Innovative Solutions Opening (ISO)

For

Treating **H**ereditary **R**are diseases with **I**n **V**ivo precision genetic m**E**dicines

THRIVE

Health Science Futures (HSF) Office

ARPA-H-SOL-25-122

Amendment No. 4

November 14, 2025

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1 INNOVATIVE SOLUTIONS OPENING SUMMARY INFORMATION

Federal Agency Name – Advanced Research Projects Agency for Health (ARPA-H), Health Science Futures Office

ISO Title – Treating Hereditary Rare diseases with In Vivo precision genetic mEdicines (THRIVE)

Announcement Type – Initial Innovative Solutions Opening (ISO) Solicitation

ISO Number – ARPA-H-SOL-25-122

Dates

- Posting Date: **September 25, 2025**
- Q&A Deadline: **October 24, 2025**
- Proposers' Day (recording release): **September 25, 2025**
- Lightning Talks and Sidebars (virtual): **October 02, 2025**
- Solution Summary Due Date/Time: **October 31, 2025 / 11:59PM ET**
- PowerPoint presentation slides Due Date and Time: **December 22, 2025 / 03:00PM ET**
- PowerPoint presentations (virtual): **January 5th through 16th, 2026**
- Proposal Due Date and Time: **February 5, 2026 / 03:00PM ET**

1.1 ISO Purpose

This publication constitutes a merit-based process in accordance with 42 U.S.C. § 290c. Any resultant award negotiations will follow all pertinent laws and regulations.

The mission of ARPA-H is to accelerate better health outcomes for everyone by advancing innovative research that addresses society's most challenging health problems. Awardees will develop groundbreaking new ways to tackle health-related challenges through high potential, high-impact biomedical and health research. ARPA-H seeks to accomplish the THRIVE goals as described in this ISO package. Ultimately, ARPA-H intends to negotiate multiple OT Agreements with proposers whose proposals are most advantageous to the Government.

It is important to note that specifically excluded are proposals that: 1) offer incremental improvements to the existing state-of-the-art, 2) make use of human embryos, human fetal tissue, or human-animal chimeras, 3) do not address cost of goods, manufacturability, and product quality, 4) do not address the objectives of the program, 5) direct policy changes, traditional education and training, or center coordination and construction of physical infrastructure, which are outside the scope of the ARPA-H mission. Furthermore, all proposals must comply with all relevant HHS regulations on research and pre-clinical studies using human stem cells:

https://stemcells.nih.gov/research-policy/guidelines-for-human-stem-cell-research

https://osp.od.nih.gov/wp-content/uploads/QA_Chimera_Policy_updated_1_Feb_2017.pdf

1.2 Program summary

THRIVE envisions a future where patients can opt for one-time therapeutic interventions designed to slow, reverse, or cure disease. THRIVE harnesses revolutionary technologies and a rapidly evolving understanding of the genetic underpinnings of the biological processes that lead to disease.

THRIVE recognizes an urgent need to support the hundreds of millions of people impacted by numerous conditions that are individually too small for commercial investments in today's market. To this end, THRIVE will first address populations with the highest unmet medical needs, i.e. patients confronting a rare disease (RD). Today, there are over 10,000 distinct RDs. Although individually rare, collectively they are common, afflicting one in ten people. Despite this epidemic, almost 95% of RDs have no approved therapies. Children, infants and newborns who compose the majority of those affected, often suffer severe disability and even premature death. THRIVE seeks age- and organ-agnostic solutions that align with performers' interests and expertise in severe, rapidly progressing genetic conditions.

At THRIVE's core is the engine to support the rapid design and development of multiple precision genetic medicines (PGMs) enabled by integrated platforms of component genetic technologies. In this program, a platform is defined as a combination of therapeutic cargo capable of correcting genetic mutations (e.g., gene editors or programmed gene insertions), and integrated delivery tools to bring the therapeutic cargo directly into targeted cells within the body (e.g., synthetic or protein nanoparticles). Platforms should be designed to target specific classes of mutations or categories of related diseases. THRIVE seeks solutions capable of addressing multiple variants within a gene, clusters of mutations, or even clusters of diseases with common genetic pathways addressable by a single solution. THRIVE also encourages solutions that include tunability of therapeutic effect (i.e., modulating technologies).

To pave the path forward and amplify impact, THRIVE will:

- Accelerate innovation and integration of therapeutic genetic technologies.
- Accelerate regulatory innovation of genetic medicines and platform evaluations in collaboration with regulatory agencies.
- Pilot viability of platforms and patient access at interventional PGM centers at expert regional centers and demonstrate scalability at virtually networked satellite clinics.
- Establish a publicly accessible data platform to enable AI-assisted iteration and growth of a robust PGM industry that serves patients everywhere.

If successful, THRIVE will change the health paradigm from a lifetime burdened by multiple prescriptions and dependent on daily medications to an unencumbered life of personalized one-time interventions that will slow, reverse, or cure chronic disease. In the near future, THRIVE will reduce the annual $1T financial burden of RDs on US taxpayers, blaze a path towards a future paradigm of treatments for common diseases, and solidify the US's position as the leader in advanced medical treatments. In the more distant future, THRIVE will enable all people to have an option to be freed from chronic medications.

NOTE: THRIVE does not seek adeno-associated virus (AAV)-mediated gene therapies that involve the addition or supplementation of a functional copy of a defective gene.

By transforming PGM platforms into a universal, widely available, and curative model for everyone, THRIVE exemplifies the type of groundbreaking, transformative healthcare innovation that aligns with the national priority of reversing chronic disease and making America healthier.

Anticipated Awards: Multiple awards are anticipated

Potential Award Instruments: Other Transaction Agreements (OT)

Cost Sharing: Cost sharing is strongly encouraged.

Agency Contact: All inquiries should be sent to THRIVE@ARPA-H.gov

2 THE PROGRAM

2.1 THRIVE Overview

Revolutionary genetic engineering tools are poised to transform the outlook for patients suffering from chronic diseases and shift the medical paradigm. Decades of iterative, foundational research has led to early solutions capable of identifying, targeting, and correcting genetic mutations, bringing us closer to cures for all diseases. Despite their transformative potential, however, genetic medicines innovation is stalling. Both technical and systemic hurdles challenge efficient development and widespread availability of genetic medicines. Biotech companies are shuttering, pharma has largely exited, and investors are losing interest in these medicines. The existential angst over the viability of genetic technologies is growing and patients are losing hope for cures.

Patients living with rare diseases have the most urgent needs. Approximately ten thousand unique rare diseases (RD) individually affect small populations but

collectively are common, afflicting 1 in 10 people. Those impacted are mostly newborns, infants, and children who suffer severe disability, reduced quality of life, and even premature death. Over 30 million Americans and their families confront such devastating fate, and yet therapeutic options for roughly 95% of RD do not exist. Furthermore, RD-related burdens cost US taxpayers roughly $1 trillion in direct and indirect costs. Despite these health economics justifications, investments into RD therapeutics are particularly low due to the commercial unviability in today's business model. Consequently, RD patients and their families face futures threatened by a lack of treatment options and inadequate systemic support.

Genetic medicine approaches to date are limited in two broad categories: i) technical and ii) real-world.

2.1.1 Technical Limitations of Current Approaches

Current genetic medicines use one of two general approaches to address genetic mutations that cause disease: a) gene therapy, which leverages the addition or supplementation of a transgene – a functional copy of the defective gene, and b) CRISPR-Cas9, which leverages double-stranded DNA breaks created by the Cas9 nuclease to correct genetic mutations. Gene therapies that utilize supplemental gene addition are limited to addressing loss-of-function mutations and have the potential to integrate into the native genomes of cells, which could theoretically lead to oncogenesis. This type of gene therapy leaves the underlying disease-causing, native mutations uncorrected. Hence, when transgene expression wanes, pre-existing conditions can re-emerge. THRIVE does not support gene supplementation gene therapy.

CRISPR-Cas9-based genetic medicines are also fundamentally limited. First-generation CRISPR relies on cells' native machinery to repair double-strand DNA breaks. This type of uncontrolled repair can lead to highly variable gene disruption and potentially pathogenic, oncogenic, or lethal variants, as well as undesirable chromosomal abnormalities and significant deletions in the target gene, raising concerns about clinical safety and efficacy. CRISPR-Cas9 also cannot correct genes in most cell types in vivo, requiring highly toxic ex vivo methods that can be fatal, particularly for the patient populations these therapies are intended to help. These technical barriers in gene disruption severely limit application to a small fraction of genetic diseases that can be treated. THRIVE does not support ex vivo CRISPR-Cas9 approaches.

Finally, solutions to precisely deliver genetic tools to relevant body's cells are still lagging. Current approaches using lipid nanoparticles (LNPs) and inactivated AAVs are limited by imprecision, inconsistency, and uncontrollability. The high doses required to deliver appropriate cargo to disease-relevant cells can cause immunogenic or off-target effects. In addition, both LNPs and AAVs have limited

cargo carrying capacities and compatibilities, leading to toxic dose requirements and adverse outcomes, including death.

2.1.2 Real-world Limitations

Misalignment between multi-stakeholder priorities has driven technical and commercial PGM failures despite billions of dollars of investments. Conflicting accountabilities prevent the collective ecosphere from efficiently and collaboratively realizing the potential of groundbreaking genetic technology innovation that is positioned to cure patients struggling to survive. Regulators accustomed to evaluating other modalities of medicines developed for large populations are limited by a lack of streamlined pathways, precedent standards, and guidelines for rapidly evolving genetic technologies especially for small populations of RDs. Academia is limited by researchers' existential need to find funding and publish. Industry is limited by an obligation to maximize investors' return on capital. Hospitals and medical systems built around a longstanding practice of creating protocols for common diseases are limited by a lack of expertise and coordinated care for genetic diseases especially in RDs. And finally, payors are limited by their goals to minimize losses, indicating an urgent need to bring costs and prices down for individual PGMs.

2.2 Overall Program Structure

To steer PGM development towards technical and commercial success and to revive venture investments in genetic medicines technologies, THRIVE presents a unique approach. First, THRIVE fuels integrated technology innovation by accelerating the development of platforms, i.e. a combination of "cargo," or the tools to correct underlying mutations, with "delivery," tools that can shepherd cargo preferentially to relevant cells in the body. THRIVE also aims to accelerate ongoing regulatory innovation for platform approvals, set critical precedents, and determine appropriate standards and references. These platforms, developed in Module 1, will be the engines enabling future sponsors to rapidly iterate countless curative PGMs with minimal to no additional regulation. Second, in parallel to the technological development thrust, THRIVE is designed to optimize the viability, sustainability, and scalability of lifesaving PGMs for patients where they are located. Modules 2 and 3 will pilot streamlined, efficient clinical trials for eligible patients to choose PGM interventions much sooner than traditional regulatory timelines allow. Patients close to expert centers will be treated without delays once each novel PGM is deemed safe with a potential for efficacy. Virtually networked expertise will allow patients at satellite clinics located at least two hundred and fifty miles from an expert center to be treated in turn, demonstrating scalability of the model.

THRIVE is a five (5) year program structured into three modules (see Figure 1). All performer teams are required to address all modules. Teams are encouraged to initiate and perform across modules in parallel. Teams are also encouraged to initiate all portfolio platforms at program kick-off.

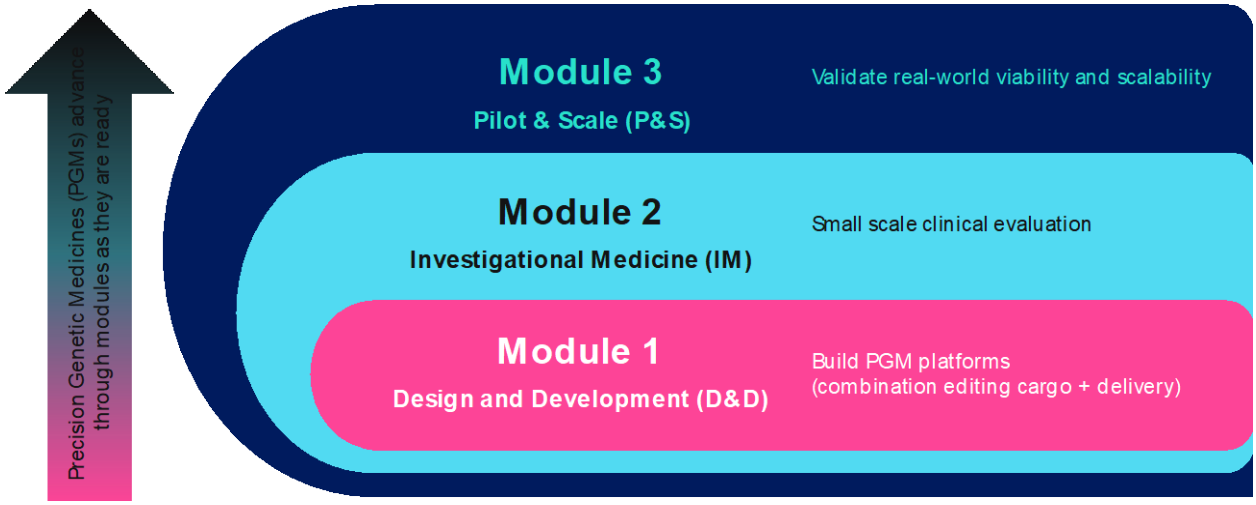

Figure 1: THRIVE is structured in three parallel modules

2.2.1 Module 1: Platform PGM(s) design and development (PGM D&D)

All performer teams are expected to strategize a portfolio of >2 PGMs in each of >2 PGM platforms (i.e., two or more PGM platforms where at least 2 RDs (or use cases) will be demonstrated for each platform). Each PGM cargo-delivery combination is considered a "platform." For example, antisense oligonucleotides (ASOs) delivered by lipid nanoparticles (LNPs) will be considered one platform; editors delivered by protein nanoparticles (PNPs) will be considered another platform; and programmable gene insertion tools delivered via synthetic polymeric nanoparticles (xNPs) would be considered another platform. Any cargo–delivery design may be proposed. THRIVE recognizes that technologies may emerge that are not yet recognized and welcomes incorporation by expert teams as they see appropriate. Performers are also encouraged to utilize expression modulators to fine tune spatio-temporal expression of therapeutic cargos. This module includes non-clinical testing for safety, off-target assessments, toxicity, and evidence of efficacy in human cells, tissues, organoids, or explanted human organs. THRIVE encourages teams to highlight RD with the highest unmet medical needs currently unaddressed by industry.

