prior research in FSHD or muscle aging?
- Has the team presented strategies to ensure a robust and unbiased approach, as appropriate for the work proposed?
- Are potential problems, alternative strategies, and benchmarks for success presented?
- If the proposed therapeutic solution is in the early stages of development, will the strategy establish feasibility and will particularly risky aspects be managed?
- Has the team presented adequate plans to address relevant biological variables, such as sex, for studies in human subjects with FSHD that will be conducted in Finals?
- Is the population that will be recruited for Finals justified in terms of the scientific goals and research strategy proposed?

Study Design

- Is the study design justified and appropriate to address the muscle endpoints proposed in the clinical studies?
- Is the scientific rationale/premise of the therapeutic based on previously well-designed preclinical and/or clinical research?
- Given the methods used to assign participants and deliver interventions, is the study design adequately powered to answer the research question(s), test the proposed hypothesis/hypotheses, and provide interpretable results?
- Is the trial appropriately designed to conduct the research efficiently?
- Are the study populations (size, gender, age, demographic group), proposed intervention arms/dose, appropriate and well justified?
- Has the need for randomization (or not), masking (if appropriate), controls, and inclusion/exclusion criteria been addressed?
- Are differences addressed, if applicable, in the intervention effect due to sex/gender and race/ethnicity?
- Are the plans to standardize, assure quality of, and monitor adherence to the clinical protocol and data collection appropriate?
- Is there a plan to obtain required study agent(s) and therapeutics?
- Is the dosing and route of administration justified?
- Are pharmacokinetic and pharmacodynamic considerations for the FSHD population well justified and appropriate (if applicable)?

Ethical Issues

- Are potential ethical issues adequately addressed?
- Is the process for obtaining informed consent or assent appropriate?
- Is the eligible genetically confirmed FSHD population available in the recruitment area and clinical center proposed?
- Are the plans for recruitment outreach, enrollment, retention, handling dropouts, missed visits, and losses to follow-up appropriate to ensure robust data collection?
- Are the planned recruitment timelines feasible and is the plan to monitor accrual adequate?

- Is the therapeutic route of administration, frequency of dosing ethical, feasible, and well-justified?
- Is the burden to research participants (time, effort, financial, physical, emotional) considered and minimized? Are proposed study plans feasible for the patient population?
- Are efforts to minimize possible risk taken? How will risk minimization be ensured?

Data Management and Statistical Analysis

- Are the procedures for data collection, management, and quality control of data adequate at clinical site(s) or at center laboratories, as applicable?
- Have the methods for standardization of procedures and quality control for how the clinical center will administer the clinical protocols and assessment measures been addressed?
- Are methods used to assign participants and deliver interventions appropriate?
- Is there a plan to submit required data and results to XPRIZE Healthspan within the proposed period (by February 2030)?

Sample Size Estimates

- Is there an analysis to support the planned sample sizes required to test the therapeutic solution?
- Were power calculations performed and a biostatistician engaged?
- Are estimates reasonable and feasible for the center and FSHD population?

Study Timeline

- Is the study timeline described in detail, taking into account start-up activities, the anticipated rate of enrollment, and planned follow-up assessments as will be required for Finals testing?
- Is the projected timeline for advancement to Finals trials feasible and well justified?
- Are regulatory materials prepared or approvals in process? Is this included in the proposed timelines?
- Are strategies in place should regulatory timelines be missed or delayed?
- Does the project incorporate efficiencies and utilize existing resources (e.g., practice-based research networks, electronic medical records, administrative database, or patient registries) to increase the rate of participant enrollment and data collection, as appropriate?
- Are potential challenges and corresponding solutions discussed (e.g., strategies that can be implemented in the event of enrollment shortfalls)?

Scale & Accessibility

Judges will assess whether therapeutic solutions proposed by teams could be adequately scaled to improve human health and function for persons with FSHD globally.

- Is it possible to scale the therapeutic delivery beyond the competition?
- Would the therapeutic be accessible to many persons or only a few?
- Are there constraints due to therapeutic administration, stability, burden of use?
- Is contamination or other safety and quality control issues a major concern for implementation during and after the competition?

- Can the financial demands for the target population to use the therapeutic be approximated at this point? If so, are these anticipated to be unduly prohibitive?

Section II. Additional Review Criteria

As applicable for the project proposed, judges will evaluate the following additional items as "pass / fail" conditions for continuing in the competition.

Protections for Human Subjects

For research that involves human subjects the judges will evaluate whether teams have or plan to obtain regulatory approval to conduct human subjects research. This should include justification for involvement of human subjects and the proposed protections from research risk relating to their participation according to the following five review criteria:

1. Risk to subjects
2. Adequacy of protection against risks
3. Potential benefits to the subjects and others
4. Importance of the knowledge to be gained
5. Data and safety monitoring for clinical studies

The judges will also evaluate the proposed plans for the inclusion (or exclusion) of individuals on the basis of sex/gender, race, and ethnicity, as well as the inclusion (or exclusion) of certain individuals to determine if it is justified. **Please note that teams that advance to the Finals must include middle-aged older adults (recommended 50-80 years) with genetically confirmed FSHD and both men and women (non-gender conforming individuals also acceptable) in their 1-year clinical trials to be considered for the FSHD Bonus Prize**.

