XPRIZE HEALTHSPAN

FINALS RULES AND REGULATIONS

4/13/26

Version 1.0

These Rules and Regulations (“Rules”) govern the Finals stage of the XPRIZE Healthspan competition. They establish the requirements and procedures for Finalist clinical trials. All competing Teams must adhere to these Rules in order to remain eligible for consideration and potential awarding of the grand prize.

These Rules complement and expand upon the Competition Guidelines. XPRIZE may update these Rules as necessary during the course of the competition to provide additional information or improve the competition’s quality. There may also be unforeseen issues that require modifications to these Rules. XPRIZE reserves the right to revise these Rules as it, in its sole discretion, deems necessary. Any changes to dates, requirements, or other key details will be communicated directly to competing teams.

Changes from previous Draft Rules and Regulations released to teams on March, 20, 2026.

1. Computerized Cognitive Assessment Battery, pages 16, 26.
    - The required Computerized Cognitive Assessment Battery by Cogstate is the newly selected battery, consisting of the Detection (DET; Psychomotor Function), Identification (IDN; Attention), One Card Learning (OCL; Visual Learning), One Back (ONB; Working Memory), Groton Maze Learning Test (GMLT; Executive Function), and International Digit Symbol Substitution Test – Symbols (IDSSTS; Processing Speed).

Table of Contents

1.Introduction and Scope

XPRIZE Healthspan is a 7-year, $101 million global competition to revolutionize the way we approach human aging.This collaborative effort brings together top scientists, clinicians, policymakers, industry experts and non-government agencies to drive new science and create a future where healthy aging is made possible for all.

Our global population is aging. In the last 100 years, public health measures like vaccination, access to clean water, lower infant and maternal mortality, and trauma care more than doubled our expected lifespan.[1,2] Yet at a population level, we have achieved these additional years of lifespan by evading early death, not by extending the period spent in relatively good health, or *healthspan*.[3] Yet there is hope; according to a 2021 report, if we could find a solution to extend healthy life by just 1 year for persons over the age of 60, it would be worth US$38 trillion, and by 10 years, US$367 trillion.[4] This concept forms the *geroscience hypothesis* - that interventions targeting the fundamental biological mechanisms of aging can improve multiple functional domains and delay or prevent age-related diseases simultaneously.[5]

Studies have implicated genetic and biological pathways that modulate healthy lifespan in animals.[6,7] Lifespan has been verifiably modulated by genetic, drug, and dietary interventions in model systems. Newer drugs, gene therapies, stem cell therapies, chemically-induced reprogramming, vaccines, and immunotherapies are now in development and show early promise in model organisms and disease conditions.[8] Many such interventions are being translated to human aging by competing teams.

The overall premise of $101M XPRIZE Healthspan is that by targeting aging with a single or combination of therapeutic solutions, it may be possible to restore function lost to age-related degradation of multiple organ systems. Teams competing in Finals may pursue testing of a variety of therapeutic interventions - including but not limited to drugs, biologics, gene therapies, devices, dietary, lifestyle, or behavioral approaches, administered alone or in combination.

During XPRIZE Healthspan Finals, Teams will conduct randomized controlled trials to conclusively demonstrate that their therapeutic solution - administered alone or in combination - can improve tests of muscle, cognition, and immune function in participants aged 50-90 years who are free of major or life-threatening disease and disability. The winning team will demonstrate that their therapeutic solution restores function by a minimum of 10 years, with a goal of 20 years. The prize awarding is based on the magnitude of functional improvement compared to controls observed in a 1 year period relative to the age-related declines expected over 10 years ($61M), 15 years ($71M), or 20 years ($81M) in a referent population.

The Judges will award the best team per award standards above (e.g. if one team exceeds 20

year threshold in all three domains - muscle, cognitive, and immune - and another team exceeds 10-years threshold in three domains, only the 20 year threshold team will be awarded the full prize purse). If more than one team exceeds a threshold equally (e.g. two teams meet the 20-year threshold), the award will be split between the highest-achieving teams.

Statement of Complicance

The competition's trials will be conducted in accordance with the Competition Guidelines and the Terms of the Competitor Agreement(s). The Finalist teams must conduct trials in accordance with local regulations, examples include ICH E6, the Code of Federal Regulations on the Protection of Human Subjects (45 CFR Part 46) in the United States, the Clinical Research Act (CRA) and Ethical Guidelines for Medical and Biological Research Involving Human Subjects overseen by the Ministry of Health, Labor and Welfare in Japan, Regulation (EU) No 536/2014 (the Clinical Trials Regulation or CTR) in Europe, or similar per the team's local or national regulatory agencies. All personnel involved in the conduct of this competition must have completed Human Subjects Protection Training as relevant to their clinical sites and local or national regulations.

XPRIZE Healthspan Finals Summary

Title: XPRIZE Healthspan Competition Finals: Clinical Trials Targeting Functional Outcomes and Biomarkers in Middle-Aged and Older Adults

Précis: XPRIZE Healthspan is a decentralized set of ten or more Finalist teams who will conduct 1-year randomized controlled phase 2 trials at their proposed clinical trial sites. It will determine whether the teams' selected therapeutic solution improves muscle and cognitive function, immune fitness, supportive biomarkers, and other aging phenotypes. Critical inclusion criteria for all teams are age range of 50-90 years and approximate balance of men and women. Teams should exclude persons for whom their therapeutic solution is contraindicated, who have difficulty communicating with study personnel, or who have dementia, an unstable chronic disease or condition, an activity of daily living (ADL) disability, or limited life expectancy.

Objectives: Our overall hypothesis is that by targeting the biology of aging, our Finalist teams can improve muscle and cognitive function, immune fitness, biomarkers and other phenotypes of aging in humans. We propose our teams to test this hypothesis using the therapeutic solution or approach as judged in earlier phases of competition in randomized controlled clinical trials.

Objective 1. To test whether the random assignment to a team's proposed therapeutic solution vs. control condition improves muscle, cognitive, and immune biomarkers by an equivalent of 10-, 15-, or 20-years. Thresholds are determined from age- and sex-similar referent cohorts.

Objective 2. To establish global research infrastructure to allow the testing of functional and mechanistic outcomes consistent with the geroscience hypothesis.

Objective 3. To evaluate safety, accessibility, and potential scalability of therapeutic solutions by judged consideration of adverse events, adherence, and tolerability of the therapeutic treatments, and feasibility of scale, delivery, administration, and commercial cost of proposed therapeutic treatments during and beyond the competition.

Exploratory Objectives: Following primary judging and awarding, the dataset generated in pursuit of XPRIZE Healthspan will also permit meta-analyses that could: 1) evaluate the effect of randomization to a therapeutic solution on biomarker "clocks" and aging phenotypes such as frailty, defined as accumulated health deficits, on self-reported quality of life measures, and on the incidence of common geriatric health conditions and syndromes; 2) explore sex-specific effects or differences in response to interventions in different groups of global participants; and 3) establish a shared biorepository and cultivate additional studies to aid in the discovery of novel pathways and therapies. Competing teams will be invited to participate in subsequent exploratory studies, though these would not affect the results of judging the primary competition.

Cohort: Each team is encouraged to complete studies of *a suggested maximum of* 200 men (~50%) and women (~50%) aged 50-90 years, with racial/ethnic competition reflective of the general population determined by each team. The *recommended* sample size at 1-year post-intervention follow-up for judging is 50 in the primary therapeutic group, or approximately 100 persons total if the team uses two-group design with 1:1 randomization scheme (note that 1:1 randomization is not required; 40 is the suggested minimum sample size in the therapeutic group). The specific population inclusion / exclusion criteria, sample size justification, intervention group, and randomization scheme must be justified by each team in their Finals Application.

Phase: Phase 2

Number of Sites: 10 Finalist Teams will be awarded. Additional teams may be invited to participate in Finals testing, but they must support their own entry and Finals participation. See Section 1, Key Roles for a complete list of operational partners, stakeholders, scientific advisors, and competition judges.

Description of Study Agent: Teams' discretion.

Study Duration: XPRIZE Healthspan Finals will have an approximately 3 to 6-month start-up phase, a ~3 to 3.5 year recruitment and treatment phase, and a 9-month analysis and judging phase.

Participant Duration: Each participant enrolled in the Team's study will participate in XPRIZE Healthspan for approximately 14 to 15 months (screening, 2 baseline assessments, 12-months intervention phase inclusive of midpoint follow-up assessments).

2. Key Roles and Responsibilities

Competing Teams

Teams should refer to the **Competition Guidelines** for detailed eligibility and registration requirements. Only approved Finalist Teams are eligible to participate in Finals. A **Finalist Team** is defined as a team that has successfully completed Semifinals Testing and is approved by the Judging Panel to participate in Finals Testing and compete for the Grand Prize. Teams must continue to adhere to the Rules and Regulations, Competition Guidelines, and Competitor Agreement to remain in good standing in the competition and must allow site visits as needed during the course of the Finals stage of competition.

Teams may still join the competition until February 2027 but may not be considered for Milestone awarding. Interested teams who did not complete a Qualifying Submission for Milestone 1 or a Semi-finals Submission for Milestone 2 must go through a Discretionary Late Registration process and be approved as a Finalist by the independent panel of Judges. Please see Section 5 of the Competition Guidelines for information on how to register a team after the standard deadline.

Teams who were ***not*** selected to receive a Milestone 2 Award (not Top 10) but still approved by Judges as a Finalist Team may choose to continue on in the competition but must financially support their use of the centralized partner-affiliated resources, the **XPRIZE Data Coordinating Center at the University of Utah (XPRIZE-Utah DCC)** and the **XPRIZE-UCSD Central Laboratories and Biorepository**. Please see the Competition Guidelines for more details.

Data Use Agreements (DUA) and **Material Transfer Agreements (MTA)** will be negotiated between Finalist Teams and the XPRIZE-Utah DCC and XPRIZE-UCSD CentralLaboratories and Biorepositories, respectively, at the start of Finals testing.

Team Liaison to XPRIZE-Utah DCC

Each Team will elect one person to serve as the Team Liaison to the XPRIZE-Utah DCC. This person:

- Must have the ability to enter data in an English database
- Will need to obtain an active directory account at the XPRIZE-Utah DCC
- Will need to sign an Electronic Data Capture agreement with the XPRIZE-Utah DCC
- Must be unblinded to the treatment arm and therefore should not administer the therapeutic or perform assessments on participants
- Will be responsible for resolving data queries

Steering Committee

Teams competing in the Finals must elect at least one and no more than three representatives to serve on the XPRIZE Healthspan Steering Committee. The Steering Committee members attend regular committee meetings (monthly for the first year of Finals, quarterly meetings thereafter). The meetings serve as a key networking opportunity between teams and provide a venue for teams to give and receive updates on trial progress, recruitment goals, scientific advances, regulatory considerations, and to troubleshoot issues for data management, specimen collections and handling, or address other competition relevant matters. These meetings will be attended by XPRIZE Operations staff, leadership of the XPRIZE-Utah DCC and XPRIZE-UCSD Central Laboratories, select SAB members, sponsors, or key stakeholders. Teams elect one representative to serve in a voting capacity as required for changes to protocols or data handling that may impact the competition or operations at their clinical site.

XPRIZE-Utah Data Coordinating Center

The Utah Data Coordinating Center (DCC) at the University of Utah serves as the centralized center for Finals data collection used for Judging. The XPRIZE-Utah DCC is tasked with providing comprehensive support for the collection, coordination, management, reporting, and storage of data required to support judging in the XPRIZE Healthspan Finals. Teams can collect additional data outside of the XPRIZE electronic data capture system (EDC) provided it does not limit testing for prize Judging.

The Roles of the XPRIZE-Utah DCC include: i) creation of a centralized EDC in REDCap that collects and monitors information supporting Finalist clinical trials; ii) development of data collection forms and data management tools; iii) providing overall study training, protocols, and a Manual of Procedures (MOP) to Teams; iv) performing quality assurance and control measures (e.g., statistical checks, data verification; v) contracting directly with non-Finalist teams who wish to continue in the competition.

Finalist Teams are REQUIRED to submit all data relevant to Judging to the XPRIZE-Utah DCC via electronic data capture using REDCap.

XPRIZE-UCSD Central Laboratories and Biorepository

The selection of the primary XPRIZE-UCSD Central Laboratory & Biorepository is pending. Additional assay services will be provided by specialized labs (e.g., IMM-AGE score and iAge Clock measures of immune function) using samples collected by teams and processed and banked at the primary XPRIZE-UCSD Central Laboratory and Biorepository. The XPRIZE-UCSD Central Laboratories will develop **Standard Operating Procedures (XPRIZE SOP)** for specimen collections and assays that will be followed by teams competing in XPRIZE

Healthspan Finals. The XPRIZE-UCSD Central Laboratories will provide teams with a detailed list of required kits and supplies for purchase, along with instructions for on-site labeling and tracking. They will also provide guidance for the batch shipment of frozen samples to the XPRIZE-UCSD Central Laboratories for tracking, assay processing, specimen management, and centralized storage.

Scientific Advisory Board

XPRIZE has appointed a panel of topical experts and big-picture thought leaders to serve as the "**Scientific Advisory Board**" (SAB) for the Competition. The SAB will remain in place throughout the Finals to advise XPRIZE regarding scientific and other elements of the Competition. Please refer to the public competition website for an up-to-date list of SAB Members. In addition to providing scientific guidance, the SAB is responsible for assisting with development of testing protocols, judging criteria, and approving and finalizing the development of these Rules and Regulations.

Judging Panel

Please refer to the public competition website for the most up-to-date information on members of the Judging Panel and Judges roles and responsibilities. Ad-hoc members of the Judging Panel will be considered and announced to Teams should the Panel feel additional subject matter expertise is necessary to review an application.

