Innovative Solutions Opening (ISO)

PROactive Solutions for Preserving Resilience (PROSPR)

Proactive Health Office (PHO)

ARPA-H-SOL-25-125

April 4, 2025[1]
Amendment 1 - April 22, 2025
Amendment 2 - May 23, 2025

[1] The final ISO is binding and supersedes the DRAFT ISO posted on December 12, 2024. Any changes to the final ISO will be made via formal amendments.

ARPA-H-SOL-25-125, PROSPR

1 INNOVATIVE SOLUTIONS OPENING (ISO) SUMMARY INFORMATION

Federal Agency: Advanced Research Projects Agency for Health (ARPA-H), Proactive Health Office (PHO)

Program Title: PROactive Solutions for Preserving Resilience (PROSPR)

Announcement Type: Solicitation

ISO Solicitation Number: ARPA-H-SOL-25-125

Dates (all times listed are Eastern Time):

- *Solution Summary Due Date for TA 1/2 Solutions* : April 25, 2025 at 2 PM
- *Extended TA3 Solution Summary Due Date*[1]: June 5, 2025 at 2 PM
- *Full Proposal Due Date*: *To be specified in feedback letters*

Anticipated awards: Multiple Other Transaction Agreements (OTs)

Agency Contact: All inquiries shall be sent to PROSPR@ARPA-H.GOV

*See ISO Sections 3 and 4 for additional information about Solution Summary and Full Proposal Submissions (e.g., to be eligible to submit a Full Proposal, a Proposer must have submitted a timely Solution Summary and received feedback from the government).

1.1 ISO Purpose

ARPA-H seeks proposals from all eligible entities (see Section 3, *Eligibility Information*) to accomplish the PROSPR program goals as described in this solicitation package. Ultimately, ARPA-H intends to negotiate multiple OT Agreements with Proposers whose proposals are most advantageous to the government.

1.2 ISO Questions and Answers

All questions regarding this ISO must be submitted to PROSPR@arpa-h.gov. ARPA-H will post Q&As to the PROSPR program website on an on-going basis and will not respond to questions directly. All questions must be submitted in English and must include the name, e-mail address, and telephone number of a point of contact. Proposers submitting questions to individual government team members (e.g., Program Manager) should not expect a response. ARPA-H will attempt to answer questions in a timely manner; however, questions submitted after the Q&A due date may not be answered. Further, duplicative questions may be combined and rephrased to streamline responses.

1.3 Proposers' Day

ARPA-H invites proposers to view the Proposers' Day video posted to SAM.gov and the

[1] ARPA-H has reopened the Solution Submission Portal exclusively for TA3 solutions. ARPA-H encourages the submission of new TA3 Solution Summaries, as well as revised Solution Summaries from previous TA3 proposers seeking to update their earlier submissions. Please note that new and/or revised submissions for TA1 and TA2 solutions will not be accepted at this time.

PROSPR Program page.

2 PROGRAM INFORMATION

2.1 BACKGROUND

Despite major advances in scientific discovery and clinical interventions that have added years to life expectancy, there has not been a corresponding increase in healthspan, the number of years spent in good health. Instead, the prevalence of chronic diseases in American adults has dramatically increased, particularly worsening with age. In the United States and elsewhere, medicines and scientific research are heavily focused on reactionary, post-symptomatic illness treatment, despite overwhelming evidence that early interventions are far more effective, and many diseases are preventable.

The Proactive Health Office (PHO) at ARPA-H is seeking solutions to extend the healthspan for Americans, with a focus on interventions aimed at early disease prevention. The PHO believes that population-level improvements in access to and adoption of disease prevention and wellness-promoting behaviors, novel early-detection methods, and prophylactic interventions could drastically improve Americans' health throughout their lives, and that system-level innovations are required for effective proactive health delivery.

In the United States, age-related chronic diseases come with an annual healthcare cost burden of nearly $1 trillion. The healthcare costs for the aging population is projected to increase by 75% if nothing is done to prevent the progressive loss of physical functioning during aging, according to a Pew Research Center Study, which will place an immense strain on our healthcare and economic resources. Currently, no preventive treatments exist for the general health decline that inevitably occurs during aging and geriatric medicine remains focused on post- symptomatic treatments.

Four major factors limiting progress in healthspan extension have been identified:

1. Health decline during aging is accepted as normal.

Aging is the most significant risk factor for a variety of diseases and yet age-associated health decline is not researched nor treated like other risk factors, such as hypertension or pre-diabetes. A major contributor to the acceptance of fatigue, muscle weakness, reduced memory, worsening hearing and vision, and many other non-disease symptoms as a "normal" part of aging, is likely because we lack therapeutic options to prevent these general health declines. However, considering that some individuals maintain excellent health far longer than others, it is clear aging does not automatically necessitate poor health and accumulation of disease but rather extending healthspan for the majority should be possible. In fact, animal studies with parabiosis, exercise, and caloric restriction demonstrate that a youthful healthy state can be maintained in older ages.

2. Geriatric medicine focuses on post-symptomatic disease treatments.

Because the early decline in health during aging is not the focus of geriatric medicine, much of the progress in healthspan research has been incidental, following specific disease targeting. This roundabout fortuitous approach slows larger-scale advancements. Aging is now known to involve systemic changes such as increased inflammation and metabolic dysfunction, which often precede age-related diseases. Drugs like Rapamycin, Ozempic, and Metformin have

shown pleiotropic effects, though most studies are limited to individuals with various diseases. Our lack of attention to the aging community before significant ailments arise contributes to a limited understanding and lack of therapeutic options for the health declines that begin for many in their 40s.

3. Clinical trials are too costly and time-consuming for age-induced health outcomes. Clinical trials are not feasible for most researchers and biotech companies despite a growing interest in therapeutics that facilitate healthy aging. For this reason, scientists are forced to conduct studies with shorter outcomes, such as those in age-related diseases after the onset of symptoms. A clinical trial with healthspan changes as the outcome could take 20-50 years, as this is time required for a typical 35-year-old to develop recognized clinical endpoints such as mortality or accumulation of disease. Considering the average clinical trial for diseases costs about $2 billion to conduct, a healthspan study could cost well over $6 billion.

4. Lack of validated surrogates for healthspan.

The major limiting factor that contributes to the cost and time requirements for human clinical trials on healthspan is the designated clinical endpoint. For some diseases, a surrogate biomarker can be demonstrated to accurately predict the clinical endpoint and can be approved by the FDA as a validated surrogate clinical endpoint. If we had a validated surrogate endpoint for long-term, age-induced outcomes, we could dramatically reduce the time and cost required for these trials. One way to measure age-induced general health is through intrinsic capacity (IC), a score generated by assessing a wide-range of physical and mental abilities. IC progressively declines with age, transitioning from peak physical health and highly functioning systems in young adulthood to a frail state or diseased state until death. Low IC has recently been demonstrated to roughly correlate with an increased risk of future chronic disease development. Blood-derived biomarkers, particularly those associated with inflammation and metabolism, have shown promising correlations with IC in older adults. However, IC studies are in their infancy, being performed in small scale, short duration studies and have not been used to generate a 20-year mortality or morbidity prediction. Further, the generalizability of current IC research is limited by low population diversity and minimal data from adults younger than 60. Now that initial studies have demonstrated the potential of IC to predict health outcomes, standardization and refinement of IC measures and analysis on a larger scale are necessary to enable their implementation in clinical and healthcare settings.

While these challenges are significant, there is progress being made in each area that will serve as the basis for exponential growth through the PROSPR program.

2.2 PROSPR PROGRAM DESCRIPTION AND SCOPE

PROSPR is a 5-year program aims to develop interventions that extend healthspan by 20 years by targeting the underlying causes of age-induced health loss and thereby prevent the onset of multiple age-related diseases simultaneously.

To facilitate the study and testing of healthspan interventions, PROSPR will first reduce the time and cost investments that currently prevent a thriving healthspan therapeutics industry from developing. By directly demonstrating that human age-induced health outcomes can be predicted by biochemical and physiological measures in a single composite intrinsic capacity (IC) score, PROSPR will remove the need for 20-year clinical efficacy trials. By focusing second-

generation interventions on those that target early health loss, PROSPR aims to preserve health in aging individuals before chronic diseases can develop. This will transform geriatric medicine into a personalized, comprehensive, preventive care model.

2.3 TECHNICAL APPROACH AND STRUCTURE

The PROSPR program has established detailed objectives for each Technical Area (TA) in Table 1. Table 2 lists deliverables for each TA and quantifiable and qualitative program metrics for each TA in Tables 3-5. Performers will be required to provide status reports during meetings with the Program Manager (PM), including detailed technical progress, financial updates, and any necessary data to validate alignment with technical milestones These reports, reviewed alongside the metrics and milestones outlined below, will be used to evaluate the progress of performer teams and their success within each phase. Performers will be required to coordinate within their team and with other performers, as directed by the PROSPR PM, the Administrative Officer (AO), and as specified in the agreed upon contract. This coordination will include the use of Agreements and Performance Assessments and general program interactions, which will be detailed in the model OT.

2.3.1 APPROACH BY TECHNICAL AREA (TA)

The three PROSPR TAs are listed below. TA1 and TA2 each have two tracks, while TA3 is a single track. All tracks and TAs are designed to run concurrently, with an expectation of ongoing collaboration and integration across teams, as outlined in the Program Structure section. Each proposal can address any number or combination of tracks, including only a single track. ARPA-H may choose to fund only a portion of any proposal. All performers are expected to collaborate with each other throughout the life of the program and will therefore have Associate Performer Agreement (APA) language included in their respective award; see Appendix A.

Technical Area 1 (TA1): *PROSPR intrinsic capacity score* (*see Table 3 for metrics*)-60 months

- TA1 Phase I (12 months) includes developing IC score (v1.0) and IC assessment technology (v1.0) and preparing for a clinical observational study to measure IC score.
- TA1 Phase II (12 months) includes refinement of IC score (v1.1) and IC assessment technology (v1.1) using data from the clinical observational study.
- TA1 Phase III (12 months) includes conducting a lifestyle intervention study to test the intervenability of IC score (v1.2) and detection capacity of the IC technology (v1.2).
- TA1 Phase IV (12 months) includes refining IC score (v2.0) and IC assessment technology (v2.0) using data from lifestyle intervention study.
- TA1 Phase V (12 months) focuses on deployment and commercialization.

TA1 is comprised of two interconnected tracks, *Track 1a* and *Track1b*.

Track 1a (PROSPR IC score)

Track 1a performers will define a single score (PROSPR IC) comprised of human physiological and biochemical components, that predicts 20-year health outcomes.

In year 1, performers will harmonize existing human datasets (see metrics for details) to identify the weighted contribution of each IC component to a composite PROSPR IC score. Two PROSPR IC scores will be generated independently, one with components weighted for

contribution to female IC and one for males, as we anticipate the contribution of certain components will vary significantly by sex. Performers can include any number of physiological and biochemical components in their initial testing but must at least include all five components of WHO-defined IC and DNA methylation. Please also note that we prefer components which do not require invasive methods of sample collection. Components should be included or excluded in the final composite PROSPR IC score based on their contribution to the accuracy of the composite score to predict 20-year health outcomes. TA1 will label the PROSPR IC score as an improved version of intrinsic capacity to leverage the existing ICD-11 (Internal Classification of Disease-11) code, accelerating its clinical use.

In year 2, *Track 1a* performers will validate and improve the accuracy of the PROSPR IC score using data provided by the decentralized or hybrid study conducted by *Track 2b* performers (see below).

In years 3 and 4, *Track 1a* performers will validate the intervenability of the PROSPR IC using data provided by the multi-modal lifestyle intervention clinical trial conducted by *Track 1b* performers (see below). Additionally, *Track 1a* performers will collaborate closely with *Track 1b* to guide technology development based on the components of the PROSPR IC score identified during the data harmonization in year 1. They will continue to guide refinements in later phases as the score improves.

Track 1a performers will compile the data from other PROSPR performers that use PROSPR IC in clinical trials. Throughout the duration of the program, performers will discuss the data with other performers and the FDA and prepare submission packages for the FDA, for surrogate endpoint designation of PROSPR IC and biochemical surrogates.

Note: *Track 1a* performers are responsible for conducting targeted analyses on biospecimen samples collected from PROSPR study participants (see below) to validate TA2 Track 2a-identified biomarkers throughout the program.

Track 1b (PROSPR IC assessment technology)

In year 1, *track 1b* performers will work closely with *Track 1a* performers to incorporate insights gained from the components of PROSPR IC score from *Track 1a* to develop in-home PROSPR IC assessment technology. PROSPR envisions a digital health platform (app) that connects with common existing health monitoring devices and wearables to assess different components of the PROSPR IC score. The platform will include methods for minimally-invasive collection of biological samples as necessary, such as blood spots or saliva, for DNA methylation and other biochemical analyses. This platform must also provide educational information in easy-to-understand language to promote health ownership.

In year 2, performers will test the technology's accuracy and user-friendliness to measure PROSPR IC in a one-year decentralized or hybrid PROSPR study. Proposals will be accepted from performers seeking to extend already existing large-scale longitudinal studies of human measures, provided they add the PROSPR TA1 *track 1b* study requirements (see Table 3). Participants will report monthly PROSPR IC score with the in-home PROSPR IC assessment technology, while clinicians conduct the same assessments during clinic visits at baseline, six

months, and at the end of the study. Each participant must be assigned a coach to virtually assist with the technology, facilitate regular engagement, and provide feedback to the performers. Starting with version 1.0, the PROSPR IC score will undergo iterative updates, progressing to version 2.0 by the end of the program. Each version will incorporate refinements and improvements based on data collected from participants in the PROSPR study, enhancing the predictive accuracy of the score over the course of the study.

Feedback on IC assessment technology accuracy, usability, and user-friendliness from participants in the TA1 *track 1b* PROSPR study will be continuously integrated into the refinement of the IC assessment technology. Starting with version 1.0, the technology will evolve through iterative updates, including milestones such as version 1.1 and 1.2, leading to version 2.0 by the end of the TA1 *track 1b* study. Each version will incorporate refinements and improvements based on participant feedback, ensuring the technology is progressively optimized throughout the study. If a technology demonstrates sufficient accuracy and technical progress at this stage, the PM may nominate the team to work with the agency's commercialization team, the Project Accelerator Transition Innovation Office (PATIO). The team would similarly iterate on its product design and business model with a goal of <$100 per consumer assessment at a realistic production volume by the end of the program.

In year 3, *Track 1b* performers will recruit a subset of participants from the TA1 *track 1b* PROSPR study into a 1-year in-home lifestyle intervention study with continued PROSPR IC monitoring facilitated by a coach and using the PROSPR IC assessment technology. The lifestyle intervention will end in year 4, and performers will continue to collect participants' PROSPR IC with PROSPR IC assessment technology to determine if health improvements are sustained or return to baseline.

The lifestyle intervention must include at least four of the following lifestyle management options for participants, weighted for their needs established during the PROSPR study: diet, exercise, stress, social engagement, sleep, poor habit management, mental health, or others. After the one-year PROSPR lifestyle intervention study, participants will continue to report their PROSPR IC score for an additional year without the coach to determine whether the PROSPR IC score remains improved, returns to baseline, or follows another trajectory.