Safety and Biohazards

Reviewers will assess whether materials or procedures proposed are potentially hazardous to research personnel and/or the environment. As with protections for human subjects, it is the responsibility of the Teams to obtain appropriate approvals and maintain safety. Biological hazards (biohazards) refer to biological substances that may pose a threat to the health of living organisms, including humans. This can include medical waste or samples of a microorganism, plants, animals or their byproducts, viruses, or toxins from a biological source that can affect human health.

Resourcing

The competing teams are responsible for funding their research and clinical studies. Though XPRIZE will provide networking opportunities with investors and funders and provide information on relevant funding announcements, teams are ultimately responsible for resourcing their own clinical research studies for the Finals. The judges and XPRIZE will review the ability of advancing teams to meet resourcing and funding goals to proceed.

PART 4. Judging, Review, and Selection Process

Review and Selection Process

FSHD Bonus Qualifying Submissions will be evaluated for scientific and technical merit by appropriate Judging Panels convened by XPRIZE Foundation. *For teams competing in both*

Healthspan and FSHD, please note that two independent Judges Panels will be convened. Separate Qualifying Submissions must be submitted for each prize track.

Completed FSHD Bonus Qualifying Submissions undergo a selection process in which only those applications deemed to have the highest scientific and technical merit (generally the top half of submissions under review) will be reviewed by Judges Panels and assigned an overall score. These applications will receive a written critique. The bottom applicants will be notified that their submission was either incomplete or not discussed by the judging panel.

Appeals of Judges Review will not be accepted.

The judges will use the questions detailed above to evaluate the teams' solutions based on:

1. Team
2. Environment & Clinical Center(s)
3. Scientific Rationale & Preliminary Data
4. Innovation
5. Approach
    a. Study Design
    b. Ethical Issues
    c. Data Management & Statistical Analyses
    d. Sample Size Justification
6. Study Timeline

Each of the above 6 categories has a possible range of 1 to 9 points, with 1 being the best and 9 being the worst. The Overall Score will also be on a 1 to 9 point scale and will reflect the judgment of the complete Qualifying Submission.

Human subject safety, financial fitness to compete (resourcing plan), safety and biohazards will also be considered as either acceptable or unacceptable.

Overall Score

The weighting of categories is a collective decision that the judges will make during the Judging Summit, which is a meeting that takes place before the presentation of the Finalist Teams. The judges will review the questions and discuss their relevance and importance for the competition. They will also consider the feedback and input from the prize operations team, Scientific Advisory Board, and Co-Title sponsors of XPRIZE Healthspan and FSHD Bonus Prize, who are the stakeholders that define the problem and the requirements for the competition.

The Overall Score may not be the average of all component scores. Judges will assign different weights to each question to reflect their relative importance and impact on the overall submission and potential success of the team in the 7-year XPRIZE FSHD Bonus Prize competition. This ensures that the judges reward the teams that demonstrate the most effective and innovative solutions to proceed to Finals.

The judges will also document the score for each of the 6 review components and provide the rationale for how these component scores drive the Overall Score.

The judges can revise or adjust the weights during the final presentation if they encounter new information or insights that affect their evaluation of the teams' solutions.

Selection Process

Applications will first be subject to administrative review and screened for completeness and merit. Judges will review screened applications deemed acceptable for review. The Judges will convene to select the Top 8 best performing teams (lowest Overall scores) for FSHD Bonis Prize. These selections will be submitted to XPRIZE and the Co-title Sponsors for review and acceptance prior to notification of teams.

Milestone 1 Awarding

The Top 8 scoring teams (lowest total scores) for FSHD Bonus Prize will be announced as Finalists (FSHD Bonus Prize) and will split a Milestone 1 prize purse of USD$2,000,000 (USD$250,000 per team) in acknowledgment of their promising research and to provide initial support for testing.

Competition Advancement

The teams selected for Milestone 1 awarded will automatically advance through to the Finals stage of testing.

Additional teams may opt to continue in the competition if their Qualifying Submission was reviewed but was not awarded. The judges' comments will be provided to teams, and teams who wish to continue are encouraged to address concerns raised by judges during the review process. Non-awarded teams should state their intent to remain in the competition and are encouraged to meet with the XPRIZE Healthspan operations team to discuss options for remaining in the competition.

Discretionary Late-Registration

A discretionary late-registration period will continue through 2027 at a progressively higher late registration fee (see Competition Guidelines). Teams registering after the deadline must first consult with the XPRIZE Healthspan Operations team and provide a letter of intent to compete. If the letter of intent to compete is approved, these teams must still complete a FSHD Bonus Qualifying Submission that will be administratively screened and reviewed by an ad hoc judges panel. Approved late-registrations are not eligible for Milestone 1 awarding and must still adhere to deadlines for submissions of data and reporting by Finalist teams.

Teams competing in XPRIZE Healthspan can transfer to the FSHD Bonus track at any point through 2027 with no additional registration fee, but must submit a letter of intent to transfer to XPRIZE for review by the FSHD Judging Panel.