Judges will not provide feedback to Finalist Teams outside of XPRIZE-managed circumstances.

The Judging Panel's decisions are final and binding. Please see the Competition Guidelines for detailed information on the Judging Panel.

Costs to Compete in Finals

Milestone 2 Awarded Finalist Teams. Top 10 Finalist Teams will be Awarded $1,000,000 USD each as an unrestricted award to support their progress in the Finals stage of the competition. These funds may not be sufficient to cover all costs to conduct trials, but are intended to partially offset the costs required to collect the data necessary for judging the Grand Prize - including clinic costs and select performance measures. Costs for the Top 10 Finalist Teams to utilize the XPRIZE-Utah DCC and the XPRIZE-UCSD Central Laboratories for the collection of data and biospecimens used for judging will be covered by XPRIZE and at no additional cost to Teams. Data from assays and analyses below will be returned to the teams.

Non-Awarded Finalist Teams. Non-awarded but Judge-approved Finalist Teams must financially support their trials, costs of data collection, and use of the centralized services provided by XPRIZE-Utah DCC and XPRIZE-UCSD Central Laboratories. General budgets for

centralized partner services will be provided, though the specific costs must be negotiated between teams and these centralized services.

An overview of cost allocations to compete in Finals is below in Table 2a. This table is illustrative and not a definitive list of all possible costs that teams may accrue in the course of their trial conduct.

Table 2a. Cost Allocation by Finals Activity

Activity	**Cost Allocation**	
	Finalist Team Budget	**XPRIZE Budget^**
Costs at Teams' Clinical Site(s)	**Teams**	
Therapeutic Solution	X	
Research Participant Recruitment & Screening	X	
Regulatory Approval (if required)	X	
Medical & Safety Monitoring or Oversight	X	
Clinical Site Operations, e.g. staffing for up to 7 assessment timepoints	X	
Participant Characteristics Questionnaires	X	
Self Reported Health, Symptoms, and Event Reports	X	
Complete Blood Count (measured at clinic)	X	
Intrinsic Capacity Assessments**	X	
Activity Level**	X	
6-minute Walk Test (6MWT)	X	
Cardiopulmonary Exercise Test (CPET)**	X	
Lower-Body Power	X	
Muscle Mass** *(team discretion)*	X	
Biospecimen Collection and Processing: e.g. whole blood, plasma, serum, nucleic acid stabilizing tubes, PBMCs, urine	X	
Biospecimen Collection Kits and Shipping Containers	X	
Cold Storage, e.g. liquid nitrogen, refrigerators, ultra-low freezers, dry ice	X	

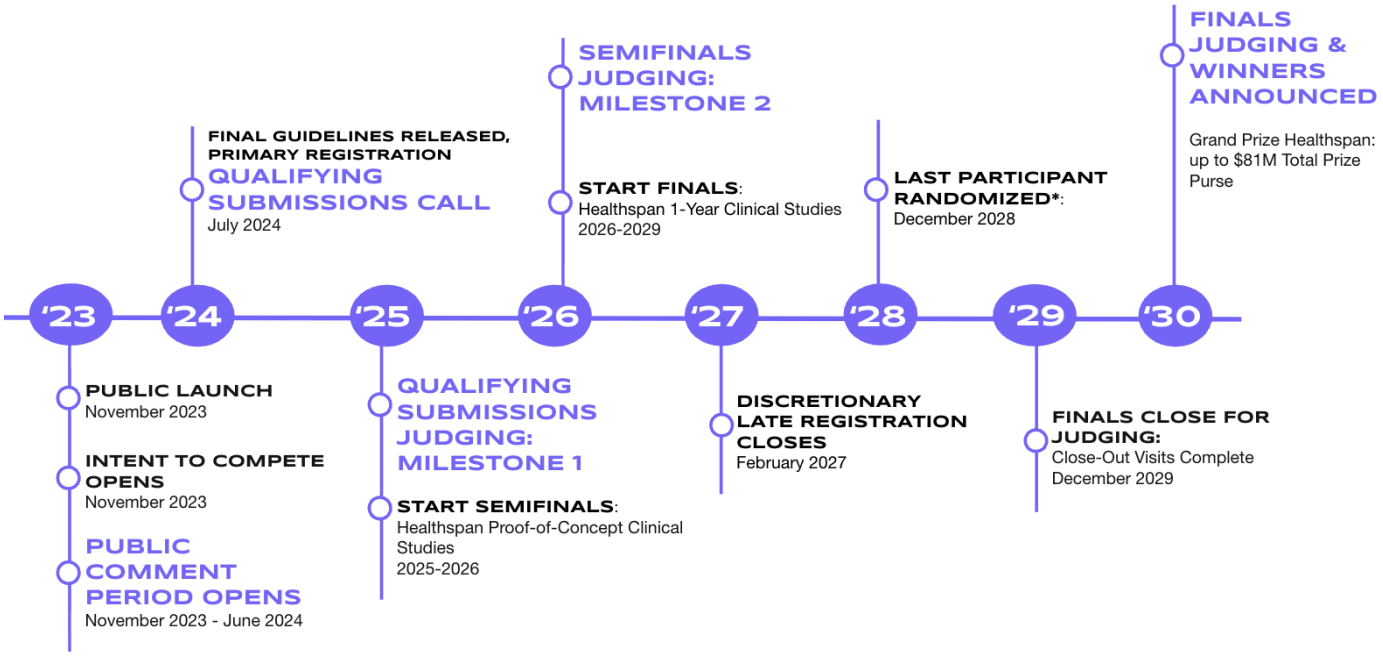
Centralized Costs for Technical Validation, Judging, Scientific Discovery^		**XPRIZE & Partners^**
XPRIZE Utah DCC Database, Data Management, Analyses for Judging		X
XPRIZE-UCSD Central Laboratories and Biorepository costs		X
Computerized Cognitive Assessment		X
Centralized Assays: Complete Metabolic Panel (fasted)		X
Centralized Assays: Hemoglobin A1c (HbA1c)		X
Centralized Assays: CMV		X
Centralized Assays: DNA / RNA isolation		X
Centralized Assays: Proteomics		X
Centralized Assays: Inflammation Age Clock (iAge)		X
Centralized Assays: Immune Age (IMM-AGE)		X
Centralized Assays: Immune Response Proxy (using banked samples)		X
Centralized Assays: circulating brain aging assays (using banked samples)		X
Centralized Assays: DNA Methylation (pending, using banked samples)		X
Centralized Assays: Metabolomics (pending, using banked samples)		X

^XPRIZE assumes costs for Milestone 2 Awarded Top 10 Finalists only; other approved Finalists must negotiate costs directly, though a fair price through XPRIZE partners will be offered

**Assessment measures denoted with double asterisks are strongly recommended but optional

3. Competition Timeline

Figure 3a. Competition Timeline Overview



*The recommended date for randomization of the final participant is December 2028. Accordingly, the last participant should be screened and enrolled no later than October 1, 2028 to allow for baseline testing and the 1-year clinical trial.

For a detailed timeline with specific dates and deadlines, please refer to the Competition Guidelines.

4. Overview of Study Design and Endpoints

PICOT Overview

Table 4a. Population, Intervention, Control, Outcome Time (PICOT) Overview

PICOT Element	Description
Population	Teams should aim to enroll ~100 adults (minimum 40 per group, suggested maximum 200 total; ~50% men and 50% women) aged 50–90 years who are free of major life-threatening disease or disability. Teams may recruit persons with evidence of functional decline, presence of a subclinical or managed condition or disease, or other *a priori* defined indicator of elevated risk of healthspan decline. Teams will define their own key criteria for inclusion / exclusion within the parameters of the suggested criteria listed in the Competition Guidelines.
Intervention	In the context of XPRIZE Healthspan, “therapeutic treatments” (or “therapeutics”, “therapeutic solutions”, or “therapeutic interventions”) refers to active drugs, biologics, devices, gene therapies, nutritional supplements, dietary interventions, lifestyle interventions or other approaches - alone or in combination. This list is not exhaustive.
Control	Teams must implement appropriate controls, including defined time controls, standard of care, or other alternatives that minimize bias. Randomization is required and masking must be used whenever possible.

Outcomes	Primary Healthspan Outcomes (measured by masked assessors using standard protocols): ● Muscle Function: Improvement beyond personalized response thresholds in: ○ Endurance Capacity (6MWT) ○ Lower-body power (Knee extensor or leg press) ● Cognitive Function: Improvement beyond personalized response thresholds in: ○ CogState computerized assessments of executive function, working memory, speed of processing/psychomotor speed and attention ● Immune Function: Improvement beyond personalized response thresholds in 2 of 3 biomarker categories measured by central lab ○ iAge ○ IMM-AGE ○ Additional biomarker to be announced prior to 2030
Time	Finalist trials start in 2026 and must conclude by December 2029. Each participant completes two baseline assessments, followed by a 1-year therapeutic intervention period inclusive of midpoint evaluations and follow-up assessments. We expect the minimum participation duration for trial participants is 14 months, with a median expected duration of 15 months.

5. Study Enrollment and Withdrawal

Participant Inclusion/Exclusion Criteria

Teams have the flexibility to define their own key elements of enrollment criteria but must adhere to the following guidance. Participants in the Finalists' trials must be 50-90 years of age. Prior to enrollment, potential participants with treatable diseases such as hypertension or diabetes will need to have those diseases adequately controlled to within acceptable limits, per each competing team's guidelines. Research participants may have evidence of some non-disabling, mild, age-related decline in function or health, which may increase the likelihood of measurable improvements with a 1-year therapeutic intervention time frame. Suggested specific eligibility criteria are described in the Competition Guidelines.

Screening and Rescreening

Teams are responsible for conducting thorough screening of all prospective participants and documenting the outcome of each screening attempt, including specific reasons for exclusion from the competition trial. This information should be tracked in sufficient detail to allow reconstruction of a CONSORT-style flow diagram for judging and audit purposes. Rescreening of individuals is acceptable and may be performed at the Team's discretion, provided that all screening and rescreening events are clearly recorded and reported. Further information regarding reporting in clinical trials can be found in the CONSORT 2025 Statement: Updated Guideline for Reporting Randomized Trials and in the CONSORT extension for n-of-1 trials. For examples of CONSORT-style reporting, see the forthcoming Rules and Regulations FAQ document.

Participant Recruitment and Retention

Enrollment of participants in Finalists' trials will be performed by a team's Clinical Center. Teams can employ recruitment strategies at their discretion as allowed by their local regulatory bodies. An estimate of the number of participants enrolled and randomized will be provided by teams in their Finals Application. The Judging Panel will review sample size estimates and evaluate the feasibility of achieving the specified sample size. Teams will determine the required sample size based on estimated therapeutic effects of the interventions being tested. It is anticipated that approximately 100 total participants will be required to achieve the large effects required to win the Grand Prize for XPRIZE Healthspan (suggested minimum 40 per group, suggested maximum 200 total).

Participant recruitment targets should strive for balance in sex (ideally, 50% female, but 40-60% balance is acceptable with accommodation for intersex individuals) and also ethnic and racial composition reflective of the geographic region from which recruitment will occur. Teams should proactively incorporate best practices to build diverse and inclusive research participant recruitment strategies.

Based on the Finals testing timeline, we recommend that all participants are screened and enrolled by October 1, 2028 (randomized by December 2028) to ensure that the trial is completed on time and the final data reports are submitted to the XPRIZE-Utah DCC prior to the data submission deadline of January 2030.

Run-In Period (Optional)

Included among the listed exclusion criteria are several that serve to identify individuals for whom retention may be compromised. These include criteria related to severely impaired function, life expectancy, and stability. At the competing team's discretion, a run-in period may be used to evaluate safety concerns or potential responses to a therapeutic, or to detect poor adherence or retention; justification and specific protocols for run-in should be reviewed and approved by Judges. Teams will not submit data from the run-in period to REDCap.

Monitoring Retention

Adherence to treatment and control conditions is important to minimize bias in the outcomes of the trials. Teams must systematically monitor and document adherence to assigned interventions (treatment or control), attendance at scheduled clinic visits, and completion of assessments within protocol-specified visit windows. Teams are encouraged to proactively implement retention strategies, subject to regulatory approval. Adherence to scheduled clinic visits and the corresponding windows surrounding these visits is systematically monitored by the XPRIZE-Utah DCC and contained in regular reports for interim review and the Healthspan Judging Panel. In interim reports to the XPRIZE-Utah DCC, recent participant attendance and completeness of data collection may be reviewed. Problems with retention will be noted, and retention strategies can be continuously refined by Competing Teams. If concerns about recruitment or retention arise, teams should submit a written explanation of contributing factors to the XPRIZE-Utah DCC and propose and implement corrective action plans.

Participant Withdrawal

Teams must implement procedures to document participant withdrawals throughout the Healthspan Finals clinical trials. All withdrawals, whether initiated by the participant, prompted by safety concerns, caused by loss to follow-up, due to protocol non-adherence, or any other reason, must be recorded with specific reasons whenever known. Responses will be tallied and

reported to the Judges by the XPRIZE-Utah DCC. Teams should ensure that withdrawal processes prioritize participant safety and ethical conduct, and that all data collected prior to withdrawal remain available for Judging and audits. Primary analysis and definition of success will be on an intention to treat basis.

6. Therapeutic Treatments

The Competition is designed to incentivize the development and testing of novel therapeutics. Each team's therapeutic solution will be described in the Final's Application and must be evaluated and approved by the Judges. Please see the Competition Guidelines for information on and examples of therapeutic treatments.

Following completion of the Finals trial, Teams may choose to offer the therapeutic solution to participants who were not randomized to the treatment group.

