XPRIZE HEALTHSPAN: QUALIFYING SUBMISSION GUIDELINES

July 31, 2024

Version 1.0

NOTE TO APPLICANTS:
This document outlines the Qualifying Submission format and judging criteria for **XPRIZE Healthspan ONLY**. Teams interested in competing in XPRIZE FSHD Bonus Prize competition should consult the FSHD Bonus Qualifying Submission Document here. Teams competing in BOTH Healthspan and FSHD bonus must submit two Qualifying Submission applications, one to each of the two prize tracks as competition stages, patient populations, and Judging Panels differ.

XPRIZE HEALTHSPAN QUALIFYING SUBMISSION

XPRIZE Healthspan will take place over 7 years with 2 Milestones along the way. Milestone 1 is the Qualifying Submission (detailed in this document) and Milestone 2 is the assessment of Semi-Finals Testing during which teams will have conducted Proof-of-Concept trials. Please see the XPRIZE Healthspan Competition Guidelines for an overview of the prize.

XPRIZE Healthspan Qualifying Submission is the first formal opportunity for prospective teams to demonstrate their ability to proceed through the competition. The Qualifying Submission is the means by which teams are initially assessed by XPRIZE Judges for their ability to ultimately compete in the XPRIZE Healthspan $101M 7-year global competition.

The Qualifying Submission is a written 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
- description of the early stage clinical testing proposed for Semi-Finals stage
- 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 Semi-Finals early stage clinical testing. Qualifying Submissions should take a risk-based approach to answering the questions herein. XPRIZE does not require all clinical studies to be completely described at the time of Qualifying Submission, but does expect teams to demonstrate the ability to fully address all criteria in the fullness of time.

PART I: OVERVIEW INFORMATION

Section I. Key Dates

Posted Date
July 31, 2024

Open Date (Earliest Submission Date)
August 14, 2024

Qualifying Submission Due Date
December 20, 2024

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

- All 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 Qualifying Submission by the due date.
- No late applications will be accepted for consideration of an award at Milestone 1.

Required Qualifying Submission Instructions
It is critical that applicants follow the instructions. Conformance to all requirements is required and strictly enforced. Competitors must read and follow all Qualifying Submission instructions in this Submission Guide. 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. The 40 best scored Qualifying Submissions will be advanced to Semi-Finals and awarded USD $250K (other teams can continue in the competition without an award, but must notify XPRIZE that they are doing this). Milestone awards are not expected to be sufficient to cover costs required to develop and test therapeutics in human studies. Evidence that sufficient funding is or will be secured by the teams will be requested to ensure competitors are able to proceed through Semi-Finals.

Prize Purse, and Milestone Awards, and Testing Information
Please see Competition Guidelines for details on XPRIZE Healthspan concept, Prize Purses (Milestone Awards 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**
  Subheadings:
  1. Scientific Rationale
  2. Preliminary Data
  3. Approach to Semi-Finals Testing
     - Study Design for Semi-Finals
     - Ethical Issues
     - Data Management & Statistical Analyses
     - Sample Size Justification
- **Study Timeline:** **1 page**
     - Use XPRIZE Excel template as a guide
- **Scale & Accessibility** **1 page**

Appendices for Judge Considerations: *no page limits*

- References
- Safety of Human Research Subjects
- 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. QUALIFYING SUBMISSIONS ANNOUNCEMENT

Section I. Qualifying Submissions Description

Purpose & Objectives

The Qualifying Submission is a written declaration of the skills and experience of the team, strengths of the clinical and laboratory facilities, review of evidence supporting the proposed therapeutic solution, and plan for Semi-Finals testing and advancement in the competition.

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
- Semi-Finals study design and approach
- Timeline
- Scale & accessibility
- Safety, human subjects protections, regulatory approvals, and resourcing plans

Teams will be required to test their therapeutic solution in human subjects in both Semi-Finals and Finals. The Qualifying Submission should indicate team readiness for clinical trials and provide a plan for how their solution will be tested in Semi-Finals early stage / proof-of-concept (PoC) clinical studies.

Section II. Semi-Finals Research Types and Testing Validation

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 Semi-Finals (and Finals) clinical trials per defined criteria in the Competition Guidelines are required.

