INNOVATIVE SOLUTIONS OPENING

FOR

GROUNDBREAKING

LYMPHATIC

INTERVENTIONS AND

DRUG

EXPLORATION

GLIDE

HEALTH SCIENCE FUTURES

ARPA-H-SOL-24-111

October 29, 2024

Amendment 1 (November 7, 2024): This amendment is to correct a typographical error in the Solution Summary due date

Amendment 2 (December 6, 2024): This amendment is to extend the Solution Summary due date

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1. INNOVATIVE SOLUTIONS OPENING SUMMARY INFORMATION

FEDERAL AGENCY: Advanced Research Projects Agency for Health (ARPA-H)

PROGRAM TITLE: Groundbreaking Lymphatic Interventions and Drug Exploration (GLIDE)

ANNOUNCEMENT TYPE: Solicitation

ISO SOLICITATION NUMBER: ARPA-H-SOL-24-111

DATES: (All times listed are Eastern Time)

- ***Proposer's Day:*** *October 1, 2024, ET*
- ***Questions & Answers (Q&A) due date***: *November 25, 2024, 2:00 PM ET*
- ***ISO Closing Date (Solution Summaries Due)***: *December 12, 2024, 2:00 PM ET*

ANTICIPATED AWARDS: Multiple Other Transaction (OT) Agreements and Cooperative Agreements (CAs)

AGENCY CONTACT: All inquiries should be sent to GLIDE@ARPA-H.gov

1.1 ISO PURPOSE

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

1.2 ISO QUESTIONS AND ANSWERS

All questions regarding this ISO must be submitted to GLIDE@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.

1.3 PROPOSERS' DAY

ARPA-H hosted a Proposers' Day in support of the GLIDE Program as described in Special Notice ARPA-H-SN-24-112. The purpose was to provide potential proposers with information on the GLIDE program, promote additional discussions, and encourage team networking.

Interested proposers were not required 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 submission of Solution Summaries, pitch decks, presentations or full proposals).

2. THE PROGRAM

2.1 GLIDE OVERVIEW

Program Overview: The GLIDE program envisions a future where doctors will have a therapeutic armamentarium targeting abnormal lymphatic structure and function, dramatically expanding the role of the lymphatic system, not only for primary lymphatic diseases but in the treatment of all chronic diseases. The program will develop therapeutic and physical interventions that alleviate, repair, and regenerate irregular or dysfunctional lymphatic vasculature, while including product design and commercialization considerations that favor broad accessibility and adoption by the community of hospitals, healthcare providers, and patients.

Today, patients with a primary lymphatic disease (LD) or a common chronic disease with underlying lymphatic dysfunction must manage often progressive and debilitating life-threatening symptoms for their entire life. Existing therapies are very limited and almost exclusively palliative.

GLIDE *will develop a variety of treatment options available for patients that address the underlying mechanisms of lymphatic dysfunction; either curing the disease state or safely stabilizing the disease and providing significant relief.*

Background and Motivation: The lymphatic system (LS) is an indispensable body system without which we could not survive. It consists of a complex network of lymphatic vessels, lymph nodes, and lymphatic organs that play a critical role in fluid balance, immune cell surveillance, and macromolecule homeostasis in almost every tissue of the human body. Normal structure and function of the LS can be altered by congenital diseases such as primary lymphedema (LE), lymphatic tumors, and malformations, or by trauma, cancer, radiation, infection, or surgical injury resulting in secondary LE. Altogether lymphatic diseases are estimated to impact more than 10 million Americans (see National Indicator Report on Cancer-Related Lymphedema). Lymphatic dysfunction has been further demonstrated to play a key role in the pathophysiology of common chronic diseases including obesity, diabetes, hypertension, heart failure (HF), inflammatory bowel disease, asthma, chronic liver disease (CLD), chronic kidney disease (CKD), HIV, sepsis, hepatitis, COVID-19, neurodegenerative disease, glaucoma, transplant rejection, and autoimmune disease.

Despite this, there are no FDA-approved treatments, therapies, or medical devices, altering lymphatic growth and function.