7. Finals Testing Study Design

Teams are required to conduct a 1-year prospective randomized controlled Phase 2 trial in which participants are randomly assigned to either an intervention or a control group. Teams may implement a two-arm design (active intervention vs. control) or incorporate additional arms — for example, subcomponents of a multi-component intervention in a factorial design — provided that a control condition is maintained in all cases.

The XPRIZE Healthspan Finals employs a before / after intervention experimental clinical study design that consists of a baseline period that includes two visits approximately 1-month apart (3-6 weeks baseline window suggested) followed by a 1-year intervention window (Figure 7a). Key features are: 2 repeat baseline measures for testing prior to randomization and 2 measures repeated at the time of follow-up (post-intervention) testing. This is intended to establish a baseline control condition (purple bars) to evaluate the magnitude of within-person change following randomization to intervention (gray-scale bars). Baseline and Follow-Up tests include those described in detail in Section 8 of this document. The repeated-assessment structure is designed to ensure that findings are robust to the measurement error, the labile nature of many physical and cognitive measures, heterogeneity in participant characteristics, variation attributable to measures taken in different clinical settings, and variability associated with different intervention approaches expected across Finalist teams and trial sites.

Figure 7b depicts how XPRIZE will determine the targeted or required change in function using longitudinal assessment in a single participant. Two assessments or measurements taken during Baseline Visits (Figure 7b, purple) and two assessments or measurements at Follow-Up Visits (Figure 7b, black) will be obtained at the Team's clinical center and used for outcome determination. Interim assessments collected at Midpoint Visits are used for safety screening, validation, and to support judging but not for award threshold determination (Figure 7b, gray). The assessment schedule is described in detail in Section 8. The proportion of positive responders (those who exceed personalized response thresholds; see Section 11) in the treated relative to control will be used for prize adjudication (see Section 12). The age- and sex-specific personalized response thresholds will be determined by XPRIZE, and will indicate the targeted or required change necessary to exceed associated 10-year, 15-year, and 20-year improvements based on referent population data (see Section 11 for details).

Figure 7a. Finals Study Design Schematic. Note: The period between repeat baseline assessments and repeat follow-up assessments is expected to be approximately 1 month, retesting within a 3 to 6 week window is acceptable.

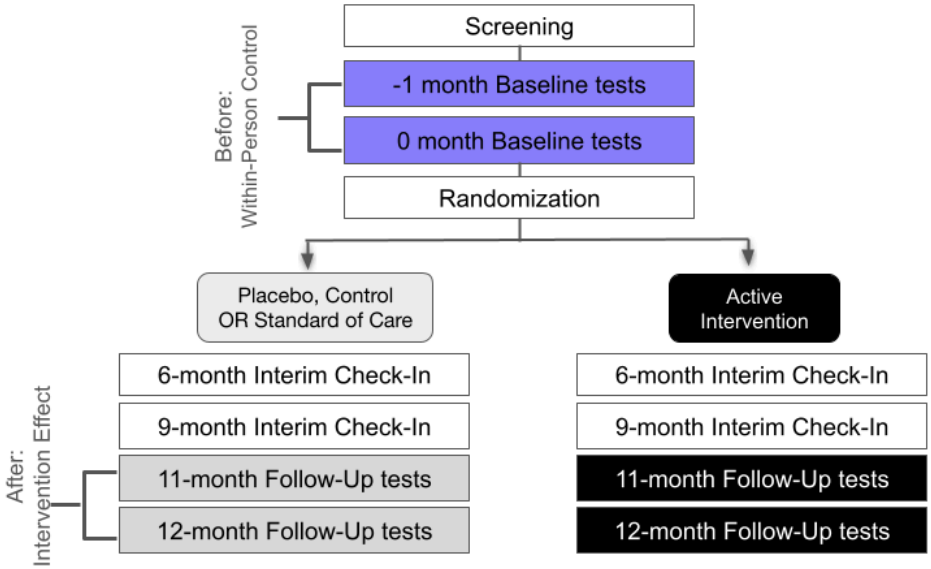
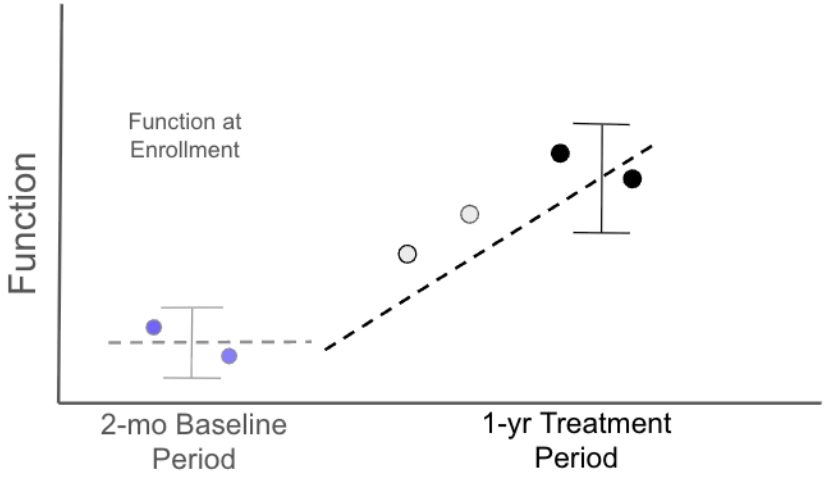


Figure 7b. Within-Person Improvement Example.



8. Competition Procedures and Schedule

Competition-Specific Study Procedures and Evaluations

As described in Competition Guidelines, Finalist Teams will conduct randomized controlled phase 2 trials to conclusively demonstrate that their therapeutic solution - administered alone or in combination - can improve tests of muscle, cognition, and immune function.

The teams can conduct this as a stand-alone trial or as a substudy within a larger or longer clinical trial.

To be considered for the Grand Prize award, teams must perform prospective clinical studies, provide necessary data to the XPRIZE-Utah DCC and XPRIZE-UCSD Central Laboratories, and must adhere to competition specific endpoint assessment protocols. Deviations from these protocols must be pre-approved by XPRIZE Operations in consultation with XPRIZE-Utah DCC and XPRIZE-UCSD Central Laboratories.

Competition Specific Assessment Schedule Table

Teams will perform endpoint assessments or biospecimen collections (see Table 8a) at two Baseline Visits (BV1, BV2), a first Midpoint Visit at 6-month post-randomization (Mid1), a second Midpoint Visit at 9-month post-randomization (Mid2), and two Follow-Up Visits (FUV1, FUV2). Judges will use the two Baseline Visits and two Follow-Up Visits to determine whether the research participant exceeded the personalized response thresholds for awarding or not. The Midpoint Visits are safety and technical validation visits.

XPRIZE-UCSD Central Laboratories will perform the assays for immune function and biomarker measures. Centralized biomarker assays will be under XPRIZE budget. Raw data will be returned to teams (see Table 8e for details).

Required vs. Optional Assessments

Required assessments will be used in the adjudication of the Grand Prize and must be conducted according to their specified protocols. Additional assessments are “recommended but optional” and identified by double asterisks (**) throughout this section. These may provide valuable information for understanding the broader impacts of interventions and alignment with other global programs (e.g., intrinsic capacity), but they will not influence judging or the determination of whether trial endpoints have been achieved. Teams may choose whether to

include these recommended assessments; their inclusion or omission will not affect judging of the primary endpoints.

Table 8a. Assessment Schedule

Visit	BV1	BV2	Mid1	Mid2	FUV1	FUV2
Study Month	**-1 mo**	**0 mo**	**6mo**	**9mo**	**11mo**	**12mo**
Determination of Participant Characteristics, Safety, Tertiary Endpoints						
Screening (team discretion)						
Participant Characteristics Questionnaires	X					X
Self Reported Health, Symptoms, and Event Reports	X	X	X	X	X	X
Complete Blood Count *(measured at clinic)*	X	X	X		X	X
Intrinsic Capacity Assessments**	X					X
Activity Level**	X	X			X	X
Determination of Primary Endpoint Assessments (Muscle, Cognition)						
6-minute Walk Test (6MWT)	X	X			X	X
Cardiopulmonary Exercise Test (CPET)**	X	X			X	X
Lower-Body Power	X	X			X	X
Muscle Mass** *(team discretion)*		X				X
CogState Computerized Cognitive Assessment	X	X			X	X
Biospecimen Collections for Central Labs & Biorepository (Immune Endpoints and Biomarkers) **- see Table 8e for detail**						
Whole blood, dried blood spot, plasma, serum	X	X	X (LV)	X (LV)	X	X
PBMCs	X	X	X		X	X
Nucleic Acid stabilizer tube		X				X
Urine (cup)	X	X	X		X	X

**Assessment measures denoted with double asterisks are strongly recommended but optional

(LV) - Low Volume. Blood collection at 6-month and 9-month Midpoint Visits will be lower volume requirements for basic clinical and safety screening.

Endpoint Assessment Measures

Training Requirements: Technicians should complete training provided by XPRIZE on standard protocols for each primary endpoint assessment. Training should be documented for each technician conducting testing to ensure adherence and consistency. In addition, testers should practice on other staff members until reliable measurements are achieved.

MUSCLE FUNCTION

Muscle function will be assessed by Endurance Capacity (6MWT) and Lower Body Power by all teams. Measures of muscle mass are strongly recommended to include for judge consideration but optional for team inclusion in Finals trial protocols.

Recommended but optional measures may be relevant for judge consideration reflecting on collective measurement characteristics, but are not used as thresholds for monetary awards. These measures also expand the science of the prize and are meaningful for alignment with other scientific programs.

Table 8b. Muscle Endpoint Assessments

Subdomain	Assessment Measure	Measured by:
Endurance Capacity*	Primary: 6-minute Walk Test (6MWT)[9]	Team
Lower Body Power*	Primary: Knee Extensor Power or Leg Press Power[10]	Team
Muscle Score – exceed threshold for % improvement in Endurance Capacity AND Lower Body Power assessments. *All teams must perform 6MWT and lower body power (by either knee extensor or leg press equipment). **The strongly recommended but optional measures are used as supportive evidence for judge consideration during grand prize determination. If teams include muscle mass assessment for judge consideration, then they must also show measurable improvement in endurance and lower body power.		

Descriptions of the tests are provided below:

Endurance Capacity *(Required)*

1) **Six-minute walk test: 6MWT *(Required)*.** The distance achieved over a brisk 6-min walk on a 30 meter length course will be assessed by all teams as a common, standardized assessment.
    a) The walk pace is set by the research participant, but must be performed as quickly as possible without running. Teams will use standardized instructions;

encouragement can be provided as patients walk as far as possible along a flat corridor for 6 minutes.

b) Recorded & Primary Measures for Judging:
    i) Total distance walked in 6-minutes *(primary*)
    ii) Recorded time per 30 meter lap
    iii) Number and duration of time stopped during 6MWT (if any)
    iv) Symptoms experienced during testing (if any)
    v) Assistance required during or after testing (if any)

Lower-Body Power *(Required)*

1. **Knee Extensor Power or Leg Press Power *(Choose 1)*.** Standardized protocols will be provided that teams can adapt to their specific equipment. Teams must use the same equipment for all testing before and after intervention.
    a) Whether using leg press or knee extensor dynamometry, XPRIZE standardized testing protocols will involve a gentle lower body warm-up, and common encouragement and instructions for the research participant to generate a contraction 'as hard and fast as possible.'
        i) Participants will perform multiple maximal efforts at given loads / speeds with at least 1-minute of rest between efforts to prevent fatigue.
        ii) Body mass on the day of testing must also be measured so that values may be normalized to allow for comparison within and between participants.
    b) Recorded & Primary Measures for Judging:
        i) Power (watts, W) normalized to body mass (*primary*).
        ii) Raw data from the team's preferred dynamometer, including torque, velocity, and time.

COGNITIVE FUNCTION

All teams must use the **CogState (https://www.cogstate.com/) digital cognitive assessment battery**. CogState digital cognitive tests provide valid and reliable measurements of cognitive function with sensitivity to individual cognitive change across a wide variety of pharmacological agents, populations, and indications (OG REFS + sensitivity /validity), and utility in preclinical Alzheimer's and CNS disease and validated for use in trials (TRIALS REFS), and acceptable sensitivity to detect change in unimpaired or early cognitive impairment in older adults (AGING REFS).[11,12,13,14,15,16] The tests have been translated and validated in approximately 100 languages; translation services may be available for a small fee if the test is not yet available in the team's native language. Primary computerized testing battery costs will be financially supported by XPRIZE for the Top 10 Finalists / Milestone 2 awardees. The digital test results are captured automatically via RedCap data management within the Utah DCC maintained system, in partnership with CogState.

The computerized assessment battery is estimated to take less than 30-minutes, and should be administered in the clinic if possible for improved standardization using CogState recommended computer / device models (options to lease devices available upon request).

The battery includes tests of executive function, working memory, speed of processing/psychomotor speed, and attention. The specific tests may change pending consultation with experts at CogState. The targeted completion time is under 30 minutes.