THRIVE seeks innovative PGM designs capable of addressing multiple variants within a gene, clusters of mutations, or even clusters of diseases with common nodal genetic pathways with a single solution. For example, multiplexed base editors (MOBEs) could be used to design therapeutics for genes with multiple disease-causing mutations, programmable gene insertions with base or prime editors could target multiple mutations within/across genes, and transfer RNA could address common codons across multiple genes with disease-causing mutations. THRIVE also challenges teams to develop solutions that address mutations leading to severe conditions in neonatal or pediatric populations that mimic adult conditions with similar genetic profiles.

A sample performer team strategy is illustrated in Figure 2. By leveraging component technologies with variable levels of complexity, teams can innovate across all modules, leveraging PGMs in lower technical, clinical, regulatory, or other risk platforms to build real-world capabilities demonstration readiness in Modules 2 and 3. In such a strategy, more complex PGMs in more complex platforms can benefit from a priori advances in Modules 2 and 3 that were driven by earlier platform PGMs.

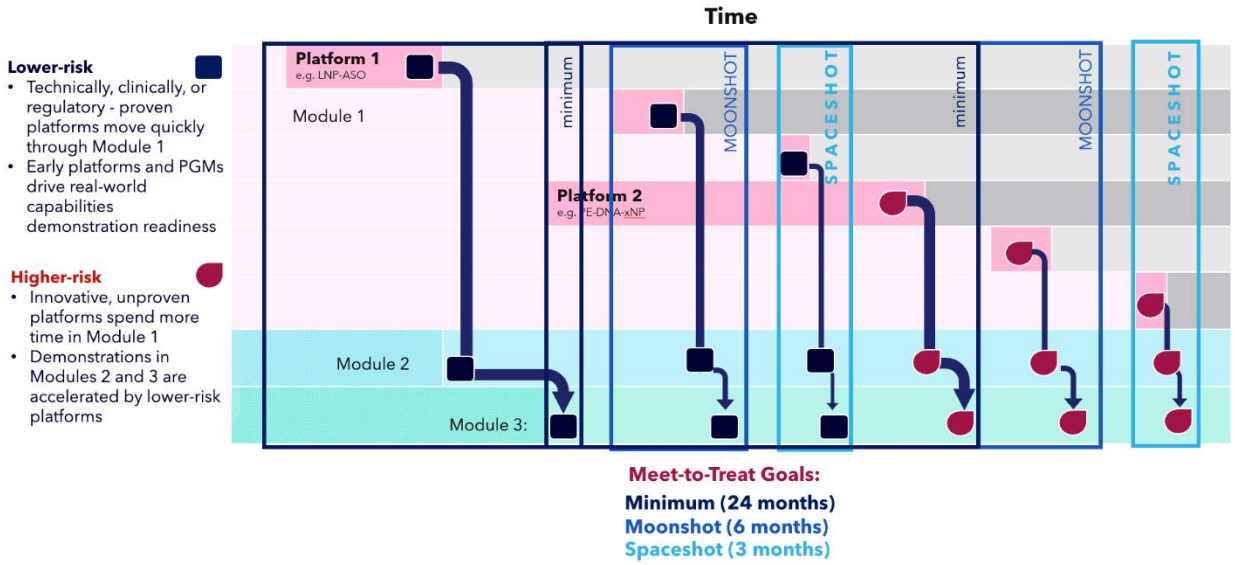

Figure 2: Sample team strategy

Enabling component technologies

1. Therapeutic cargo

THRIVE is technology and organ agnostic. ASOs, CRISPR-based, and other precision editing tools may be leveraged alone or in combination. Other technologies with the potential to correct genetic mutations may be brought into THRIVE.

2. Targeted, preferential cell-specific delivery

THRIVE seeks versatile precision delivery tools with broad cargo carrying capacity and cargo compatibility that allow for in vivo administration. THRIVE also seeks tools capable of reaching multiple organs preferentially. For example, virus-like particles (VLPs), polymeric or protein nanoparticles (PNPs), or other synthetic nanoparticles (xNPs) might all be engineered to preferentially deliver therapeutic cargo to specific disease-relevant cells while avoiding off-target cells and/or tissues. THRIVE will favor solutions that can be manufactured with cell-free, synthetic processes to enable low-cost, efficiency at scale.

3. Spatio-temporal expression modulators

THRIVE encourages teams to incorporate tunability into their solutions, e.g. inhibitory and activating small molecules, bio-responsive delivery vehicles, optogenetic molecules, temperature, focused ultrasound, focused magnetic charges, and epigenetic regulators.

Measuring off-target effects

THRIVE recognizes the potential for unintended and harmful clinical consequences of off-target effects from PGMs that edit, replace, or modulate genetic expression. To address this, THRIVE aims to make publicly available a dynamic and robust library of tools, assays, standards, and references available to future PGM developers. In partnership with gene editing consortiums and others, THRIVE will contribute its data outputs to an open-source database. Performers, in collaboration with regulatory authorities, will establish standards and references for PGM platforms, specifically for measuring unintended chromosomal aberrations from investigational therapeutic interventions using the following criteria for initial guidance:

- Performers must consult with a gene editing consortium representative at a minimum annually to align with the latest methods, protocols, and reporting norms/standards. This consultation can/will be coordinated through the ARPA-H Program Manager.
- FDA guidelines require that performers ascertain the existence of off-target effects and, if unintended edits are detected above the assigned lower frequency, they must conduct studies on functional implications (e.g., oncogenesis, cell fitness, gain of function, loss of function) of off-targets in vivo to determine if the safety risk is unacceptable. Functional implications of off-target edits can include gain of function (GOF) events. For example, activation of an inactive or weakly expressed gene can theoretically occur. The downstream effect of the newly activated gene can in turn lead to adverse clinical effects, including oncogenesis or other untoward functional biology. Performers must use highly sensitive methods that can detect low frequency events.
    - Performers must use at least 1 in silico method to find likely locations and at least 2 physical (non-computational) methods, of which at least 1 must be a cellular assay on relevant cell types. At least 2 replicates are required.
    - Chromosomal re-arrangements must be tested by at least 1 method that detects aberrations of ≥5 Mb in size (e.g., karyotyping) and at least 1 method that detects aberrations between 5kb-5Mb (e.g., long-range PCR sequencing, optical genome mapping, target locus amplification). On-target, hybrid capture next generation sequencing (NGS), and long-range sequencing must detect similar frequencies of <10% of large (>30bp) insertions/deletions to prove that no inter-chromosomal translocations occur.

2.2.2 Module 2: Investigational Medicine (IM)

To accelerate real world treatments for patients in need, every PGM that successfully meets minimum metrics in Module 1 (see Table 2) is eligible for immediate advancement to Module 2 upon agreement by the cross-functional, multi-disciplinary team and the THRIVE PM. Unanimous alignment from all team members, including regulatory advisors, on the body of evidence demonstrating safety and potential for efficacy is required to proceed. With ethics guidance and patient advocacy engagement, patients and their advocates will be presented with the option to try a THRIVE PGM. Potential risks, including knowable and unknowable outcomes, will be weighed against evidence-informed potential benefit of slowing or stopping disease progression. Patients have ultimate decision-making authority to trial any new medicine within THRIVE.

Initial PGM administration will occur at an expert hub established during THRIVE, under close monitoring and with expert RD and other clinical expertise and capabilities. Team and regulatory acceptance of administration of the same PGM to a second patient at the expert hub will enable that PGM to advance to Module 3 where administration of that same PGM to a third patient will occur at a satellite clinic.

2.2.3 Module 3 (SSO): Real-world viability Pilots and Scaling (P&S)

To demonstrate ability to administer novel PGMs to patients where they reside, teams are required to onboard at least one satellite clinic located farther than 250 miles from a central expert center if in the US. Central expert centers will help up-skill all experts and ensure capabilities to enable diagnosis, PGM receipt and handling, PGM clinical administration, and patient care and long-term follow up. Sustainability and scalability of a robust future for PGMs will be piloted by treating eligible patients who opt in at satellite centers with appropriate levels of clinical expertise and operational capabilities. Module 3 solutions require piloting comprehensive RD patient solutions, from identification, diagnosis, treatment, and clinical long-term follow-up at satellite clinics virtually networked to partnered expert centers.

Modules 2 and 3 will establish long-term clinical follow-up capabilities within expert hubs, enabling the monitoring of treated patients for at least 15 years, as required by regulators. THRIVE also encourages lifetime follow-up of patients to aid monitoring and refine artificial intelligence (AI) assistance through machine learning (ML) for future PGM development.

2.2.4 THRIVE – Regulatory Facilitation

Given that ARPA-H is not a regulatory agency, all teams are required to demonstrate regulatory competency and to thoroughly describe their regulatory strategies assuming NO reliance on ARPA-H facilitation.

THRIVE will facilitate regulatory guidance for each performer team, to accelerate pathway innovation and establish standards and references for distinct platforms of

PGMs. Together with technical engineers, clinicians, and patient advocates who understand and respect the science, regulators may evaluate studies in real time and jointly determine the limits of each platform and their components, with a rigorous focus on safety. Regulators may also provide real-time guidance and drafting of necessary submission documents, to optimize and surpass traditional timelines. This approach aims to enable emergency use authorization (EUA)-type submission and review timelines, facilitating the initiation and approval of each PGM and platform developed within THRIVE. To mitigate potential misalignment between regulatory authorities and expedite submission and review processes beyond the scope of EUA reviews and responses, the THRIVE PM team will hold monthly regulatory affairs meetings with each performer team as well as conduct quarterly cross-performer team meetings to identify obstacles and devise alternative strategies.

THRIVE will facilitate accelerated platform regulation by supporting performers to innovate multiple PGMs within single investigational new drugs (INDs), allowing non-clinical evidence to be cross-referenced across PGMs. Clinical trials are encouraged to be designed as single-phase, open-label trials with approximately 10-20 patients. Appropriate numbers of participants will be disease dependent. Similarly, safety and efficacy goals will also be disease dependent. Compelling evidence of efficacy within acceptable margins of safety will depend on biomarkers derived from bodily fluids, radiographic imaging, digital tools, or other means, leading to accelerated approvals. After two PGMs within a single platform achieve regulatory approval, the platform itself will be submitted for platform approval. Full approval for individual PGMs will be requested twelve months post accelerated approval, given absence of serious adverse events or irreversible adverse events attributable to the PGMs or platform (See Figure 3, Figure 4).

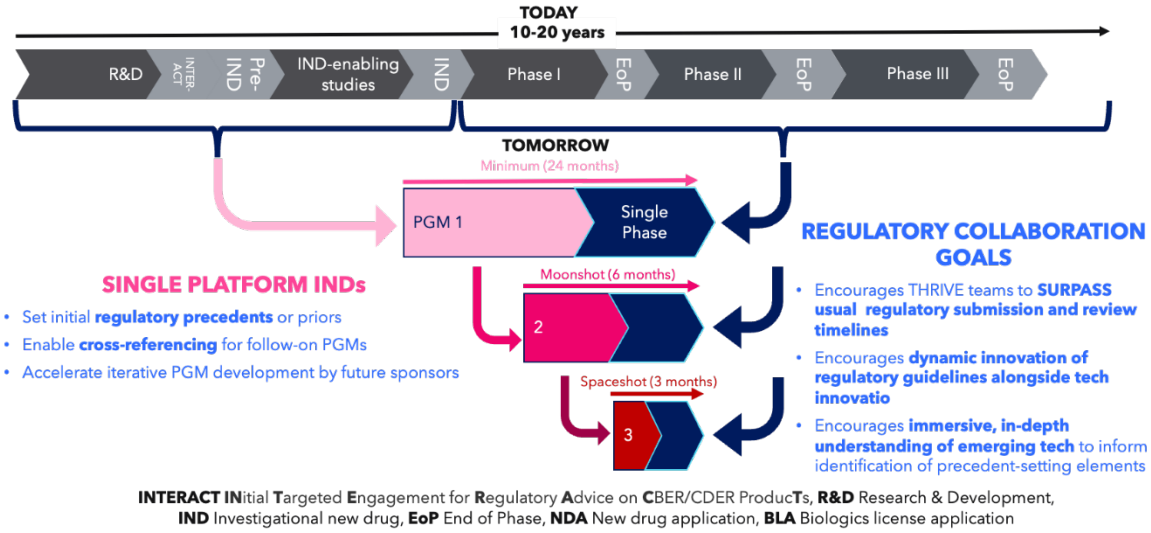

Figure 3: Platform INDs accelerate rapid PGM iterations

Traditional Clinical Trials

Phase	Purpose	# of Participants	Duration	Success
1	Safety & dosage	**20-100** healthy volunteers or people with the disease/condition	Several months	70%
2	Efficacy & side effects	Up to **several hundred** people with the disease/condition.	Up to 2 years	33%
3	Efficacy & monitoring of adverse reactions	**300-3,000** volunteers who have the disease or condition	1-4 years	25-30%

THRIVE Clinical Trial Goals

Phase	Purpose	# of Participants	Duration	Success
Single phase • Combined phase 1/2/3 • Novel designs	**Safety, dosage, efficacy** BIOMARKER evidence	**~10-20 patients** • Actual # will be disease-dependent • No healthy volunteers	**≤12 months**	**Accelerated approval**

Figure 4: Expedited clinical trials lead to accelerated approvals

2.2.5 THRIVE Data Platform

THRIVE data outputs will be ingested into an available, federated data platform to enable future scaling of PGM design and development accelerated by AI/ML. Relevant publicly available as well as sourced proprietary pools and lakes of data [e.g. Undiagnosed Diseases Network (UDN), Oxford-Harrington Rare Disease Centre, Rare as One (Chan Zuckerberg Initiative), Rare Diseases International (RDI), UK Genomics, National Organization for Rare Diseases (NORD) and The Alliance for Regenerative Medicine (ARM)], in addition to data generated by THRIVE performer teams at each step (i.e. diagnostic sequencing, PGM generation, screening and optimization, non-clinical safety and efficacy, as well as pre-clinical and clinical safety, efficacy, and long-term follow-up data) will be consolidated. Outputs from other ARPA-H programs [e.g. Genetic Medicines and IndiVidualized Therapies for Everyone (GIVE); Rare Disease AI/ML for Precision Integrated Diagnostics (RAPID); ML/AI-Aided Therapeutic Repurposing in eXtended uses (MATRIX); Performance and Reliability Evaluation for Continuous Modifications and Useability of Artificial Intelligence (PRECISE-AI), Advancing Clinical Trial Readiness (ACTR); Platform Accelerating Rural Access to Distributed and Integrated Medical Care (PARADIGM); Biomedical Data Fabric (BDF); and others] may also be incorporated into the platform as appropriate. THRIVE's data platform will enable future developers to leverage PGM-focused ML and AI to rapidly bring PGMs to more patients in the future. A networked expert data platform managed at hubs will be connected to satellite clinics allowing scaling of all THRIVE solutions.