In year 5, *Track 1b* nominated performers will work with ARPA-H PATIO and its partners to commercialize the in-home PROSPR IC score assessment technology, validating progress toward the affordability objective and optimizing deployment within the health system workflow. Performers will also discuss approval of the PROSPR IC assessment technology with the FDA for clinical and in-home use of the IC assessment for patient IC measurement. Further, *track 1b* performers will work with payers to develop a strategy for covering the consumer costs and propose a plan for in-home screening and monitoring outside the FDA-regulated clinical diagnosis pathway.

Note: Annual discussions with the FDA are a requirement for TA1 (*track 1a and 1b)* performers to advance to the next phase of the program. The FDA encourages early engagement so that they may provide guidance on where additional data may be needed for validation. TA1 performers must provide an update on their progress with these FDA interactions to the PROSPR PM as part of the quarterly status meetings.

Note: *Track 2b* performers are responsible for providing biospecimen samples collected from PROSPR study participants to *Track 1a* to support the validation of TA2-identified biomarkers throughout the program.

Technical Area 2 (TA2): Repurposing FDA-approved interventions for healthspan extension *(see Table 4 for metrics)-60 months*

- TA2 Phase I (12 months) includes identifying intervenable biomarkers and preparing for a phase 3 decentralized clinical trial for drug repurposing.
- TA2 phase II (6 months) includes finalizing clinical trial study requirements and sharing identified biomarkers.
- TA2 Phase III (12 months) focuses on conducting the phase 3 decentralized clinical trial.
- TA2 phase IV (12 months) continues data collection and monitoring.
- TA2 phase V (18 months) concludes phase 3 trial and involves engaging with the FDA for regulatory approval.

TA2 is comprised of two interconnected tracks, *track 2a* and *track 2b*.

Track 2a (Biochemical markers)

Performers will collect clinical data and blood samples from existing clinical trials where a therapeutic intervention has demonstrated broad health improvements to identify biochemical markers (genes, metabolites, proteins, etc.) consistently responsive across interventions. These biomarkers will be shared with TA1 performers for potential inclusion in the composite PROSPR IC score. We encourage performers to consider trials of the following treatments: rapamycin, metformin, GLP-1, acyclovir, naltrexone, and somatostatin. Performers must have letters from trialists agreeing to share the stored blood samples for omics analysis. *Track 2a* will conduct comprehensive omics analyses on these blood samples to identify biochemical changes during an 18-month funding period. Throughout the funding period, *Track 2a* will collaborate closely with TA1 *Track 1a and 1b* performers to integrate identified biochemical markers into the TA1 *track 1a*-developed PROSPR IC score and TA *track* 1b-developed PROSPR study design. The biochemical markers identified by *Track 2a* will be tested by *Track 2b* in a Phase 3 clinical trial using FDA-approved drugs to determine whether the biomarkers are responsive to these interventions.

Track 2b (FDA-approved drugs)

TA2 *track 2b* performers will identify up to two FDA-approved drugs with strong safety data and evidence of multimorbidity reduction in humans or evidence of healthspan, frailty, or lifespan improvement in preclinical animal models, and conduct a 3-year, phase 3 randomized clinical trial, conducted in a decentralized manner (DCT). The trial will test the drug's efficacy for improving PROSPR IC, the biomarkers identified in phase 1 of TA2, and health outcomes in 60-year-old participants. *Track 2b* performers will work with the FDA on decentralized clinical trial design and validated surrogate endpoints for healthspan. *Track 2b* performers will also share IC data with TA1 performers during the clinical trial to allow TA1 to determine whether PROSPR IC

is responsive to pharmacological interventions in humans.

Note: Track 2b performers are responsible for sharing IC data and the findings of their targeted analyses of intervenable biochemical markers (identified by Track 2a) from clinical trial study participants with TA1-Track 1a performers. This enables TA1-Track 1a performers to compile the data and prepare submission packages to the FDA for the validated surrogate endpoint designation of PROSPR IC and biochemical surrogates.

Technical Area 3 (TA3): *Second-generation interventions (see Table5 for metrics)-60 months*

- TA3 Phase I (18 months) includes preclinical validation using aged animal models.
- TA3 Phase II (18 months) includes IND-enabling studies to evaluate the safety, pharmacokinetics, and behavior of second-generation interventions.
- TA3 Phase III (6 months) focuses on establishing IRB approval and preparing for the clinical trial.
- TA3 Phase IV (18 months) focuses on the first-in-human clinical testing of second-generation interventions to assess safety and efficacy in a Phase 1b clinical trial.

TA3 focuses on identifying the most efficacious interventions that can extend human healthspan. TA3 performers will propose interventions with strong evidence of extending healthspan, lifespan, or reducing frailty symptoms in preclinical rodent models. Performers must provide evidence of optimized intervention delivery and address treatment-specific challenges to enable long-term use in animals as part of the supporting data in their proposal.

TA3 will begin with multiple teams. TA3 performers are expected to collaborate and share data, both among the TA3 performers (specifically the preclinical method of IC assessment) and with performers in TAs 1 and 2 to ensure the overall success of the program. Therefore, performers will have Associate Performer Agreement (APA) language included in their respective award; see Appendix A.

In phase 1, TA3 performers will conduct preclinical testing of their intervention in outbred rodents beginning about mid-age until advanced age, evaluating the efficacy of the intervention to maintain or improve health (cognitive ability, metabolic function, muscle strength, immune function, cardiovascular function, sensory function, etc.) during aging. TA3 performers must ensure reproducibility of results through external validation by an independent group at an independent research site. TA3 will assess model health using a method they develop to test components of the PROSPR IC, as closely identified in TA1, ideally using automated, non-subjective measures. Although each team is responsible for developing pre-clinical IC measures, the PROSPR PM may require performers switch to another team's rodent PROSPR IC protocol at any time during the program.

Innovative therapeutics with the highest safety profile and greatest efficacy in aged animal models will be prioritized for the phase 1b human clinical trials conducted within this TA. Performers may propose various interventions such as small molecules, organelle transplant, or lifestyle mimetics.

Selection for TA3 teams to advance to next phases of the PROSPR program will take place twice: once at the end of the phase I (Y2), and again at the conclusion of IND-enabling studies (Y3). Ultimately, ARPA-H anticipates two teams will be selected to proceed to human clinical trials. The final team(s) must work with TA1 and TA2 performers during phase III (Y4) to incorporate TA1 *track1a*-developed PROSPR IC and biochemical surrogates into their clinical trial design.

Table 1: The general program objectives by TA

TA1: PROSPR IC Score: *Predict 20-year health outcomes*	• Harmonize existing datasets to identify key physiological and biochemical changes of age-induced health outcomes. • Develop a sex-specific PROSPR IC score for predicting 20-year mortality and multi-morbidity outcomes. • Build in-home PROSPR IC assessment technology for consistent monitoring of health and allow proactive health management. • Establish a multi-modal decentralized or hybrid lifestyle intervention study to collect data on the responsiveness of the PROSPR IC score and biochemical markers (from TA2) to lifestyle interventions. • Collect empirical evidence demonstrating that these lifestyle interventions can improve or maintain general wellness in relatively healthy, aging individuals. • Engage with the FDA to advance PROSPR IC and biochemical markers toward validated surrogate endpoint designation in collaboration with TA2. • Engage with the FDA to obtain approval of in-home PROSPR assessment technology. • Commercialize PROSPR IC assessment technology (<$100 out of pocket) • Begin strategies for securing insurance coverage to enable early health intervention and preventive care.
TA2: Repurposing approved interventions: *Accelerate creation of a healthspan industry*	• Identify common biochemical changes shared between multiple FDA-health improving drugs using omics data from blood samples obtained from existing clinical trials. • Demonstrate the utility of PROSPR IC (from TA1) and biochemical markers as surrogate endpoints in place of disease accumulation or mortality in phase 3 clinical trials. • Utilize repurposed drugs to provide first-generation healthspan therapeutics and generate the clinical data necessary for establishing feasibility of short-term efficacy trials for healthspan extension. • Build a consensus on decentralized trials for non-diseased populations.
TA3: Second-generation interventions: *Extend human health by 20 years*	• Test second-generation interventions that target age-related health decline through rigorous efficacy and safety preclinical trials. • Develop a preclinical method in rodents to assess the components of PROSPR IC as closely as identified in TA1.

	• Test safety and efficacy of candidate intervention in Phase 1b human clinical trial.
Accessibility Requirements	Performers must develop solutions that account for health inequalities, considering cost and accessibility of care, and ensure protection of all protected groups. These considerations must be addressed prior to program onset.

2.3.2 DELIVERABLES AND TRANSITION ACTIVITIES

Table 2. Overall deliverables and transition activities

Technical Area	Deliverables and Transition Activities
TA1	A highly accurate and easy-to-measure intrinsic capacity score (PROSPR IC score) that quantifies age-associated health changes, responds to interventions, and predicts 20-year health outcomes.
	A user-friendly proactive health management tool (in-home PROSPR IC assessment technology) that offers a personalized, patient-centered experience based on the PROSPR IC score.
	Deployment strategies that ensure regulatory approval and reimbursement pathways for PROSPR IC.
	PROSPR IC as an FDA-validated surrogate endpoint.
	Intervenable endpoint surrogates for early prediction of healthspan changes and adverse health outcomes.
	A multi-modal decentralized/hybrid lifestyle intervention study.
	Empirical evidence demonstrating that lifestyle interventions can improve or maintain general wellness in relatively healthy individuals.
TA2	Intervention-responsive biomarkers, identified through omics analysis of blood samples collected in existing clinical trials.
	Repurposed drugs that extend healthspan in aged individuals.
	Establishment of a basis for consensus around decentralized clinical trials for aged, non-diseased populations.
	Establishment of a regulatory pathway for interventions targeting age-induced intrinsic capacity decline.
TA3	Phase 1b clinical trial for an affordable and accessible novel medicine that extends healthspan in aged individuals by improving or maintaining intrinsic capacity.
	Preclinical assessment protocol of PROSPR IC measures.

All TAs	• Integrate TA1 deliverables (PROSPR IC and in-home PROSPR IC assessment technology) into clinical trial designs throughout the program (TA1 lifestyle intervention trial, TA2 Phase 3 drug-repurposing trial, TA3 second-generation Phase 1b clinical trial) to demonstrate clinical utility of PROSPR IC and validate its responsiveness to intervention for designation as a validated surrogate endpoint. • Integrate TA2 identified biomarkers from existing clinical trials into clinical trial designs throughout the program (TA1 lifestyle intervention trial, TA2 Phase 3 drug-repurposing trial, TA3 second-generation Phase 1b clinical trial) to demonstrate clinical utility of biochemical surrogates and validate their responsiveness to intervention for surrogate endpoint designation. • Use TA2-identified biomarkers from existing clinical trials to guide necessary modifications to the in-home PROSPR IC technology. • Leverage insights gained from TA2 clinical trial data to guide the design of clinical trial in TA3.
All TAs	• Engage with FDA to receive early guidance on data needed to progress with the program. • Demonstrate long-term planning to sustain the project by identifying potential funding and commercialization partners. • Establish clear guidelines for intellectual property rights and licensing agreements early in the research process. • Focus on accessibility and demonstrate that the team is advocating for partnerships that promote and promise accessibility to ≥75% of US communities.

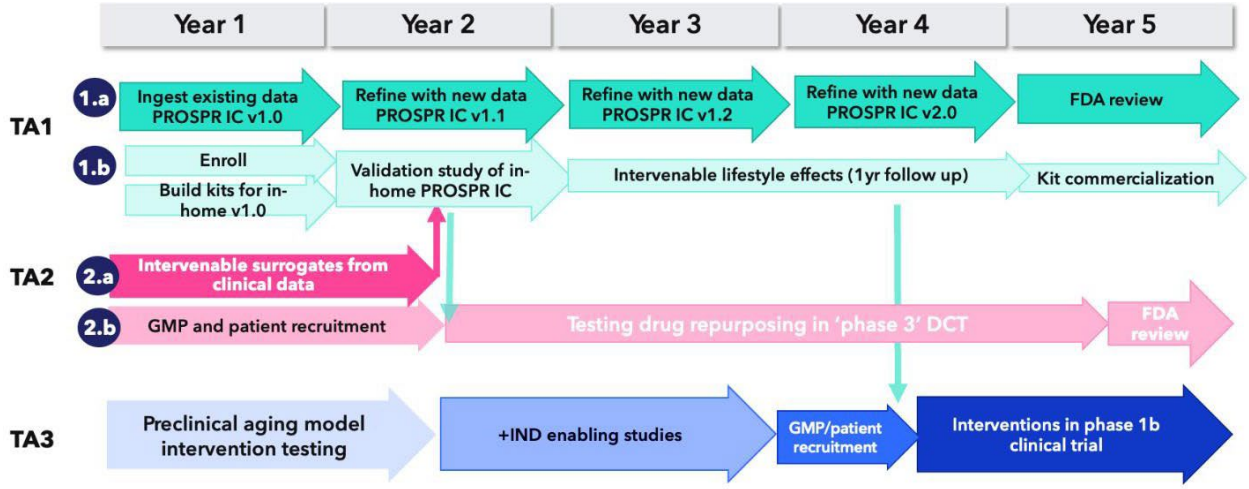
2.3.3 PROGRAM STRUCTURE

The PROSPR program structure is based on the timeline shown in Figure 1. PROSPR will depend on multidisciplinary teams to bring expertise in various scientific domains, and has been designed to transfer information across the TAs. Performers may submit proposals that address any one of three TAs or can combine more than one TA or tracks to address broader, multi-disciplinary challenges. However, regardless of the number of TAs included in the proposal, performers must plan for integration and data sharing with other teams. Any performer that does not meet the accessibility, data sharing plan, and attendance requirements may not progress to subsequent phases. Progression into future phases is determined by the ARPA-H PM and is based on funding availability, performer progress toward phase metrics, and probability of success in future phases. Performers who remain in the program must continue to meet all the required metrics, including the following integration areas:

- TA1 performers will provide PROSPR IC technology to TA2 performers before the end of Phase 2 to use in their phase 3 clinical trial design using FDA-approved repurposed drugs. Data from this trial will support the designation of PROSPR IC as a surrogate endpoint to shorten timelines for healthspan extension trials.
- TA1 performers will provide PROSPR IC technology to TA3 performers before the end of TA3 Phase III to incorporate measures into phase 1b clinical trial of second-generation intervention design.

- TA1 *Track 1a* and *Track 1b* performers will collaborate for the duration of the program to coordinate the PROSPR IC score with the assessment technology.
- TA2-*Track 2a* performers will share identified biochemical biomarkers with TA1 and TA2-*Track 2b* performers during TA2 Phase 2 to allow performers to validate these biomarkers as surrogate endpoints in the lifestyle intervention trial and phase 3 trial for FDA-approved drug repurposing, respectively.
- TA1_*Track 1a* performers are responsible for preparing the FDA submission package for PROSPR IC and biochemical markers as validated surrogate endpoints. All PROSPR performers are required to share data with TA1 performers for the FDA discussions as needed.

Figure 1: The PROSPR Timeline and TA interactions.