1. **Detection (DET; Psychomotor Function).** The DET is a measure of psychomotor function and uses a well-validated simple reaction time paradigm with playing card stimuli. In this test, the playing cards all depict the same joker, and the participant is asked to press the Yes key as soon as the card in the center of the screen turns face up. The software measures the speed and accuracy of each response.
2. **Identification (IDN; Attention)**. The IDN test is a measure of visual attention and uses a well-validated choice reaction time paradigm with playing card stimuli. In this test, the playing cards are either red or black jokers, and the participant is asked whether the card displayed in the center of the screen is red, responding by pressing the Yes key when the joker card is red and No when it is black. The software measures the speed and accuracy of each response.
3. **One Card Learning (OCL; Visual Learning).** The OCL test is a measure of working memory and uses a well-validated pattern separation paradigm with playing card stimuli. In this test, the playing cards are identical to those found in a standard deck of 52 playing cards (without the joker cards), and the participant is asked whether the card displayed in the center of the screen was seen previously in the test, responding by pressing the Yes or No key. The software measures the speed and accuracy of each response.
4. **One Back (ONB; Working Memory):** The ONB test is a measure of concentration and working memory and uses a well-validated n-back paradigm with playing card stimuli. In this test, the playing cards are identical to those found in a standard deck of 52 playing cards (without the joker cards), and the participant is asked whether the card displayed in the center of the screen is the same as the card presented immediately previously, responding by pressing the Yes or No key. Because no card has been presented yet on the first trial, a correct first response is always No, and the software measures the speed and accuracy of each response.
5. **Groton Maze Learning Test (GMLT; Executive Function):** The GMLT is a validated measure of problem solving and executive reasoning based on a standardized maze-learning paradigm. Participants are presented with a 10 × 10 grid (100 locations) containing a hidden 28-step pathway, where each box represents a potential move location within the grid array. Participants are required to identify the hidden pathway while adhering to predefined search rules: movements must not be diagonal, must not

skip boxes (i.e., no jumping), must not retrace steps along the pathway, and following an error, participants must return to the last correct location. At each step, only the most recently selected box remains visible, and performance feedback is provided via visual and auditory cues (green check marks for correct responses and red crosses for errors). If two consecutive errors occur, the last correct location (head of the path) is highlighted to prompt return. Twenty-one (21) psychometrically matched alternate pathways are available, and the software records each move as correct or incorrect, enabling detailed error analysis.

6. **International Digit Symbol Substitution Test – Symbols (IDSSTS; Processing Speed):** The IDSSTS is a processing speed assessment based on the traditional pencil-and-paper Digit Symbol Substitution Test. In this task, participants are shown a legend that pairs nine symbols with the digits 1 through 9, followed by a conveyor belt of empty boxes labeled with numbers displayed in the center of the screen. For each highlighted box, participants must select the symbol that corresponds to the displayed number from the symbol options presented at the bottom of the screen. Participants are instructed to place as many correct symbols into the boxes as possible within the allotted time, and performance is measured by the total number of correct responses.

Table 8c. Cognitive Endpoint Assessments

Subdomain	**Assessment Measure**	**Measured by:**
Memory	CogState One Back Test	Team
Visual Learning	CogState One Card Learning	Team
Executive Function & Processing	CogState Groton Maze Learning Test CogState International Digit Symbol Substitution Test	Team
Attention	CogState Identification	Team
Psychomotor	CogState Detection	Team
Circulating Biomarkers (Supportive)	*For Judge Consideration:* *e.g. Glial Fibrillary Acidic Protein (GFAP), Neurofilament Light Chain (NfL), phosphorylated tau (p-tau)*[17]	Central Lab
Cognitive Summary Score – exceed threshold in >50% of selected cognitive function subcategory tests **NOTE: Additional tests could be named.** Blood-based biofluid based biomarkers of brain aging will be measured by central or regional laboratories and used as supportive evidence for judge consideration.		

Biomarker Assessments of Brain Aging or Cognitive Function

The judges will review changes in biomarkers associated with brain aging and cognition. Biomarker assays will not replace the computerized battery for grand prize awarding or thresholding. However, these biomarker measures expand the science of the competition and support alignment with other scientific programs. Supportive biomarker assays will use banked aliquots of plasma or serum. These biomarker assays will be measured by an XPRIZE-UCSD Central Laboratory supported by XPRIZE operational budget. All biomarker data generated centrally will be returned to the competing Finalist team. These assays will be considered collectively with other computerized assessment data and may be influential to teams at the cusp of a response threshold.

IMMUNE FITNESS

Table 8d. Immune Endpoint Assessment Measures

Subdomain	Assessment Measure	Measured by:
Immune Cell Response to Challenge	Dynamic cell response to pathogen or stimulation – or a proxy measured centrally using banked biospecimen (to be determined)	Central Lab
Immune cell composition	Immune Age (IMM-AGE Score)[18]	Central Lab
Inflammatory status	Inflammatory Age (iAge) Score[19]	Central Lab
Other Circulating Biomarkers (Supportive)	*For Judge Consideration:* *Multi-omic analyses and select assays may be used by judges in support of the above, pending development*	Central Lab
Immune Summary Score – exceed threshold for % improvement in 2 out of 3 measures. **NOTE:** Assays will be performed centrally by XPRIZE Healthspan contracted laboratories. Teams will complete standardized collectio and handling of peripheral blood mononuclear cells, plasma, serum, and whole blood. All biomarker data generated centrally will be returned to the competing Finalist team. **NOTE: Additional tests could be named.** Blood-based biofluid based biomarkers of immune aging will be measured by central laboratories supported by XPRIZE operations and may be used as supportive evidence for judge consideration.		

In brief, all teams must collect peripheral blood mononuclear cells (PBMCs), plasma, serum, and whole blood per standardized operation procedures (SOPs) and ship biospecimens to a Central Laboratory for assays. Data from these assays will be automatically logged with the XPRIZE-Utah DCC and analyzed against normative data for judging; raw data will also be returned to teams. The following assays will be run centrally:

1. **Immune Cell Response to Challenge *(pending)*** is a measure of immune resilience or response kinetics based on pathogenic exposure or stimulus. A proxy measure of dynamic immune response using banked samples that reflects immune fitness and resilience to exposure will be identified, developed, and validated; prior to implementation using team provided biospecimen, Finalist teams will be consulted.

2. **Immune Cell Composition - IMM-AGE** requires collection of whole blood processed by standard procedures into PBMCs and serum. The samples will be processed by central laboratories in a standardized manner with multiple deep phenotyping modalities profiled.
3. **Inflammatory Status - Inflammation Age (iAge)** requires collection of whole blood for gene expression and plasma or serum separated for cytokine and chemokine determination by a central laboratory.
4. **Other Supportive Measures *(pending)*.** Novel unified metrics of immune aging may be developed or validated during the course of competition and will be considered as supportive of the above primary immune biomarkers listed above. Teams will be consulted prior to any additional testing or consideration of novel biomarkers that may influence evaluations. All raw data generated by central laboratories will be returned to teams.

Tertiary Endpoints

To support judging considerations above, the following Tertiary Endpoint Assessments may be included following discussion with Finalist Teams. These include changes in outcomes that are not domain specific, patient reported outcomes, self-reported health events, adherence, novel biomarkers, and clinical risk factors. Examples are listed below, but these are not final. Final tertiary and safety measures will be announced in 2026.

Strongly Recommended but Optional Tertiary Endpoints

Cardiopulmonary Exercise Test (CPET) - Peak VO_2 *(Recommended but optional*).** The gold standard for endurance capacity and aerobic fitness is standardized CPET testing involving an incremental exercise test while wearing a mask to analyze exhaled gases (oxygen/CO2) and a heart rate monitor to find peak oxygen consumption[20].

a) <u>All teams are encouraged to adopt CPET testing</u>. If a team would like to include CPET testing for peak VO2 in addition to 6MWT as an 'Endurance Capacity' endpoint assessment measure, CPET testing data will be considered by judges in Grand Prize determination.
b) Suggested equipment and set-up:
    vi) Teams can use either treadmill or cycle ergometer, but teams must use the same equipment for testing before and after intervention.
    vii) The set-up for testing includes the teams chosen exercise equipment, heart rate monitor, mask and metabolic cart.
    viii) When possible, the XPRIZE recommends teams use a modified Balke protocol, and encourage participants during the test. The modified Balke protocol is a a submaximal treadmill test used to assess cardiorespiratory

fitness by walking at a constant speed (e.g., around 3.0-3.3 mph for treadmill test) with gradual, incremental increases in incline (e.g., 2.5% every few minutes) until a target respiratory exchange ratio (RER) >1.05 is reached. A version of the test that uses a cycle ergometer can be used if treadmill testing is unavailable at the clinic. Teams may adopt alternative protocols already in use at their clinic with justification and notification of XPRIZE-Utah DCC and XPRIZE operations staff.

ix) The protocols must include low intensity warm up on a treadmill or bike, followed by gradually increasing intensity (speed/incline or resistance) every few minutes, that proceeds to near maximal fatigue and exhaustion.

c) A supervising physician or appropriate clinical or technical personnel should decide if the participant is safe to complete the symptom-limited phase (peak test). The physician, physician delegate, exercise physiologist or appropriate clinic technician must oversee procedures and ensure safety and adequate adherence to protocols.

d) Recorded & Primary Measures for Judging:
   i) VO2 Peak is defined as the highest 30-second average of VO2 (L/min) achieved during the exercise test before rest starts (*primary*) from measurements of the participants Oxygen Uptake (VO_2) & Carbon Dioxide Production (VCO_2) during the test
   ii) Maximum heart rate during the test
   iii) Ventilatory thresholds during the test
   iv) Ratings of perceived exertion (RPE's) using 6-20 scale with RPE of 9 ("very light"), 13 ("somewhat hard"), 15 ("hard"), and 17 ("very hard")

Muscle Mass *(Recommended but Optional)***

Muscle mass is not a required judged criteria for muscle function. The judges will prioritize performance-based measures of muscle function over muscle mass, but measures of muscle mass and body composition will still be viewed as supportive of the judged criteria for muscle.

Teams are encouraged to adopt muscle mass assessments using biospecimen or imaging equipment available at their clinic. The team's proposed therapeutic solution may be hypothesized to increase muscle mass independent of function.

Acceptable measures of muscle mass include:

1. **Urinary D3 Creatine Dilution Method *(Recommended).*** XPRIZE recommends Total Muscle Mass measured in participants using a D3 creatine dilution[21]. Briefly, participants will take a tablet with 30mg of D3-creatine and provide a fasting, morning urine sample 72-144 hours later. Deidentified samples labeled creatinine will be assayed from urine by laboratories at University of California, Berkeley, per negotiation with Finalist teams prior

to start of trial recruitment in Finals.

a. Recorded & Primary Measures:
    i. Creatine pool size (*primary*) calculated by UC Berkeley Labs as: (131.1/134.1) x [amount of D3-Cr dosed (g) – amount of D3-Cr excreted (g)] / (mean steady-state D3-Cr enrichment ratio)
    ii. Recorded measures by team:
        1. Amount of D3-Cr dosed and date dosed
        2. Date of urine collections

2. **Computed Tomography (CT) Muscle Volume or Magnetic Resonance Imaging (MRI)** [22,23]**.** Quantitative CT can be used to assess the muscle area from a single slice or muscle volume from a stack of slices covering a whole muscle, following segmentation. MRI may be used coupled with analysis algorithms for muscle mass assessment or body composition analysis. The specific outcome measurements will depend on the clinic's protocols and will be negotiated by the Finalist team with XPRIZE and the XPRIZE-Utah DCC directly prior to the start of trial recruitment in finals.

Examples of Additional Tertiary and Safety Assessment Measures

Changes in outcomes that are not domain specific could include but are not limited to:

- Frailty defined as the accumulation of age-related health deficits[24,25]
- Self-reported health and symptoms
- Self-reported rates of major health events, including but not limited to:
    - Falls
    - Fractures
    - Pneumonia, severe respiratory illness, or other severe acute illness
    - Hospitalizations
    - Other major health events

Recommended but optional tertiary assessment measures:

- Intrinsic capacity[26] including assessments of:
    - 4-m walk at usual speed and chair stand test (locomotion)
    - Handgrip-strength and mini-nutritional assessment (vitality)
    - Patient Health Questionnaire-9 (PHQ-9) depression score (psychological)
    - Self-reported vision and hearing questionnaires (sensory)
- Activity level recorded from wearable device or step tracker

Changes in biomarkers of aging and clinical risk factors
(*assays performed by XPRIZE-UCSD Central Laboratories from banked samples will be covered by XPRIZE operational budgets and raw data will be returned to teams*)

- Molecular and cellular biomarker measures consistent with biological age deceleration, may include but is not limited to: proteomic, metabolomic, and DNA-methylation based biomarkers
- Blood pressure
- Body weight and / or body composition
- Metabolic, kidney, bone, or lipid biomarkers (from proteomic analysis)
- Brain aging, Alzheimer's disease and dementia biomarkers (e.g. neurofilament light chain, glial fibrillary acidic protein, plasma p-tau immunochemical assays)[59]

Determination of Research Participant Characteristics

Research participant general characteristics will be evaluated by questionnaires at baseline and measures denoted with asterisk* will be queried again at follow-up. Specific survey questions and participant characteristics will be discussed and finalized with the top 10 teams regarding relevant demographics, languages, and cultural considerations.

- Age (not date of birth)
- Reported sex at birth
- Race / ethnicity
- Socioeconomic status: income level, occupation, education
- Medical history (or change in medical conditions at follow-up*)
- Smoking history*
- Alcohol or substance use and history*
- Current medication use*

Laboratory and Biological Specimens Procedures

Specimen Collection & Biomarker Assays

Teams will collect biospecimen at two Baseline Visits (BV1, BV2), a Midpoint Visit at 6 months post-randomization (Mid1), at 9 months post-randomization (Mid2), and two Follow-Up Visits (FUV1, FUV2). XPRIZE Healthspan XPRIZE-UCSD Central Laboratories will perform the clinical and pre-specified biomarker measures (Table 8e, below).

- Category 1. Assays to be performed by teams at their clinical testing site. Teams are responsible for screening measures and time-sensitive measures, like complete blood counts (CBC) for safety.
- Category 2. Collections required by teams. Teams are responsible for collecting, processing, and batch-shipping samples. Example tube types are shown but exact tubes, volumes, and standardized operating procedures (SOPs) will be determined in consultation with Finalist Teams. Efforts will be made to collect no more than 80-100ml

of blood at any given time point. The total amounts will be negotiated with teams during study start-up and alternative collections can be determined on a case-by-case basis should the team's maximum collection limits fall below the recommended collection amount for XPRIZE Healthspan.