Early-stage / Proof-of-Concept Trials Description

Early-stage / PoC trials are typically short (less than 30-60 days), small (5-20 people receive therapeutic treatment), and relatively inexpensive studies that are used to help design and justify larger clinical trials.

Early stage / PoC trials can be used to show feasibility of approach, develop or participant recruitment or study methods, evaluate best dosing / formulation / route of administration / protocol / combination, provide initial estimates of safety, and generate supportive data useful for planning the 1-year clinical trials required for Finals testing. Early-stage/PoC trials may or may not include an untreated control group, commonly feature dose-finding or

pharmacokinetic / pharmacodynamic studies, and may use criteria for success that differ from efficacy trials (e.g. statistical significance criteria $p < 0.05$ may not be necessary as "go / no-go" decision criteria). We allow our teams the flexibility to define these features needed to demonstrate feasibility and readiness. These features for Semi-Finals testing should be detailed in the Qualifying Submission document section "**4. Approach to Semi-Finals**"

The early-stage / PoC studies proposed for Semi-Finals are intended to be prospectively performed as part of this competition. However, a team may have previously completed such studies on their therapeutic solutions. In such cases, submission of this data and analysis reports for Semi-Finals judging may be allowable, determined on a case-by-case basis.

Semi-Finals Timeline
The Semi-Finals clinical studies must be complete with submission of analysis reports, data, and applications for Finals submitted to XPRIZE for judging of Milestone 2 by 2026. The Team's anticipated timelines for Semi-Finals will be evaluated by judges to ensure readiness and likelihood of success. A timeline document should be included in the application. A Timeline template is included here. Qualifying Submissions are encouraged to download and modify the template, or they may use a similar timeline. Relevant components can be added, deleted, or otherwise modified to fit Team's clinical studies proposed for Semi-Finals.

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 Judging Information

Section I. Primary Judging Criteria

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

Overall Score
Judges will provide an Overall Score to reflect their assessment of the likelihood for the project to improve muscle, cognitive, and immune function or exert a sustained meaningful change in the underlying biology of aging in older adults. Judges will consider the 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. For example, a project that by its nature is not innovative may still be meritorious.

Team

- Are the Team Leaders or scientific director / team leader, collaborators, and other researchers well suited to testing the therapeutic?
- Does the team have appropriate experience and training?

- If the team is collaborative, do the investigators leading the team have complementary and integrated expertise; are their leadership approach, governance and organizational structure appropriate for the competition?
- With regard to the proposed team leadership, do investigators leading the team and key personnel have the expertise, experience, and ability to organize, manage and implement the clinical trials required for Semi-Finals and Finals and meet milestones and timelines?
- Does the team have appropriate expertise in study coordination, data management and statistics?
- For teams that will use multiple clinical centers, 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 environment, research populations, or collaborative arrangements?
- Are the laboratory/testing centers appropriate for clinical studies?
- Does the application adequately address the ability to conduct the trial at the proposed site(s) or centers? Are the plans to add or drop enrollment centers, as needed, appropriate?
- If international site(s) is/are proposed (either multiple clinical centers, or a site located in a different country from the competing Team), does the application adequately address the complexity of executing the clinical trial?
- 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 & Preliminary Data

- Is the prior research that serves as the key support for the proposed project rigorous?
- Are the scientific rationale, the proposed hypothesis, and intervention approach well supported by preliminary data, clinical and/or preclinical studies, or information in the literature or knowledge of biological mechanisms?
- What is the quality of the preliminary evidence provided by the team? Did the team generate this preliminary data, or another group?
- Is it possible to rigorously test the therapeutic in a clinical trial in human subjects?
- Will additional understanding of the mechanisms or effects of this therapeutic be needed to advance therapeutic development?

Approach to Semi-Finals Testing

- Are the overall strategy, methodology, and analyses well-reasoned and appropriate for the early stage / PoC trials proposed for Semi-Finals?

- Are the competing team's plans of proposed clinical studies rigorous and supported by prior research?
- Has the team presented strategies for Semi-Finals testing 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 appropriately managed?
- Is the population that will be recruited for Semi-Finals justified?