2.3.4 PROGRAM METRICS AND TIMELINE

Tables 3-5 provide the milestones and metrics expected and used to track progress throughout the duration of the program. Performers will be required to formally report progress against the agreed upon metrics on a quarterly basis or as needed to the PROSPR PM and to the designated collaborating team(s). Technical progress toward the program metrics, data sharing, and collaboration with teams from other TAs are significant factors for continuation into subsequent phases.

Table 3: Expected milestones and metrics per phase in TA1 (PROSPR IC score)

TA1 Phase I (v1.0 Development) - 12 months	
Track 1a	
Ingest existing longitudinal databases	• At least three of the following used: Canadian Longitudinal Study of Aging (CLSA), All of Us, Baltimore Longitudinal Study of Aging (BLSA), Mass General Brigham Biobank, Coronary Artery Risk Development in Young Adults (Cardia), and UK Biobank. • Database study participants reflect the general population.

	• Combined data from study participants is demonstrated to be generalizable relative to the target population based on Performers' statistical analysis and includes adult datasets starting from at least 35 years of age. • Collectively, the chosen datasets provide coverage of all IC subdomains, disease risk, all-cause mortality, and morbidity. Note: individual datasets are not required to have all of these health outcomes.
Data harmonization	• Data cleaning, normalization, and validation are performed to ensure at least 95% consistency across datasets
DNAm or other sequencing	• As needed, completed DNA-methylation or other sequencing and analysis using existing biospecimens with linked clinical data.
IC components and measures	• Includes all five components of WHO-defined IC (cognition, locomotion, vitality, sensory function, and psychological capacities) and DNA methylation. • Each IC component contributes to the overall score based on a weighted calculation. • Minimum factor loading for any IC indicator is ≥ 0.3, with no significant cross-loading observed. • IC measures include at least one validated assessment for each of the five IC subdomains. • At least 80% of IC measures are designed to be compatible with digital health platforms, including wearables. • IC measures requiring biospecimen collection prioritize non-invasive methods (e.g., blood spots or saliva) with a total collection and processing time of ≤10 minutes.
V1.0 PROSPR IC score	• PROSPR IC scores are developed independently for males and females. • Demonstrates a clear distribution across different age groups in adults >35. • Capability Demo (v1.0): 20-year mortality or multi-morbidity prediction, AUC ≥ 0.90, 95% CI, R^2 ≥ 0.5. • PROSPR IC score validated against multiple outcomes, including two of the following: functional ability, hospitalizations, multi-morbidity, and mortality.
Data security and storage	• Data security and protection measures meet industry regulations (e.g., HIPAA, GDPR) and data governance best practices. • Data collected, stored, and managed using industry standard data models or formats (e.g., OMOP, CDSIC, LinkML for electronic health records; FASTA, VCF for genomic data) and APIs. • Data is FAIR (findable, accessible, interoperable,

	reusable), with a preference for standard and open APIs such as FHIR, the Global Alliance for Genomics and Health (GA4GH) APIs (DRS, Passports, Phenopackets, etc.), or similar access mechanisms.
Regulatory compliances	• Engaged at least once with the FDA to ensure accurate measurement and assessment of IC components by incorporating FDA guidance into study protocols and methodologies.
Track 1b	
In-home PROSPR IC assessment tech (v1.0)	• Integrates with various available wearable devices and sensors to assess the physiological components of PROSPR IC v1.0. • Include methods for collecting non-invasive biospecimens, (e.g. blood spot, saliva, etc.) for biochemical analysis with collection success rate of ≥ 95% and a total collection and processing time of ≤10 minutes. • Capability Demo (v1.0): Real-time data synchronization (≤ 5 sec) and analysis capabilities (≤ 10 sec) with ≤ 99.9% uptime. • User-friendliness aiming for Task Success Rate (TSR) >80%, a low (2-5 min) Time to Task (TOT), and user satisfaction rating ≥ 3.5/5.0 using standardized questionnaire to assess overall usability and navigation. • Includes a patient education platform that explains each component of PROSPR IC (v1.0), the meaning of scores, and the significance of score changes in lay terms. • Provides options for data sharing with healthcare providers and researchers with user consent obtained in 100% of cases. • Scalable to support at least 4K participants.
PROSPR study (Design)	• Incorporated the measurement of IC score and PROSPR IC assessment tech (v1.0) into the study design. • Obtained IRB approval for decentralized/hybrid trial. • Trained 100% clinical staff and coaches for new study protocol and technology orientation. • 100% completion of electronic informed consent from all participants. • Enrolled >1K patients that reflect the general population, aged 35-75 with no chronic health conditions, non-extreme end BMI, and no cognitive dysfunction, breakdown of male and female patients that reflects the general population. Note: Extending existing studies is allowed. • Established unique ID links between study participants and wearables.

Regulatory compliances	• Engaged at least once with the FDA to align the human study design with regulatory standards. • Documented and incorporated all FDA feedback and comments into the study design.
TA1 Phase II (v1.1 Development) - 12 months	
Track 1a	
V1.1 PROSPR IC score	• Model accuracy and reproducibility validated and refined with emergent data from PROSPR IC study. • Individual IC measurements remain statistically correlated with changes in PROSPR IC score (v1.1). • Capability Demo (v1.1): 20-year mortality or multi-morbidity prediction AUC ≥0.95, 95% CI, R2 ≥ 0.5. • Similar AUC (±0.05) when analyzing different age groups. • Similar AUC (±0.05) when analyzing males and females.
Metrics additional requirements	• Performed targeted analyses on samples collected from PROSPR study participants to validate *TA2-Track 2a* identified biomarkers and establish baseline measures.
Regulatory compliances	• Conducted at least one meeting with the FDA.
Track 1b	
In-home PROSPR IC assessment tech (v1.1)	• Capability Demo (v1.1): Data accuracy and consistency: ≥80% correlation between device measurement and clinician assessments. Measurements yielded ≥90% consistency over repeated trials. • Reliability: ≥ 95% successful sync rate with wearable devices and sensors, and ≥ 99% uptime. • User experience: user satisfaction rating ≥ 4.0/5.0 on standardized usability scales. Task Success Rate (TSR) >80%, low (2-5 min) Time to Task (TOT).
PROSPR study (Observational)	• Attrition rate < 15%. • Achieved ≥ 80% data completion for all data sources. • Demonstrated inter-rater reliability ICC ≥ 0.75 and data consistency ≥ 90% across all sources throughout the study.
Metrics additional requirements	• Biospecimen samples collected from PROSPR study participants shared with *Track 1a.* • Distributed in-home PROSPR IC assessment tech to TA2-*Track 2b* performers for use in clinical trial. • TA2-*Track 2a* intervenable biochemical surrogates used to inform any refinements to the in-home PROSPR IC assessment technology (v1) for measuring new markers.

Data security and storage	• Data security and protection measures meet industry regulations (e.g., HIPAA, GDPR) and data governance best practices. • Data collected, stored, and managed using industry standard data models or formats (e.g., OMOP, CDSIC, LinkML for electronic health records; FASTA, VCF for genomic data) and APIs. • Data is FAIR (findable, accessible, interoperable, reusable), with a preference for standard and open APIs such as FHIR, the Global Alliance for Genomics and Health (GA4GH) APIs (DRS, Passports, Phenopackets, etc.), or similar access mechanisms.
Regulatory compliances	• Conducted at least one meeting with the FDA to review and align the study design.
TA1 Phase III (v1.2 development) - 12 months	
Track 1a	
V1.2 PROSPR IC score	• Model accuracy and reproducibility validated and refined with emergent data from PROSPR IC study. • Individual IC measurements remain statistically correlated with changes in PROSPR IC score (v1.2). • Capability Demo (v1.2): 20-year mortality or multi-morbidity prediction AUC ≥0.95, 95% CI, $R^2 \geq 0.5$. • Similar AUC (±0.05) when analyzing different age groups. • Similar AUC (±0.05) when analyzing males and females.
Metrics additional requirements	• Performed targeted analyses in samples collected from PROSPR lifestyle intervention participants to validate intervenable biomarkers (identified by TA2-Track 2a). Achieved an AUC ≥ 0.70 in predicting lifestyle intervention response and a correlation coefficient ≥ 0.5 between biomarker changes and clinical outcomes. • Completed re-analysis of intervenable biomarkers (identified by TA2-Track 2a) using data shared by Track 2b. Achieving an AUC ≥ 0.80 and a correlation coefficient ≥ 0.5 between biomarker changes and clinical outcomes.
Track 1b	
In-home PROSPR IC assessment tech (v1.2)	• Capability Demo (v1.2): Data accuracy and consistency: ≥80% correlation between device measurement and clinician assessments. Measurements yielded ≥90% consistency over repeated trials. • Reliability: ≥ 95% successful sync rate with wearable devices and sensors, and ≥ 99% uptime. • User experience: user satisfaction rating ≥ 4.5/5.0 on standardized usability scales. Task Success Rate (TSR) >80%, low (2-5 min) Time to Task (TOT).

	• Coaching feature effectiveness: ≥ 80% of participants improve PROSPR IC score and reduced risk of functional decline, multi-morbidity, and mortality (OR ≥0.70, 95% CI).
PROSPR study (Lifestyle intervention)	• The multimodal lifestyle intervention study incorporates at least four of the following management techniques: diet, exercise, stress, social engagement, sleep, mental health, poor habit management, or others. • Maintained an attrition rate of <30%. • Achieved ≥80% data completion across all data sources. • Achieved inter-rater reliability with ICC ≥ 0.75 and data consistency ≥ 90% across all data sources throughout the study.
Regulatory compliances	• Conducted at least one meeting with the FDA to review and align the study design.
TA1 Phase IV (v2.0 development) - 12 months	
Track 1a	
V2.0 PROSPR IC score	• Model accuracy and reproducibility validated and refined with emergent data on lifestyle effects. • Measurements must remain statistically correlated with changes in PROSPR IC score (v2.0). • Demo (v2.0): 20-year mortality or multi-morbidity prediction AUC ≥0.98, 95% CI, R^2 ≥ 0.5. • Similar AUC (±0.05) when analyzing different age groups separately. • Similar AUC (±0.05) when analyzing males and females.
Metrics additional requirements	• Completed targeted analysis in new samples collected from PROSPR lifestyle intervention participants to validate TA2-intervenable biomarkers (identified by Track 2a). Achieved an AUC ≥ 0.70 in predicting lifestyle intervention response and a correlation coefficient ≥ 0.5 between biomarker changes and clinical outcomes. • Completed re-analysis of intervenable biomarkers (identified by TA2-Track 2a) using data shared by Track 2b. Achieving an AUC ≥ 0.80 and a correlation coefficient ≥ 0.5 between biomarker changes and clinical outcomes.
Regulatory compliances	• Provided status report of discussions with the FDA for validated surrogate endpoint designation of PROSPR IC (v2.0).
Track 1b	
In-home PROSPR IC assessment tech (v2.0)	• Capability Demo (v2.0): Data accuracy and consistency: ≥80% correlation between device measurement and clinician assessments. Measurements yielded ≥90%

	consistency over repeated trials. • Reliability: ≥ 95% successful sync rate with wearable devices and sensors, and ≥ 99% uptime. • User experience: user satisfaction rating ≥ 4.8/5.0 on standardized usability scales. Task Success Rate (TSR) >80%, low (2-5 min) Time to Task (TOT). • Coaching feature effectiveness: ≥ 60% of participants maintain their improved PROSPR IC score over the additional year and reduced risk of functional decline, multi-morbidity, and mortality (OR ≥0.70, 95% CI).
PROSPR study (Health ownership)	• Collected and logged data for all participants throughout the 12-month study. • Achieved >80% participant adherence to reporting PROSPR IC score without the coach. • Concluded PROSPR study by the end of Phase IV.
Metrics Additional requirements	• Distributed in-home PROSPR IC assessment tech to TA3 performers for use in clinical trial.
Transition and adoption	• Began the regulatory approval process for the in-home PROSPR IC assessment technology (v2.0) and developed a comprehensive plan to address any remaining regulatory requirements. • Developed commercialization plan for the in-home PROSPR IC assessment technology (v2.0) in collaboration with ARPA-H partners and the ARPA-H Project Accelerator Transition Innovation Office (PATIO). • Initiated the development of an insurance action plan following consultations with the Center for Medicare & Medicaid Innovation (CMMI) and the Centers for Medicare & Medicaid Services (CMS).
TA1 Phase V (Deployment and commercialization) - 12 months	
Track 1a	
Transition and adoption	• Incorporated FDA feedback and submitted the qualification package for surrogate endpoint designation of PROSPR IC (v2.0)
Track 1b	
Transition and adoption	• Completed all regulatory requirements for the finalized prototype of in-home PROSPR IC assessment technology (v2.0). • Maintained ongoing engagement with ARPA-H partners and PATIO on the commercialization plan for in-home PROSPR IC assessment technology (v2.0), including an engagement plan with Executives-in- Residence (XIRs) and Entrepreneurs-in-Residence (EIRs), targeting a consumer cost of around $100.

	• Continued engagement with CMMI and CMS to advance the development of an Insurance Action Plan

TA1 (PROSPR IC to predict 20-year health outcomes)	
Out-of-scope criteria	Track 1a (PROSPR IC): • Single disease prediction/focus. • Proposals that lack DNA-methylation integration with relevant health metrics or omit key metrics from IC subdomains. Track 1b (In-home PROSPR assessment technology): • Technologies that require more than one year for refinement or manufacturing. • Technologies that are not compatible with current wearables/sensors. • Technologies that do not comply with applicable health regulations and standards. • Technologies without integrated data security. (PROSPR study): • Single-site or multi-site centralized trial. • Single lifestyle intervention.