- Category 3. Biomarkers by XPRIZE-UCSD Central Laboratories. All raw data generated by XPRIZE identified Central Labs and partnered laboratories will be returned to teams. XPRIZE continues to expand the science and data resources for teams and the prize, including opportunities to support high-throughput assays and novel platforms. Teams can opt out of measures not used for judging. Raw data will be returned to teams.

Table 8e. Biospecimen Collections and Proposed Assays

Visit	**BV1**	**BV2**	**Mid1**	**Mid2**	**FU1**	**FU2**
Study Month	**-1 mo**	**0 mo**	**6mo**	**9mo**	**11mo**	**12mo**
Assays to be performed by teams at their clinical testing site (data sent to Utah DCC)						
Whole Blood for CBC *(required)*	X	X	X		X	X
Collections required by teams (batch ship specimen to XPRIZE-UCSD Central Lab & Biorepository)						
Plasma (EDTA)	X	X	X (LV)	X (LV)	X	X
Serum (SST)	X	X	X (LV)	X (LV)	X	X
Whole Blood (K2 EDTA)	X	X	X (LV)	X (LV)	X	X
Dried Blood Spot	X	X	X	X	X	X
PBMCs (tube TBD)	X	X	X		X	X
Proteomic Stabilizer Blood (PROT1)	X	X			X	X
Nucleic Acid Stabilizer Tube		X				X
Urine (cup)		X	X			X
Biomarkers by XPRIZE-UCSD Central Laboratories (uses banked samples)						
Complete Metabolic Panel (fasted)	X	X			X	X
Hemoglobin A1c (HbA1c)	X	X			X	X
CMV	X					X
DNA / RNA isolation		X				X
Inflammation Age Clock (iAge)	X	X			X	X

Immune Age (IMM-AGE)	X	X			X	X
Pending: Immune Response Proxy	X	X			X	X
Pending: circulating brain aging assays	X	X			X	X
OPTIONAL BIOMARKERS - permit use of banked samples (pending biomarker partnerships)						

LV - Low Volume; mid-point visits will collect specimen for safety or validation, but lower collection volumes anticipated

Specimen Processing & Shipment

Specimen Processing: Detailed SOPs will be developed in consultation with Finalist Teams for processing at clinical sites, ideally with minimal processing (less than 1-2 hour total processing time) for specimen preparation / centrifugation, cold storage, cell isolation and freezing of PBMC pellets at clinical sites prior to shipment to XPRIZE-UCSD Central Laboratories.

Biospecimen Shipment. All plasma, serum, whole blood, PBMCs and urine will be shipped to the XPRIZE-UCSD Central Laboratories. Each site will ensure compliance with local laws concerned with the packaging and shipment of biohazardous samples.

Quality Evaluation

Quality Assurance. XPRIZE-UCSD Central Lab and specialized biomarker laboratories will monitor the quality of the sample collection and processing at each Finalist Team Clinical Site via:

- centralized training resources for site technicians at start of Finals
- review of collection/processing/shipping forms and specimens

Finalist Clinical Trial Site Equipment Records. Each Team Clinical Site is responsible for the maintenance of records for equipment performance and freezer performance and temperature checks. Specific equipment criteria required for specimen integrity will be informed by the XPRIZE-UCSD Central Laboratories per their SOPs in consultation with Finalist teams.

Specimen Storage

Teams are responsible for short-term storage of samples prior to shipment to XPRIZE-UCSD Central Laboratories. The central biorepository will feature appropriate tracking software, freezer alarm systems, power systems, and human systems for ultra-low freezer and cryogenic storage long-term. All specimens will be de-identified and logged into the XPRIZE-UCSD Central Laboratories tracking system. Retrieval and use of specimens will be communicated to teams per use agreements that will be negotiated with Finalist Teams.

Study Assessments by Visit

The order of assessments during visits could affect results, and the order of assessment completion should be similar at baseline and follow-up visits when possible. A suggested order of assessments by each clinical visit is presented below; these will be refined in Manual Operating Procedures (MOPs) developed with input by Finalist Teams. The double asterisk (**) indicates a recommended but optional assessment.

Recruitment, Screening, Consent

All participants must be consented prior to research procedures. Screening assessments are the competing team's responsibility and discretion. Teams will report the number of participants recruited to the XPRIZE-Utah DCC. If the participant is screened out after recruitment the team will report the reason for screening failure.

Baseline Visit 1 (approximately 1 month prior to randomization)

- Vitals - body temperature, height, weight, blood pressure, pulse rate
- Fasted Blood Draw
    - Complete Blood Count - measured at clinic
    - Processing specimen for XPRIZE-UCSD Central Laboratories and Biorepository
- Snack Opportunity
- Participant Characteristics Surveys (*in clinic or remote*), including:
    - Age (not date of birth)
    - Reported sex at birth
    - Race / ethnicity
    - Socioeconomic status (e.g., income level, occupation, education)
    - Medical history
    - Smoking history
    - Alcohol or substance use and history
    - Current medication use
- Self Reported Health, Symptoms, and Event Reports (*in clinic or remote*)
- Activity levels** *(in clinic or remote monitoring*)
- 6-minute Walk Test (6MWT)
- Lower Body Power Test
- CogState Computerized Cognitive Assessments
- Optional but recommended: ideally conducted after primary endpoint assessments:
    - Cardiopulmonary Exercise Test (CPET)**
    - Imaging for muscle mass / body composition**
- Intrinsic Capacity Assessments** (*recommended but optional)*

    - 4-m walk at usual speed (locomotion)
    - 30-second repeat chair stand test (locomotion)
    - Handgrip-strength (vitality)
    - Mini-nutritional assessment or similar (vitality)
    - Patient Health Questionnaire (PHQ-9) or similar (psychological)
    - Self-reported vision and hearing questionnaires (e.g. likert scales) (sensory)

Baseline Visit 2 (at or prior to randomization)

- Vitals - body temperature, weight, blood pressure, pulse rate
- Fasted Blood Draw
    - Complete Blood Count - measured at clinic
    - Processing specimen for XPRIZE-UCSD Central Laboratories and Biorepository
- Urine collection
- Snack Opportunity
- Self Reported Health, Symptoms, and Event Reports (*in clinic or remote*)
- Activity levels** (*in clinic or remote monitoring*)
- 6-minute Walk Test (6MWT)
- Lower Body Power Test
- CogState Computerized Cognitive Assessments
- Optional but recommended ideally conducted after primary endpoint assessments *(same visit or stand-alone visit)*:
    - Cardiopulmonary Exercise Test (CPET)**
    - Imaging for muscle mass / body composition**

Randomization

Participants must be randomized to the active therapeutic solution(s) or a placebo / control / standard of care condition. The randomization method is the responsibility of the competing team. While 1:1 randomization is recommended, it is **not** mandatory. The randomization scheme must be justified by the team and reviewed by judges in the Finals Application.

Midpoint Visit 1 (6-months post-randomization)

- Vitals - body temperature, weight, blood pressure, pulse rate
- Fasted Blood Draw
    - Processing specimen for XPRIZE-UCSD Central Laboratories and Biorepository
- Urine collection
- Snack Opportunity
- Self Reported Health, Symptoms, and Event Reports

Midpoint Visit 2 (9-months post-randomization)

- Vitals - body temperature, weight, blood pressure, pulse rate
- Fasted Blood Draw
    - Complete Blood Count - measured at clinic
    - Processing specimen for XPRIZE-UCSD Central Laboratories and Biorepository
- Urine collection
- Snack Opportunity
- Self Reported Health, Symptoms, and Event Reports (*in clinic or remote*)

Follow-up Visit 1

- Vitals - body temperature, weight, blood pressure, pulse rate
- Fasted Blood Draw
    - Complete Blood Count - measured at clinic
    - Processing specimen for XPRIZE-UCSD Central Laboratories and Biorepository
- Snack Opportunity
- Self-reported health, symptoms, and major health events *(in clinic or remote*)
- Activity levels** (*in clinic or remote monitoring*)
- 6-minute Walk Test (6MWT)
- Lower Body Power Test
- CogState Computerized Cognitive Assessments
- Optional but recommended ideally conducted after primary endpoint assessments *(same visit or stand-alone visit)*:
    - Imaging for muscle mass / body composition**
    - Cardiopulmonary Exercise Test (CPET)**

Follow-up Visit 2 / Final Study Visit

- Vitals - body temperature, weight, blood pressure, pulse rate
- Fasted Blood Draw
    - Complete Blood Count - measured at clinic
    - Processing specimen for XPRIZE-UCSD Central Laboratories and Biorepository
- Snack Opportunity
- Close-out Participant Characteristics Surveys
    - Changes in socioeconomic status over trial: income level, occupation, education
    - Changes in smoking behavior over trial
    - Changes in alcohol or substance use over trial
    - Current medication use
- Self-reported health, symptoms, and major health events (*in clinic or remote*)
- Activity levels** (*in clinic or remote monitoring*)

- 6-minute Walk Test (6MWT)
- Lower Body Power Test
- CogState Computerized Cognitive Assessments
- Optional but recommended ideally conducted after primary endpoint assessments *(same visit or stand-alone visit)*:
    - Intrinsic Capacity Assessments**
        - 4-m walk at usual speed (locomotion)
        - 30-second repeat cChair stand test (locomotion)
        - Handgrip-strength (vitality)
        - Mini-nutritional assessment or similar (vitality)
        - Patient Health Questionnaire (PHQ-9) or similar (psychological)
        - Geriatric Depression Scale (GDS) or similar in native language (psychological)
        - Center for Epidemiological Studies Depression Scale (CES-D) or similar (psychological)
        - Self-reported vision and hearing questionnaires (e.g. likert scales) (sensory)
    - Imaging for muscle mass / body composition**
    - Cardiopulmonary Exercise Test (CPET)**

Early Termination Visit

Should the team's trial be terminated for an unforeseen reason, it is recommended to complete the assessments in the next scheduled follow-up visits if possible and safe for participants. The visit assessments should be recorded and reported to XPRIZE-Utah DCC, noting any deviations from protocol required.

Unscheduled Visit

An unscheduled visit may be needed to complete or re-do an endpoint assessment due to experimental failure, address a safety concern, conduct additional monitoring of symptoms, or other unexpected reasons. The team should report unscheduled visits to the XPRIZE-Utah DCC and note the reason for the unscheduled visit, noting deviations from protocol.

9. Assessment of Safety

Potential Risks and Benefits

Risks and benefits to participants should be clearly explained in the informed consent document. Some known risks and benefits of participating in clinical trials are described below, but it is the responsibility of the teams to carefully consider all risks and benefits and to work with their regulatory body (e.g., Institutional Review Board [IRB]) to clearly relay them to participants.

Known Potential Risks

Participation in clinical trials may involve risks. The investigational treatment may not be effective and could be less beneficial than standard care. There is a possibility of experiencing side effects, including unknown or unexpected risks. Participants may also be asked to complete additional study visits, procedures, or tests, which may require extra time and could cause discomfort. In some cases, participants may be assigned to a placebo or control group and may not receive the therapeutic treatment. All foreseeable risks must be explained to participants, but some risks may be unforeseeable.

Known Potential Benefits

Potential benefits of participating in clinical trials include access to therapeutic treatments that are not yet widely available and increased medical monitoring during the study period. Participants may receive additional health assessments and follow-up that could provide useful information about their health. Participation may also contribute to scientific knowledge and support the development of improved therapeutic treatments. It is important to note that benefits cannot be guaranteed.

Participant Safety

Competing teams and clinical centers, not XPRIZE, are ultimately responsible for all clinical practice-related issues and the clinical safety of all study participants. All competing teams must conduct safety monitoring in accordance with institutional and national regulatory requirements. Teams must ensure that all risks to study participants related to their involvement in the XPRIZE Healthspan trials are minimized, including those resulting directly from the investigational interventions. All study participants should undergo systematic safety assessments throughout the study period. Teams are responsible for actively monitoring and appropriately managing all safety events throughout the course of their studies.

This section outlines the definitions, expectations, and procedures for submitting required safety parameters to the XPRIZE-Utah DCC. These safety assessments should be **in addition to** all standard safety assessments and reporting procedures required by each team's study protocol, independent data and safety monitoring board (DSMB), Sponsor, applicable Regulatory Oversight Committee (ROC) (e.g., Institutional Review Board [IRB] or Independent Ethics Committee [IEC]), and national regulatory agencies. Competing teams and clinical centers are responsible for engaging their own DSMB or ROC, reviewing study data related to the overall safety of study participants, and preparing safety reports for their respective DSMB or ROC whenever participant safety issues arise. Teams are required to submit all reports from their individual DSMB to the XPRIZE-Utah DCC promptly using a shared part 11 compliant document storage platform.

The Utah DCC follows International Council for Harmonization (ICH) guidelines ICH E6 (R3): Good Clinical Practice (GCP) and ICH E2A: Clinical Safety Data Management- Definitions and Standards for Expedited Reporting to guide the capture and reporting of safety parameters. Competing teams in the XPRIZE Healthspan competition will have varying types of interventions with specific safety requirements and applicable regulations.

For the purpose of submitting safety reports to the XPRIZE-Utah DCC, **all competing teams will be required to use the safety parameters, definitions (Adverse Events, Serious Adverse Events, Unanticipated Problems) and classifications (Severity, Relationship to Study Intervention, Expectedness) detailed in this section.** This may require teams to categorize parameters into a definition that isn't originally captured per study protocol.