2.3 Program Progress

2.3.1 Objectives, Metrics and Points

To evaluate the progress and effectiveness of a proposed solution in achieving the stated program objectives, the following will serve as the basis for determination of team performance and satisfactory progress to warrant continued work within THRIVE. Although the program objectives, metrics and point system are specified below, proposers should note that the government has identified these goals with the intention of bounding the scope of effort while affording maximum flexibility,

creativity, and innovation of proposed solutions to the goals. Proposals must cite alignment of their quantitative and qualitative success criteria described here.

Program Objectives and associated **metrics** used to assess team performance (Table 1).

Time limits assigned to each objective are noted for minimal, moonshot and spaceshot goals. Teams unable to meet minimal time limits may be down-selected from program advancement.

Objectives	Go	Reiterate	Down-selection	Time Allotted per PGM* (Months)	MOON SHOT	SPACE SHOT
Team portfolio strategy, including platforms and PGMs TPP** alignment	All parameters clearly defined and agreed upon by cross-functional multidisciplinary team, including PAG	Team review unlocks opportunities for expedited development	Lack of team consensus	3	2	1
Platform and PGMs Design and Development	PGM platform selection, tech component innovation, and strategy to evaluate safety and efficacy	Team review identifies gaps in confidence and proposes further studies	• Lack of team consensus • Inability to demonstrate safety • Lack of alternative PGM platform(s) innovation	24	12	6
Experimental medicine***	Unanimous team alignment to proceed to patient treatment	Invite outside consultants	Lack of team consensus	1 (after safety studies)	0.5	0
Clinical validation at hub	Safe and efficacious treatment of patient(s)	Team and regulatory review uncovers questionable safety or efficacy requiring more studies	• Lack of team consensus • Inability to demonstrate appropriate safety and efficacy in patient(s) • Lack of alternative PGM platform(s) innovation	24 (after safety acceptance)	6	3
Regulatory acceptance of PGM and platform and agreement to treat all	Agreement to allow platform cross-referencing for future innovative PGMs	Team and regulatory review uncovers questionable safety or efficacy requiring more studies	• Lack of team consensus • Inability to demonstrate appropriate safety and efficacy in patient(s) • Lack of alternative PGM platform(s) innovation	3 (after clinical testing completed)	2	1
Treatment of patient at remote hub (pilot → scale)				6 (after regulatory agreement)	3	0
Payor reimbursement approval				3 (after regulatory agreement)	2	0

*New time clocks start at kickoff of each new PGM or platform project pursued by a team.
**Sample TPP (Appendix C)
***Clinical validation requires *unanimous agreement* across multidisciplinary cross-functional teams, including bioethics, and patient choice to proceed.

Table 1: Program Objectives and Time Limits

Metrics evaluate individual PGM readiness to advance through modules. Each PGM must meet minimum metrics in each module before advancing to the next module. (Table 2 and Table 3). Teams, in agreement with THRIVE management, may elect to return a PGM to an earlier module if appropriate before re-advancing. Teams are encouraged to quickly identify and reiterate addressable issues with eligible PGMs. Teams unable to meet minimum metrics may be down-selected from program advancement.

Points are assigned to specific objectives and metrics to incentivize teams to push the boundaries of what is currently possible. Points will also be used to compare progress across teams and may be used for determining team down-selection (See Table 2 and Table 3).

Teams are encouraged to begin innovating all modules at program initiation. Team strategies that acknowledge the need to innovate across all modules starting at program initiation will be favorably reviewed.

Each metric is assigned points. Teams collect points by achieving specific metrics.
Total points amassed by each team are reviewed periodically. Low scoring teams may be down–selected.

Criteria	Metric	MINUMUM*	Pts	MOONSHOT	Pts	SPACESHOT	Pts
TPP	Aligned TPP with relevant PAG(s) acceptance (months)	≤3	10	≤2	50	≤1	100
Platform Design	Clinically validated cargo, i.e. past regulatory approvals, e.g. ASO	Yes	10	---	---	---	---
	**Clinically validated delivery, i.e. past regulatory approvals, e.g. LNP	Yes	10	---	---	---	---
	Some clinical validation of cargo or delivery i.e. in trials	---	--	Yes	50	No	100
PGM Design	# Mutations addressed	>1	25	>2	50	≥5	100
	# Diseases targeted	>1	25	>2	50	≥5	100
	# Ped – Adult Pairs	>1	25	>2	50	≥5	100
Efficacy	% On-target editing	≥50	25	≥75	50	100	100
	On:Off target cell ratio (disease physiology relevant)	≥3:1	25	≥5:1	50	≥9:1	100
	Use of animal models	Yes	10	---	---	No	100
	Evidence of disease impact	Slowed	25	---	---	Regression	100
Safety	% Off target effect	≤25	25	≤10	50	0	100
	% Bystander effect	≤25	25	≤10	50	0	100
Tunability	Modulation of effect, i.e. on/off or up/down	Non-specific On/Off	25	Cell-specific On/off	50	Incremental Up/down	100

*Minimum metrics must be met for each PGM before advancing to Module 2

Table 2: Module 1 - Metrics and Points

Criteria	Metric	MINIMUM	Pts	MOONSHOT	Pts	SPACESHOT	Pts
Module 2 (HSF) Demo at central hub	Expertise (e.g. PI, clinical research coordinator, diagnostic geneticist, clinical multi-disciplinary specialists, bioinformatics, ethics, pharmacist et.al.) (months)	≤36	25	≤24	50	≤12	100
	Capabilities (e.g. rWGS, devoted RD cloud network connectivity, patient web portals, mobile apps, digital recordkeeping, federated accessible cloud data storage (months)	≤48	25	≤36	50	≤24	100
	Trial initiation (weeks)	≤4	25	≤2	50	≤1	100
	# Trial phases	≥1	25	---	---	Single	100
	# patients treated (n)	≥10	25	≤10	50	≤5	100
	Trial duration (months)	≥12	25	≤12	50	≤6	100
	Accelerated approval to treat all (weeks)	≤ 4	25	≤ 3	50	≤ 2	100
Module 3 (SSO) Pilot and scale to remote clinics	Medical expertise commensurate with local standards (months)	≤36	25	≤24	50	≤12	100
	Capabilities (e.g. Network connectivity, mobile sample collection, telemedicine, mobile app, PGM administration with critical care capabilities (months)	≤36	25	≤24	50	≤12	100
	Number of remote clinics	1	25	2	50	3	100
Meet-to-Treat	**Time in months**	**≤ 24**	25	**≤ 6**	50	**≤ 3**	100

Table 3: Modules 2 and 3 - Metrics and Points

At the time of submission, proposers must:

- Propose to meet all objective criteria and metrics for each module.

Performance reporting will be required throughout the program, and will include:

- Monthly and ad hoc check-ins by the ARPA-H THRIVE team will assess progress towards team advancement or down-selection.
- Monthly status reports outlining technical, clinical, regulatory, financial, timelines, risks and mitigations will be required at regular meetings with the ARPA-H THRIVE team. Evaluation criteria will include progress towards program objectives, metrics, points amassed, and operational success.
    - Team down-selection may occur based on: (1) inability to meet minimum timelines on program objectives; (2) lack of progress towards advancing PGMs and platforms towards regulatory approval; (3) overall points amassed; (4) number of distinct RD patient populations impacted; and (5) success in piloting and scaling capabilities demonstrations at central hubs and satellite clinics; and (6) availability of funding.
- ARPA-H may request performer and sub-performer data and arrange visits to their facilities as deemed necessary throughout the program to validate technical progress.
- Attendance at the check-in meetings must include the performer team leads and the project manager; However, other members of performer teams may be requested by the ARPA-H THRIVE team as necessary.
- Commercialization strategy plan, which includes:
    - a customizable clinical trial template for each platform innovated at the time of biologics licensing application (BLA),
    - a customizable manufacturing process for each platform innovated at the time of market approval authorization (MAA),
    - an IP access strategy, and
    - a scaling strategy by end of program.
- Working in partnership with the ARPA-H THRIVE team, performer teams will provide annual reports detailing their progress made in discussions with regulatory authorities to ensure regulatory standards are met or developed.
    - These updates will be evaluated against agreed upon metrics and objectives to monitor progress and outcomes across modules. ARPA-H may elect not to advance individual PGM(s) or platform(s) from module to module, pending data generated and overall team progress.
    - The ARPA-H THRIVE PM may also recommend revised team membership arrangements.

2.3.2 Requirements for making the treatment widely available

ARPA-H is committed to affordable health care for all geographic regions of the country. ARPA-H will review all conforming proposals and performers throughout the program to ensure that metrics and milestones prioritize end-user needs regarding affordability, independent of geographic region.

To address potential misperceptions about the program and educate patients on the benefits of solutions developed in THRIVE, performers with ARPA-H will actively engage in conversations and workshops with relevant patient advocacy groups on how best to inform and educate patients on the new treatment option.

2.4 General Requirements

2.4.1 Team Requirements

Either multi-party agreements (MPTA) or prime/subawardee(s) arrangements may be proposed. Please see Appendix D for MPTA requirements.

It is expected that proposals will require cross-functional, multidisciplinary teams with the expertise and capabilities needed to achieve the goals of all three Modules. ARPA-H encourages proposer teams to encompass a variety of organizational types (e.g., commercial organizations, academic institutions, patient advocacy organizations, etc.), to ensure expertise and capabilities requirements are fulfilled, future commercialization is optimized, and adherence to project timelines is managed (Figure 5).

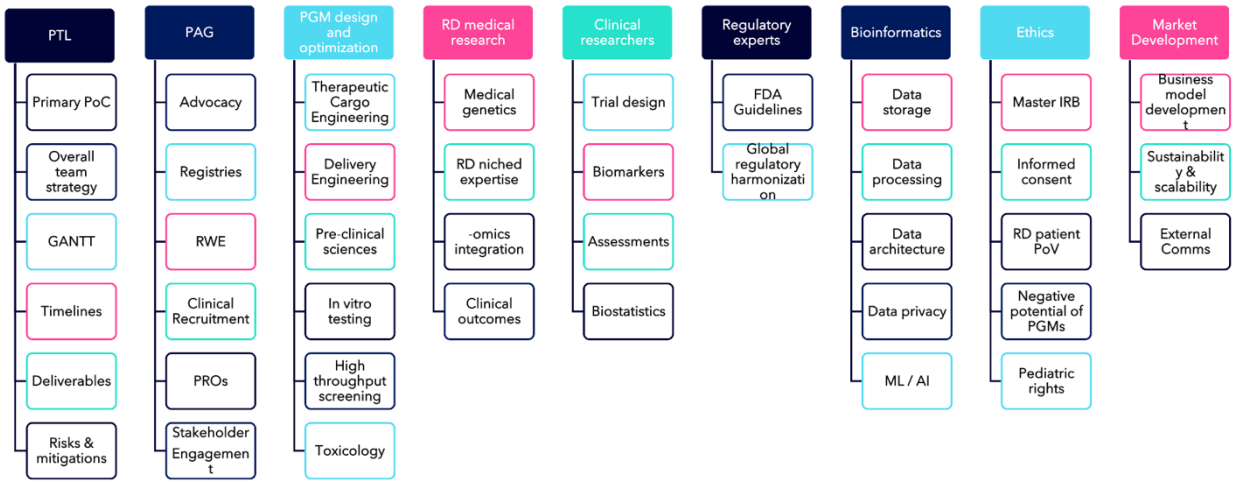

Figure 5: Recommended team expertise and capabilities

Teaming partners should submit a one-page profile with their contact information, a brief description of their technical capabilities, and the desired expertise from other teams, as applicable at the THRIVE Teaming Profile Form, which may be found here: Teaming link. Submissions to this platform will remain open through the Full Proposal submission deadline, but interested parties are highly encouraged to submit them well ahead of Solution Summaries to identify potential teaming partners in a timely manner. Profiles will be made available for all prospective proposers to review. All parties are encouraged to seek complimentary expertise and skills to optimize their team's overall submission to participate in and collaboratively achieve goals and objectives set in THRIVE.

Performers will be required to coordinate within their team and other performers for the benefit of the THRIVE program. Lessons learned are expected to be shared amongst the program teams. Opportunities to discuss progress across teams will be provided and team participation expected.

Proposals must be submitted by the prime proposer or the MPTA Program Team Lead (PTL), who is the team member that will represent the Team throughout submissions in response to this ISO, negotiations, and post-award administration of the OT. The prime proposer or PTL will be responsible for submissions in response to this ISO on behalf of the team, under single integrated submissions that encompass the entirety of the Team's proposed solution. Prime proposers and PTLs may only submit one proposal as the Program Team Lead. However, prime proposers, PTLs, and other team members may participate in multiple teams under separate submissions.

All communications, networking, and team formation are the sole responsibility of the Teams. Proposer's Day will serve as a networking platform strategizing and assembling team members. Furthermore, teams are anticipated to include collaborations between multiple academic institutions and for-profit organizations with disparate component technologies, capabilities, and expertise, including procedural and operational capabilities. Furthermore, it is required for each team to include leadership members from relevant patient advocacy communities with relevant experience.

The ARPA-H THRIVE team may recommend teaming performers together to successfully meet program end goals and to successfully bring together the highest performing teams. The purpose of this process is to successfully bring together the highest performing teams to meet all the technical metrics and to successfully achieve the medical breakthroughs for THRIVE. Each Team will be responsible for data-sharing, technology transfer, personnel management and communication when working collaboratively with their team members and other Teams, in each phase of the program.

A full-time Project Manager/Integrator (PMI) with extensive experience in novel drug development, particularly in RD and preferably also in genetic medicines, must be budgeted for in the proposal. This PMI should be onboarded by performers upon successful award to ensure efficient communication between team members and with ARPA-H. This PMI function must be contained within the prime proposer or PTL entity.

ARPA-H will hold a Proposers' Day (see section 4.2) to further describe the goals, structure, metrics, milestones, and point system of the program, as well as to facilitate the formation of proposer teams and enable sharing of information among interested proposers.

2.4.2 Award Strategy

The ISO constitutes a merit-based solicitation, and the number of awards made will depend on the quality of the proposals received and the availability of funds. Award(s) will be made to proposers whose solutions are determined to be the most advantageous to the Government, consistent with this ISO.

The Government reserves the right to select for negotiation all, some, one, or none of the proposals received in response to this ISO. 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 with phases or options for continued work, as applicable.

The Government reserves the right to request any additional necessary documentation to support the negotiation and award process. Further, 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.