Figure 2. TA1 Timeline

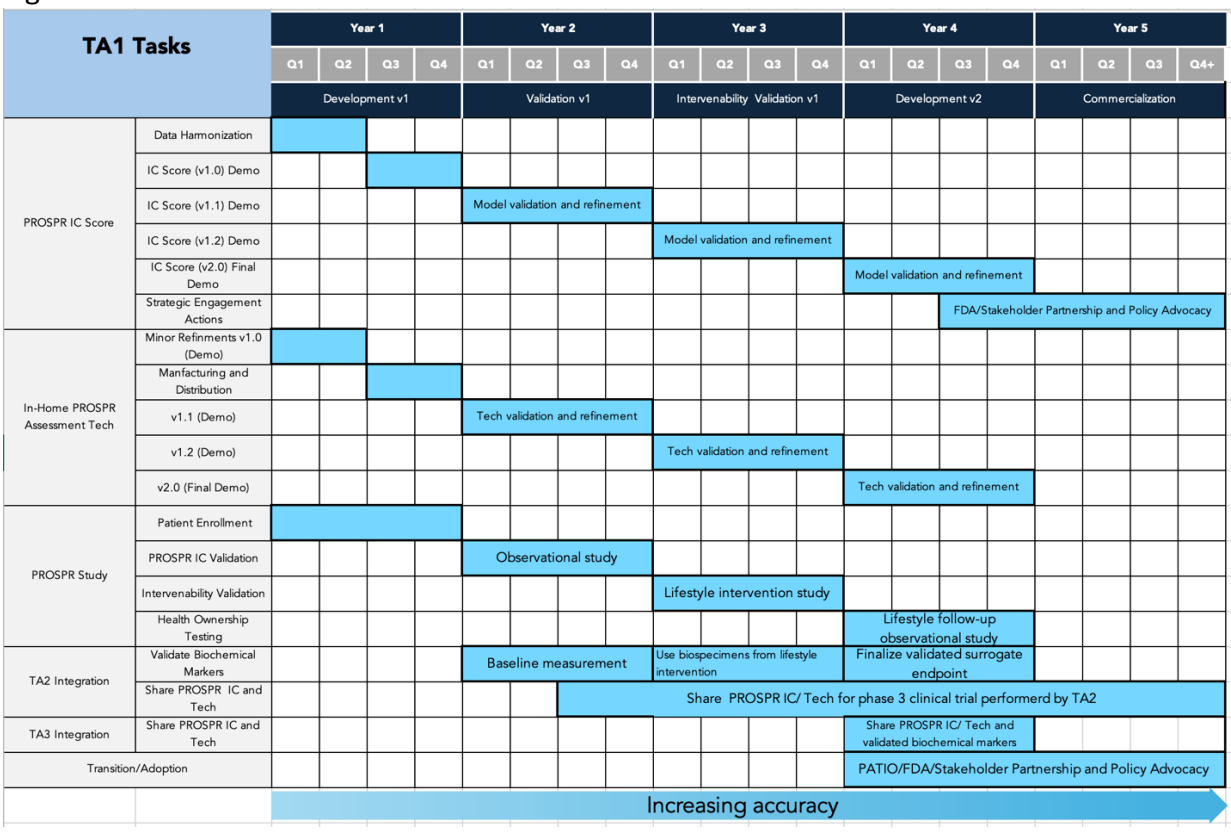


Table 4: Expected metrics per phase in TA2 (Repurposing FDA-approved interventions)

TA2 Phase I (Development and trial design)-12 Months	
Track 2a	
Ingest existing biospecimen and databases	• Obtained ~4-5K blood samples and linked data from existing clinical trials where treatments have demonstrated improvements in multi-morbidity (e.g., rapamycin, metformin, GLP-1, acyclovir, naltrexone, somatostatin, TNFa or other inflammatory inhibitors). • Corresponding clinical data and metadata includes patient demographics, clinical trial details, health status and medical history of participants, outcomes and response to intervention, laboratory results and other relevant data.
Omics analysis	• Completed comprehensive omics sequencing and analysis on at least 70% of the samples collected.
Intervenable biomarkers	• Identified biomarkers show a significant dose-response relationship with the intervention ($p<0.05$) using appropriate statistical method. • Identified biomarkers show consistent directional changes across at least three independent clinical trials • Evaluated the performance of individual biomarkers and multi-marker panels, aiming for an AUC ≥ 0.75 in predicting treatment response and a correlation coefficient ≥ 0.5 between biomarker changes and clinical outcomes.
Metrics additional requirements	• Reported and logged secure storage of all omics data in cloud infrastructure. • Shared data with TA1 and *Track 2b* as it was generated.
Data security and storage	• Data security and protection measures meet industry regulations (e.g., HIPAA, GDPR) and data governance best practices. • Data collected, stored, and managed using industry standard data models or formats (e.g., OMOP, CDSIC, LinkML for electronic health records; FASTA, VCF for genomic data) and APIs. • Data is FAIR (findable, accessible, interoperable, reusable), with a preference for standard and open APIs such as FHIR, the Global Alliance for Genomics and Health (GA4GH) APIs (DRS, Passports, Phenopackets, etc.), or similar access mechanisms.
Track 2b	
Clinical trial design	• Integrated the PROSPR IC score (v1) and in-home PROSPR IC assessment technology (v1) developed by TA1 into the clinical trial design.

	• Designed a three-year decentralized phase randomized clinical trial with two treatment groups (each can be either single drugs or combination therapies) plus controls, involving participants aged 60-65 years. • Developed the study to assess health outcomes, PROSPR score, all-cause mortality, all-cause hospital visits, and multi-morbidity at the end of the trial. • Planned validation of identified intervenable biochemical surrogates in clinical trial participants. • Clinical trial design meets FDA approval requirements. • IRB submission.
Metrics Additional requirements	• Identified a GMP manufacturer for clinical trial
Regulatory compliances	• Conducted at least one meeting with the FDA to review and align DCT study design.
TA2 Phase II (Finalizing development and trial design)- 6 Months	
Track 2a	
Omics analysis	• Completed 100% omics sequencing and analysis
Intervenable biomarkers	• Identified biomarkers show a significant dose-response relationship with the intervention ($p<0.05$) using appropriate statistical method. • Identified biomarkers show consistent directional changes across at least three independent clinical trials • Evaluated the performance of individual biomarkers and multi-marker panels, aiming for an AUC ≥ 0.75 in predicting treatment response and a correlation coefficient ≥ 0.5 between biomarker changes and clinical outcomes.
Metrics additional requirements	• Reported and logged secure storage of all omics data in cloud infrastructure. • Shared data with TA1 and *Track 2b*.
Track 2b	
Clinical trial design	• Obtained IRB approval. • Completed patient recruitment in alignment with the FDA Clinical Trial Guidance. • Distributed PROSPR IC assessment technology (v1) acquired from TA1 performers to participants in the clinical trial.
Metrics additional requirements	• Secured GMP-grade material for clinical trial.
TA2 Phase III (Clinical trial and validation) – 12 months	
Track 2b	
Clinical trial	• Attrition rate < 15%. • Acceptable safety profile with no new or unexpected adverse events, as per FDA guidelines.

Metrics additional requirements	• Data collected and logged for the 12-month study. • IC data and data from surrogate biomarkers validated in phase 3 clinical trials, have been shared with the TA1 team as data is collected.
TA2 Phase IV (Clinical trial and validation) – 12 months	
Track 2b	
Clinical trial	• Concluded Phase 3 clinical study with an attrition rate < 15%. • Acceptable safety profile with no new or unexpected adverse events, as per FDA guidelines.
Metrics additional requirements	• Data collected and logged for the 12-month study • IC data and data from surrogate biomarkers validated in phase 3 clinical trials, have been shared with the TA1 team as data is collected.
Data security and storage	• Data security and protection measures meet industry regulations (e.g., HIPAA, GDPR) and data governance best practices. • Data collected, stored, and managed using industry standard data models or formats (e.g., OMOP, CDSIC, LinkML for electronic health records; FASTA, VCF for genomic data) and APIs. • Data is FAIR (findable, accessible, interoperable, reusable), with a preference for standard and open APIs such as FHIR, the Global Alliance for Genomics and Health (GA4GH) APIs (DRS, Passports, Phenopackets, etc.), or similar access mechanisms.
TA2 Phase V (Clinical trial completion and FDA review) – 18 months	
Track 2b	
Clinical trial	• Concluded phase 3 clinical trial. • Clinical trial design and results meets FDA approval requirements. • Demonstrated significant improvement in the primary health outcomes compared to the control group and individual baseline measurements (PROSPR score, all-cause hospital visits, multi-morbidity). • Achieved improvement in patient-reported outcomes and quality of life metrics compared to the control. • Established an acceptable safety profile with no new or unexpected adverse events as per FDA guidelines. • Achieved a significant correlation ($p < 0.05$) between improved health outcomes and the PROSPR IC score, as well as biochemical surrogates, with a $r \geq 0.5$. • Achieved a high retention rate of study participants ≥85%, including minorities.
Metrics additional requirements	• Data was collected and logged in secure storage.

	• IC data and data from surrogate biomarkers validated in phase 3 clinical trials, have been shared with the TA1 team as data is collected.
Transition and adoption	• Application submitted to FDA

TA2 (Drug repurposing)	
Out-of-scope criteria	Track 2a (Intervenable biomarkers): • RNA-sequencing. • Other biospecimens besides blood. Track 2b (FDA-approved drugs): • Drugs approved for conditions unrelated to aging or age-related diseases, unless there is compelling evidence of their benefit in an aging context. • Drugs known to have severe interactions with other medications commonly used by older adults. • Drugs that require careful monitoring and have a narrow margin between therapeutic and toxic doses. • Clinical trials targeting individuals with chronic conditions or extreme BMI. • Single-site or multi-site centralized trial.

Figure 3. TA2 Timeline

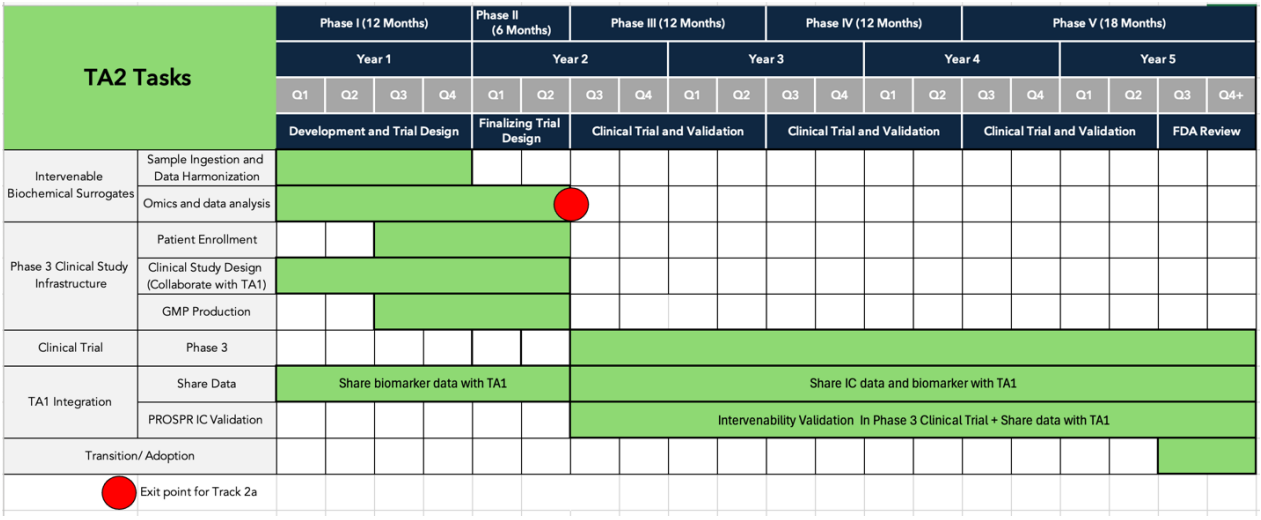


Table 5: Expected metrics per phase in TA3 (Second-generation interventions)

TA3 Phase I (Preclinical) - 18 months

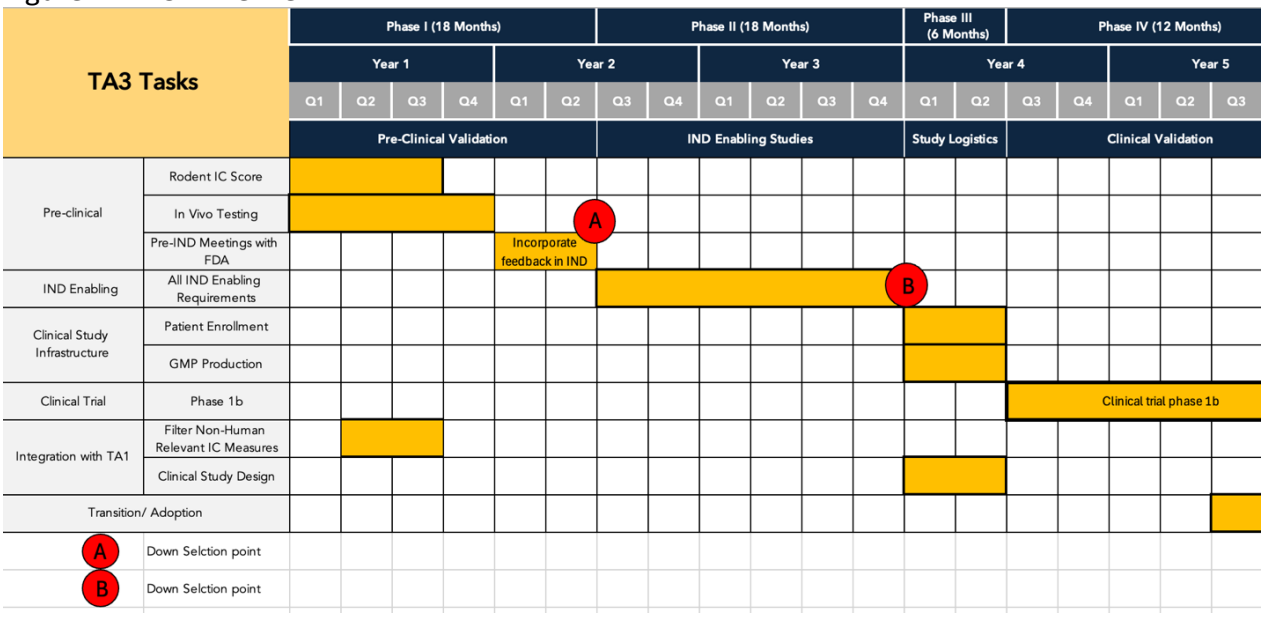
Pre-clinical PROSPR IC	• Established preclinical IC measures that correlate with human PROSPR IC (v1), with $R^2 \geq 0.7$. • Demonstrated sex-related differences in animals. • Demonstrated age-related decrease in IC composite score similar to humans. • Measures are repeatable within the same animal. • Measures are reproducible in ≥ 90% of tested animals.
In vivo preclinical study	• Assessed the effect of second-generation intervention on preclinical IC measures at 2 or more distinct timepoints following treatments. • Intervention maintained or improved at least five health metrics in the preclinical IC model (including cognitive ability, metabolic function, muscle strength, immune function, cardiovascular function, sensory function, etc.) during aging with $p<0.05$. • Demonstrated therapeutic efficacy in ≥ 90% of treated animals, with no significant toxicity observed in major organ systems (e.g. liver, kidney, heart) • Study design included appropriate control groups (e.g., young animals, vehicle-treated) and sufficient sample sizes to reach statistical power of ≥ 80%.
Metrics additional requirements	• TA3 used information shared by TA1 to remove IC measures that are not reflective of human changes during aging.
Regulatory strategy and compliance	• For interventions showing promise, scheduled a pre-IND meeting with the FDA 6 months before the end of Phase I, upon PM approval. Note: For biologics or novel therapies other than small molecules, earlier engagement may be necessary. • Established detailed plans for IND enabling studies, incorporating FDA feedback and ensuring adherence to regulatory guidelines. • Completed pre-IND documentation. • Required interventions showing promise to secure partners for GLP and GMP manufacturing before advancing to Phase II. • Note- for medical devices IDE studies replace IND studies
TA3 Phase II (IND enabling) - 18 months	
IND enabling studies	• Meets/exceeds IND enabling criteria, including safety pharmacology, toxicology, and pharmacokinetics studies. • Achieved a NOAEL (No Observed Adverse Effect Level) that supports the proposed starting dose for clinical trials.