Safety Parameters

Safety parameters submitted by the competing teams should include the following:

- Standard baseline medical assessments, including medical history (e.g., comorbidities) and physical examinations (e.g., vital signs)
- General clinical laboratory evaluations:
    - A complete blood count (CBC) to include White Blood Cell count (WBC), Red Blood Cell (RBC), platelet count, hemoglobin (HGB), hematocrit (HCT), mean corpuscular volume (MVC), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), red cell distribution width (RDW), mean platelet volume (MPV), and nucleated red blood cells (NRBC) (count and %). *The CBC will be performed by the teams at their clinical trial site(s).*
    - A comprehensive metabolic panel (CMP) to include creatinine, blood urea nitrogen (BUN), chloride, sodium, potassium, carbon dioxide, glucose, albumin, alanine transaminase (ALT), aspartate transa-inase (AST), total bilirubin, and alkaline phosphatase. *The CMP assays will be performed by XPRIZE-UCSD*

Central Laboratories and raw data will be reported to the Utah DCC and Finalist teams).

Competing teams should provide the XPRIZE-Utah DCC with the reference ranges for CBC used for their specific study populations.

Submission to the XPRIZE-Utah DCC

Competing teams must notify the XPRIZE-Utah DCC within **7 days** of any serious adverse events (SAEs), halting, suspension, pause, or termination of a study site or study. In addition, teams must submit adverse events (AEs), and unanticipated problems (UPs) to the XPRIZE-Utah DCC **at least quarterly** throughout the competition. The XPRIZE-Utah DCC will be responsible for sending quarterly reports for AEs and UPs to the XPRIZE staff. SAEs will be reported by the DCC to XPRIZE staff within 7 days of receiving notification from the Team.

The XPRIZE staff and Healthspan judges will review aggregate safety parameters submitted to the XPRIZE-Utah DCC periodically to assess each team's continued eligibility for the XPRIZE Healthspan competition. At their discretion, after review of AEs, UPs or SAEs, XPRIZE staff may also choose **independently at any time** to require a team to withdraw from the Healthspan competition, **even if the team's DSMB** and/or applicable regulatory bodies have not **required study halting or stopping.**

The XPRIZE-Utah DCC will not request any identifiable data and will not accept submissions containing free-text fields. Teams must ensure that all data submitted to the XPRIZE-Utah DCC are in English and fully deidentified.

Definitions of Adverse Events (AEs)

An **Adverse Event (AE)** is defined as any untoward medical occurrence associated with the use of an intervention in humans, whether or not considered intervention-related. An event constitutes a disease, a set of related signs or symptoms, or a single sign or symptom. This can, therefore, be any unfavorable and unintended physical sign, symptom, laboratory parameter, or disease entity that develops or worsens in severity during the course of the study, whether or not considered related to the investigational interventions.

Definition of Serious Adverse Events (SAEs)

A **Serious Adverse Event (SAE)** is any untoward medical occurrence in a participant that:

- results in death; or
- is life-threatening (the patient was, in the view of the study team, in immediate danger of death from the event as it occurred); or
- requires inpatient hospitalization or prolongs an existing hospitalization; or

- results in a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions; or
- results in congenital anomaly/birth defects; or
- is any other important medical event, based upon appropriate medical judgment, may jeopardize the participant's health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition.

A planned hospitalization for a previously identified disease/condition is not considered an SAE.

Definition of Unanticipated Problems (UPs)

An Unanticipated Problem is defined as any incident, experience, or outcome that meets **all** the following criteria:

- Unexpected in terms of nature, severity, or frequency given (a) the research procedures that are described in the protocol-related documents, and (b) the characteristics of the participant population being studied; and
- Related or possibly related to participation in the research ("possibly related" means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
- Suggests that the research places participants or others at a greater risk of harm (including physical, psychological, economical, or social harm) than was previously known or recognized.

Classification of an Adverse Event/Serious Adverse Event

Severity

The severity, which is a measure of intensity, of the adverse event will be categorized by the study team as follows:

Mild	Sign or symptom that does not interfere with usual activity or is transient, resolved without treatment
Moderate	Interferes, but does not hinder, usual activity; may require treatment
Severe	Symptom(s) causing severe discomfort and significant impact on usual activity and requires treatment or intervention.

Note: "Severe" does not necessarily indicate that an event is "serious".

Relationship to Study Intervention

The relationship of the adverse event to the investigational intervention will be categorized by the study team as follows:

Not Related	The event is completely independent of study intervention administration, and/or evidence exists that the event is definitely related to another etiology. There must be an alternative, definitive etiology documented by the clinician.
Possibly Related	There is some evidence to suggest a causal relationship, and other factors (e.g., the participant's clinical condition, other concomitant events) may or may not have contributed to the event. The clinical event, including an abnormal laboratory test result, occurs within a reasonable time after administration of the study intervention and follows a clinically reasonable response on withdrawal. Although an event may rate only as "possibly related" soon after discovery, it can be flagged as requiring more information and later be upgraded to "definitely related", or downgraded to "not related," as appropriate.
Definitely Related	The clinical event, including an abnormal laboratory test result, occurs in a plausible time relationship to the study intervention administration and cannot be explained by concurrent disease or other drugs or chemicals. The response to withdrawal of the study intervention should be clinically plausible. The event must be pharmacologically or phenomenologically definitive, with use of a satisfactory rechallenge procedure if necessary.

Expectedness

The expectedness of the adverse event will be categorized by the study team as follows:

Expected	An event is considered expected if it is known to be associated with the underlying condition or is related to the study intervention and is mentioned in the protocol, informed consent, or other study documents. An event may be expected despite the study participant's clinical state immediately prior to the event.
Unexpected	An event is considered unexpected if the nature, severity, or frequency of the event is not consistent with the risk information previously described for the intervention(s) as described in study documents such as the protocol, informed consent form, patient instructions, investigators brochure, instructions for use, or any other supporting document.

Special considerations for XPRIZE Healthspan Trials

Given the unique nature of interventions in aging populations, competing teams are recommended to consider the following when categorizing safety parameters:

- Advanced Age: Assessment of severity of AE/SAEs should take into account participants' baseline functional status and age-related comorbidities.
- Multi-System Effects: Interventions may have pleiotropic effects across multiple organ systems. Events affecting more than one system should be submitted separately for each affected system.
- Long-Term versus Acute Effects: It is important to distinguish between acute adverse events and gradual changes that may represent either therapeutic effects or delayed adverse reactions.
- Polypharmacy Interactions: For teams with drug interventions, special attention should be paid to potential drug-drug interactions given the high likelihood of concomitant medications in aging populations.
- Biomarker Changes: Asymptomatic laboratory abnormalities may be graded based on clinical significance and degree of deviation from normal ranges specific to aging populations.

10. Clinical Site Monitoring

Clinical Site monitoring may be conducted to ensure that the rights and well-being of human subjects are protected, that the reported data submitted for Judging are accurate, complete, and verifiable, and that the conduct of the trial adheres to the Rules & Regulations and is compliant with the Competitor Agreement. Each Clinical Center is expected to perform internal quality management of study conduct, data collection, documentation and completion based on their own quality management plans.

Scheduled site visits may be conducted by XPRIZE operations staff or Judges at any time throughout the duration of Finals, with the frequency determined through collaborative discussion of the above parties or informed by data verification checks (e.g. additional monitoring if discrepancies are found). Site visits may assess protocol adherence, perform source data verification to confirm that case report form (CRF) entries match original records, and review a sample of informed consent forms and regulatory documents. Site visits may also include viewing the informed consent process, examining adverse event documentation and safety reporting, interviewing study staff, reviewing training records, inspecting facilities and equipment, and assessing data management and quality systems. Corrective actions will be relayed to teams, and teams must respond with a corrective action plan.

11. Statistical and Analytical Considerations

Statistical Criteria

The therapeutic intervention administered to participants in the intervention group must produce improvements in muscle, cognitive, and immune function, such that **at least 20% of participants in the intervention group exceed their personalized response threshold across all three domains**, with 20% representing the difference in percentage points between intervention and control arms.

However, in addition to meeting the 20% criterion, Teams must demonstrate to the Judges that their findings were likely not due to random chance differences in responder proportions between the control and intervention arms of the trial even if the control response rate is 0 given the sample size chosen. To meet this statistical analysis requirement, Team trial results must show that the lower bound of a **90% one-sided confidence interval (CI)** for the difference in intervention responder proportions relative to control group responder proportions **is at least 15%** (see Appendix C). These calculations are especially important in unlikely cases where many individuals reach intervention responder status in the control arm of the study.

The primary analysis and definition of success will be on an intention to treat basis. We do not require adjustments for multiple comparisons across the studies being pursued by the different competitors for Grand Prize Judging Criteria, as the winning team will be determined by the greatest, possibly adjusted, responder rate.

Analysis Datasets

The XPRIZE-Utah DCC will be responsible for assembling, managing, and preparing datasets used for analysis and reporting based on data entered by Teams into the REDCap database. The XPRIZE-Utah DCC will also prepare public use datasets as requested by XPRIZE to support transparency and future research (e.g., meta-analyses). Data to be included in the public use and future research use datasets will be described in the Data Use Agreement (DUA) with Finalist Teams prior to starting finals trials.

Clean, de-identified, analysis datasets will be constructed for each trial and will include:

- baseline datasets
- primary analysis datasets
- interim reporting datasets
- final locked datasets

Dataset structure and specifications for the primary analysis endpoints will be standardized across all trials to ensure comparability, though supportive measures and tertiary endpoints may vary across trials. Annual safety datasets will be prepared using the same standardized specifications.

Although Teams can construct their own datasets independently of the XPRIZE-Utah DCC and perform their own analyses, these datasets and analyses will not be used for Judging.

Primary Analysis: Responder / Non-Responder Analyses Using Personalized Response Thresholds

The primary analytical framework for XPRIZE Healthspan Finals trials focuses on individual responder proportions in the intervention and control arms of the Team trials. Each participant will be classified as a responder or non-responder according to whether they achieve their pre-specified, personalized response threshold in each domain (see description below). A simple 2 x 2 contingency table analysis will be used to calculate and compare the proportions of responders in the intervention (I_R/I_{total}) vs. control group (C_R/C_{total}; see Table 11a).

Table 11a. Example 2x2 contingency table

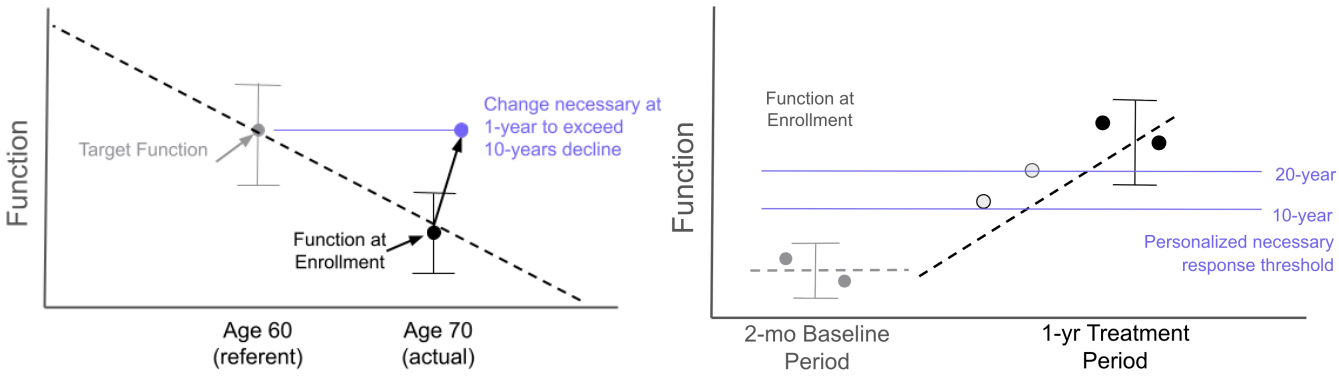
Group	Responders	Non-Responders	Total Participants
Intervention	I_R	I_N	I_{total}
Control	C_R	C_N	C_{total}
To be eligible for grand prize awarding, $(I_R / I_{total}) - (C_R / C_{total}) \geq 20\%$.			

Personalized response thresholds define the level of improvement each participant must achieve in muscle, cognitive, and immune function for the Team to count that participant as a 'responder'. These thresholds are at the individual (or 'personalized') level in that they are specific to an individual participant's age, sex, and baseline values rather than one that reflects a common or shared threshold value for all participants.

The personalized response thresholds will be determined by XPRIZE, and will indicate the change necessary to exceed 10-year, 15-year, and 20-year declines based on an analysis of referent populations. The methods and equations used for determining thresholds for awarding will be released in late 2026 or early 2027. Please see the forthcoming FAQ document for more background information on the use of personalized response thresholds.

Figure 11a depicts how XPRIZE will determine the personalized response threshold (based on age, sex, and function [i.e., measurement value at baseline testing]) an individual must exceed to demonstrate a change in function equivalent to the expected change over, in this example, 10 years based on analysis referent cohorts.

Figure 11a. Defining Personalized Response Thresholds



The use of personalized thresholds ensures that improvements reflect clinical and physiologically meaningful changes relative to each participant's expected aging trajectory as opposed to random fluctuations, covariate (e.g., dietary changes, stress level, etc.) induced variability, or simple biological differences between participants. The XPRIZE-Utah DCC will calculate the average of measurement values at Baseline (i.e., BV1, BV2) and the average of measurement values at Follow-Up visits (i.e., FV1, FV2). Average Baseline and Follow-Up measurements will be reported.

If the participant's follow-up value meets or exceeds their personalized response threshold for 10, 15, or 20 years, they are considered a **responder** for that threshold level. If the follow-up value does NOT meet the threshold for 10, 15, or 20 years, they are a **non-responder** for that threshold level.