In all cases, the government Agreements Officer (AO) will have sole discretion to negotiate all terms and conditions with proposers. 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, 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.

2.4.3 Accessibility Requirements

ARPA-H is committed to proportionate healthcare access irrespective of race, ethnicity, sex, disability, geography, employment, insurance, and socioeconomic status. To achieve this, teams must prioritize availability and affordability in their innovative PGM designs, ensuring that the advantages of ARPA-H funded research extend to as many RD populations and patients as possible. THRIVE will require Patient Advocacy Group (PAG) leader team membership to inform real-life meaningful qualitative endpoints and to advocate for patient-centric policies and partnerships with government agencies and the private sector. THRIVE will also drive central government regulatory and federal and state payor and policy collaborations.

2.4.4 Associate Performer Agreement

To facilitate the open exchange of information, performers will have Associate Performer Agreement (APA) terms included in their award, which requires teams to closely cooperate as an Associate Performer with other Associate Performers. It is anticipated that, at a minimum, this will include requirements to:

a) Maintain a close working relationship that drives towards THRIVE program goals.

b) Share information, data, technical knowledge, expertise, resources, inventions, and other intellectual property to the maximum extent practicable in furtherance of THRIVE's intended objectives; and
c) As deemed necessary by the Associate Performer, enter into a written agreement with other Associate Performers setting forth specific procedures related to the foregoing and to memorialize IP sharing arrangements.

This APA requirement will establish a common understanding of expectations to guide the open exchange of ideas and establish a collaborative foundation for the THRIVE project. Please note that ARPA-H is not a party to the APA.

2.4.5 IP Strategy

ARPA-H recognizes that patents for related technologies that may be leveraged by performing teams are held by other entities that are not part of the proposing team. To ensure the successful commercialization proposed solutions, performer teams must address the following elements as part of the commercialization plan:

1. **Propose a Comprehensive IP Strategy**: Teams must provide a detailed strategy demonstrating how they will navigate the existing IP landscape. This strategy must show that they have identified necessary patents and established a clear plan for securing access to such IP.
2. **Meet Commercialization Plan Requirements**: The commercialization plan should reflect explicit consideration of IP constraints and include actionable steps that ensure the proposed solution can be brought to market effectively. This plan should clearly demonstrate that the team has the capability and agreements in place to support the commercialization terms proposed in response to Section 2.5.2 of this ISO. Teams are required to demonstrate that their path to market is viable and that they have addressed any potential IP obstacles that could hinder commercialization and how they intend to overcome them.
3. **Secure Licensing and Negotiation**: Teams are encouraged to proactively negotiate with current patent holders to secure any necessary licenses. It is essential that these negotiations cover terms that will be applicable during and after the project (i.e., the post-THRIVE period). Notional or actual agreements with existing patent holders should be described in the commercialization plan.

By meeting these requirements, performer teams can ensure that their proposed solutions are not only innovative but also commercially viable under the program guidelines.

2.5 Other Program Considerations

2.5.1 Cost Share

To incentivize stakeholders from academia, industry, private and PAG-led nonprofits and ventures to engage in building privately owned customized, branded solutions in

the future, THRIVE strongly **encourages** cost-share. If proposing cost share, performer team cost proposals must reflect all performance costs (i.e., inclusive of both ARPA-H and performer - sourced contributions, both monetary and in-kind) throughout the five years to demonstrate the proposer's cost-share. .

Cost sharing includes any costs a reasonable person would incur during ordinary competitive business to carry out the proposed solution, that is not directly paid for by the Government under this OT or another exiting contract or financial assistance instrument. There are two (2) types of cost-sharing: Cash Contributions or In-Kind Contributions. Cash contributions are the preferred method of fulfilling the performer's cost-share; however, the Government will consider in-kind contributions that directly support the proposed solution. Both types are further detailed below:

(1) Cash: Cash contributions refer to direct, monetary payments made by the performer (or third party) to directly support the proposed solution. These contributions include, but are not limited to:

- Direct financial payments for salaries, supplies, services, equipment purchases, and operational expenses.
- Funding for the purchase of new laboratory equipment, computers, and software licenses.
- Payments for external consultants, contractors, travel, and accommodation costs.
- New Independent Research and Development (IR&D) funds that support research related to the proposed solution and is not recoverable under an indirect expense pool.

(2) In-Kind Contributions: In-kind contributions refer to non-monetary inputs provided by the performer (or third party) that directly support the proposed solution. These contributions include goods, services, and resources with **verifiable market value,** and can include:

- Uncompensated personnel time and effort contributed by project staff.
- Use of *existing* laboratory equipment, machinery, and tools not included in any indirect expense pool.
- Supplies and consumables from *existing* inventories.
- Access to laboratory space, office space, and meeting rooms.
- Analytical and technical services, including data analysis and equipment maintenance.
- Clinical services for trials and patient recruitment.
- Access to proprietary databases, datasets, and research libraries.
- Non-cash licensing of *existing* intellectual property.

The following are examples of unacceptable cost-sharing:

- Sunk costs or costs incurred before the start of the proposed project.
- Resources that were funded by the Government under a separate contract or financial assistance vehicle.
- Foregone fees or profits.
- Foregone General & Administrative (G&A) or cost of money applied to a base of Independent Research & Development (IR&D).
- Bid and proposal costs.
- Value claimed for intellectual property or prior research, unless it is being delivered under this OT with a minimum of Government Purpose Rights and is directly related to the proposed solution.
- Parallel research or investment, i.e., research or other investments that might be related to the proposed project, but which is not directly part of the proposed solution. Typically, this includes activities that would have been undertaken regardless of whether the proposed project is awarded.
- Off-Budget Costs, i.e., costs that will not be risked by the proposer in performance of the proposed project, will not be considered when evaluating cost share.
- Costs that were incurred for the proposed solution after the beginning of negotiations, but prior to the date the OT becomes effective, may be counted as cost-share if and to the extent that the Agreements Officer determines that: (1) the party other than the Federal Government incurred the costs in anticipation of the OT; and (2) it was appropriate for the entity to incur the costs before the OT became effective in order to ensure the successful implementation of the OT.

The following must be provided to substantiate fulfillment of cost-share:

1. A Description of each cost share item proposed.
2. Proposed Dollar Value of each cost share item proposed; and
3. The Valuation Technique used to derive the cost share amounts (e.g., vendor quote, historical cost, labor hours and labor rates, number of trips).
4. Supporting documentation that substantiates the valuation technique.
5. The burden of proof for substantiating cost share requirements is borne by the proposer.

2.5.2 Post-THRIVE IP licensing and PGM Pricing

THRIVE anticipates a robust PGM industry post-THRIVE. To that end, teams must propose post-THRIVE commercialization terms and conditions including but not limited to aspects related to Platform IP licensing/royalties and PGM pricing. Proposals that incentivize solutions for RD and rewarding all THRIVE performers will

be favorably reviewed. The negotiated terms will be incorporated into the resulting OT. Proposers should align their proposed terms to the following THRIVE objectives:

1. Deprioritizing component technology siloes and driving towards integrated IP platforms.
2. Incentivizing solutions that continue to prioritize small patient populations post-THRIVE.
3. Favorable PGM Platform IP licensing terms to reward all THRIVE performers.
4. Enabling consistent individual PGM dose pricing across all markets.
5. Promoting a future of precision genetic medicine clinics, both expert and satellite.
6. Collaborating with other THRIVE performers to collectively determine a path forward that enables a robust industry for diverse entities post-THRIVE.

To illustrate these goals, a sample notional pricing and licensing term construct is depicted in Figure 6 and the subsequent narrative.

*Eligible Patient Population (Market Size)	IP and Pricing (in perpetuity)	Owner creators	Non-owner creators
n≤5000	IP Licensing	• Fees **NTE $K per license** • No cost	**90% discount**
(Lower commercial opportunity)	PGM Pricing	• No limits • **Pricing must be consistent across all markets**	
n>5000	IP Licensing	• No limits • No cost	**50% discount**
(Higher commercial opportunity	PGM Pricing	• Pricing **NTE $K per dose or per year** • **Pricing must be consistent across all markets**	

*Global patient populations

Figure 6: Sample Team Commercialization Terms and Conditions Strategy

In this example:

- THRIVE performers who succeed in obtaining regulatory approval for a PGM Platform or an individual PGM during THRIVE are considered owner creators of the PGM Platform IP or the individual PGM IP.
- THRIVE performers who succeed in obtaining regulatory approval for a novel PGM Platform may leverage the Platform IP to create future PGMs at their discretion.
- Pricing for PGMs created with a THRIVE platform IP must be consistent across all geographies and markets.
- ALL THRIVE PGM Platforms that achieve regulatory approval during THRIVE must adhere to proposed commercialization T&C's.

Commercialization for patient populations $\leq$ 5,000 globally:

- Total annual licensing and royalty fees for any THRIVE platform IP required to develop more PGMs may not exceed $K per licensee.

- THRIVE PGM Platform licenses are offered at a 90% discounted rate compared to the standard market rate being offered under similar terms to entities who did not substantially participate in THRIVE.
- The individual PGM dose price of any PGM that results from THRIVE or any subsequent PGM derived from a THRIVE PGM IP Platform will be at the discretion of each future sponsor.

Commercialization for patient populations >5,000 globally:

- Licensing fees for any THRIVE platform IP may be offered to future sponsors at any cost deemed reasonable by the owner creators.
- THRIVE PGM Platform license shall be offered to non-owner creators who participated in THRIVE at a 50% discounted rate compared to the standard market rate being offered under similar terms to entities who did not substantially participate in THRIVE.
- The individual PGM dose price of any PGM that results from THRIVE or any subsequent PGM derived from a THRIVE PGM IP Platform cannot exceed $K per dose if a single intervention or $K (same $K per dose) per year if multiple doses are required.

Proposers are reminded that the above sample licensing and price scheme is merely intended to give a general illustration of the types of commercialization terms and conditions THRIVE expects proposers to address. The specific price points and discounts are notional and should not be construed to represent baselines or expectations by THRIVE. Proposers should use the objectives described earlier in this section as the guidelines for devising their respective post-THRIVE commercialization terms and conditions.

2.5.3 AAV Cost Share

THRIVE discourages the use of AAV delivery. Furthermore, supplemental transgene expression solutions will not be accepted. However, THRIVE recognizes that AAV may be leveraged by some teams as part of their strategy to de-risk otherwise untested therapeutic cargo. To this end, THRIVE will support a maximum of 20% of AAV costs. Therefore, if a performer is employing the use of AAV along with other approaches, AAV costs must be segregated from the rest of the proposal. Performers are required to seek cost-share and in-kind support from other sources to fund any funding gaps.

3 ELIGIBILITY INFORMATION

3.1 Eligible Proposers

All responsible sources capable of satisfying the Government's needs may submit a proposal to this ISO. Specifically, universities, non-profit organizations, small businesses and other than small businesses are eligible and encouraged to propose to this ISO. ARPA-H encourages geographically dispersed teams - particularly team members (e.g., companies, institutions, investigators, etc.) new to federal awards - in

order to tap into the wide-range of talented performers and groundbreaking technologies available throughout the entirety of the U.S.

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 three awards to a particular person or entity. ARPA-H encourages entities to submit their research ideas notwithstanding this perceived limitation. Any proposal received will be fairly considered for award and, if it is of interest to ARPA-H, will be selected for an award.

3.1.1 Prohibition of Performer Participation from Federally Funded Research and Development Centers (FFRDCs) and Other 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 may 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 proposed performer team member.

- 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; OR, 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 solicitation, contact THRIVE@ARPA-H.gov.

- If a potential team believes an FFRDC has a unique capability without which their solution is unachievable, they may provide documentation as part of their Solution Summary submission demonstrating they have exhausted all other options. ARPA-H will consider the documentation to determine if inclusion of the FFRDC is necessary for the Solution.

3.2 Non-U.S. Entities

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. However, non-U.S. entities are encouraged to collaborate with domestic U.S. entities. 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. § 3059)) or entities suspended or debarred from business with the Government.

3.3 System for Award Management (SAM)

All proposers must have an active registration in SAM.gov for their 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 as well as renewals may take more than 14 business days to process in SAM.gov. SAM.gov is independent of ARPA-H and thus ARPA-H representatives have no influence over processing timeframes.

4 SUBMISSION PROCESS

4.1 Submission Process Overview

The submission process for THRIVE is as follows:

1. Proposer's Day (optional)
2. Solution Summary submission
3. PowerPoint presentation
4. Full Proposal submission
5. Review of Full Proposals
6. Feedback and awards

4.2 Proposer's Day

ARPA-H will host a Proposers' Day in support of the THRIVE Program as described in Special Notice ARPA-H-SN-25-122. The purpose is to provide potential proposers with information on the THRIVE program, promote additional discussions, and encourage team networking.

Interested proposers are not required to but are strongly encouraged to attend, and materials formally presented during Proposers' Day will be posted to SAM.gov.

ARPA-H will not reimburse potential proposers for participation at Proposers' Day (or time and effort related to any response related to this ISO, including submission of Solution Summaries, presentations or full proposals).

Participants are required to register no later than the date listed in the Section 1of this ISO. This event is not open to the press.

4.3 General Submission Information

The official ISO and attachments are those posted on the System for Award Management (SAM) at SAM.gov. This announcement and any references to external websites herein constitute the total solicitation. If proposers cannot access the referenced material posted in the announcement found at https://www.sam.gov/, please contact the administrative contact listed herein.

Solution Summaries, PowerPoint presentation submissions, and Full Proposals submitted in response to this solicitation must be written in English and must be consistent with the content and formatting requirements of Appendix A (Solution Summary Format and Instructions), and Appendix B (Full Proposal Format and Instructions). The PowerPoint presentation submission must be consistent with the content and formatting requirements of 4.3.2.

Proposers are responsible for submitting Solution Summaries, PowerPoint presentations, and Full Proposals via the ARPA-H Solution Submission Portal and ensuring receipt by the date and time specified in the ISO. No other method of submission is permitted.

Registration is required to submit via the ARPA-H Solution Submission Portal, and registration may take several business days to process. It is recommended to register well in advance of the Solution Summary submission deadline as late submissions resulting from delays with registration will not be accepted or considered.

4.3.1 STEP 1: Solution summary submission

Solution Summary submissions **are required**. Solution summaries may not exceed three (3) pages, excluding the cover page, references, and Rough Order of Magnitude (ROM). The Government will not review any content beyond the first three (3) pages. Official transmittal letter is not required. Based on the evaluation of Solution Summaries, proposers will be either encouraged or discouraged for PowerPoint presentation submission.