Regulatory strategy and compliance	• Conducted at least three strategic meetings with regulatory consultants to ensure the study design and regulatory submission strategy are robust. • Submitted IND application to the FDA.
TA3 Phase III (Patient recruitment and logistics) - 6 months	
Clinical trial	• Obtained IRB approval. • Completed patient recruitment (participants aged 60-65, no chronic disease present, no extreme BMI), 100% of participants signed the informed consent. • Completed and passed GMP manufacturing, with documentation of 100% compliance and no critical findings. • Adhered to FDA Clinical Trial Guidance. • Collaborated with TA1 and TA2 to incorporate PROSPR IC and biochemical surrogate endpoints in clinical trial design. • Used an electronic data capture system and data analytics tools to support centralized monitoring.
Metrics additional requirements	• Collaborated with TA1 and TA2 to incorporate PROSPR IC and biochemical surrogate endpoints in the clinical trial design, with endpoints defined and documented.
Regulatory strategy and compliance	• Consulted regulatory guidelines and sought early feedback.
TA3 Phase IV (Clinical Trial) - 18 months	
Clinical trial	• Conducted safety and efficacy testing in patient study. • Measured PROSPR IC and biomarkers in clinical trial participants, achieving at least 80% data collection completion rate. • Assessed if the second-generation intervention has the potential to significantly maintain or improve PROSPR IC throughout the trial duration. • Assessed if the second-generation intervention can restore function or improve health outcomes.
Regulatory strategy and compliance	• Continuously assessed and updated risk mitigation strategies throughout the trial, with risk assessments conducted quarterly and mitigation plans updated accordingly. • Consulted regulatory guidelines and sought early feedback from regulatory agencies, with documented consultations and received feedback incorporated into the trial design. • Used an electronic data capture system and data analytics tools to support centralized monitoring, with at least 95% data integrity and real-time monitoring capabilities.
Transition and adoption	• Successfully transitioned to the clinic or larger

	commercial entities

TA3 (Second-generation interventions)	
Out-of-scope criteria	Second-generation interventions: • Interventions with evidence only *in vitro*. • Interventions that require more than 18 months before starting IND-enabling studies. • Interventions that require surgery for administration. • Proposal requesting funding solely for conducting a clinical trial. Preclinical IC measures: • Single-sex rodent studies. • Protocols that require >6 months to establish • Measurements excluding cognitive function. • Genetically modified, disease models, or inbred rodents* * Exceptions to the rodent model proposed may be considered in cases where preliminary data strongly suggests the therapeutic will extend healthspan in non-disease contexts and justification is provided that use of another rodent model is strongly advantageous relative to outbred strains. Diseases or accelerated models will not be considered.

Figure 4. TA3 Timeline



2.3.5 PROSPR DATA SHARING PLAN

Proposers are generally required to share deidentified/sanitized data collected during the project with other PROSPR performers, and potentially other federal agencies. This ensures transparency and collaboration within and beyond the program. Proposers must provide detailed plans for handling data storage and computing needs. This includes addressing

challenges related to managing and processing the data. These plans may be updated as the program progresses, in concurrence with PM and ARPA-H. The Data Management and Sharing Plan (DMSP) should adhere to industry-standard data formats to ensure compatibility and ease

of integration with ARPA-H and other federal agency platforms. The DMSP should also include strategies for situations where sharing data openly might harm the commercial value of the technology. This includes considering how to protect intellectual property or competitive advantage.

3 ELIGIBILITY INFORMATION

3.1 Eligible Applicants

All responsible sources capable of satisfying the Government's needs may submit a proposal to the ISO. Specifically, universities, non-profit organizations, small businesses and other than small businesses are eligible and encouraged to propose to this ISO.

3.1.1 Prohibition on Performer Participation from Federally Funded Research and Development Centers (FFRDCs) and Government Entities

ARPA-H is primarily interested in responses to this solicitation from commercial performers, academia, non-profit organizations, etc. In certain circumstances, FFRDCs and Government Entities will have unique capabilities that are not available to proposing teams through any other resource. Accordingly, the following principles will apply to this solicitation.

FFRDCs and Government entities, including federal Government employees, are not permitted to respond to this solicitation as a prime or sub-performer on a proposed performer team.

If an FFRDC or Government entity has a unique research idea that is within the technology scope of this solicitation that they would like considered for funding, contact this email address: PROSPR@arpa-h.gov.

If an FFRDC or Government entity, including a federal Government employee, is interested in working directly with the Government team supporting the research described by this, the party should contact: PROSPR@arpa-h.gov.

If a potential prime performer believes that an FFRDC has a unique capability without which their solution is unachievable, potential prime performers should be aware that they will have to provide documentation as part of their abstract submittal showing that they have exhausted all other options in order for ARPA-H to consider the inclusion of the FFRDC in the proposed solution.

3.1.2 Non-US Entities

ARPA-H will prioritize awards to entities (organization and/or individuals) that will conduct funded work in the United States. However, non-U.S. entities may participate to the extent that such participants comply with any necessary nondisclosure agreements, security regulations, export control laws, and other governing statutes applicable under the circumstances. In accordance with these laws and regulations, in no case will awards be made to entities organized

under the laws of a covered foreign country [as defined in section 119C of the National Security Act of 1947 (50 U.S.C. Ch 44 § 3059)]; a foreign entity of concern meeting any of the criteria in section 10638(3) of the CHIPS and Science Act of 2022; [an individual that is party to a malign foreign talent recruitment program, as defined in Section 10638(4) of the CHIPS and Science Act of 2022; or entities suspended or debarred from business with the Government.

3.1.3 Award Limitations

While there is statutory language that may suggest ARPA-H is limited in the number of awards it may make to one entity, there are circumstances in which ARPA-H may make more than four awards to a particular person or organization. ARPA-H encourages organizations to submit their research ideas notwithstanding this perceived limitation. Any proposal received will be fairly considered for award and, if it is most advantageous, will be selected for an award.

3.2 System for Award Management (SAM)

A Proposer must have an active registration in SAM (www.sam.gov) for its proposal to be found conforming. Proposers must maintain an active registration in SAM.gov with current information at all times during which a proposal is under consideration and/or a current award from ARPA-H is held. Information on SAM.gov registration is available at SAM.gov.

NOTE: New registrations and renewals may take more than 14 business days to process in SAM. The SAM is independent of ARPA-H and thus ARPA-H representatives have no influence over processing timeframes.

4 SUBMISSION AND EVALUATION PROCESS

The PROSPR selection process is based on the following steps designed to maximize efficiency, transparency, and integrity:

- Eligible entities submit Solution Summary Packages
- Government verifies eligibility and then reviews eligible Solution Summaries to determine whether a full proposal is encouraged or discouraged.
- Proposers are notified whether they are encouraged to submit a full proposal or not.
- Eligible entities submit full proposals.
- The government reviews full proposals to determine conformance to the ISO, including Program scope and minimum requirements.
- The government reviews conforming full proposals against criteria 1-3 and determines the Proposals that are most advantageous. The most advantageous proposals will be selected for award negotiations based on available funding and Program needs.
- Proposers are notified whether a proposal (1) was determined non-conforming and was not considered further; (2) has been selected for award negotiations or

(3) the proposal has not been selected for award negotiations. High-level feedback will be provided to proposers who submit conforming proposals, either verbally or in writing (subject to government discretion).

- In addition to the notices mentioned above, the government may request clarification from any proposer at any stage of the process. Requests for clarification do not allow for proposal revisions.

4.1 Solution Summary Submission Requirement and Guidance

Solution Summary submissions are mandatory. See Appendix B (Solution Summary Format and Instructions).

4.2 Solution Summary and Proposal Submission Information

NOTE: Non-conforming submissions that do not follow ISO instructions may be rejected without further review at any stage of the process.

4.2.1 General. All Solution Summaries and full proposals submitted in response to this solicitation must be submitted in English and must be consistent with the content and formatting requirements of Appendix B (Solution Summary Format and Instructions) and Appendix C (Full Proposal Format and Instructions).

4.2.2 Submission Portal. All Solution Summaries and full proposals shall be submitted via the ARPA-H Solution Submission Portal (https://solutions.arpa-h.gov/). Proposers must register in advance of submissions.

4.3 Solution Summary and proposal Submission Deadlines

4.3.1 The closing date of this solicitation, as established in Section 1, is the final date Solution Summaries will be accepted.

4.3.2 ~~The estimated due date for full proposals is provided in Section 1.~~ The final full proposal due date will be provided at the time of Solution Summary feedback.

4.4 Proprietary Information

Proposers are responsible for clearly identifying proprietary information. Submissions containing proprietary information must have the cover page and each page containing such information clearly marked with a label such as “Proprietary.” Other incorrect markings (e.g., Confidential) will bear no weight.

5 REVIEW AND EVALUATION OF FULL PROPOSALS

5.1 Conforming Proposal Submissions

5.1.1 Conforming submissions contain all requirements detailed in this ISO. Full proposals that fail to include required information will be deemed non-conforming and may be removed from further consideration. To be considered conforming, the proposal must meet the following elements:

- The proposed concept is applicable to the PROSPR Program.
- The Proposer meets the eligibility requirements.
- The proposal meets the submission requirements.
- The proposal meets the content and formatting requirements in the attached Appendices.
- The Proposer's concept has not already received funding or been selected for award negotiations for another funding opportunity (whether from ARPA- H or another government agency).
- The full proposal is submitted by a Proposer that submitted a timely and responsive Solution Summary.

5.1.2 Non-conforming proposal submissions may be removed from consideration. Proposers will be notified of non-conforming determinations via email correspondence if the determination results in the submission not moving forward for further consideration because it is not responsive to this ISO.

5.2 Proposal Evaluation Criteria

The following criteria, listed in descending order of importance, will guide the government's evaluation of Proposals that have been determined to be conforming and thus eligible for further consideration.

5.2.1 Overall Scientific and Technical Merit

The proposed technical approach is innovative, feasible, achievable, and complete. Task descriptions and associated technical elements provided are complete and in a logical sequence with all proposed deliverables clearly defined such that a final outcome that achieves the goal can be expected as a result of award. The proposal identifies major technical risks and planned mitigation efforts are clearly defined and feasible.

In addition, the evaluation will take into consideration the extent to which the proposed intellectual property (IP) rights structure will potentially impact the Government's ability to transition the technology.

5.2.2 Proposer's capabilities and/or related experience

The proposed technical team has the expertise and experience to accomplish the proposed tasks. The proposer's prior experience in similar efforts clearly demonstrates an ability to deliver products/data that meet the proposed technical performance within the proposed budget and schedule. The proposed team has the expertise to manage the cost and schedule. Similar efforts completed/ongoing by the proposer in this area are fully described, including identification of other Government entities.

5.2.3 Budget Analysis

The proposed price is reasonable and consistent with the proposed technical approach. To determine reasonableness, the evaluation may also take into consideration the projected societal impact and value the proposed technical solution offers.

When price and value analysis are inconclusive, a cost realism analysis may be performed to ensure proposed costs are realistic for the technical and management approach, accurately

reflect the technical goals and objectives of the solicitation, the proposed costs are consistent with the proposer's technical approach and reflect a sufficient understanding of the costs and level of effort needed to successfully accomplish the proposed technical approach.

Proposals shall clearly indicate whether resource-sharing is included/proposed.

5.3 EVALUATION AND SELECTION PROCESS

It is the policy of ARPA-H to ensure impartial, equitable, comprehensive proposal evaluations based on the evaluation criteria listed above and to select the source (or sources) whose offer meets ARPA-H's mission objectives and programmatic goals.

ARPA-H will conduct a scientific and technical review of each conforming proposal. All proposal evaluations will be based solely on the evaluation criteria above.

Relative to the evaluation criteria, the Government will evaluate each conforming proposal in its entirety, documenting the strengths and weaknesses. Based on the identified strengths and weaknesses, ARPA-H will determine whether a proposal will be selected for award negotiation. Proposals will not be evaluated against each other during the scientific review process, but rather evaluated on their own individual merit to determine how well the proposal meets the criteria stated in PROSPR ISO.

An award will be negotiated with a proposer(s) whose proposal is determined to be the most advantageous to the Government, consistent with instructions and evaluation criteria specified herein and based on availability of funding.

5.4 Handling Of Selection Sensitive Information

It is the policy of ARPA-H to protect all proposals as selection sensitive information and to disclose their contents only for the purpose of evaluation and only to screened personnel for authorized reasons, to the extent permitted under applicable laws. Restrictive notices notwithstanding, during the evaluation process, submissions may be handled by ARPA-H support contractors for administrative purposes and/or to assist with technical evaluation.

All ARPA-H support contractors are expressly prohibited from performing ARPA-H sponsored technical research and are bound by appropriate nondisclosure agreements. Input on technical aspects of the proposals may be solicited by ARPA-H from non-Government consultants/experts who are strictly bound by appropriate non-disclosure requirements. No submissions will be returned.

5.5 Evaluation and Award General Guidelines

5.5.1 The government reserves the right to select for negotiation all, some, one, or none of the proposals received in response to this ISO. If warranted, portions of resulting awards may be segregated into pre-priced options. In the event the government desires to award only portions of a proposal, negotiations will commence upon selection notification. The government reserves the right to fund proposals in phases with options for continued work, as applicable.

5.5.2 The government reserves the right to request any additional necessary documentation to support the negotiation and award process. The government reserves the right to remove a proposal from award consideration should the parties fail to reach agreement on award terms, conditions, price, and/or if the Proposer fails to provide requested additional information in a timely manner.

5.5.3 In all cases, the government will have sole discretion to negotiate all instrument terms and conditions with selectees. ARPA-H will apply publication or other restrictions, as necessary, if it is determined the research resulting from the proposed effort will present a high likelihood of disclosing sensitive information including Personally Identifiable Information (PII), Protected Health Information (PHI), financial records, proprietary data, any information marked Sensitive but Unclassified (SBU), etc. Any award resulting from such a determination will include a requirement for ARPA-H concurrence before publishing any information or results on the effort. At a minimum, all awards will include a requirement for Performer teams to submit information for review to ARPA-H before publishing.

6 GENERAL REQUIREMENTS AND INFORMATION

6.1 PROPOSING TEAMS

It is expected proposals will involve teams with the expertise needed to achieve the goals for the proposed TA(s). Specific content, communications, networking, and team formation are the sole responsibility of the proposer. Proposers must submit a single, integrated proposal led by a Principal Investigator (PI), under a single prime awardee that addresses all program phases and metrics, as applicable.

Investigators may serve as the Principal Investigator under a single prime proposal. Investigators may participate in multiple proposals within a sub-proposer/sub-awardee. If an entity, proposed as a sub-awardee, is part of multiple successful teams (i.e., award recipients), the Government may establish Associate Performer Agreements (APAs) with the applicable prime awardees. The requirement for an APA will be dependent on the types of services/supplies provided by the sub-awardee, and the specific terms and conditions will be negotiated for each award (e.g., depending on the circumstances, subperformers may not receive compensation in the form of ARPA-H funding for the same services more than once).

Additionally, an institution/organization can only submit one proposal as a Prime. In terms of a university with multiple departments or a private or non-profit organization with multiple departments or divisions, each division/department may be counted as an institution who is eligible to submit a full proposal as the Prime proposer.

6.2 HEALTH DATA PROTECTION AND PRIVACY

- PROSPR program deliverables will NOT include raw health data (e.g. names and other identifying information). Performers must de-identify the health data to be included within any program deliverable.