It is important to emphasize that the probability of an individual surpassing their response threshold for any one of the three domains (i.e., being labeled a 'responder' for that domain) purely by chance will likely be small based on the referent population data that will be used to establish the very strict and challenging personalized response thresholds. Therefore, the probability that the same individual will surpass thresholds for all three domains by chance (i.e., be labeled an overall responder) will be even smaller. With this in mind, it is anticipated that the number of responders in the control arm of a study will be close to 0. This suggests that responders in the intervention arm will likely be due to a *bona fide* intervention effect and not a simple covariate effect or imbalance of covariates between a control and intervention arm of a

study. Analysis of Team's trial data may also depend on the accommodation of covariates that could explain an unusually high response rate in the control arm of a study (see below).

The XPRIZE-Utah DCC will perform analyses comparing proportions of responders and non-responders in intervention vs. control groups, adjusting for pre-specified covariates if needed. These covariates will likely depend on the Team's study population (e.g., disease conditions, smoking status, etc.), the mechanism of action of the therapeutic solution (e.g., BMI adjustment for intentional weight loss trials), and general characteristics of the individuals in each arm (e.g., demographic and socioeconomic factors).

Statistical analyses used for Judging will be conducted using data masked to treatment conditions. Analyses of primary endpoints and responder / non-responder status will be standardized across studies to ensure comparability and consistency in Judging.

Analysis of Tertiary Endpoint(s)

Additional analyses will be performed by the XPRIZE-Utah DCC on tertiary endpoints and those deemed *supportive* to judging (e.g., biomarkers, muscle mass). These will be considered by judges as change with intervention relative to change in the control group, and not evaluated against personalized response thresholds for responder / non-responder analyses. Additional study-specific analyses may be performed independently by each Team, but will not be included as a judged component of Finals.

Safety Analyses

Analyses of adverse event (AE) data performed by the XPRIZE-Utah DCC will be limited to endpoints necessary to support XPRIZE safety monitoring requirements (e.g., event counts, symptoms questionnaires, change in safety labs like CBC and CMP). Study Teams remain responsible for collecting and reporting all AEs to appropriate oversight bodies and regulators.

Adherence and Retention Analyses

Adherence to scheduled clinic visits and the corresponding windows surrounding assessment dates will be systematically monitored by the XPRIZE-Utah DCC and contained in regular reports for interim review and judging.

Teams are encouraged to prospectively collect adherence data using objective and/or auditable methods appropriate to the intervention. Suggested approaches to monitor adherence to the intervention may include:

- Pill counts, electronic medication monitoring, or pharmacy records
- Device logs, wearables, or software usage records

- Session attendance logs or protocol checklists
- Other objective indicators of intervention exposure, when applicable

These data may be used by Judges in consideration of scalability, commercial utility, generalizability, and post-competition impact (i.e. if a product is highly effective, but with low adherence, this may have implications for scale and impact post-competition)

Exploratory Analyses

XPRIZE-UCSD Central Laboratories and XPRIZE-Utah DCC may conduct additional exploratory analyses to expand the science of the competition and accelerate discovery. This could include meta-analyses, novel biomarker analyses, inter-intervention comparisons, and others. Teams will be consulted for use of data and exploratory analysis beyond judging of the competition; data from exploratory biomarker assays will be returned to teams.

Teams are permitted to conduct their own exploratory analyses that will not be included in Judging. Although not mandatory, teams are encouraged to use the Competition to explore and provide evidence for novel biomarkers, clinical risk factors, or clinical outcome assessments, or sex-specific responses.

Sample Size

Teams are advised to enroll approximately 100 participants (50 intervention, 50 control) after accounting for attrition. However, Teams may enroll a minimum of 80 (40 per group) and up to 200 participants (more than 200 may present considerable logistical and timeline concerns).

Teams are required to submit their own sample size plans as a part of the Finals Application for judge review. The plan must justify the expected sample size along with any assumptions (e.g. level of certainty, attrition, etc.). Team justifications should demonstrate that their chosen sample size is sufficient to show at least 20% difference in responder proportions between groups; and that the difference in responder proportions in the intervention group compared to control has a one-sided 90% confidence lower bound of at least 15% (see above).

Teams are also encouraged to analyze the probability that an individual might achieve 'responder' status by chance alone or through unrelated factors (such as dietary changes). Using accessible datasets and published literature, teams can examine 10-, 15-, and 20-year improvements in the competition's measurements (or similar measurements). These analyses can inform study design decisions, support statistical power calculations, estimate expected responder rates in control groups, reveal potential effects from covariates or confounding variables, and build familiarity with the scientific and intervention testing principles underlying the competition. Please see **Appendix C** for additional guidance on sample size justification.

Measures to Minimize Bias

Control or Standard of Care Group

Teams must include defined time controls, standard of care, or other alternative as appropriate for the proposed approach to minimize confounding and bias.

Randomization / Masking Procedures

To minimize bias, randomization to the intervention group is *required*, and masking or blinding procedures must be implemented wherever possible throughout the conduct of the trial. This includes participant blinding (participants are unaware of their treatment allocation) and assessor blinding (investigators and study staff responsible for clinical assessments and endpoint evaluation are unaware of each participant's treatment allocation). Although there may be circumstances in which blinding a participant is not feasible (e.g., a lifestyle-based intervention), the blinding of investigators/staff who are performing outcome assessments is essential to reduce bias and ensure that outcome measurements are objective and not influenced by expectations about the treatment. The XPRIZE-Utah DCC must be aware of the randomization allocation for each participant. This means the team liaison to the XPRIZE-Utah DCC will need to be unblinded for the purpose of data entry.

Breaking the Study Blind/Participant Code

Breaking the study blind will involve strictly observed predefined procedures. The study blind may be broken for emergency patient safety (e.g., serious adverse events needing specific treatment), or by accidental breaches (e.g., different packaging, staff error). Both cases require immediate notification to the XPRIZE operations team and the XPRIZE-Utah DCC. The XPRIZE-Utah DCC may contact the team for analysis to assess bias and management with minimal access to codes to preserve data integrity. Teams are strongly recommended to use participant codes that do not jeopardize masking of conditions in the event of an accidental breach.

12. Judging and Awarding

Grand Prize Award Levels by Thresholds of Functional Improvement

To win, teams must demonstrate that a minimum of 20% of participants in the intervention group achieved or exceeded their **personalized response thresholds** for muscle, cognitive, **and** immune function. To count toward the 20%, a participant must achieve their thresholds for the measures described in Section 7 in ***all three domains*** (not corrected for multiple comparisons). If there are responders in the control group, the 20% requirement is assessed as an absolute difference between groups. For example, if 5% of participants in the control group meet their response thresholds, at least 25% of participants in the intervention group must do so to satisfy the 20% criterion. As described in Section 11, Team trial results must show that the lower bound of the 90% one-sided confidence interval for the intervention responder proportion compared to the control responder proportion is at least 15%.

As outlined in the **Competition Guidelines**, the Judging Panel will award the Grand Prize to the team with greatest proportion of participants to achieve the highest of three potential awarding thresholds:

> "**10 Year Functional Improvement:** The best team who conclusively demonstrates, to the satisfaction of the Judging Panel, a functional improvement of at least **10 years** in all three systems (muscle, cognition, and immune), compared with controls, through a therapeutic intervention lasting 1 year (or less) is eligible to win **$61 Million** of the purse. This purse is paid out only if no team achieves the award at the 15 year or 20 year functional restoration level.
>
> **15 Year Functional Improvement:** The best team who conclusively demonstrates, to the satisfaction of the Judging Panel, a functional improvement of at least **15 years** in all three systems (muscle, cognition, and immune), compared with controls, through a therapeutic intervention lasting 1 year (or less) is eligible to win **$71 Million** of the purse. This purse is paid out only if no team achieves the award at the 20 year functional restoration level.
>
> **20 Year Functional Improvement:** The best team who conclusively demonstrates, to the satisfaction of the Judging Panel, a functional improvement of at least **20 years** in all three systems (muscle, cognition, and immune), compared with controls, through a therapeutic intervention lasting 1 year (or less) is eligible to win **$81 Million** of the purse."

See Section 11 above for details on personalized threshold levels, analyses of responders / non-responders, and proportions of participants required to meet threshold to be considered a ‘win’ at a given threshold for Functional Improvement.

Grand Prize Awarding - Potential Contingencies

More Than One Team Meets Threshold For Awarding

If more than one team meets the same threshold level the prize purse will be split. For example, if two teams similarly meet the required proportion of participants above the 20-year functional improvement level, both teams would be named as “Grand Prize Winner” and the $81M prize purse would be split by the two teams.

Team Meets Awarding Thresholds But With Judges Concern

The magnitude of effects of the therapeutic across muscle, cognitive, and immune endpoints is the primary consideration for awarding. In addition, judges will consider the sum of observed effects of the team’s therapeutic solution on supportive biomarkers, clinical risk factors, estimates of safety, and the anticipated scalability, accessibility, and potential for impact of the therapeutic solution after the competition. These Judging Panel considerations may factor into judges’ recommendations for awarding. Should the judges identify a reasonable concern - for example, a team wins functional improvement threshold but with considerable safety concern based on trial evidence - this will be reflected in their recommendations for awarding of the Grand Prize.

No Team Meets Minimum Threshold (10-Year)

Should no team meet the lowest threshold of 10-Year Functional Improvement, the Judging Panel holds the authority to make a recommendation for awarding the ‘best team’ to serve as “Grand Prize Winner.” The ‘best team’ judgement will be based on: 1) the magnitude of effects across muscle, cognitive, and immune endpoints (primary consideration for awarding), and 2) the sum of observed effects of the team’s therapeutic solution on supportive biomarkers, clinical risk factors, estimates of safety, and the anticipated scalability, accessibility, and potential for impact of the therapeutic solution after the competition (tertiary considerations for awarding of the Grand Prize). The Judging Panel will make recommendations for monetary awarding level based on the factors above. This ‘best team’ recommendation will then be reviewed by XPRIZE Foundation leadership and Co-Title and select sponsors for consideration of sub-award levels (e.g. less than $61M).

Teams Fail to Complete Clinical Trials for Competition Judging

Should no team complete the competition within the allotted time for data analysis and awarding, Judges may recommend a time extension that will be reviewed by Co-Title sponsors and XPRIZE Foundation leadership.

13. Quality Assurance and Quality Control

The quality of Finalist trials depends on Team's committing to integrity measures such as: maintaining randomization schemas, accurately assessing participant eligibility, recording dropouts and adherence, measuring outcome variables without bias, preventing premature release of results, monitoring and assessing protocol adherence, and avoiding biases in the analysis of results. Quality control (QC) procedures should be devised to monitor screening, data and specimen collection, follow-up, clinical measurements, collection of forms, data entry procedures, and implementation of interventions. Teams are strongly recommended to consult with a biostatistician and skilled technical consultants starting at the design phase of the trials and continue to engage with them through the final analysis and dissemination phase.

The XPRIZE-Utah DCC will conduct data monitoring activities and independent statistical review to ensure the reliability of study results and compliance with competition rules and study procedures. The XPRIZE-Utah DCC electronic data capture (EDC) system will incorporate extensive and comprehensive data validation rules to support accurate and complete data collection. Standardized reports will be developed and reviewed to monitor data quality and consistency across competing teams. EDC validation rules and data monitoring reports will evaluate missingness, outliers, distributions, patterns, and relationships within and across submitted variables. These procedures are designed to identify anomalies that may indicate data errors, deviations from approved protocols, or systematic irregularities. Statistical QC procedures will be performed to identify non-random patterns, implausible irregularities, or other indicators inconsistent with authentic data generation. Findings from statistical QC reviews may prompt further review, including requests for clarification, data correction, or additional documentation.

Monitoring approaches are risk-based and adaptive, with increased scrutiny applied when unusual patterns or deviations from expected responses are observed. All data monitoring and statistical QC activities will be conducted in a manner consistent with principles of fairness, transparency, and reproducibility, and are intended to protect the scientific integrity of the competition and its outcomes.

Trainings and Support

At the Team Summit, to be held at the University of Utah on August 12, 2026, training will be provided to Teams on data entry into REDCap and instruction will be provided for all required SOPs. Teams should make every effort for at least one team member to attend in-person. Virtual attendance for additional team members may be available but is not guaranteed.

Trainings will be administered by the XPRIZE-Utah DCC, recorded, and made available for future viewing. Teams should distribute the recordings to clinic and research staff responsible

for performing assessments. The DCC will be available to provide support in English on data-related issues within the scope of the XPRIZE-Utah DCC database (i.e., support will not be provided on issues external to the Competition). Each Team will elect one liaison to interface with the DCC for addressing study site issues with data.

14. Ethics and Protection of Human Subjects

Ethical Standards

Each Finalist Team is solely responsible for the ethical design and execution of its study and for compliance with all applicable local, regional, and national regulations. Finalist teams should demonstrate a strong understanding of the ethical and regulatory guidelines governing human subjects' participation in clinical trials. Examples include knowledge of Good Clinical Practice (GCP) and relevant regulations like the Declaration of Helsinki and the International Conference on Harmonisation (ICH) guidelines. Teams are responsible for ensuring that participant safety, autonomy, and welfare are prioritized at all stages of study design, conduct, and reporting. Teams must comply with all laws and regulations which apply to their participation in the prize. XPRIZE reserves the right to expel teams who do not uphold reasonable standards of safety and ethics.

Institutional Review Board

Each Team must obtain approval from an Institutional Review Board (IRB), Independent Ethics Committee (IEC), or similar regulatory body prior to initiating any participant-facing study activities. Documentation of approval must be maintained by the Team and provided to XPRIZE prior to initiating Finals trials.