See Appendix A for the required Solution Summary format.

4.3.2 STEP 2: PowerPoint presentation submission

All proposers that have submitted the solution summaries will receive feedback letters that will encourage or discourage the submission of PowerPoint presentations and a Gantt chart for the next stage. ARPA-H solution summary feedback is provided to ensure that potential proposers are making an informed decision on the investment of time and resources associated with subsequent Steps. Instructions for Step 2 (PowerPoint presentations) are provided below. The presentation format template will be posted on SAM.gov.

Instructions for PowerPoint presentation submission.

1. **Required documents to be submitted for the PowerPoint presentation stage. Please submit:**
    a. PowerPoint slides
        i. A template will be provided with the feedback letter. Please follow the instructions provided in the template.
        ii. **1 title slide, 1 cover page slide, and not-to-exceed 18** content slides are allowed. See details below.

b. Gantt chart for the entire project in an editable format.
    i. Excel is preferred. No template is provided.
    ii. The granularity and thoughtfulness of the Gantt chart/timeline will be evaluated.
    iii. The full Gantt chart provides the proposing teams with the opportunity to assign all team member organizations to the tasks and subtasks, thereby demonstrating the expected responsibilities of all organizations.
c. Optional: Appendix PDF with supporting documents is allowable but is not required. No template is provided. This document is not part of mandatory review by ARPA-H. Please note that Appendix slides in PowerPoint are not allowed, and any additional information that proposers provide must go into the PDF document.

2. Logistical considerations

a. All documents required for the PowerPoint presentation must be provided **by 3pm Eastern Time Zone, Monday, December 22, 2025**, through the submission portal.
b. The ARPA-H team will review the documents and will reach out to each proposer's point of contact to schedule a virtual PowerPoint presentation that will occur from **January 5th through 16th, 2026**. Proposers will be given several time/date options to choose from.
c. ARPA-H may have additional questions. ARPA-H will send half of the questions 24 hours in advance of the virtual presentation to allow for preparation and will ask the other half during the presentation ad hoc.
d. The presentations will take place virtually, with **15 min** for presentations and **up to 20 minutes** for questions from ARPA-H. The presenters will be timed and stopped after the allotted 15 minutes. The reviewers will be anonymous.
e. After ARPA-H completes its evaluation of PowerPoint presentations, we will send **encourage/discourage** letters to all proposers for submission of full proposals. Specific and clarifying instructions will be provided to each encouraged team in feedback letters. Full proposals are expected to be the last stage of the review process after which the selection for award negotiations will be made.

3. PowerPoint presentations – Two focus areas must be included on the main slides

a. **Focus area #1** - Propose a development path that highlights potential **regulatory pathways and strategies**. (**5-8** slides)
    i. Regulatory strategy is a very important section of the presentation and must be elucidated in detail using schemas, diagrams, text, images, and other tools to demonstrate substantial regulatory competency of the proposing team. Prior experience of expert team members should be evident from the presentation.
    ii. As part of the strategy, please discuss nonclinical, clinical, and

CMC components. Please customize your strategy to your technology and diseases as well as to the most important objective of the program, which is to create precedents for platform approvals of the future.

iii. The regulatory strategy must be provided assuming **no** reliance on ARPA-H facilitation with regulatory agencies.
iv. Please show timeline of activities.
v. Teams are encouraged to provide multiple potential approaches to regulatory pathways for their products. This is needed to demonstrate that a team is able to creatively think about regulatory strategies given the existing regulatory uncertainty around platformization approaches. Proposers are encouraged to show how the proposers will apply existing regulatory pathways to platformization. Proposers are encouraged to propose potential regulatory pathways to explore regulatory flexibilities. As appropriate for each specific project, proposers must show how to platformize CMC, pharm/tox, clinical, how to leverage regulatory documents, how to leverage international clinical experience, designations, compassionate use mechanisms, and other regulatory mechanisms.
vi. Proposers must describe their specific experiences with patient engagement and collaboration with patient communities. Teams are encouraged to discuss how the proposed clinical development will aim to serve all patients with selected diseases in the future (beyond the timeline of the THRIVE program).
vii. Proposers must demonstrate how follow-on drug products will be able to go through the development to licensure faster and more efficiently as compared to the first/initial/lead drug product(s) developed from the same platform. Proposers must clearly demonstrate how relevant learnings will be used.
viii. Proposers must describe their preliminary thinking on valuable inputs into payer dossiers for future payer coverage pursuits (e.g., adding an additional clinical trial endpoint that is important for payors).

b. **Focus area #2** - Propose a feasible path to **sustainable deployment model during and post THRIVE** (**2-4** slides)
    i. Proposers must describe a sustainable path from the proposed clinical development through licensure to a broader commercial setting for multiple products and diseases. The goal is to understand how the proposing teams think about sustainable development of therapies for patients post THRIVE. Discuss how the proposed therapies could be delivered at a nationwide scale. Describe a model (strategies and workstreams) for deployment of these medicines on-demand.

ii. Given that therapies for rare and ultra-rare diseases are rarely commercially viable, proposers must prove their model or approaches **can be replicated and sustained**. It is important to recognize that various incentives and disincentives naturally exist among the proposing organizations. It is typical for an innovator organization to protect its own know-how, thereby preventing replication across the U.S. healthcare organizations. Please describe incentives (i.e., what's in it for you) to transfer knowledge and IP to other players. A combination of incentives and not a single incentive is preferred. The strategy must **not rely on goodwill alone**.

iii. Please discuss sustainable clinical operations across two geographically separated clinical sites including patient recruitment, treatment, and follow-up. Show how the therapy deployment will occur at another clinic (a satellite clinic or another institution). Please ground the discussion in the route of administration and anticipated side effect profile of proposed products. Describe patient engagement incentives and feasible long-term strategy for patients to stay involved in long-term follow up (at least 5 years).

iv. The proposed strategy and plan must work in the existing business and economic environment. For example, when proposing your strategy, do not rely on hypothetical changes in the IP law, in the American healthcare system, in policy, and so on. However, the FDA guidance documents (drafts or final) or recent publications may be used to support such strategy.

4. PowerPoint presentations – Other slides to include

a. 1-2 slides only: Please describe selected disease(s) and selected platform technology(ies) and specific drug products pursued as part of the proposed project. Please indicate the team's knowledge or awareness of the natural history of the selected disease or using patients as their own control.

b. Maximum 2 slides: Describe the **Intellectual Property (IP)** strategy. Specifically,

i. Proposers must provide the proposer's strategy on IP. Proposers must clearly describe how existing IP and innovations under THRIVE will be combined.

ii. Proposers should identify components of the proposed technologies that will or may require 3rd party rights in the future to ensure freedom to operate (FTO) after the licensure and beyond the THRIVE program timeline.

iii. Proposers should provide their thinking on whether the IP position will be incentivizing or disincentivizing (blocking) replication of the proposed model after the THRIVE program is

concluded. The proposed plan must work in the existing business and economic environment and with the existing IP framework.

c. Maximum 2 slides: Describe **economics and cost of goods** (COG) for proposed drug products
    i. Proposers must demonstrate understanding of economics of the proposed drug products. If logistics/distribution/administration components are critical pieces for the overall COG, then please note any patient engagement and experience considerations.
    ii. Proposers should identify cost synergies and economies of scale across products and diseases.
    iii. Proposers should provide deas on how to bring COG down to ≤$1k per patient. Proposers must describe which levers in the COG structure will be pulled to reduce the cost, discuss which components are scalable and which are not, and discuss gradual or staged path to the moonshot COG, i.e., how moderate COG reductions could be achieved first before further cost reductions could be achieved.
    iv. Please note that **drug pricing discussion is not permitted**.
d. 1 slide only**: High level Gantt chart** – slide is required but not presented.
    i. In addition to the full Gantt chart in Excel requested above, proposers must also provide a high-level version of that chart on one slide.
    ii. Proposers must identify the critical path and demonstration of project management competency on the team, which are critical for the project.
e. 1 slide only: **Budget** – slide required but not presented
    i. Proposers must submit a rough order of magnitude (ROM) budget. Please refer to the feedback letter for any guidance provided for the proposer's specific budget.
    ii. At minimum, Proposer's budget slide must show a breakdown by year, and cost share component must be identified for each year (if proposed). Any other breakdown is encouraged as relevant for each proposed project, especially by disease, by platform, etc.

5. PDF Appendix (optional)

a. Additional information is not required but could be included in the PDF appendix. Formal evaluation will not be conducted on materials in the PDF Appendix.
b. Appendix slides are not allowed as part of the PowerPoint slide deck but may be included in the separate PDF document.
c. If a proposer has ever received regulatory feedback from any regulatory body that is pertinent to this proposal, please consider including that original verbatim feedback in the supporting PDF document as proof of

such feedback.

Note: Please only include the information requested in this section for the PowerPoint presentation. Do NOT include any information requested below for the Full Proposal Submission.

4.3.3 STEP 3: Full Proposal Submissions

All proposals submitted in response to this ISO must comply with the content and formatting requirements.

See Appendix B for the required Full Proposal format.

Appendix B- VOL III Administrative & National Policy Requirements Document Template OTs is required to be submitted for OT Full Proposals.

4.4 Solution Summary, PowerPoint presentation, and Full Proposal Submission Deadlines

Please see Section 1 for submission deadlines. Submissions, unless changed via amendment to the ISO, must be submitted by those deadlines. Accordingly, proposers should not wait until the last minute to submit.

4.5 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."

NOTE: "Confidential" is a classification marking used to control the dissemination of U.S. Government National Security Information as dictated in Executive Order 13526 and should not be used to identify proprietary business information.

ARPA-H is responsible for handling submissions in accordance with applicable federal law.

4.6 Funding Restrictions

Pre-award costs will not be reimbursed unless pre-award agreement is negotiated prior to award.

4.7 Questions and Answers

All questions regarding this ISO must be submitted to THRIVE@arpa-h.gov. ARPA-H will post Q&As to the ARPA-H ISO Website and SAM.gov on an on-going basis and may not respond directly to email inquiries. All questions must be in English and must include the name, email address, and telephone number of a point of contact, and should be submitted by the Q&A deadline posted with other key dates. 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 due date may not be answered. Further, duplicative questions may be combined and rephrased to streamline responses.

5 PROPOSAL REVIEW PROCESS

Proposals to THRIVE will be reviewed in two steps as follows (Figure 7):

Step 1: Evaluation of Solution Summary (Proposers are encouraged or discouraged to move to Step 2).

Step 2: Evaluation of PowerPoint presentations (Proposers are encouraged or discouraged to move to Step 3).

Step 3: Evaluation of Full Proposals.

5.1 Evaluation Criteria

Solution Summaries, PowerPoint presentations, and Full Proposals will be evaluated using Evaluation Criteria #1-4, listed in descending order of importance.

5.1.1 Evaluation Criteria #1: Technical Merit

The proposed technical approach is innovative, feasible, and complete. Task descriptions and associated technical elements provided are complete and in a logical sequence with all proposed deliverables clearly defined such that an 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. The proposal represents a revolutionary change rather than an incremental advance.

5.1.2 Evaluation Criteria #2: Potential Contribution and Relevance to the ARPA-H Mission

ARPA-H's mission is to accelerate better health outcomes for everyone by supporting the development of high-impact solutions to society's most challenging health problems. To that end, factors considered may include potential future R&D, commercial, and/or clinical applications of the project proposed including whether such applications may have the potential to address areas of unmet need within biomedicine and improve health outcomes; degree to which the proposed project has the potential to transform biomedicine; and potential for the project to take an interdisciplinary approach.

5.1.3 Evaluation Criteria #3: 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 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 or commercial activities where they have led or participated.

In terms of capability, the Government shall assess the Volume III bio-sketches provided for the performer team members including the PI, Project Manager, key technical personnel, Regulatory and Commercialization experts, and any other key personnel on the project team as requested by ARPA-H.

5.1.4 Evaluation Criteria #4: Cost Realism

Price and/or value analysis will assess the reasonableness and overall value of the proposed price provides to the Government for the selected technical solution.

If these analyses are inconclusive, cost realism analysis may be performed to ensure that the costs align with the technical and management approaches, accurately reflect the goals and objectives, and are consistent with the proposer's scope of work, demonstrating a clear understanding of the necessary costs and effort. The effort should leverage all relevant prior research to maximize the benefits of available funding.

NOTE: ARPA-H discourages cost strategies that involve proposing low-risk ideas with minimum uncertainty and staffing with junior personnel merely to remain competitive. Instead, proposers should include rationale for any proposed resource sharing relative to the solution’s goals and are encouraged to propose the best technical solutions, seeking novel approaches that genuinely reflect the required level of effort and associated risks.

5.2 Conforming Submissions

Full Proposal submissions must conform to the instructions in the ISO. Conforming submissions contain all material requirements detailed in this ISO. Submissions that fail to include required information may be deemed non-conforming and may be removed from further consideration and/or rejected without further review. A submission may be deemed non-conforming under this ISO if it fails to meet one or more of the following solicitation requirements:

- The proposed concept is applicable to the THRIVE program.
- The proposers meet the eligibility requirements.
- The submission meets the submission requirements, including content and formatting requirements in the attached instructions.
- The proposer’s concept has not received funding or been selected for award negotiations for another funding opportunity (whether from ARPA-H or another Government agency).

Proposers will be notified of non-conforming determinations via email correspondence.

Please note that ARPA-H reserves the right, at its discretion, to reject as "non-conforming", submissions that it determines are duplicative of previously submitted solution summaries and proposals under this or other ARPA-H solicitations.

At its discretion and pursuant to its best interest, the Government may: contact all, some, one, or none of proposers to clarify submission information, request additional information/ documentation, or otherwise address conformance issues; and/or choose to waive minor informalities or omissions when determining whether a submission is conforming.

5.3 Solution Summary Review Process

ARPA-H will review and respond to all proposers submitting solution summaries. Solution summaries will be reviewed to provide potential proposers with feedback on whether ARPA-H is interested in the proposed solution/concept. Proposers will be notified of the Government's decision on whether they are encouraged or not encouraged to give a PowerPoint presentation. Feedback notifications will be provided to the administrative and technical points of contact noted on the solution summary cover page.

5.4 PowerPoint Presentation Review Process

ARPA-H will review and respond to all proposers giving a PowerPoint presentation. PowerPoint presentations will be reviewed to provide potential proposers with feedback on whether ARPA-H is further interested in the proposed solution/concept. Proposers will be notified of the Government's decision on whether they are encouraged or not encouraged to submit a Full Proposal. Feedback notifications will be provided to the administrative and technical points of contact noted on the solution summary cover page.