- Sharing of any program information and/or program deliverables will be controlled and in accordance with the negotiated terms of the resulting Agreement. Program information will be shared during the period of performance, within the PROSPR Government team (e.g. the IV&V team and other key Government stakeholders).
- The associated Intellectual Property rights for all program deliverables will be negotiated with each selected Performer prior to Agreement award. Program information will be controlled in accordance with the Agreement, and all PROSPR deliverables will be appropriately marked as negotiated by the Performer and ARPA- H.

6.3 SCIENTIFICALLY APPROPRIATE REPRESENTATION IN CLINICAL STUDY POPULATIONS

ARPA-H is committed to healthcare access for all those who need it, where they need it. Aging affects all people. Therefore, PROSPR will ensure that all performers have a clear plan to enroll clinical study populations that aim to match the demographics of the US population.

7 ADMINISTRATIVE AND NATIONAL POLICY REQUIREMENTS

7.1 Organizational Conflicts Of Interest (OCI)

Proposers are required to identify and disclose all facts relevant to potential organizational conflicts of interest (OCI) involving the proposer's organization and any proposed team member (proposed subawardee). Although the FAR does not apply to OTs, ARPA-H requires OCIs be addressed in the same manner prescribed in FAR subpart 9.5. Regardless of whether the proposer has identified potential OCIs under this section, the proposer is responsible for providing a disclosure with its proposal. The disclosure must include the proposer's and, as applicable, proposed team members' OCI mitigation plans. The OCI mitigation plan(s) must include a description of the actions the proposer has taken, or intends to take, to prevent the existence of conflicting roles that might bias the proposer's judgment and to prevent the proposer from having unfair competitive advantage. The OCI mitigation plan will specifically discuss the disclosed OCI in the context of each of the OCI limitations outlined in FAR 9.505-1 through FAR 9.505-4. The disclosure and mitigation plan(s) do not count toward the page limit.

7.2 Agency Supplemental OCI Policy

In addition, ARPA-H restricts performers from concurrently providing professional support services, including Advisory and Assistance Services or similar support services (e.g., Project Intermediary Agreement services), and being a technical performer. To address the Agency's policy, performers must complete required information in Appendix C.

7.3 Intellectual Property

Proposers must provide a good faith representation the proposer either owns or possesses the appropriate licensing rights to all intellectual property that will be utilized for the proposed effort. Proposers should appropriately identify any desired restrictions on the Government's use of any Intellectual Property contemplated under the award instrument in question. This includes both noncommercial items and commercial items. Respondents should utilize the prescribed format within the Administrative & National Policy Requirements Document Template (Volume 3 of full proposals as outlined in Appendix C) when asserting restrictions. If no restrictions are intended, then the proposal should state "NONE."

7.4 Animal Subject Research

Award recipients performing research, experimentation, or testing involving the use of animals shall comply with the laws, regulations, and policies on animal acquisition, transport, care, handling, and use as outlined in: (i) 9 CFR parts 1-4, U.S. Department of Agriculture rules that implement the Animal Welfare Act of 1966, as amended, (7 U.S.C. § 2131-2159); (ii) the Public Health Service Policy on Humane Care and Use of Laboratory Animals, which incorporates the "U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training," and "Guide for the Care and Use of Laboratory Animals" (8th Edition)." Proposers must complete and submit the Vertebrate Animal Section worksheet for all proposed research anticipating Animal Subject Research. All Animal Use Research must undergo review and approval by the local Institutional Animal Care Use Committee (IACUC) prior to incurring any costs related to the animal use research.

7.5 Human Subjects Research

All entities submitting a proposal for funding that will involve engagement in human subjects research (as defined in 45 CFR § 46) must provide documentation of one or more current Assurance of Compliance with federal regulations for human subjects protection, including at least a Department of Health and Human Services (HHS), Office of Human Research Protection Federal Wide Assurance. All human subjects research must be reviewed and approved by an Institutional Review Board (IRB), as applicable under 45 CFR § 46 and/or 21 CFR § 56. The entities human subjects research protocol must include a detailed description of the research plan, study population, risks and benefits of study participation, recruitment and consent process, data collection, and data analysis. Recipients of ARPA-H funding must comply with all applicable laws, regulations, and policies for the ARPA-H funded work. This includes, but is not limited to, laws, regulations, and policies regarding the conduct of human subjects research, such as the U.S. federal regulations protecting human subjects in research (e.g., 45 CFR § 46, 21 CFR § 50, § 56, § 312, § 812) and any other equivalent requirements of the applicable jurisdiction.

The informed consent document utilized in human subjects research funded by ARPA-H must comply with all applicable laws, regulations, and policies, including but not limited to U.S. federal regulations protecting human subjects in research (45 CFR § 46, and, as applicable, 21 CFR § 50). The protocol package submitted to the IRB must contain evidence of completion of appropriate human subjects research training by all investigators and key personnel who will be involved in the design or conduct of the ARPA-H funded human subjects research. Funding cannot be used toward human subjects research until ALL approvals are granted.

7.6 Electronic Invoicing and Payments

Performers will be required register in and to submit invoices for payment for invoicing in the Payment Management Services (PMS) system. PMS is a centralized payment and cash management system. ARPA-H other transaction payments are made by PMS, operated by PSC, in accordance with Department of the Treasury and OMB requirements. PMS guidance can be found here: https://pms.psc.gov/training/grant-recipient-training.html.

7.7 Government-Furnished Property/Equipment/Information

Government-furnished property/equipment/information may be provided to selected

Performers. Any instances of GFP/GFE/GFI will be specifically negotiated.

7.8 Associate Performer Agreement

Associate Performer Agreements (APAs) may be required for proposers negotiating an award under the PROPSR Program. An APA is an agreement between non-Federal entities working in furtherance of an ARPA-H agreement that requires the parties to share information, data, technical knowledge, expertise, or resources. See Appendix A for more information related to anticipated APAs in support of the PROSPR Program.

APPENDIX A: Associate Performer Agreement (APA) Information

An Associate Performer Agreement (APA) is an agreement between non-Federal entities or Federal contractors (hereinafter Contractor) working in furtherance of an ARPA-H agreement that requires the parties to share information, data, technical knowledge, expertise, or resources. An Associate Contractor is defined as a party to an APA. ARPA-H is not a party to an APA.

Each resulting award will have the same or similar language:

Submission of a conforming proposal or receipt of an award under an ARPA-H solicitation is not conditioned on Associate Performers or their subcontractors selling, furnishing, or relinquishing proprietary information or confidential data (e.g., intellectual property).

a) It is recognized that success of the research effort depends in part upon the open exchange of information between the various Associate Performers involved in the effort. This is intended to ensure that there will be appropriate coordination and integration of work by the Associate Performers to achieve complete compatibility and to prevent unnecessary duplication of effort. By executing this Agreement, the Performer assumes the responsibilities of an Associate Performer. For this APA, the term Performer includes subsidiaries, affiliates, and organizations under the control of the Performer (e.g., subcontractors).

b) Work under this Agreement may involve access to proprietary information or confidential data from an Associate Performer. Associate Performers and their subcontractor are not required to sell, furnish, or relinquish proprietary information or confidential data developed at private expense unless mutually agreed. To the extent that such data is received by the Performer from any Associate Performer for the performance of this contract, the Performer hereby agrees that any proprietary information or confidential data received shall remain the property of the Associate Performer and shall be used solely for the purpose of the research effort. Only that information received from another performer, in writing, and is clearly identified as proprietary or confidential shall be protected in accordance with this provision. A Performer's obligation to retain such information in confidence will be satisfied if the Performer utilizes the same controls to avoid disclosure, publication, or dissemination of its own proprietary information. The receiving Performer agrees to hold such

information in confidence as provided herein so long as such information is of a proprietary/confidential or limited rights nature.

c) The Performer hereby agrees to closely cooperate as an Associate Performer with the other Associate Performers on this research effort. This involves as a minimum:

- maintenance of a close liaison and working relationship;
- maintenance of a free and open information network with all Government-identified associate Performers;

- delineation of detailed interface responsibilities;
- entering into a written agreement with the other Associate Performers setting forth the substance and procedures relating to the foregoing, and promptly providing the Agreements Officer with a copy of same; and,
- receipt of proprietary information from the Associate Performer and transmittal of Performer proprietary information to the Associate Performers subject to any applicable proprietary information exchange agreements between associate Performers when, in either case, those actions are necessary for the performance of either.

d) In the event that the Performers and the Associate Performer are unable to agree upon any such interface matter of substance, or if the technical data identified is not provided as scheduled, the Performer shall promptly notify the ARPA-H Program Manager. The Government will determine the appropriate corrective action and will issue written guidance to the affected Performer(s).

e) The Performer agrees to insert in all subcontracts hereunder which require access to proprietary information belonging to the Associate Performer, a clause which shall conform substantially to this language, including this paragraph (e).

f) Associate Performers for this research effort include:

Contractor (POC Details)	Technical Area

APPENDIX B: Solution Summary Format and Instructions

A. General Instructions

All Solution Summaries must be submitted in English and use a non-serif font type with a readability like that of Calibri, Avenir Next, Arial, or New Century 11-point font. Smaller non-serif fonts may be used for figures, tables, and charts. Margins may be no less than one inch in width. Solution Summaries are limited to: a cover page, one page for a graphical and written abstract, five pages written summary solution, a Rough Order of Magnitude page, and References. No tables of contents shall be provided. The government may not review pages beyond total; and any Solution Summary submitted that exceeds page limit will only be reviewed at ARPA-H's discretion.

B. Cover Page

The cover page should follow the following format:

Solicitation #	ARPA-H-SOL-125
Solution Summary Title	
Submitter Organization	
Type of Organization	Choose all that apply: Large business, small disadvantaged business, other small business, HBCU, MI, other educational, or other nonprofit
Technical Point of Contact (POC)	Name: Mailing Address: Telephone: Email:
Administrative POC	Name: Mailing Address: Telephone: Email:
Total Estimated Budget	Total: $
Place(s) of Performance	
Other Team Members (subperformers, including consultants) if any	Technical POC Name: Organization: Organization Type:
TA(s) and tracks covered	

C. Graphical and written abstract

The graphical and written abstract page should be a single page before the five-page Solution Summary. The graphical abstract should be a visual representation of the summary solution. The written abstract should include which TA(s) and tracks are being proposed.

D. Proposed Work (5 page maximum, to include requirements in paragraph E)

1. In terminology appropriate for a non-specialized, scientific audience (minimal jargon), explain how the proposed work will address the technical area(s) of the PROSPR program. Explain the concept's potential to be disruptive compared to existing or emerging technologies, including anything with pre-existing funding, and how the proposed approach will go far beyond current commercial capabilities.

2. Describe the final deliverables for the project, one or two key interim milestones, and the overall technical approach used to achieve project objectives. Describe the background, theory, simulation, modeling, experimental data, or other sound engineering or scientific practices or principles that support the proposed approach.

3. TA/track specific information to include:

TA1, track1a: Describe which databases you will use, which health and biochemical measures will be included for consideration in PROSPR IC composite score, how data will be harmonized to account for missing data in individual databases and generate a 20-year prediction of mortality, disease risk, or morbidity.

TA1, track1b: Describe the technology for in-home IC assessment, which measures the technology can assess, what distribution capabilities are, etc. Describe the decentralized approach for the PROSPR study, the lifestyle intervention study, including the use of coaching and which interventions will be used.

TA2, track 2a: Describe which clinical trials will be used and the justification for inclusion and the original indication and whether the trialist have agreed to share the samples. Describe the approach to identify common biomarkers for healthspan based on the trials identified, and which omics will be screened.

TA2, track 2b: Describe the FDA-approved drug proposed and any human or preclinical evidence to warrant repurposing for healthspan extension. Describe the hybrid or decentralized clinical trial approach.

TA3: Describe the preclinical or human evidence demonstrating healthspan extension effect of the proposed intervention. Describe the intervention and whether it is currently ready for use in humans or what is needed first. Describe the approach to test intrinsic capacity in rodents. Describe the approach to conduct a clinical trial to test the intervention in humans.

E. Team organization and capabilities (included in 5-page maximum with paragraph D)

Indicate the roles and responsibilities of the organizations and key personnel that comprise the Performer Team. Provide the name, position, and institution of each key team member and describe in 1-2 sentences the skills and experience they bring to the team. This section should be included in the 5-page written summary solution section.

F. Rough Order of Magnitude (ROM)
Please include a basis of estimate (BOE) to support the proposed project budget, as well as the total project cost including cost sharing, if applicable. The BOE should also include a breakdown of the work by direct labor, labor hours, subcontracts, materials, equipment, other direct costs (e.g., travel), profit, cost sharing, and any other relevant costs. Proposers must ensure the BOE encompasses all applicable costs and should modify the above to best reflect the Proposer's expected costs. The BOE does not count toward the page limit.

APPENDIX C: Full Proposal Format and Instructions

1. General Instructions

a. All Proposals must be submitted in English and use a non-serif font type with a readability like that of Calibri, Avenir Next LT Pro Light, Arial, or New Century 11-point font. Smaller non-serif fonts may be used for figures, tables, and charts. Margins may be no less than one inch in width.

b. Documents must be clearly labeled with the ISO number, proposer organization, and proposal title/proposal short title (in the header of each page). Use the following Title Format: "TA #, Volume I_XYZ Institution", "Volume II_XYZ Institution", "Volume II Supporting Documents", etc. Proposals must address one specific Technical Area.

c. Conforming full proposals should consist of three volumes as follows plus three attachments as described:

- Appendix D: Volume I, Technical and Management Proposal,
- Appendix D: Volume II, Cost Proposal, and
- Appendix D: Volume III, Administrative and Policy Requirements Submission
- Attachment: Cost Spreadsheet
- Attachment: Statement of Work (SOW)
- ~~Attachment: Rare Disease Prioritization Spreadsheet (applies to TA1 & TA2)~~

2. Summary of Full Proposal Requirements, including page limits:

Volume I, Technical and Management Proposal	
Volume Element	Page Limit
Cover Page	1
A. Executive Summary	30
B. Solution Fit with PROSPR	
C. Technical Plan	
D. Management Plan	
E. Capabilities	
F. Commercialization Plan	
G. Statement of Work (SOW)	N/A, use provided template/format
H. Schedule and Milestones	N/A use provided template/format in the Model OT
I. Data Management and Sharing Plan	N/A (estimated 2 pages)

(DMSP)	
J. References	N/A

Volume II, Cost Proposal	
Volume Element	Page Limit
A. Cover Page	1
B. Cost Proposal Spreadsheet(s), including for subcontractors at any tier	N/A, use provided template/format
C. Cost and Pricing Data Support	N/A
D. Model OT with proposed Changes (Recommended, but not required if (e.g., no edits suggested.)	N/A, use Model OT provided
Volume III, Administrative and Policy Requirements Submission	
Volume Element	Page Limit
Cover Page	1
A. Team Member Identification	N/A, use provided template/format
B. OCI Affirmations and Disclosure	
C. Research Security Disclosure	
D. Novelty of Proposed Work	
E. Intellectual Property (IP)	
F. Technical Data and Computer Software	
G. Patents	
H. Ability to Meet Programmatic Goals with IP/Patent Implications	
I. Human Subjects Research	
J. Representations Regarding Unpaid Delinquent Tax Liability or a Felony Conviction Under any Federal Law	
K. Software Component Standards	
L. Cybersecurity	