Study Design

- Is the Semi-Finals study design justified and appropriate? Will it address feasibility measures or biomarkers that will be clear, informative and relevant to evaluate the Semi-Finalist team for readiness to conduct 1-year clinical trials?
- For Teams considering submission of data from previously conducted early-stage/PoC trials, is the previous study well-designed?
- Given the methods used to assign participants and deliver interventions, is the study design adequate to provide interpretable results?
- Is the Semi-Final study designed to conduct the research efficiently?
- Are the Semi-Final early stage / PoC appropriate and well justified with respect to: study populations (size, gender, age, demographic group), proposed intervention details, and duration?
- Has the need for randomization (or not), masking (if appropriate), and inclusion/exclusion criteria been addressed?
- 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 well justified and appropriate (if applicable)?

Ethical Issues

- Are potential ethical issues adequately addressed?
- Is the process for obtaining informed consent or assent appropriate?
- Are the plans for recruitment appropriate and ethical?
- Is the team's therapeutic, dosing, route of administration, and frequency ethical and well-justified?
- Is the burden (time, effort, financial, physical, or emotional) to the research participant considered and minimized?
- Are efforts to minimize possible risk taken? How will risk minimization be ensured?

Data Management and Statistical Analysis

- Are the procedures for data management and quality control of data adequate at clinical center(s) or at center laboratories adequate and well justified?
- Have the methods for standardization and quality control of procedures been addressed?
- Are methods used to assign participants to treatment arms appropriate (if needed)?

- Is there a plan to complete data analysis for Semi-Finals and submit required data and results to XPRIZE for judging?

Sample Size Justification

- Is there an analysis or other justification to support the planned sample sizes for Semi-Finals?
- Are estimates reasonable and feasible for the center?
- Was a biostatistician engaged, or will one be consulted during Semi-Finals?

Study Timeline
SEMI-FINALS = ONE YEAR
Consult the Timeline example document here *or you are welcome to use a similar timeline to suit your Semi-Finals testing plan. We recommend downloading and modifying. To modify the template, please add or delete rows corresponding to your planned activities, and slide or extend bars to indicate active time per activity.*
XPRIZE activities and judging footprint are approximate and included for reference.

Judges will evaluate the following:

- Is the study timeline adequately described, taking into account start-up activities, recruitment, and planned follow-up assessment for Semi-Finals (2025-2026)?
- Is there a proposed plan for how the Semi-Finals studies will expedite transition to Finalists' 1-year clinical trials?
- Are regulatory materials prepared or approvals in process, and 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 to increase the rate of participant enrollment, study start-up, and data collection, as appropriate?
- Are potential challenges that may impact timeline and corresponding solutions discussed (e.g. drug or therapeutic access, funding limitations, recruitment)?

Scale & Accessibility
Judges will assess whether therapeutic solutions proposed by teams could be adequately scaled to improve human health and function 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 Judging 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 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.

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 Semi-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

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 Qualifying Submissions undergo a selection process in which only those applications that are fully complete and deemed to have the scientific and technical merit will be reviewed by Judges Panels and assigned an overall score. These judged applications will receive a brief 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. Approach to Semi-Finals Testing
    a. Study Design
    b. Ethical Issues
    c. Data Management & Statistical Analyses
    d. Sample Size Justification
5. Study Timeline
6. Scale & Accessibility

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 assessment 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 Semi-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, 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, impact on the overall submission, and potential success of the team in the 7-year XPRIZE Healthspan competitions. This ensures that the judges reward the teams that demonstrate the most effective and feasible solutions for the XPRIZE Healthspan challenge to proceed to Semi-Finals.

The judges will also document the score for each of the 6 judged components and provide the rationale for how these component scores result in 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 40 best performing teams (lowest Overall scores) for XPRIZE

Healthspan. 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 40 best performing teams (lowest total scores) for XPRIZE Healthspan will be announced as Semi-Finalists. The Semi-Finalists will split a total Milestone 1 prize purse of USD$10,000,000 awarded (USD$250,000 per team) in acknowledgment of their promising research and to provide initial support for the next-stage of testing (Semi-Finals) in the competition.

Competition Advancement

The teams selected for Milestone 1 awarded will automatically advance through to the Semi-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 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 Semi-Finals (see Competition Guidelines). Teams registering after the deadline must first consult with the XPRIZE Healthspan prize operations team and provide a 2-page letter of intent to compete. If the letter of intent to compete is approved, these teams must complete a 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 adhere to all deadlines for submissions of data and reporting by Semi-Finalist teams.