Lymphatic vessels (LV) are translucent, tiny, and fragile and often overlooked in anatomical studies; additionally, LVs are found in almost every tissue/organ throughout the human body with regional heterogeneity in phenotype. Designing therapies that can target the lymphatic system specifically has been difficult and surgical interventions require significant extra training and skill. Today, clinicians have no pharmacological, gene, or cell therapies that have been specifically formulated or optimized for lymphatic dysfunction. Existing physical interventions and therapies to normalize function, such as compression garments or manual decongestive drainage, are strictly palliative and cumbersome. In the last few decades, several surgical and interventional procedures to decompress obstructive lymphatics have emerged but are still considered experimental with limited insurance coverage and access.

To address the underlying causes of abnormal lymphatic structure and function, treatment approaches must consider how they address key features of lymphatic dysfunction including:

1. Obstructed and abnormal flow
2. Leaky vessels, permeability, and excess fluid accumulation
3. Poor vessel contractility and transport capacity
4. Abnormal lymphatic growth

GLIDE will address two key issues in the treatment of lymphatic dysfunction: 1) decompression of obstructed lymphatics and 2) normalization of lymphatic function. Decompression of distended lymphatic vessels and their surrounding tissues that are the consequence of obstructed lymphatic flow provides immediate relief of tissue swelling and organ dysfunction and can be lifesaving. However, decompression is often a temporary measure that must be continued or repeated to maintain quality of life and healthy organ function. For an extended solution, normalization of function through repair or regeneration of damaged lymphatic vessels is an attractive approach but requires further development and refinement of techniques.

We are in urgent need of cures in the form of repair and regeneration that would restore healthy lymphatic flow for an extended period. Both decompression and lymphatic repair have seen clear demonstrations of proof of concept in the hands of experts at specialized centers, but both need advancements in technology to bring these benefits to a wider population.

ARPA-H will be the catalyst that moves lymphatic medicine from the fringes into the mainstream and opens the benefits of lymphatic medicine to a much broader range of disorders, such as autoimmune disease, HF, CKD, and CLD. We believe that the scientific methodologies to accomplish our aims already exist but are spread among a disparate group of scientists and clinicians. What is needed is an organized effort to bring these technologies together under a shared goal to realize the promise of lymphatic medicine in clinical practice.

2.2 PROGRAM STRUCTURE, TIMELINE AND TECHNICAL APPROACH

The GLIDE program will develop a portfolio of physical devices and pharmacologic, genetic and cell therapeutics to target lymphatic dysfunction through:

1. Decompression of an obstruction of lymphatic flow and/or abnormal lymph accumulation.
2. Repair and regeneration of the lymphatic system's structure and function.

To accomplish these goals, GLIDE is structured into two technical areas (TAs) focused on physical interventions and pharmacologic, gene and cell therapeutic interventions, respectively, and three phases to support translation from idea to market:

Phase I encompasses platform development, proof-of concept research, and feasibility investigations.

Phase II addresses clinical viability and risk assessment.

Phase III provides initial confidence to establish the foundation for clinical trial success with support through Phase I clinical trials. ARPA-H will select the disease indication that the performing team pursues into clinical efforts in Phase III. Continuation into Phase III will be determined by ARPA-H and will be based on technical progress made in prior phases and available funding. (Figure 1. GLIDE Program Structure & Timeline)

Further, GLIDE offers *two pathways to success* with different timelines to support translational research and commercialization for technology at various technical readiness levels (TRLs) as outlined in the ARPA-H Technology Readiness Level Guide. Proposers must assess the maturity of their proposed solution and self-report the TRL and decide between one of two appropriate pathways regardless of TA.

The Activator pathway -> focuses on transformative early-stage solutions with limited or no preliminary data collected. Proposals must demonstrate how the approach will revolutionize the state of care for lymphatic disease and dysfunction if successful. The phases of the Activator path include:

Phase I - Discovery and Development (up to 36 months).
Phase II - Preclinical studies (18 months).
Phase III– Clinical focused primarily on safety and securing regulatory approvals (up to 6 months).