3. Volume I: Technical and Management Proposal

a. The maximum page count for Volume I is thirty (30) pages, with exclusions as noted in the table above. ARPA-H encourages conciseness to the maximum extent practicable. No other supporting materials may be submitted for review. Note that while the Government's evaluation of Volume I is limited to the sections included in the page count limitations, it will be reviewing all sections. The other documents may be used to cross-check the proposal and will also inform feedback for proposers whose full proposals are determined most advantageous and selected for award negotiations.

b. At the bottom of Volume I information is a summary of proposal elements recommended for inclusion in proposals based on each TA and track proposed, as well as recommendations for all proposals. These elements should be incorporated into the 30-page Volume I submission however the proposer deems most appropriate.

c. Volume I should include the following components:

1) Cover Page

1	Solicitation #	ARPA-H-SOL-25-125
2	Full Proposal Title	
3	Technical Approach (TA) Selection	
4	Prime Awardee/entity submitting the proposal	
5	Unique Entity Identifier of primer proposer/awardee (UEI)	
6	Type of Organization and website URL if applicable	Choose all that apply: Large Business, Small Disadvantaged Business, Other Small Business, Historically Black Colleges and Universities (HBCUs), Minority Institution (MI), Other Educational or Other Non-Profit (including non- educational government entities) (NOTE: The Small Business Administration's (SBA) size standards determine whether or not a business qualifies as small.). Size standards may be found here: https://www.ecfr.gov/current/title-

		13/chapter-I/part-121#121.201
7	Date of Submission	
8	Technical Point of Contact (POC)	Include salutation Last Name: First Name Mailing Address: Telephone: Email:
9	Administrative POC	Include salutation Last Name: First Name Mailing Address: Telephone: Email:
10	Other Team Members (sub-performers, including consultants) if applicable.	Technical POC Name: Organization: Organization Type:
11	Total funds requested from ARPA-H, and the amount of cost share (if any)	Total: $
12	Place(s) of Performance	

2) Executive Summary. Provide a synopsis of the proposed project including answers to the following questions:

- What is the proposed work attempting to accomplish or solve?
- How is it done today? What are the limitations of present approaches?
- What are the key technical challenges in your approach, and how do you plan to overcome these?
- What is new about your approach? Why do you think you can be successful at this time?
- Who cares? If you succeed, what difference will it make?
- What are the risks? Identify any risks that may prevent you from reaching your objectives as well as any risks the program itself may present. Please also describe plans to mitigate these risks at a high level.
- How much will your project cost?
- What are your milestones to check for success consistent with PROSPR metrics
- To ensure equitable access for all people, how will cost, accessibility, and user experience be addressed in your project?
- How might this program be misperceived or misused (and how can we prevent that from happening)?

3) Solution Fit with PROSPR

Clearly describe what the team is trying to achieve and the difference it will make (qualitatively and quantitatively) if successful relative to PROSPR's vision and metrics. Provide an overview of the current and previous research and development (R&D) efforts related to the proposed research and identify any challenges associated with such efforts including any scientific or technical barriers encountered during such efforts or challenges in securing sources of funding as applicable. Describe the innovative aspects of the project in the context of existing capabilities and approaches clearly delineating the uniqueness and benefits of this project in the context of the state of the art, alternative approaches, and other projects from the past and present. Describe how the proposed project is revolutionary and how it significantly rises above the current state-of-the-art. Describe the deliverables associated with the proposed project as well as how the project will integrate into existing clinical workflows and successfully improve patient care.

4) Technical Plan

Outline and address technical challenges inherent in the approach and possible solutions for overcoming potential problems. This section should provide appropriate measurable milestones (quantitative if possible) at intermediate stages of the program to demonstrate progress, a plan for achieving the milestones, and a simple process flow diagram of the final system concept. The technical plan should demonstrate a deep understanding of the technical challenges and present a credible (even if risky) plan to achieve the program goal. Discuss mitigation of technical risk.

5) Management Plan

a) Provide a summary of the expertise of the team, including any subperformers, and key personnel who will be doing the work. A Principal Investigator (PI) for the project must be identified, along with a description of the team's organization, including the breakdown by TA. All teams are required to identify a Project Manager.

b) Provide a clear description of the team's organization including an organization chart that includes, as applicable:
- the programmatic relationship of team members
- the unique capabilities of team members
- the task responsibilities of team members
- the teaming strategy among the team members and
- key personnel with the amount of effort to be expended by each person during each year.

c) Provide a detailed plan for coordination, including explicit guidelines for interaction among collaborators/sub-performers of the proposed effort.

Include risk management approaches. Describe any formal teaming agreements required to execute this program.

6) Capabilities
Describe organizational experience in relevant subject area(s), existing intellectual property, specialized facilities, and any Government-furnished materials or information. Discuss any work in closely related research areas and previous accomplishments.

7) Commercialization Plan
Briefly outline your current understanding of your technologies target market and the size of that market. Identify 2-3 key competitive technologies operating in the market and their limitations. Outline ownership plans for existing and future IP across the team. Identify ideal partners (e.g. private industry, investors, etc.), that may be pursued to secure funding, manufacturing, and marketing following the award period. Plans shall include completion of the following table:

IP Category (Trade Secret, Patent, or Data)	USPTO# and Docket # and Application #	IP Title	Summary of Intended Use in Project	Asserted rights for Government related to PROSPR Program (Government Purpose, Unlimited, Limited.)	Name of Person or Entity Asserting Restrictions (who owns the IP?)	Funding Source (Federal Government, other, or Mix**)

8) Statement of Work

a) The SOW should provide a detailed task breakdown, citing specific tasks for each TA and their connection to the milestones and program metrics. Each Phase of the program should be separately defined. The SOW must not include proprietary information. Please note the technical proposal must stand on its own as the SOW cannot be used to supplement the 15 pages of the technical proposal.

b) For each task/subtask, provide:

- A detailed description of the approach to be taken to accomplish each defined task/subtask.
- Identification of the primary organization responsible for task execution (prime awardee, sub-awardee(s), by name).

- A measurable milestone, i.e., a deliverable, demonstration, or other event/ activity that marks task completion. Include completion dates for all milestones. Include quantitative metrics.
- A definition of all deliverables (e.g., data, reports, software) to be provided to the Government in support of the proposed tasks/subtasks.

c) It is recommended the SOW be developed so that each TA and phase of the program is separately defined.

9) Schedule and Milestones
Using the provided format in the Model OT, provide a detailed schedule showing tasks (task name, duration, work breakdown structure element as applicable, and performing organization), milestones, and the interrelationships among tasks. The task structure must be consistent with that in the SOW. Measurable milestones should be clearly articulated and defined in time relative to the start of the project.

10) Data Management and Sharing Plan (DMSP)

a) This is recommended to be no more than 2 pages.

b) The DMSP shall include all information included in the 6-Element plan format recommended by the National Institutes of Health (to view the 6-Element suggested format visit: https://grants.nih.gov/grants/forms/data-management-and-sharing-plan-format-page). Note this plan will not be specifically evaluated against Criteria 1-3 but will likely be used to inform feedback for proposals who are selected for award negotiations.

c) The plan shall demonstrate, on a high level for the proposal stage, how health data will be sourced and preserved while ensuring the integrity of the data collected throughout the period of performance. The plan shall account for addressing that health data that will be collected by Performers in the PROSPR Program will remain confidential and not be subject to secondary analysis or sharing (outside of the government) without the explicit consent of the health data owner.

11) References
Add a list with the cited literature.

12) Technical Proposal elements

TA1. PROSPR IC to predict 20-year health outcomes
TA1 aims to collect empirical evidence that lifestyle interventions can improve or maintain general wellness in relatively healthy individuals. This initiative aims to enable individuals and healthcare providers to detect early health changes and support improved long-term health outcomes. Assuming proposal plans and evidence of successful implementation are similar,

priority will be given to proposals that cover both tracks.

Track 1a (PROSPR IC) proposal should:

- Demonstrate the team's capability in managing large-scale clinical and omics data, including plan for data mining, harmonization, and health trajectory modeling.
- Describe any prior work or methodologies utilized in health trajectory modeling and outcomes.
- If applicable, provide details about the model including the type of data used, the number of participants whose data was used to develop the model, maximum level of model accuracy achieved.
- Explain how existing databases would be leveraged to supplement the data already collected and enhance the model, if applicable.
- Justify cost per unit of data generated.
- Describe which longitudinal studies will be included, which IC or biochemical measures will be included for assessment in the composite score.
- Outline a plan to make inferences about missing components of the overall IC composite score.
- Provide evidence of access to the longitudinal data proposed to incorporate into their analysis.

Note: Performers with access to at least three of the required longitudinal studies (see Table 3) will be considered advantageous.

Track 1b (in-home PROSPR IC assessment technology) proposal must:

- Describe the current Technology Readiness Level (TRL) of this device/kit.
- Detail features of the technology and how it will connect to existing wearables and sensors to enhance data collection and monitoring health metrics (list compatible existing wearables and data synchronization method).
- Explain the parameters that will be used to assess intrinsic capacity and overall health including thresholds.
- Describe the percentage accuracy of the technology and provide data to support.
- Describe any testing or validation processes that have been undertaken to ensure reliability.
- Outline strategies for personalizing user guidance based on individual data and preference.
- Outline quality assurance processes in place to ensure the reliability and performance of the technology being developed (testing protocols, validation procedures and metrics for success).
- Provide plans for commercialization, targeting a cost of ≤ $100 per consumer by the end of the program.
- Describe plans for securing insurance coverage to enable early health intervention and preventive care.
- Proposals must demonstrate the team's capability in technology development.
- Highlight what makes the technology novel or innovative compared to existing

technologies.
- Address data management and sharing protocols.
- Outline plans for a three-year decentralized or hybrid longitudinal study (PROSPR Study) with three phases: 1. observational phase, 2. multimodal lifestyle intervention trial, 3. observational follow-up; include methods for collecting intrinsic capacity measures and biospecimens.
- Describe the recruitment strategies.
- Include plans addressing attrition to ensure ~1K participants complete the study and outline clear retention strategies, especially for younger participants and minority groups in their proposal.
- Describe inclusion and exclusion criteria.
- Include a power analysis to determine sample size.
- Detail participant retention strategies for each phase of the study, with specific plans for maintaining engagements of minority and younger participants.
- Clearly define lifestyle intervention details, intervention duration and follow up periods.
- Detail clinical data analysis plan, including approaches for handling missing data.
- Proposers seeking to extend an existing study must provide a comprehensive overview of the study's characteristics, including details on the existing data and biospecimens available for analysis.

TA2. Repurposing FDA-approved interventions
The PROSPR program will accelerate the clinical development of two repurposed drugs with a high safety profile and demonstrated efficacy to restore function and prevent decline.

Track 2a. (Intervenable biomarkers). All proposals should include the following information:

- Provide a detailed list of existing clinical trials planned for omics analysis.
- Include rationale for selecting each trial and provide evidence that selected clinical trials improved multi-morbidity.
- Include letters from trialists confirming willingness to share stored blood samples for omics analysis.
- Provide a power analysis to determine sample sizes needed for biochemical surrogate discovery.
- Demonstrate the team’s capability in managing big data, multi-omics analysis, as well as the ability to mine, harmonize data, and develop biomarkers.
- Detail the omics platforms to be used (e.g. proteomics, metabolomics, lipidomics).

Track 2b (FDA-drug repurposing). All proposals should include the following information:

- Describe the repurposed drug, its original indication, and its effects on relevant biological pathways.
- Provide a detailed rationale for the drug’s expected effectiveness.
- Present evidence of the drug’s efficacy from existing studies or preliminary data.
- Summarize the drug’s safety profile, including known side effects and their impact on the new use.
- Summarize preclinical and clinical data supporting the drug’s potential efficacy and

safety, including any modifications or new formulations that were used.
- Explain any new or updated understanding of the drug's mechanism of action.
- Detail the regulatory pathway for repurposing.
- Detail the plan for manufacturing the drug, including any changes in production processes or quality control measures.
- Include an analysis of the risk-benefit ratio for prolonged use in older adults and any known drug-drug interactions, particularly with medications common in elderly populations.
- Specify any changes in dosage or any modifications to drug formulation for the new use.
- Outline the design of phase 3 decentralized clinical trial including procedures for remote safety monitoring, adverse event reporting, technology and infrastructure, endpoints (primary, secondary and experimental), patient populations, dosing regimens, etc. Note: endpoints that are specific to the intervention should be used in addition to IC.
- Provide a power analysis to determine the required sample size for the primary endpoints.
- Outline clear retention and recruitment strategies, especially for minority groups.
- Include plans for meeting FDA or other regulatory body guidelines for repurposing drugs.

Note: Priority will be given to proposals that comprehensively characterize the drug's safety and efficacy, detail its mechanism of action, and include robust *in vivo* and human evidence.

TA3. Second-generation interventions

The PROSPR program will catalyze the development of novel interventions to prevent health decline, restore function, and enhance overall health. Proposers will be required to test the efficacy and safety of their intervention using a thorough assessment of health measures developed in outbred rodents. Priority will be given to proposals with a detailed characterization profile, known mechanism of action, and robust behavioral and functional *in vivo* data. Proposals based solely on *in vitro* data or those requiring high-throughput screening will not be considered.

All proposals should:

- Describe known mechanism of action, including how the intervention affects aging-related pathways or processes. Note: May include standalone therapy or combination therapy.
- Include data demonstrating the pleiotropic effect of the second-generation intervention.
- Provide available data demonstrating significant functional and behavioral improvements in aged or frail animal models (e.g. improvements in lifespan, healthspan or frailty index or improvements in both cognitive and physical function).
- Provide evidence of improved health and function in response to therapeutic intervention in at least two tissues or organ systems.
- All preliminary data must include the number of times independent experiments were

performed, statistical information, and number of animals in each study (N).
- Show long-term effect by measurements at multiple time points.
- Show significant modulation of target pathway(s).
- Provide data demonstrating the optimization of specificity and efficacy for the second-generation intervention to enhance its therapeutic potential.
- Show that the optimized modality and route of administration enable stable, long-term effects while reducing risk.
- Highlight what makes the intervention novel or innovative compared to existing therapies.
- Outline the study design plan, including animal models, dosing regimens, and endpoints to be evaluated.
- Outline the development plan for advancing the intervention from preclinical to clinical stages, including any additional studies or modifications needed.
- Include an analysis of the risk-benefit ratio for prolonged use in older adults and any known drug-drug interactions, particularly with medications common in elderly populations.
- Provide data on the safety profile of the intervention, including any observed side effects or adverse reactions in preclinical studies.
- Include a plan for scalability of clinical doses with consistent quality at a low cost.
- Describe plans for entry into appropriate FDA regulatory programs and processes.

The PROSPR program will support the development of preclinical health measures in rodents. These measures aim to enhance the likelihood of translating findings into clinical applications.