Informed Consent

Teams must obtain informed consent from all participants prior to enrollment. Informed consent documents and processes must be written at an appropriate reading level in the participant's native language, and should be as non-technical as is practically possible. XPRIZE recommends that the informed consent document clearly describes, at a minimum:

- The purpose of the study and procedures involved
- Potential risks and anticipated benefits
- Alternatives to participation
- The voluntary nature of participation and the right to withdraw at any time without penalty
- How participant data and biospecimens will be collected, used, stored, and shared
- Use of data / specimen for future research
- And, if a participant withdraws, that they can have their data removed from the public deidentified database

Special protections must be implemented for vulnerable populations in accordance with applicable regulations. Teams must include language on how their data will be used during the XPRIZE competition. Sample suggested informed consent language can be found in the Appendix Section.

Participant Data and Confidentiality

Teams are responsible for protecting participant privacy and confidentiality in accordance with applicable data protection laws and regulations (e.g., HIPAA, GDPR, or regional equivalents).

All data transferred to the Utah DCC and biospecimens transferred to Central Laboratories and Biorepository will be fully de-identified prior to transfer. Neither XPRIZE nor the Utah DCC nor the Central Laboratories will receive direct identifiers and will have no means to reidentify participants. Teams must ensure that any data shared with third parties, including the DCC and Central Laboratories, will be handled using appropriate technical and administrative safeguards. Teams must also abide by the conditions set forth in the **Data Use Agreement (DUA)**.

Future Use of Data and Stored Specimens

Use of participant de-identified data or centrally stored biospecimens for scientific discovery and advancement should be clearly disclosed in the informed consent process and approved by their IRB/IEC. The future use of de-identified data and banked specimens for scientific advancement beyond judging requirements is strongly encouraged. XPRIZE requests Finalist teams include language in their consent documents to allow the opportunity for scientific expansion during and future analyses beyond the duration of the team's finals trial. However, a team may opt out of select use of data with rationale provided in advance of Finals, and local regulatory agencies may request participant right to opt out of specific uses of data or specimen (e.g. genetic testing).

15. Data Handling and Record Keeping

Data Collection and Management Responsibilities

Teams are responsible for establishing secure, well-documented systems to manage screening, enrollment, trial visits, safety data, and outcome data throughout their Finals clinical trial. Common data elements that will be used for judging or reviewed by judges will be entered by teams into the XPRIZE-Utah DCC electronic data capture system, REDCap. Teams should ensure accurate, timely data entry with procedures in place to handle quality control, verification, corrections, and protocol deviations. At study closeout, the XPRIZE-Utah DCC will follow a defined process for database locking, archiving, and version control to ensure integrity of final datasets.

Protocol Deviations

Teams must maintain a log of protocol deviations, including explanation and corrective actions. XPRIZE, Judges, and the XPRIZE-Utah DCC may ask to view protocol deviation logs. Significant or repeated deviations may trigger additional oversight or review.

Publication and Data Sharing

Teams are encouraged to disseminate their findings responsibly and transparently. Data sharing should follow ethical, legal, and regulatory requirements, including use of de-identified datasets and appropriate data-use agreements. The specific methods and timelines for dissemination are at the discretion of each Team, provided participant privacy requirements are upheld. As noted

XPRIZE and its operational partners may conduct secondary analyses or meta-analyses using de-identified datasets and biospecimens submitted to the XPRIZE-Utah DCC or Central Laboratories. Team Leaders will be considered partners or co-investigators in any subsequent analyses and will retain rights for acknowledgement on publications that use data or specimens from their team’s trial. Teams will be provided access to data from new assays or analyses obtained from their team’s specimens or trial data.

Appendices

A. Abbreviations and Key Terms

6MWT - Six Minute Walk Test

90% CI / LCL - 90% Confidence interval / Lower confidence level

AE- Adverse Event; any unfavorable, unintended, and/or untoward occurrence, i.e. disease, sign, or symptom (including an abnormal laboratory finding) that is temporarily associated with the use of an intervention, medical therapy, or procedure.

BV - Baseline Visit; two clinical visits to establish pre-treatment status of endpoint assessments and participant characteristics. The BV assessments for an individual participant will be averaged to establish a starting point for personalized thresholds.

CANTAB - Cambridge Neuropsychological Test Automated Battery

CBC - Complete Blood Count, to be measured at the Finalist Team's Clinical Site; measured as clinical risk factor and safety marker.

CMP - Complete Metabolic Panel, 14-analytes measured as clinical risk factor and safety markers.

CMV - Cytomegalovirus status; key covariate for immune function assays.

CogState Digital Assessment Battery

DET - Detection; Psychomotor Function
GMLT - Groton Maze Learning Test; Executive Function
IDSSTS - International Digit Symbol Substitution Test – Symbols; Processing Speed
IDN - Identification; Attention
OCL - One Card Learning; Visual Learning
ONB - One Back; Working Memory

Competition Guidelines - Document that establishes the high-level requirements and summary of operations for the XPRIZE Healthspan competition.

CONSORT - Consolidated Standards of Reporting Trials; a guideline and flowchart used in clinical trials to visually track participants through the study, from initial screening to final analysis, showing numbers enrolled, randomized, allocated to groups, lost to follow-up, and included in the analysis, ensuring transparency and clarity in reporting a trial's progress and validity.

CPET - Cardiopulmonary Exercise Testing by treadmill or cycle ergometer to determine VO2 maximum or peak VO2. This is an optional but strongly recommended measure of exercise capacity.

CRF - Case Report Form

CT - Computed tomography; an optional imaging based measure of muscle mass.

DSMB - Data and Safety Monitoring Board

DUA - Data Use Agreements

D3Cr - Urinary D3 Creatine method to measure muscle mass using UC Berkeley's patent protected mass spectrometry based assay. This is an optional but strongly recommended biospecimen based measure of muscle mass.

FV - Follow-Up Visit; two clinical visits to establish post-treatment status of endpoint assessments and participant characteristics. The two follow-up visits (FV1, FV2) will be the key assessment points used to evaluate change over baseline for responder / non-responder threshold analyses.

HbA1c - Hemoglobin A1c; measured as clinical risk factor and safety marker.

iAGE - Inflammatory Aging Clock; multi-dimensional score measured by Central Laboratories used to evaluate immune function.

IMM-AGE - Immune Age Score; multi-dimensional score measured by Central Laboratories used to evaluate immune function.

Intrinsic Capacity - the World Health Organization's (WHO) concept for measuring an individual's physical and mental abilities, focusing on five key domains: cognition, locomotion, sensory, vitality, and psychological well-being, to promote healthy aging. This is an optional but strongly recommended measure of functional ability.

IRB - Institutional Review Board; Group made up of scientists, physicians and potentially patient advocates that is formally convened and assigned to review and monitor research and development studies and/or clinical trials involving human subjects. The IRB can make suggestions, and approve or disapprove defined protocols and procedures. Their role is to protect the rights and well-being of people participating in a study and/or trial.

Judging Panel - impartial and independent evaluation team with subject matter and technical expertise to judge the Competition in accordance with the XPRIZE Healthspan Competition Guidelines and Rules and Regulations.

MTA - Material Transfer Agreements

MOP - Manual of Operating Procedures

PBMC - Peripheral Blood Mononuclear Cells, biospecimen to be collected by teams and shipped for central analyses of immune function markers and storage.

SAB - Scientific Advisory Board; A select group of topical experts and big-picture thought leaders who contribute their wisdom, knowledge and guidance to various aspects of the prize including, but not limited to: (i) assisting with the establishment of qualifications for prospective Judges; (ii) recommending members of the Judging Panels; (iii) assisting with development of testing protocols and judging criteria; (iv) and providing input toward the development of the Competition Guidelines.

SAE - Severe Adverse Event; Critical and potentially life-threatening occurrences that demand immediate attention and intervention.

SOP - Standard Operating Procedure; Uniformly written procedures, with detailed instructions to record routine operations, processes and practices followed within the Competition. The SOPs help define the expectations XPRIZE has for a team's standard practices and daily processes conducted to assure execution of research tasks in accordance with guidances to improve validity of Grand Prize judging. Should local / state / federal regulations conflict with XPRIZE defined SOPs, XPRIZE operations should be notified to resolve potential discrepancies.

Steering Committee - Multi-stakeholder group in which representatives of each Team competing in the Finals serve in a voting capacity for changes to protocols or data handling that may impact the competition or operations at their clinical site, as required. Committee Meetings also serve the purpose of teams giving and receiving updates on trial progress, recruitment goals, scientific advances, regulatory considerations, and to troubleshoot issues for data management, specimen collections and handling, or addressing other competition relevant matters with representatives of XPRIZE Operations staff, XPRIZE-Utah DCC and XPRIZE-UCSD Central Laboratories, and other key stakeholders such as members of SAB, Sponsors, etc.

XPRIZE-UCSD Central Laboratories and Biorepository - To be named; facility designated by XPRIZE to provide standardized laboratory testing and biospecimen processing services for Finalist Teams

XPRIZE-Utah DCC - University of Utah Data Coordinating Center, the XPRIZE data coordination and management center

B. Key Contacts

XPRIZE Operations - Healthspan@xprize.org

XPRIZE-Utah Data Coordinating Center - DCC.XPRIZE.Healthspan@hsc.utah.edu

XPRIZE-UCSD Central Laboratories - TBD

C. Sample Size Guidance

To assist teams in selecting an appropriate study sample size, an example reference guide is provided in Table C. The table presents example scenarios for selected sample sizes (n = 40, 50, 100 per group) and observed differences in responder proportions between treatment and control groups (Δp = 20%, 22%, 25%) and under differing control responder rates (0% and 4%). For each scenario, the table shows the number needed in the treatment group (k) to achieve the respective proportion difference and the corresponding one-sided 90% lower confidence limit (LCL), calculated using the Newcombe method, assuming equal numbers of participants in the treatment and control groups.

Table C. Sample Size Guidance

Control responders = 0%

n per group	**Δp = 20%** (k → 90% LCL)	**Δp = 22%** (k → 90% LCL)	**Δp = 25%** (k → 90% LCL)
40	8 → 12.1%	9 → 14.2%	**10 → 16.4%** ✓
50	10 → 13.0%	11 → 14.7%	**12 → 16.5%** ✓
100	**20 → 15.1%** ✓	**22 → 16.9%** ✓	**25 → 19.6%** ✓

Control responders = 4%

n per group	**Δp = 20%** (k → 90% LCL)	**Δp = 22%** (k → 90% LCL)	**Δp = 25%** (k → 90% LCL)
40	10 → 10.0%	11 → 12.2%	12 → 14.5%
50	12 → 11.4%	13 → 13.2%	**14 → 15.0%** ✓
100	24 → 14.0%	**26 → 15.9%** ✓	**29 → 18.6%** ✓

* Δp = difference in responder proportions between treatment and control arms. A check mark (✓) indicates that the number of responders (k) in the treatment group meets both the ≥20% responder requirement and the ≥15% one-sided 90% lower confidence limit (LCL) criterion.

Table C includes two illustrative control-group assumptions of 0% and 4% responders. These scenarios are provided for planning purposes only. As an example, with n=40 participants in the treatment group, observing k=8 responders (20%) yields a one-sided 90% LCL of 12.1%, which does not meet the 15% threshold. Observing 10 responders (25%) in the same group,

however, yields a LCL of 16.4%, satisfying both the ≥20% responder proportion criterion and the ≥15% LCL requirement.

This table is intended as a guide only. Teams should use it alongside prior evidence and relevant literature to inform and justify their proposed sample size. Teams that anticipate observing responders in the control group should account for this in their study design and sample size justification, as higher control responder rates will reduce the observed difference in proportions and will affect the resulting one-sided 90% LCL. We do anticipate that it would be unlikely for a large proportion of control participants to spontaneously meet responder thresholds across all three domains simultaneously. While some variability or practice effects may occur within individual domains, achieving a ≥10-year improvement by chance would be difficult in one domain and even more unlikely across all three. Randomization schemes other than 1:1 should also be accounted for.

D. Suggested Informed Consent Language

Below are key sections and sample language that may be useful for your consent form:

1. Purpose & Data Collection

- Sample: "We are collecting your health information and biospecimens (like blood/urine) for this study. With your permission, these will be sent to a central research repository - including University of Utah Data Coordinating Center and the XPRIZE-UCSD Central Laboratories and Biorepository - for analysis and for future research. This work is part of a global research project sponsored by the US Non-Profit XPRIZE Foundation"

2. Future Use & Storage

- Sample: "Your de-identified data and samples may be stored and used for an unlimited time for future research studies, which might be similar to this one or completely different. Researchers from universities, government, or health companies may apply to use them."
- Option: "You can choose specific types of future research (e.g., health-related, disease-specific, or general research) or decline future use."

3. Data Security & Sharing

- Sample: "Before sharing, your name, address, and other direct identifiers will be removed. While we protect your privacy, no system is 100% secure. Future researchers must follow strict rules to protect your information but cannot identify you personally."

4. Withdrawal & Voluntary Participation

- Sample: "Participation is voluntary; you can refuse to participate in this clinical study without affecting your care."
- Sample: "You can withdraw consent for future use, but data already used or shared cannot be retrieved."

5. Checklist for Choices (for Participant Clarity)

- The default option is for all data / samples to be used for future research, but as required by team institution or ethics board, research participants may opt out of future use for specific purposes.
- Sample: "All data and samples collected in this research study may be used for future research. Please indicate your choice to decline participation in future research:"
    - ___ Yes, allow my data/samples only for research, but not data related to genetic testing or genetic material like DNA.
    - ___ No, do not allow my data/samples for future research.

These are **suggestions only.** You may follow specific standard language as required by your regulatory agency or ethics oversight committees. Be clear, acknowledge use by centralized partner services and XPRIZE, use simple language, allow specific choices (opt-in/out), explain de-identification, and state that withdrawal is possible.

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