The Accelerator pathway -> focuses on technologies with some demonstrated proof of concept but requiring additional feasibility investigation up to early efficacy data or prototyping. Appropriate technologies must still require at least 18 months of research, development, and optimization during Phase I of GLIDE. The Accelerator path will lower barriers to validating the efficacy of the approach and propel the solution toward successful commercial transition. The phases of the Accelerator path include:

Phase I - Later-Stage Research and Development (R&D) (up to 18 months)
Phase II - Preclinical studies (18 months),
Phase III - Clinical Trials (up to 24 months).

At the time of submission, proposers **must**:

1. **Select One Technical Area:** Determine if the "primary mode of action" applies to TA1: Physical Intervention or TA2: Pharmacologic, Gene and Cell Therapies.

2. **Determine Your Path to Success:** Evaluate the technical readiness of your technology as a product of commercialization. The technical rationale for choosing the activator or accelerator track must be defined in the proposal.
   - **Activator (TRL 1)**: Proof-of-concept demonstration
   - **Accelerator (TRL 2)**: Feasibility technology

3. **Define Rare & Chronic Disease:** identify two or more disease indications including suspected or targeted mechanism of action for their proposed solution. Submissions

must include at least one rare and one chronic disease/disorder impacted by lymphatic dysfunction with recent literature citation and/or evidence supporting the presence of lymphatic dysfunction in their chosen disease indications. At the beginning of Phase III, ARPA-H will select 1 of the 2 indications for clinical trials. Examples of disease indications include but are not limited to:

Table 1. Examples of Disease Indications

Examples of rare diseases with demonstrated lymphatic dysfunction:	**Examples of chronic diseases w/ demonstrated lymphatic dysfunction:**

• Lymphatic Malformations
• Complex Lymphatic Anomalies:
  o Gorham's Stout Disease (GSD)
  o Generalizing Lymphatic Anomaly (GLA)
  o Kaposiform Lymphangiomatosis (KLA)
  o Central conducting lymphatic anomaly (CCLA)
• Castleman Diseases
• Lymphangioleiomyomatosis (LAM)
• Kaposi Sarcoma
• Milroy Disease
• Primary Intestinal Lymphangiectasia
• Noonan Syndrome
• Turner Syndrome
• Primary Lymphedema
	• Secondary Lymphedema
	• Lipedema
	• Inflammatory Bowel Disease
	• Cardiovascular Disease
	• Pulmonary Fibrosis
	• Cancer
	• Organ Transplantation
	• Chronic Liver Disease
	• Chronic Kidney Disease
	• Autoimmune Disorders
	• Glaucoma
	• Neurodegenerative Diseases
	• Obesity
	• Filariasis
	• HIV
	• COVID
	• Lymphangitis

2.2.1 TECHNICAL AREAS (TAs)

Technical Area 1 (TA1): Restore Flow through Physical Interventions – TA1 focuses on developing technology to enhance surgery, microsurgery, interventional radiology, nuclear medicine, compression, or other physical/mechanical (e.g. neuromodulation) means to restore obstructed flow through the LS. Proposers are encouraged to integrate the latest advances in biomaterials, sensors, and artificial intelligence/machine learning (AI/ML)-practices to their proposed physical intervention approach, ensuring that the approach represents a significant, revolutionary (non-incremental) improvement to the current clinical practice. Solutions that are minimally invasive or non-invasive, or interventions that can be done at the same time as existing standard interventional or surgical procedures (such as lymph node dissections or biopsies) are viewed favorably. Physical interventions can include, among others, smart compression, cutting edge surgical tools and interventional radiology devices, and/or lymphatic modulating and reparative implants.