All proposals should:

- Provide rational for the chosen rodent and strain.
- Demonstrate the team's capability to generate preclinical health measures.
- Include a power analysis and justification for the number of rodents being tested.
- Describe the criteria and benchmarks for standardizing the preclinical health measures.
- Describe strategies for ensuring data integrity and reproducibility.
- Describe strategy for exclusion of preclinical measures that are not relevant to human IC as data from TA1 becomes available.
- Describe strategy for testing responsiveness of IC score to various positive and negative interventions.
- Address any regulatory and ethical considerations related to the development and use of the preclinical health measures.
- Provide technical details on any automation technology and process being used.

A. For performers who pursue cell therapy or organelle therapy, proposal must include:

- Source justification: Provide rational for the chosen cells source (e.g., iPSCs, adipose tissue-MSCs, etc.)/organelle isolation for mass production and differentiation.
- Technical plan: Describe methods to verify cell-specific/organelle-specific characteristics and optimize conditions for therapeutic potential (e.g., enhancing

immunosuppressive function, homing capability, post-engraftment survival, bioactivity, internalization, biodistribution, and targeting).

- Administrative route and scaffold: Describe the appropriate route of administration and a biocompatible scaffold for cell delivery with reduced risk.
- Regenerative capacity testing: Outline the plan to assess regenerative and repair capabilities.

B. Proof-of-concept data required:

- Cell product quality: Demonstrate purity and percent viability after storage of finished cell product. For engineered cells, data must confirm genomic stability, absence of mutations and plasmid integration into the reprogrammed cells.
- Efficacy and durability in small animals.
- Safety data in small animals (e.g. absence of tumorigenicity, immune rejection, etc.).
- Scalability plan: Discuss how cells will be produced consistently, at low cost, and in quantities sufficient for clinical use. Identify potential GLP and cGMP manufacturing partners.

4. Volume II: Cost Proposal

There is no maximum page count for Volume II. The Cost Proposal shall be comprised of the editable Excel Cost Proposal spreadsheet and associated supporting materials ideally provided in a single attachment (e.g., Adobe pdf) led by a Cover page as follows.

a. Cover Page

1	Solicitation #	ARPA-H-SOL-25-119
2	Full Proposal Title	
3	Technical Approach (TA) Selection	
4	Prime Awardee/entity submitting the proposal	
5	Unique Entity Identifier of primer proposer/awardee (UEI)	
6	Type of Organization and website URL if applicable	Choose all that apply: Large Business, Small Disadvantaged Business, Other Small Business, Historically Black Colleges and Universities (HBCUs), Minority Institution (MI), Other Educational, or Other Non-Profit (including non-educational government

		entities) (NOTE: The Small Business Administration's (SBA) size standards determine whether or not a business qualifies as small.). Size standards may be found here: https://www.ecfr.gov/current/title-13/chapter-I/part-121#121.201
7	Technical Point of Contact (POC)	Include salutation Last Name: First Name: Mailing Address: Telephone: Email:
8	Administrative POC	Include salutation Last Name: First Name: Mailing Address: Telephone: Email:
9	Other Team Members (sub-performers, including consultants) if applicable and type of organization for each	Technical POC Name: Organization: Organization Type:
10	Total proposed cost separated by base and option(s) (if any)	
11	Name, address and telephone number of the proposer's cognizant auditor (as applicable)	
12	Date proposal was submitted	
14	Proposal validity period (Minimum of 120 days)	

b. Cost Proposal Spreadsheet

1) ARPA-H Standard Excel Cost Proposal Spreadsheet (See Attachments). All tabs and tables in the cost proposal spreadsheet should be developed in an editable format with calculation formulas intact to allow traceability of the cost proposal. The cost proposal spreadsheet must be used by the prime organization and all subcontractors at any tier.

2) While the prime proposer is ultimately responsible for submission of all required documents, subcontractor cost proposal spreadsheets may be

submitted directly to the Government by the proposed subcontractor via email to PROSPR@ARPA-H.gov. Subcontractor proposals should include Interdivisional Work Transfer Agreements or similar arrangements between the awardee and divisions within the same organization as the awardee.

c. Cost and Pricing Data Support

1) In addition to using the cost proposal spreadsheet, the cost proposal must include documentation to support the proposed price/budget. Supporting documentation must be in sufficient detail to substantiate the summary cost estimates and should include a description of the method used to estimate costs (e.g., vendor quotes). For indirect costs provide the most current indirect cost agreement (e.g., Colleges and Universities Rate Agreement, Forward Pricing Agreement, Provisional Billing Rates, etc.).

2) Cost and pricing support may also facilitate a value analysis by the Government through information other than detailed cost and pricing data. Proposers are encouraged to include information related to value-added resources or conditions that are not immediately obvious in the Cost Proposal Spreadsheet or the traditional forms of cost and pricing support information like vendor quotes (e.g., intended intellectual property terms and conditions with perceived future value).

d. Model OT

Proposers may suggest edits to the model OT for consideration by ARPA-H and provide a copy of the model OT with track changes (i.e., 'Redlines') as part of the full proposal package. Proposers must include comments providing rationale for any suggested edits of a non-administrative nature. Suggested edits may be rejected or negotiated at ARPA-H's discretion.

Submission of proposed edits to the Model OT will facilitate more efficient negotiations.

5. Volume III: Administrative & National Policy Requirements Document Template

- The Administrative and National Policy Requirements document must be completed in full. Do not delete any portion of this document.
- All pages shall be formatted for printing on 8-1/2 by 11-inch paper with 1-inch margins and font size not smaller than 11-point. Font sizes of 8- or 10-point may be used for figures, tables, and charts. There is no page limit for this document.
- The Administrative and National Policy Requirements document must be in .pdf, .odx, .doc, or .docx formats. Submissions must be written in English.

a. Cover Page

1	Solicitation #	ARPA-H-SOL-25-119
2	Proposal Title	
3	Proposer Organization	
4	Technical Point of Contact (POC)	Name: Address: Telephone: Email:
5	Administrative POC	Name: Address: Telephone: Email:
6	Date of Proposal Submission	
7	Proposal Validity Period (minimum 120 days)	

b. Team Member Identification

[Provide a list of all team members including the prime, subawardee(s) (including consultant(s)), as applicable. Identify specifically whether any are a non-US organization or individual. Use the following format for this list. Note: Consultants (e.g., 1099s) are considered subperformers and must be listed.]

PRIME		
Individual Name:	Organization:	Non-U.S. Organization: ☐ Yes ☐ No Non-U.S. Individual: ☐ Yes ☐ No
SUBAWARDEES/CONSULTANTS		
Individual Name:	Organization:	Non-U.S. Organization: ☐ Yes ☐ No Non-U.S. Individual: ☐ Yes ☐ No
Individual Name:	Organization:	Non-U.S. Organization: ☐ Yes ☐ No Non-U.S. Individual: ☐ Yes ☐ No

c. Organizational Conflict of Interest Affirmations and Disclosure

[In accordance with the ISO, provide the following information.]

1) Are any of the proposed individual team members or their respective organizations (whether prime or subawardee or consultant) currently providing Systems Engineering Technical Assistance (SETA), Partnership Intermediary Agreement (PIA) or similar support to ARPA-H?

☐ No ☐ Yes

2) Did any of the proposed individual team members or their respective organizations (whether prime or subawardee or consultant) provide SETA or similar support to ARPA-H within one calendar year of this proposal submission?

☐ No ☐ Yes

[If you answered "Yes" to c.1) OR c.2), provide the following information for each applicable team member:

- The name of the ARPA-H office receiving the support;
- The prime contract number;
- Identification of proposed team member (subawardee, consultant) providing the support; and an OCI mitigation plan.

3) Are there any other potential Organizational Conflicts of Interest involving any of the proposed individual team members or their respective organizations (whether prime or subawardee or consultant)?

☐ No ☐ Yes

[If yes, provide the following information for each applicable team member:
Identification of applicable team member; and
An OCI mitigation plan.]

d. Research Security Disclosure

[In accordance with National Security Presidential Memorandum (NSPM)-33 and the associated White House Office of Science and Technology Policy Implementation Guidance[1], which requires certain individuals to disclose potential conflicts of interest (COI) and commitment (COC), PIs and other senior/key personnel[2] that will serve as prime and subawardees are required to complete the Current and Pending (other) Support Common Form as well as the Biographical Sketch Common Form. These forms can be found at: https://www.nsf.gov/bfa/dias/policy/nstc_disclosure.jsp]. Existing forms/formats that contain the same information may also be used.

1) In populating these forms, the following is required for each PI and other Senior/Key Personnel (whether they are supporting the prime or a subawardee (at any tier)).

- Other organizational affiliations and employment
- Other positions and appointments[3]

- Participation in any foreign government-sponsored talent recruitment program(s)[4]
- Current and pending support/Other support. For researchers, "Other Support" includes all resources made available to a researcher in support of and/or related to all of their professional R&D efforts, including resources provided directly to the individual rather than through the research organization, and regardless of whether or not they have monetary value (e.g., even if the support received is only in-kind, such as office/laboratory space, equipment, supplies, or employees). This support includes:

    - All resources made available, or expected to be made available, to an individual in support of the individual's research and development efforts, regardless of (i) whether the source is foreign or domestic; (ii) whether the resource is made available through the entity applying for a research and development award or directly to the individual; or (iii) whether the resource has monetary value;
    - In-kind contributions requiring a commitment of time and directly supporting the individual's research and development efforts, such as the provision of office or laboratory space, equipment, supplies, employees, or students. This includes resource and/or financial support from all foreign and domestic entities, including but not limited to, (i) gifts provided with terms or conditions, (ii) financial support for laboratory personnel, and (iii) participation of student and visiting researchers supported by other sources of funding; and
    - Private equity, venture, or other capital financing.

2) For consultants, please additionally list the following (Note: current, pending, and other support not required):

- Other organizational affiliations and employment
- Other positions and appointments
- Participation in any foreign government-sponsored talent recruitment program(s)

3) Foreign Participation

a) Do any members of the proposed team have any contracts associated with participation in programs sponsored by foreign governments, instrumentalities, or entities, including foreign government-sponsored talent recruitment programs? If yes, please provide a list of contracts and the nature of the sponsorship.

☐No ☐ Yes

b) Do any members of the proposed team receive direct or indirect support (including, but not limited to, financial) that is funded by a foreign government-sponsored talent recruitment program, even where the support is provided through an intermediary and does not require membership in the foreign government- sponsored talent recruitment program. If yes, please provide a list of individuals and the nature of the support received.

☐ No ☐ Yes

c) Do any members of the proposed team have/participate in any other foreign government sponsored or affiliated activities. In accordance with 42 USC § 19232, individuals are prohibited from being a party in a malign foreign talent recruitment program.

☐ No ☐ Yes

d) Do any of the proposed individual team members or their respective organizations (whether prime or subawardee or consultant) participate in any foreign government-sponsored talent recruitment program(s)?

☐ No ☐ Yes

By submitting this document to ARPA-H, you are certifying that the information provided in this section is current, accurate, and complete. This includes, but is not limited to, information related to current, pending, and other support (both foreign and domestic) as defined in 42 U.S.C. §6605.

By submitting this document to ARPA-H, you are also certifying that, at the time of submission, no members of the proposed team are a party in a malign foreign talent recruitment program.

By submitting this document to ARPA-H, you acknowledge that misrepresentations and/or omissions may be subject to prosecution and liability pursuant to, but not limited to, 18 U.S.C. §§287, 1001, 1031 and 31 U.S.C. §§3729-3733 and 3802.

e. Novelty of Proposed Work

[Performers shall not receive alternative funding for the same purposes as an agreed upon ARPA-H award. At the discretion of the program team and the Agreement Officer, additional reporting may be required.]

Has the proposed work been submitted to any other Government solicitation?

☐ No ☐ Yes

If yes, provide the following information:

Solicitation number _____
Agency/Office _____
Proposed work has already received funding or a positive funding decision. ☐ No ☐ Yes ☐ Decision pending

f. Intellectual Property (IP)

[Note: The Government will assume unlimited rights to all IP not explicitly identified as restricted in the proposal.]

g. Technical Data and Computer Software

Are you asserting any IP restrictions on any technical data or computer software that will be delivered to the Government?

☐ No ☐ Yes

[If yes, list all anticipated proprietary claims to results, prototypes, deliverables, or systems supporting and/or necessary for the use of the proposed research, results, prototypes and/or deliverables. Provide a short summary for each item asserted with less than unlimited rights that describes the nature of the restriction and the intended use of the intellectual property in the conduct of the proposed research. Use the following format for these lists.]

NONCOMMERCIAL				
Technical Data and/or Computer Software To be Delivered with Restrictions	Summary of Intended Use in the Conduct of the Research	Basis for Assertion	Asserted Rights Category	Name of Person Asserting Restrictions

COMMERCIAL				
Technical Data and/or Computer Software To be	Summary of Intended Use in the Conduct	Basis for Assertion	Asserted Rights Category	Name of Person Asserting

Delivered with Restrictions	of the Research			Restrictions

h. Patents

Does the proposed effort involve using patented inventions that are owned by or assigned to the proposing organization or individual?

☐ No ☐ Yes

[If yes, provide documentation proving ownership or possession of appropriate licensing rights to all patented inventions to be used for the proposed project. If a patent application has been filed for an invention, but it includes proprietary information and is not publicly available, provide documentation that includes: the patent number, inventor name(s), assignee names (if any), filing date, filing date of any related provisional application, and summary of the patent title, with either: (1) a representation of invention ownership; or (2) proof of possession of appropriate licensing rights in the invention (i.e., an agreement from the owner of the patent granting license to the proposer).]

i. Ability to Meet Programmatic Goals with IP/Patent Implications

[Describe how IP assertions and/or patent implications impact the ARPA-H PROSPR programmatic goals.]

j. Human Subjects Research

Does the proposed work involve Human Subject Research?

☐ No ☐ Yes

[If yes, provide evidence of or a plan for review by an institutional review board (IRB). Please include evidence of a Federalwide Assurance for the Protection of human subjects. Please also complete the below table for each organization, including team members and subawardees, performing HSR. Add row as needed.]

Organization Performing HSR	Federalwide Assurance Number	Approved IRB Protocol (Y/N)

k. Representations Regarding Unpaid Delinquent Tax Liability or a Felony Conviction Under Any Federal Law

[Complete the following statements.]

The Proposer represents that –

(i) It is ☐ is not ☐ a corporation that has any unpaid Federal tax liability that has been assessed, for which all judicial and administrative remedies have been exhausted or have lapsed, and that is not being paid in a timely manner pursuant to an agreement with the authority responsible for collecting the tax liability,

(ii) It is ☐ is not ☐ a corporation that was convicted of a felony criminal violation under a Federal law within the preceding 24 months.

l. Software Component Standards

Does your solution include software components that are proprietary or do not include commercial-friendly-open-source licenses?

☐ No ☐ Yes

[If you answered yes, please provide a technical plan in accordance with Section 6.1 of the ISO.]

m. Cybersecurity

Does your organization implement a cybersecurity program leveraging industry and/or government standards to secure and defend your systems, networks, and/or data?

☐ No ☐ Yes

[If yes, provide a brief description of the program in your DMSP, including the specific standard(s) that guide the program, the abilities of the organization to respond to a cybersecurity incident, and how the organization assesses the security posture of their systems and/or networks. If no, provide an explanation.]

ATTACHMENT 1: Model PROSPR Other Transaction Agreement (OT)

(see attachment)