5.5 Full Proposal Review Process

ARPA-H will conduct a scientific review of each conforming Full Proposal, evaluating proposals on how well the submission meets the criteria stated in this ISO.

Upon conclusion of Full Proposal reviews, the proposer will be notified that:

1. ARPA-H has not selected the proposal; or
2. ARPA-H has selected the proposal for funding pending award negotiations, in whole or in part; or
3. ARPA-H requires an explanation of any unclear elements in the submitted proposal. Based on that discussion, ARPA-H may or may not select the proposal or select the proposal in whole or in part and enter negotiations.

Notifications and/or feedback will be provided to the administrative and technical POCs noted on the proposal cover page.

5.6 Reporting

The number and types of reports will be specified in the individual award document. As a typical model, ARPA-H expects the reporting will include monthly financial status reports, monthly technical status reports, quarterly reports, and an end-of-module reports. The reports shall be prepared and submitted in accordance with the procedures contained in the award document and mutually agreed on before award. Reports and briefing materials will also be required as appropriate to document progress in accomplishing program metrics. A Final Report that summarizes the project and tasks will be required at the conclusion of the performance period for the award, notwithstanding the fact that the research may be continued under a follow-on vehicle.

5.7 Handling of Competition Sensitive Information

It is the policy of ARPA-H to protect all proposals as competition 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.

6 POLICY REQUIREMENTS AND MISCELLANEOUS OTHER INFORMATION

6.1 Controlled Unclassified Information (CUI) on Non-Federal Information Systems

Information on Controlled Unclassified Information (CUI) identification, marking, protection, and control is incorporated herein and can be found at 32 CFR § 2002.

6.2 Organizational Conflicts of Interest (OCI)

Proposers are required to identify and disclose all facts relevant to potential or actual OCIs involving the proposer's organization and any proposed team member (proposed sub-awardee). Although the FAR does not apply to OTs or this ISO overall, ARPA-H requires OCIs be addressed in the same manner prescribed in FAR subpart 9.5. Regardless of whether the proposer has identified potential or actual OCIs under this section, the proposer is responsible for providing a disclosure with its proposal. If a potential or actual OCI has been identified, the disclosure must include the proposers', 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.

6.2.1 Agency Supplemental OCI Policy

ARPA-H restricts Performers from concurrently providing professional support services, including Advisory and Assistance Services or similar contracted support services, in addition to performing as an R&D technical Performer. Therefore, as part of the FAR 9.5 disclosure requirement above, a Proposer must affirm whether the proposer or any proposed team member is providing professional support services to any ARPA-H office(s) under: (1) a current award or subaward; or (2) a past award or subaward that ended within one calendar year prior to the proposal's submission date.

[Proposers shall follow the instructions in and complete Volume III (see Appendix B) to address the requirements of this ISO Section.]

Note: An OCI based on a proposer currently providing professional support services as described above cannot be mitigated.

6.2.2 Government OCI Procedures

The Government will evaluate OCI mitigation plans to avoid, neutralize, or mitigate potential OCI issues before award and to determine whether it is in the Government's interest to grant a waiver. The Government will only evaluate OCI mitigation plans for proposals selected for potential award based on the evaluation criteria and funding availability.

The Government may require proposers to provide additional information to assist the Government in evaluating the OCI mitigation plan.

If the Government determines a proposer failed to fully disclose an OCI or failed to provide the affirmation of ARPA-H support as described above; or failed to reasonably provide additional information requested by the Government to assist in evaluating the proposer's OCI mitigation plan, the Government may reject the proposal and withdraw it from consideration for award.

6.2.3 Research Security Disclosures

Conforming proposals selected for negotiations of a potential award will undergo a Research Security Review (RSR). The RSR involves a review of the Proposer's disclosures made as part of the Administrative & National Policy Requirements Document and a validation and comparison of those disclosures utilizing publicly available information and commercially available information tools. Section 10631 of the CHIPS and Science Act of 2022 prohibits Federal research agencies, such as ARPA-H, from providing R&D awards on any proposal in which a covered individual is participating in an MFTRP. It also requires Federal agencies to require recipient

institutions to prohibit covered individuals participating in MFTRPs from working on projects supported by federal R&D awards.

In accordance with National Security Presidential Memorandum 33, research organizations should identify and mitigate conflicts of commitment (COCs) and conflicts of interest (COIs) to receive federal funding. COCs and COIs involving foreign countries of concern (FCOCs), including the People's Republic of China, the Russian Federation, the Islamic Republic of Iran, and the Democratic People's Republic of Korea (also known as North Korea), will require risk mitigation plans. A research organization proposing to this ISO must provide research security disclosures as described in the Administrative & National Policy Requirements Document and the Office of Science and Technology Policy identified Common Forms. The Common Forms are required for all senior or key personnel.

ARPA-H will conduct an RSR of each Proposer and their senior or key personnel after a proposal is selected for negotiations of a potential award. The RSR is not part of the ARPA-H scientific merit review process. The reviews include assessments of potential risks associated with covered individuals' disclosed or undisclosed participation in MFTRPs, funding received from FCOCs, collaboration with FCOC entities (including researchers and research institutions that's have been identified on various entity lists), foreign ownership control or influence with regards to FCOCs identified in proposals, and the pursuit of foreign patents stemming from U.S. Government funded research prior to obtaining U.S. patent protections.

If ARPA-H determines the Proposer fails to provide all requisite research security disclosures or reasonably provide additional information requested by ARPA-H to assist in evaluating the Proposer's disclosures and/or research security mitigations, ARPA-H may remove the proposal from award consideration. The format for this submission can be found in the Administration and National Security Document Template (Appendix B)

6.3 Intellectual Property

Proposers must provide a good faith representation that the proposer either owns or possesses the appropriate licensing rights to all IP that will be utilized for the proposed effort. Further, it is desired that all non-commercial software (including source code), software documentation, and technical data generated and/or developed under the proposed project is provided as a deliverable to the Government. IP delivered to the Government should align with project or Program goals and should be aligned with the level of Government funding provided to generate and/or develop the IP.

6.4 Human Subject Research

A proposal for funding that will involve engagement in human subject research (HSR) (as defined in 45 CFR § 46) must provide documentation of one or more current Assurance(s) 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 HSR must be reviewed and approved by an Institutional Review Board (IRB), as applicable under 45 CFR § 46 and/or 21 CFR § 56. The entity's HSR 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 ARPA-H funded work. This includes, but is not limited to, laws, regulations, and policies regarding the conduct of HSR, 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 HSR 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 HSR training by all investigators and key personnel who will be involved in the design or conduct of the ARPA-H funded HSR. Funding cannot be used toward HSR until ALL approvals are granted.

6.5 Animal Subject Research

All entities submitting a proposal for funding that will involve engagement in animal subjects 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:

- 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); and,
- 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 provide documentation of a current Animal Welfare Assurance (AWA) on file with the Office of Laboratory Animal Welfare (OLAW).

The Proposer must complete and submit the Vertebrate Animal Section (VAS) for all proposed research anticipating animal subject research. A guide for completing the VAS can be found at https://olaw.nih.gov/sites/default/files/VASchecklist.pdf worksheet for all proposed research anticipating Animal Subject Research (ASR).

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. For all proposed research anticipating animal use, proposals should briefly describe plans for IACUC review and approval.

6.6 Electronic Invoicing and Payments

Performers will be required to register in, and submit invoices for payment through, the Payment Management Services (PMS) https://pms.psc.gov.

6.7 Software Component Standards

The health- and healthcare data eco-system is complex and multi-dimensional with a variety of standards for data models, data transmission protocols, data routing methods, etc. that are similar to and extend the International Standards Organization (ISO) Open Systems Interconnection Model (OSI). ARPA-H programs are likely to involve research that touches on multiple layers of the OSI model, from low-level radio frequency (RF) based protocols for transmission of data from implantable devices (potentially OSI layers 1-5), to secure and fault tolerant networking protocols for medical devices (potentially OSI layers 3-6), to the exchange of health information including Electronic Health Records, lab results, and medical images related to a patient between healthcare facilities and health data brokers, including (but not limited to) Health Information Exchanges (HIE) and Trusted Exchange Framework and Common Agreement (TEFCA) Qualified Health Information Networks using protocols such as HL7 FHIR (Fast Healthcare Interoperability Resources, OSI Layer 7). This diversity requires careful consideration of the most appropriate standards to be used for the specific technologies in development and the layer at which they operate.

ARPA-H is committed to advancing interoperability in today's health ecosystem through the adoption of open, consensus-driven standards and laying the foundation for emerging technologies to interoperate in the health ecosystem of the future through the evolution of these standards across all layers of the health data information technology (IT) eco-system. With that in mind, we anticipate that the Performer will develop software and data communication components that fall into three categories:

(1) components that can leverage today's existing standards without impeding the R&D,

(2) components where extensions to existing standards will be necessary to unlock new capabilities in an interoperable way, and

(3) components in areas where consensus-based standards do not yet exist or where use of standards would seriously limit the ability to efficiently conduct R&D.

Whenever such an existing standard is available that meets the scientific, technical, and research needs of the proposed effort, proposers must use the existing standard instead of creating their own. In cases where an existing standard provides only partial functionality, proposers should expand upon the existing standard, ideally in a way that does not prohibit or interfere with backward compatibility, and create sufficient documentation for the Office of the National Coordinator for Health Information Technology (ONC), and the U.S. Department of Health and Human Services (HHS) agencies or standards organizations, to evaluate extensions for potential inclusion in the standard (including open Application Programming Interfaces (APIs) and open data formats). In the case of information relating to health-

and healthcare data at higher layers of the OSI model, all health IT components should adhere to or (as needed) expand upon applicable national standards adopted by HHS, including the ONC (e.g., Fast Healthcare Interoperability Resources (FHIR) and United States Core Data for Interoperability (USCDI)). Technical solutions that contain software elements, commercial-friendly open-source licenses (e.g., MIT, BSD, or Apache 2.0) are preferred. If an open, consensus-based standard does not yet exist, the Proposer should identify the aspects that lack an open standard, describe a plan to develop a general-purpose open data model and to prototype new open APIs. A strong proposal will explain how the Performer will enhance data interoperability (including semantic interoperability) and expand the availability of open, consensus-based standards and data models.

A proposal must include a technical plan to align with applicable standards based on the OSI layer at which they are operating including (but not limited to) HHS-adopted health IT standards (45 CFR Part 170 Subpart B). For the full description of standards adopted in CFR Part 170, Subpart B, please review the complete text of the regulations; a strong technical solution will also outline integration with the Trusted Exchange Framework and Common Agreement (TEFCA). Adhering to international standard ISO/IEEE 11073 will enable broad support for current and future devices, especially those developed internationally. At other layers of the OSI model, and for software components operating outside the network stack (e.g., health databases, Picture Archiving and Communication Systems (PACS), etc.) other standards will be relevant, and strong technical solutions will seek to utilize or expand upon appropriate open, consensus-based standards. If a technical solution requires an extension of existing standards or development of technologies outside of the standards, the Proposer must schedule a meeting with ARPA-H representatives prior to proposal submission to discuss the deviation to the standards.

6.8 Genomic Data Sharing

A resulting award will include the requirement to comply with NIH's Genomic Data Sharing (GDS) Policy (NOT-OD-14-124). Information about the GDS policy can be found at: https://grants.nih.gov/grants/guide/notice-files/NOT-OD-24-157.html.

6.9 Government Furnished Property/Equipment/Information

None is anticipated under THRIVE.

6.10 i-Edison

The award document for each proposal selected for funding will contain a mandatory requirement for patent reports and notifications to be submitted electronically through i-Edison (https://www.nist.gov/iedison).

6.11 Draft OT

Proposers that are interested in previewing OT terms and conditions included in ARPA-H programs are referred to the ARPA-H Model OT that is publicly available. THRIVE intends to use this Model OT as a baseline; however, proposers should not

include redlines or exceptions to terms and conditions during Full Proposal submissions. Negotiations of the terms and conditions in the OT will commence if, and once proposers are selected for negotiation. During the negotiation phase, proposers will be given an opportunity to respond to specific terms and conditions based on a version of the OT that will be tailored to the program and proposed solution.

6.12 Section 508 of the Rehabilitation Act (29 U.S.C. § 749d)

All electronic and information technology acquired or created through this ISO must satisfy the accessibility requirements of Section 508 of the Rehabilitation Act (29 U.S.C. § 749d).

APPENDIX A: SOLUTION SUMMARY FORMAT AND INSTRUCTIONS

A. General Instructions

All Solution Summaries must use a font type not smaller than 12-point font. Smaller font may be used for figures, tables, and charts (but should be legible). Margins may be no less than 1.0" inch in width. Solution Summaries are limited to three (3) pages, exclusive of a cover page, references, target product profile, team organization and capabilities, and Rough Order of Magnitude (ROM). No tables of content shall be provided. The government may not review pages beyond three (3) total; and any Solution Summary submitted that exceeds three (3) pages will only be reviewed at ARPA-H's discretion. Solution Summaries should be submitted in a PDF format to ARPA-H Solution Submission Portal. Attachments and embedded links shall not be included. The Solution Summary should address why the proposed idea is relevant to the ARPA-H mission and the proposed THRIVE program. The Solution Summary should demonstrate the technical merit, user experience, commercial viability, and team qualifications for this proposed idea. Proposers should frame their responses using at least the first 4 of the 10 ARPA-H Heilmeier Questions (HQs):

1. What health problem are you trying to solve? Articulate your objectives using absolutely no jargon.
2. How is it done today, and what are the limits of current practice?
3. What is new in your approach, and why do you think it will be successful?
4. Who cares? If you succeed, what difference will it make?

And include the following items:

- ✓ Team qualifications
- ✓ R&D timeline—what you can accomplish in the agreed upon project timelines?
- ✓ Rough Order of Magnitude (ROM)

B. Cover Page

The cover page should follow the format below. The cover page does not count towards the page limit.