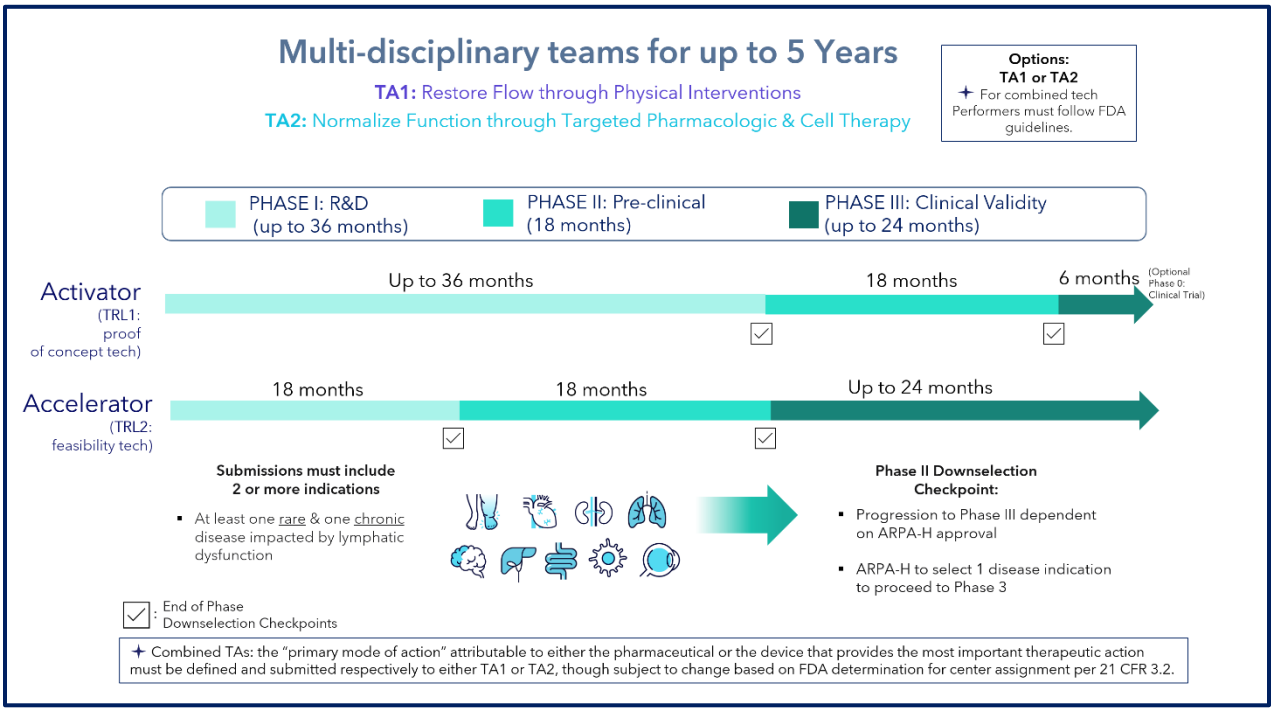
Proposals should consider how the physical intervention may:

- Improve access to and efficacy of devices and surgical procedures which decompress (relieve blockage) of the lymphatic system.
- Directly address the underlying causes of lymphatic dysfunction or obstructed flow.
- Proactively reduce disease incidence for susceptible individuals.

Technical Area 2 (TA2): Normalize Function through Targeted Pharmacologic, Gene, and Cell Therapy - TA2 focuses on platform development and therapeutic identification of pharmacologic, genetic, or cellular approaches to repair, regenerate, and/or relieve obstruction causing lymphatic dysfunction. Proposers are requested to consider high-throughput LD relevant screens and leverage AI, when appropriate to identify viable therapeutic and/or targets to modulate, repair, and/or regenerate lymphatic vasculature. Proposers are also encouraged to identify the best pathway to maximize success while maintaining urgency and delivering viable lead candidates for possible commercialization. Pharmacologic solutions for consideration include small molecules, biologics (e.g. antibody drug conjugates), and cell and gene therapy solutions as well as mechanisms to boost drug delivery into the lymphatic system with high specificity and sustained dosage to minimize off-target effects, reduce drug-resistance, and improve safety. Proposals should consider:

- New drug discovery through lymphatic-relevant high-throughput screens
- Rational drug design and target identification with AI-assistance
- Repurposing existing drugs
- Delivery methods
- Leveraging diagnostic technology
- Potential combinations with interventional modalities from TA1
- The impact of sex and age as a biological variable on the therapy's safety, efficacy and pharmacokinetic (PK) profile

Figure 1: GLIDE Program Structure and Timeline



2.2.2 GLIDE DOWNSELECTION CHECKPOINTS & PHASE III PROGRESSION

The GLIDE program has established detailed **quantifiable and qualitative program metrics for each TA in Tables 1 and 2** with phase-specific metrics to ensure performers succeed as they progress toward a viable therapeutic or physical intervention solution that is both groundbreaking and clinically viable in their ability treat and/or manage LD.