SOLUTION SUMMARY COVER LETTER

<TEAM OR PROGRAM TEAM LEAD ORGANIZATION LOGO (OPTIONAL)>

Innovative Solutions Opening	ARPA-H-SOL-25-122
Solution Summary Title	
Submitter Organization (Prime Proposal or Program Team Lead)	

Type of Organization	**Choose all that apply:** Academic Institutions, Large Business, Small Disadvantaged Business, Other Small Business, Historically Black Colleges and Universities (HBCUs), Minority Institution (MI), Other educational, or other Nonprofit (including non-educational government entities). (Note: The Small Business Administration's (SBA) size standards determine whether a business qualifies as small.). Size standards may be found here: https://www.ecfr.gov/current/title-13/chapter-I/part-121#121.201
Technical Point of Contact (POC)	Name: Mailing Address: Telephone: Email:
Administrative POC *(Authorized to Negotiate Award)*	Name: Mailing Address: Telephone: Email:
Unique Entity Identifier (UEI) of Program Team Lead	
ARPA-H Share (A):	Total: $
Performer Cost Share (if applicable) (B):	Total: $
Total Cost of Performance (A+B):	Total: $
Place(s) of Performance	
Other Team Members (please indicate if they are team members or commercial vendors/consultants)	Technical POC Name: Organization: Organization Type:

CONCEPT SUMMARY

Describe the Solution Summary concept with minimal jargon and explain how it addresses the goals of the THRIVE program.

INNOVATION AND IMPACT

Clearly identify the outcome(s) sought and/or the problem(s) to be solved with the proposed technology concept. Describe how the proposed effort represents an innovative and potentially revolutionary solution to address the technical challenges outlined in the THRIVE ISO. Explain the concept's potential to be disruptive compared to existing or emerging technologies and how the proposed approach will go far beyond current existing capabilities. To the extent possible, provide quantitative metrics in a table that compares the proposed technology concept to current and emerging technologies, which may include:

- A progression of increasingly complex technical challenges.
- State of the art / emerging technology "baseline."
- Aggressive metrics in for each year of the proposed project.
- Summary of specific outcomes from the proposed research.

PROPOSED WORK

Describe the final deliverable(s) for the project, key interim milestones, and the overall technical approach used to achieve project objectives. Discuss alternative approaches considered, if any, and why the proposed approach is most appropriate for the project objectives. Describe the background, theory, simulation, modeling, experimental data, or other sound engineering and scientific practices or principles that support the proposed approach. Provide specific examples of supporting data and/or appropriate citations to scientific and technical literature. Identify adoption challenges to be overcome for the proposed technology to be successful. Describe why the proposed effort addresses the THRIVE ISO and the key technical risks. At a minimum, the Solution Summary should address:

- Does the approach require one or more entirely new technical developments to succeed?
- How will technical risk be mitigated?
- What use cases, capabilities, or demonstrations will be featured?

PORTFOLIO

Proposers must include a strategic portfolio including greater than two PGM platform and greater than two PGM ((i.e., two or more PGM platforms where at least 2 RDs (or use cases). Portfolios and platforms should align with the team's proposed capabilities and expertise. An overall GANTT for the team's overall strategy must be included with each proposal.

TARGET PRODUCT PROFILES

Proposers must include a target product profile (TPP) for each PGM proposed. The TPPs should thoughtfully outline the desired characteristics, features, and performance specifications of the product being developed. Target goals with respect to affordability and accessibility should be reflective of the best estimates and predictions at the time of writing. General guidelines, examples, and templates of a TPP, with required key metrics for impact on disease indications, are provided as attachments (See Attachment 1). No more than two pages per TPP.

TEAM ORGANIZATION AND CAPABILITIES

Indicate the roles and responsibilities of the organizations and key personnel that comprise the Project 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. Be specific about the expertise, experience and capabilities of each team member, especially as it aligns with the team's overall portfolio of platforms and PGMs proposed.

Separately, please complete the below table for key personnel on a separate page of the solution summary. If included in the Table for Key Personnel, this information will not count towards the (3) page Solution Summary page limit, however, the Table for Key Personnel must still not exceed (1) page in length.

Organization	Last Name	First Name	City	State	Country

ROUGH ORDER OF MAGNITUDE (ROM)

Please include a ROM by module. Further estimates based on year, platform, PGM are encouraged. The ROM should encompass all applicable costs and proposers should modify the below to best reflect expected costs. The ROM should also include a breakdown of the work by direct labor (fully burdened), labor hours, consultants/vendors, materials, equipment, other direct costs (e.g., travel), profit, cost sharing, and any other relevant costs. The ROM does not count toward the page limit. The below table may be used for this breakdown:

Categories	Module 1	Module 2	Module 3	Total
Direct Labor (Fully burdened)				
Labor hours				
Vendors/Consultants				
Materials				
Equipment				
Travel				
Other Direct Costs				
Total				
ARPA-H Share				

Performer Cost Share (if applicable)				

Proposers must ensure the ROM encompasses all applicable costs and should modify the above to best reflect the proposer's expected costs. The ROM does not count toward the page limit.

APPENDIX B: FULL PROPOSAL FORMAT AND INSTRUCTIONS

Full proposals must follow this guidance. Full proposals should consist of three volumes as follows:

1) Volume I, Technical and Management Proposal,
2) Volume II, Cost Proposal, and
3) Volume III, Administrative and Policy Requirements Submission

Summary of Full Proposal Requirements, including page limits.

Volume I, Technical and Management Proposal	
Volume Element	Page Limit
Cover Page	1
A. Executive Summary	20
B. Solution Fit with THRIVE	
C. Technical Plan	
D. Management Plan	
E. Capabilities	
F. Commercialization Plan	
G. Statement of Work (SOW)	Proposer format
H. PGM Platforms Portfolio	2, use provided template/format
I. Target Product Profiles	2 (maximum per TPP), use provided template/format
J. Schedule and Milestones	N/A, use Attachment 3 of the ARPA-H Model OT as a template.
K. Data Management and Sharing Plan (DMSP)	N/A (estimated 2 pages)
L. References	N/A
Volume II, Cost Proposal	
Volume Element	Page Limit
Cover Page	1
A. Cost Proposal Spreadsheet(s), including for team members, consultants and vendors at any tier	N/A, use provided template/format
B. Cost and Pricing Data Support	N/A

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. National Security Disclosure and associated biosketches	
D. Novelty of Proposed Work	
E. Intellectual Property (IP)	
F. Software Component Standards	
G. Human Subjects Research	
H. Animal Subjects Research	
I. Representations Regarding Unpaid Delinquent Tax Liability or a Felony Conviction Under any Federal Law	
J. Cybersecurity	

The page limitation includes all figures, tables, and charts. All pages shall be formatted for printing on 8-1/2 by 11- inch paper. Margins must be 1-inch on all sides, font size should be no less than 12 point (Avenir Next LT Pro font), and page numbers should be included at the bottom of each page.

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: "Volume I_XYZ Institution", "Volume II_XYZ Institution", "Volume II Supporting Documents", etc.

I. Volume I, Technical and Management Proposal

The maximum page count for Volume I is twenty (20) pages, with exclusions as noted in the table above. The cover page and sections G-J below are not included in the page count. However, for all sections, 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 against criteria 1-4 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.

Volume I should include the following components:

Cover Page

Solicitation #	ARPA-H-SOL-25-122
Full Proposal Title	
Rare Disease Indication	

Chronic Disease Indication	
Prime Proposer/Program Team Lead	
Unique Entity Identifier (UEI) of Prime Proposer/Program Team Lead	
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 NONPROFIT (including non-educational government entities) (NOTE: The Small Business Administration's (SBA) size standards determine whether a business qualifies as small.). Size standards may be found here: https://www.ecfr.gov/current/title-13/chapter-I/part-121#121.201
Date of Submission	
Technical Point of Contact (POC)	Include salutation Last Name: First Name Mailing Address: Telephone: Email:
Administrative POC	Include salutation Last Name: First Name: Mailing Address: Telephone: Email:
Other Team Members (please indicate if they are team members or commercial vendors/consultants)	Technical POC Name: Organization: Organization Type: UEI:
ARPA-H Share (A):	Total: $
Performer Cost Share (if applicable) (B):	Total: $
Total Cost of Performance (A+B):	Total: $
Place(s) of Performance	

A. 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 is the competitive landscape?*

- What are the key technical challenges in your approach, and how do you plan to overcome these?
    - *Is your study design inclusive with respect to demographics or social identities?*
    - *Have you considered collaborations that will expand the inclusivity of your study cohorts?*
- What is new about your approach? Why do you think you can be successful at this time?
    - *Who will benefit from your solution?*
    - *What health outcomes are you accelerating?*
- 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 THRIVE metrics?
- To ensure equitable access for all people, how will cost, accessibility, and user experience be addressed in your project?
    - *What is the expected target cost for the product?*
- How might this program be misperceived or misused (and how can we prevent that from happening)?

B. Solution Fit with THRIVE: Clearly describe what the team is trying to achieve and the difference it will make (qualitatively and quantitatively) if successful relative to THRIVE'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.

C. 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.

D. Management Plan: Provide a summary of the expertise of the team including all team members and key personnel who will be doing the work. All teams are required

to identify a Project Manager/Integrator (PMI) to serve as the primary POC to communicate with the ARPA-H PM team and OT/Contracts equivalent for each award instrument (e.g., Contracting Officer), coordinate the effort across the team, organize regular performer meetings or discussions, facilitate data sharing, and ensure timely completion of milestones and deliverables. 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 and the teaming strategy among the team members; and key personnel with the amount of effort to be expended by each person during each year. Provide a detailed plan for coordination including explicit guidelines for interaction among team members of the proposed effort. Include risk management approaches. Describe any formal teaming agreements required to execute this program.

A PMI candidate resume or a qualification requirements description (if a specific PMI is not identified at the time of proposal) must be provided as part of the proposal.

E. Capabilities: Describe organizational experience in relevant subject area(s), existing intellectual property, specialized facilities, and any government-furnished materials or information. Describe any specialized facilities to be used as part of the project, the extent of access to these facilities, and any biological containment, biosafety, and certification requirements. Discuss any work in closely related research areas and previous accomplishments.

F. Commercialization Plan: Briefly outline your current understanding of your technologies target market and the size of that market. Identify competitive technologies operating in the market and their limitations. **Be sure to fully address the IP Strategy requirements in section 2.4.5**. Identify partners (e.g. private industry, investors, etc.), required to secure funding, manufacturing, and marketing following the award period. Plans shall include completion of the following table: 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 THRIVE Program (Government Purpose, Unlimited, Limited.)	Name of Person or Entity Asserting Restrictions (who owns the IP?)	Funding Source (Federal Government, other, or Mix**)

*Rights definitions may be found in the ARPA-H Model OT

G. Statement of Work (SOW): The SOW should provide a detailed task breakdown, citing specific tasks for each Module and their connection to the milestones and program metrics. Each Module 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 20 pages of the technical proposal.

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 (i.e., team member 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.

It is recommended the SOW be developed so that each Module of the program is separately defined.

H. Schedule and Milestones: Using the provided format, 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.

I. Data Management and Sharing Plan (DMSP) (recommend NTE 2 pages) 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 1-4, but will likely be used to inform feedback for proposals who are selected for award negotiations.

J. References: Add a list with the cited literature.

II. 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.

Cover Page

Solicitation #	ARPA-H-SOL-25-122

Full Proposal Title	
Rare Disease Indication	
Chronic Disease Indication	
Prime Proposer/Program Team Lead	
Unique Entity Identifier (UEI) of Prime Proposer/Program Team Lead	
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 NONPROFIT (including non-educational government entities) (NOTE: The Small Business Administration's (SBA) size standards determine whether a business qualifies as small.). Size standards may be found here: https://www.ecfr.gov/current/title-13/chapter-I/part-121#121.201
Technical Point of Contact (POC)	Include salutation Last Name: First Name Mailing Address: Telephone: Email:
Administrative POC	Include salutation Last Name: First Name: Mailing Address: Telephone: Email:
Other Team Members (including consultants) if applicable and type of organization for each	Technical POC Name: Organization: Organization Type: UEI: CAGE:
ARPA-H Share (A):	$
Performer Cost Share (if applicable) (B):	$
Total Cost of Performance (A+B):	$
Name, address and telephone number of the proposer's cognizant auditor (as applicable)	
Date proposal was submitted	
Commercial and Government Entity (CAGE) Code	
Proposal validity period (Minimum of	

150 days)	

A. Cost Proposal Spreadsheet: ARPA-H Standard Excel Cost Proposal Spreadsheet (template will be distributed with Solution Summary feedback). 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 Program Team Lead and all team members. The Program Team Lead submission must encompass the totality of all costs for performance for all Team Members, inclusive of cost share. Costs should clearly be segregated by performance year to ensure that required cost share is demonstrated.

While the Program Team Lead is ultimately responsible for submission of all required documents, all team members' cost proposal spreadsheets may be submitted directly to the government by the proposed team member via email to THRIVE@ARPA-H.gov. Proposals should include Interdivisional Work Transfer Agreements or similar arrangements between the awardee and divisions within the same organization as the awardee.

B. Cost and Pricing Data Support: 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.).

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).

C. Salary Cap: None of the federal funds awarded under this program shall be used to pay the salary of an individual at a rate more than the rate identified by the Office of Personnel Management for Executive Level II positions. Nor may the proposed and later negotiated salaries escalate more than the Executive Level II rate for the purposes of invoicing for salary support.

Note: The salary rate limitation does not restrict the salary that an organization may pay an individual working under an award; it merely limits the portion of that salary that may be paid with federal funds.

D. Profit/Fee: Proposal of profit/fee is not allowed.

III. Volume III, Administrative and Policy Requirements Submission

Cover Page

Solicitation #	ARPA-H-SOL-25-122
Full Proposal Title	
Rare Disease Indication	
Chronic Disease Indication	
Prime Proposer/Program Team Lead	
Unique Entity Identifier (UEI) of Prime Proposer/Program Team Lead	
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 NONPROFIT (including non-educational government entities) (NOTE: The Small Business Administration's (SBA) size standards determine whether a business qualifies as small.). Size standards may be found here: https://www.ecfr.gov/current/title-13/chapter-I/part-121#121.201
Technical Point of Contact (POC)	Include salutation Last Name: First Name Mailing Address: Telephone: Email:
Administrative POC	Include salutation Last Name: First Name: Mailing Address: Telephone: Email:
Other Team Members (including consultants) if applicable and type of organization for each	Technical POC Name: Organization: Organization Type: UEI: CAGE:
ARPA-H Share (A):	
Performer Cost Share (B):	
Total Cost of Performance (A+B):	
Name, address and telephone number of the proposer's cognizant auditor (as applicable)	
Date proposal was submitted	
Commercial and Government Entity (CAGE) Code	

Proposal validity period (Minimum of 150 days)	

1. TEAM MEMBER IDENTIFICATION

[Provide a list of all team members. 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 team members and must be listed.]

PROGRAM TEAM LEAD		
Individual Name:	**Organization:**	Non-U.S. Organization: ☐ Yes ☐ No Non-U.S. Individual: ☐ Yes ☐ No
OTHER TEAM MEMBERS		
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

2. ORGANIZATIONAL CONFLICT OF INTEREST AFFIRMATIONS AND DISCLOSURE

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

a. Are any of the proposed individual team members or their respective organizations (including consultants) currently providing Systems Engineering Technical Assistance (SETA), Partnership Intermediary Agreement (PIA) or similar support to ARPA-H? ☐ No ☐ Yes

b. Did any of the proposed individual team members or their respective organizations (including consultants) provide SETA or similar support to ARPA-H within one calendar year of this proposal submission? ☐ No ☐ Yes

[If you answered "Yes" to 2.a OR 2.b, 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 (consultant/vendor) providing the support; and
- An OCI mitigation plan.]

c. Are there any other potential Organizational Conflicts of Interest involving any of the proposed individual team members *or* their respective organizations (including consultants) ☐ No ☐ Yes

[If yes, provide the following information for each applicable team member:

- Identification of applicable team member; and

- An OCI mitigation plan.]

3. 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), PMI and other senior/key personnel[2] that will serve under team members 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].

a. In populating these forms, the following is required for the PMI and other Senior/Key Personnel (whether they are supporting the Program Team Lead of any other team member)).

i. Other organizational affiliations and employment

ii. Other positions and appointments[3]

iii. Participation in any foreign government-sponsored talent recruitment program(s)[4]

iv. 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:

1. 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;
2. 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

[1] GUIDANCE FOR IMPLEMENTING NATIONAL SECURITY PRESIDENTIAL MEMORANDUM 33 (NSPM-33) ON NATIONAL SECURITY STRATEGY FOR UNITED STATES GOVERNMENT-SUPPORTED RESEARCH AND DEVELOPMENT (whitehouse.gov)

[2] In addition to the Principal Investigator or Program/Project Director, Senior/Key Personnel includes individuals who contribute to the scientific development or execution of a project in a substantive, measurable way, whether or not they receive salaries or compensation under the award. These include individuals whose absence from the project would significantly impact the approved scope of the project; in other words, were the individual to leave the program, the change would be so substantial that ARPA-H would need to be notified.

[3] Both foreign and domestic, including affiliations with foreign entities and governments. This includes titled academic, professional, or institutional appointments whether or not remuneration is received, and whether full-time, part-time, or voluntary (including adjunct, visiting, or honorary).

[4] The term "foreign government-sponsored talent recruitment program" or "foreign government-sponsored talent recruitment programs" means an effort directly or indirectly organized, managed, or funded by a foreign government or institution to recruit S&T professionals or students (regardless of citizenship or national origin, and whether having a full-time or part-time position). Compensation could take many forms including cash, research funding, complimentary foreign travel, honorific titles, career advancement opportunities, promised future compensation, or other types of remuneration or consideration, including in-kind compensation.

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

3. Private equity, venture, or other capital financing.

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

i. Other organizational affiliations and employment

ii. Other positions and appointments[3]

iii. Participation in any foreign government-sponsored talent recruitment program(s)

c. Foreign Participation:

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

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

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

Do any of the proposed individual team members or their respective organizations (including consultants) 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.

4. Novelty of Proposed Work

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

5. Intellectual Property (IP)

All proposers must provide a good faith representation that they either own or possess the appropriate licensing rights to all intellectual property (IP) used in the proposed effort. This information will be requested in a full proposal. Proposers must comply with applicable laws and regulations and identify any desired restrictions on the Government's use of IP (both noncommercial and commercial items). Proposers are encouraged to use a format similar to that shown in the tables below. If no restrictions are intended, state "NONE."

[In accordance with the ISO, provide the following information, as applicable. *Note: The Government will assume unlimited rights to all IP not explicitly identified as restricted in the proposal.*]

A. 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 Delivered with	**Summary of Intended Use in the Conduct of the**	**Basis for Assertion**	**Asserted Rights Category**	**Name of Person Asserting Restrictions**

Restrictions	Research			

B. 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).]

C. ABILITY TO MEET PROGRAMMATIC GOALS WITH IP/PATENT IMPLICATIONS

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

6. 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 5.1.2 of the ISO.]

7. HUMAN SUBJECTS RESEARCH (HSR)

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 vendor/consultants, performing HSR. Add row as needed.]

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

8. ANIMAL USE RESEARCH (ASR)

Does the proposed work involve animal use? ☐ No ☐ Yes

[If yes, provide a brief description of the plan for Institutional Animal Care and Use Committee (IACUC) review and approval. Please also provide the Vertebrate Animal Section (VAS) worksheet (https://olaw.nih.gov/sites/default/files/VASchecklist.pdf), provided evidence of each applicable organization's Animal Welfare Assurance, and compete the below table for each organization, including team members and consultants/vendors, performing ASR. Add rows as needed.]

Organization Performing ASR	Approved IACUC Protocol (Y/N)	Completed VAS (Y/N)	Animal Welfare Assurance Number

9. 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.

10. 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, 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.]

Does your organization have experience with managing and securing Controlled Unclassified Information (CUI)?
☐ No ☐ Yes

[Describe how the proposing institution, team members and consultants organization manage CUI, including details of access control for research designated as CUI, information systems security protocols, storage, communicating unclassified fundamental research with foreign nationals, and risk mitigation strategies for unclassified research that may ultimately become CUI as the research proceeds.]

APPENDIX C: TARGET PRODUCT PROFILE

The Target Product Profiles (TPP) for all PGMs. Located below provide specific guidance on the acceptable product specifications for products submitted to the THRIVE program.

Additional templates for proposer's use and examples of TPPs for reference can be found in Attachment 1.

Sample Target Product Profile (TPP)

Performer teams will be required to create and align on a TPP for each PGM and PGM platform innovated. Below is an example TPP published by the FDA with demonstrative suggestions only. Potential proposers are also encouraged to review the FDA package insert CASGEVY, an approved ex vivo gene editing medicine for sickle cell disease for illustrative purposes. Teams are highly encouraged to review both and consider all aspects in creating their TPP for review with the ARPA-H THRIVE team.

A Target Product Profile (TPP) is a planning tool for therapeutic candidates based on FDA ***Guidance for Industry and Review Staff Target Product Profile – A Strategic Development Process Tool.***

The CBER Office of Cellular, Tissue and Gene Therapies (OCTGT) web page for industry education also has a Webinar on TPP

Product Targets	**Minimum Acceptable Result**	**Ideal Results**
Primary Product Indication	Precision genetic medicine for patient with _specific indication – e.g. list of mutations, or clinical diagnoses or symptoms or syndromes	Precision genetic medicine for patient with _ (broader indication) _____
Patient Population	Specific demographics and diagnosis, e.g. Adults >18 and < 65 with _____	People of all ages with _____
Treatment Duration	Once	Once
Delivery Mode	Route of administration	Route of administration

Dosage Form	Drug form, e.g. lyophilized powder in glass vials	Drug form, e.g. lyophilized powder in glass vials
Regimen	Administration, e.g. infusion over ##minutes	Administration, e.g. infusion over ##minutes
Efficacy	Endpoints: e.g. genetic markers of targeted effect, biomarkers, digital markers or patient-reported outcomes on validated tools; other acceptable outcomes	Endpoints: e.g. broader parameters
Risk/Side Effect	Devoid of e.g. undesirable off-target effects, germ cell effects, etc. _____	Devoid of e.g. any off-target effects, germ cell effects, etc. _____
Therapeutic modality	PGM Platform (e.g. ASO-LNP, BE-xNP, mRNA-xNP, PE-AAV)	
Formulation (CMC)	Details	

APPENDIX D: MINIMUM EXPECTATIONS FOR THRIVE OT AGREEMENT MULTI-PARTY TEAMING AGREEMENT (MPTA)

General

If an MPTA arrangement is chosen, the resulting OT will be executed by ARPA-H and one team member who is designated as the team's Program Team Lead (PTL). However, the agreement will establish privity of contract between ARPA-H and all team members. This flat structure will allow for greater continuity and in-scope direction of the program by the ARPA-H Program Manager. Teams will be required to execute a Multi-Party Teaming Agreement (MPTA) prior to award. While ARPA-H will not be a party to this Agreement, MPTAs must contain the minimum conditions set forth here.

Team members will be required to execute a Multi-Party Teaming Agreement (MPTA) with all members of their team to outline the terms and conditions of their established relationship, as parties to the resultant OT. ARPA-H is not a party to MPTAs, but the OT will require that the MPTA terms and conditions comply with the minimum expectations set forth in Appendix D and the MPTA will be required to be executed prior to award.

Organizational

1. All entities who are responsible for the success of the THRIVE Project must be a member of the multi-party team and must be parties to the Other Transaction. Members must either sign individually or be represented by an entity that is authorized to sign on all members' behalf.
2. The agreement must define the entity (company, institution, etc.) who will sign the award document and subsequent modifications on behalf of the multi-party team (i.e., "The Program Team Lead"). This entity will also be responsible for submitting invoices, receiving payments, and distributing accordingly.
3. A Commercialization Partner must be defined and must, by means of the other transaction and MPTA, have license to all the necessary background and foreground IP to allow for commercialization of IP developed or generated under the THRIVE agreement. These licenses/commitments must be such that they allow for commercialization efforts to continue after the OT's period of performance, be able to comply with the post-THRIVE commercialization terms.
4. The Commercialization Partner and Program Team Lead may be the same entity.
5. The MPTA must provide for streamlined on-ramping and off-ramping procedures of team members without adverse impact on post-THRIVE commercialization and other overall THRIVE objectives.

Intellectual Property (IP)

1. The Commercialization Partner must have access and license to the IP necessary to pursue and comply with the post-THRIVE commercialization terms.
2. The Commercialization Partner must be identified and consistent. Their rights to the IP necessary for commercialization must be clearly defined and survive expiration of the agreement.

Communication

1. The Government must be able to interact and share information directly with any team member throughout performance, including to provide in-scope guidance, and to do so without obtaining approval from any other team member.
2. All members of the team must be parties to the OT agreement.

Logistical

1. Delivery of the signatory page of the executed MPTA to the Agreements Officer.

APPENDIX E: ABBREVIATIONS

AAV	Adeno-Associated Virus
AI	Artificial Intelligence
AMI	Advanced Manufacturing Incubators
APECx	Antigens Predicted for Broad Viral Efficacy through Computational Experimentation
ARM	Alliance for Regenerative Medicine
ARPA-H	Advanced Research Projects Agency for Health
ASGCT	American Society of Gene and Cell Therapy
ASO	Antisense Oligonucleotide
ASR	Animal Subject Research
AWS	Amazon Web Services
BDF	Biomedical Data Fabric
BE	Base Editor
BGTC	Bespoke Gene Therapies Consortium
BID	Business Innovation Division
BLA	Biologics License Applications
BOE	Basis of Estimate
CAGE	Commercial and Government Entity Code
CBER	Center for Biologics Evaluation and Research
CDER	Center for Drug Evaluation and Research
CFR	Code of Federal Regulations
CMMI	Center for Medicare and Medicaid Innovation
CMS	Centers for Medicare & Medicaid Services
COE	Community Outreach and Engagement
COGs	Cost Of Goods
CRISPR	Clustered Regularly Interspaced Short Palindromic Repeats
CRISPR-Cas9	CRISPR-associated protein9
CTMI	Clinical Trial Management Institutions
CTMS	Clinical Trial Management Systems
CUI	Controlled Unclassified Information
CZI	Chan Zuckerberg Initiative
DARPA	Defense Advanced Research Projects Agency
DIRO	ARPA-H Director's Office
DNA	Deoxyribonucleic Acid
EMA	European Medicines Agency
ePRO	Electronic Patient-Reported Outcome
ESGCT	European Society of Gene and Cell Therapy
eVLP	Engineered Virus-Like Particle
FAR	Federal Acquisition Regulation
FDA	Food and Drug Administration

FFRDCs	Federally Funded Research and Development Centers
FY	Fiscal Year
GIVE	Genetic Medicines, Immunotherapies and Vaccines for Everyone
HSF	Health Science Futures
HSR	Human Subject Research
IACUC	Institutional Animal Care and Use Committee
IP	Intellectual Property
IRB	Institutional Review Board
ISO	Innovative Solutions Opening
ITDI	Information Technology and Data Innovation
LNP	Lipid Nanoparticle
MAA	Market Approval Authorization
MATRIX	ML/AI-Aided Therapeutic Repurposing in Extended Uses
MHRA	Medicines and Healthcare products Regulatory Agency
ML	Machine Learning
MOBE	Multiplexed Orthogonal Base Editor
mRNA	Messenger RNA
NCATS	National Center for Advancing Translational Sciences
NIH	National Institutes of Health
NIIMBLE	National Institute for Innovation in Manufacturing Biopharmaceuticals
NIST	National Institute of Standards and Technology
NORD	National Organization for Rare Disorders
NP	Nanoparticle
OCI	Organizational Conflicts of Interest
OCTGT	Office of Cellular, Tissue and Gene Therapies
OT	Other Transaction
PACE	Phage-Assisted Continuous Evolution
PAG	Patient Advocacy Group
PASSIGE	Prime-Editing-Assisted Site-Specific Integrase Gene Editing
PaVe-GT	Paving the Way for Rare Diseases Gene Therapies
PE	Prime Editor
Ped	Pediatric
PGM	Precision Genetic Medicine
PHI	Protected Health Information
PI	Principal investigator
PII	Personally Identifiable Information
PM	Program Manager
PMDA	Pharmaceuticals and Medical Devices Agency

PNP	Protein Nanoparticle
Pre-IND	Pre-Investigational New Drug Application
Pts	Points
PTL	Program Team Lead
QVR	Query View Report
R&D	Research and Development
RADIANT	Real-time Analysis and Discovery in Integrated and Networked Technologies
RAPID	Rapid Access to Programmable Individualized Drugs
RD	Rare Disease
RDI	Rare Diseases International
RePORTER	Research Portfolio Online Reporting Tools Expenditures and Results
RNA	Ribonucleic Acid
ROM	Rough Order of Magnitude
RSO	Resilient Systems Office
rWGS	Rapid Whole Genome Sequencing
SAM	System for Award Management
SBU	Sensitive but Unclassified
SCGE	Somatic Cell Gene Editing
SETA	Systems Engineering and Technical Assistance
SSO	Scalable Solutions Office
TA	Technical Area
THRIVE	Treating Hereditary Rare Diseases with in vivo Medicines
TIN	Tax Identification Number
TPP	Target Product Profile
tRNA	Transfer RNA
UARCs	University Affiliated Research Centers
UDN	Undiagnosed Diseases Network
UEI	Unique Entity ID
VCs	Venture Capitalists
xNA	Nucleic acid (DNA or RNA)
xNPs	Polymeric, Synthetic, Protein or Other Nanoparticle