ARPA-H may request performer data as deemed necessary throughout the program to validate technical progress. The performer's progress will be evaluated in alignment with the program metrics outlined in Section 2.3 Technical Metrics and Objectives and will be used to assess success within each phase by GLIDE's PM. Failure to meet the metrics within each phase may result in downselection from GLIDE. Additionally, any performer that does not meet the accessibility, product development, and attendance requirements may not progress to the subsequent phases.

Continuation into Phase III will be determined by ARPA-H and will be based on technical progress made in prior phases and available funding.

2.2.3 DATA MANAGEMENT AND SHARING PLAN (DMSP)

GLIDE encourages all teams to consider the importance of data sharing opportunities that may be possible during the GLIDE program. All proposals are required to include a data management and sharing plan that address the following points:

1. What type of data will be generated? Explain rationale for what scientific data will be preserved and what will be shared.

2. Will specialized tools, software, or code be needed to access or manipulate shared data, and if so, provide the purpose and rationale?
3. What are the common data standards that apply to scientific data and metadata to enable interoperability and safety?
4. What is the timeline for data preservation and access?
5. Outline your plan for data access, distribution, reuse, and privacy considerations.
6. Describe activities and individuals to ensure compliance and oversight.

Teams are encouraged to leverage existing large databases from multiple research centers (e.g. All of Us Initiative) to determine novel insight into lymphatic physiology and pathology and contribute research findings to these resources. Unless an exception is approved by the GLIDE PM, proposers will openly share deidentified/sanitized data acquired during the period of performance with the scientific community. Any member of the scientific community may have access to the deidentified/sanitized data; registration to a specific repository website is acceptable, but approval needs to be automatic. The specific repository where data will be deposited will be chosen in agreement with the ARPA-H PM. The proposers will need to present explicit solutions to address the significant data storage and computing challenges presented by the program with the understanding that the plans and repository may change later in the program. The DMSP must address any instances where open sharing of data may jeopardize the technology's commercial potential. With PM approval and proper justification, proposers may restrict access to even the sanitized/deidentified data generated during the period of performance.

2.3 TECHNICAL AREA METRICS AND OBJECTIVES

ARPA-H will meet with GLIDE performers monthly to review progress towards the metrics and milestones defined below. Achievement of all metrics as agreed to by ARPA-H is part of the basis for initiation of moving to the next phase. Key overall program metrics and milestones are listed in this section below. Proposers may propose quantitative metrics and milestones for the PM to consider that may be better suited for their specific technology. However, the proposers must provide a justification for these revisions to the metrics and milestones as specified below. A full target product profile (TPP) outlining the minimum and ideal functionality of the technology developed in each TA must be included with all submission materials. An example of a TPP can be found in Appendix D.

TABLE A. Overall GLIDE Program GOALS	
Disease Target & Proposal Strategy	• Address chronic disease challenges or lymphatic dysfunction through modulation of the lymphatic system. • Develop therapeutic intervention through decompression with physical intervention to improve lymphatic flow, and normalize lymphatic system through targeted pharmaceutical, gene or cell therapeutic solutions to repair and/or regenerate LVs.
GENERAL GOALS	
Leveraging Computational Intelligence and Big Data Management	• All performers should leverage and share data in a smart and collaborative way using FAIR Data Principles (Findable, Accessible, Interoperable and Reusable), including submission to public database repository as relevant. • Apply current state-of-the-art approaches to leveraging AI and ML approaches to increase speed, efficiency, or predictiveness of the team's therapy technology. • Utilize AI/ML to aid in the design and discovery effort of therapeutic intervention, when possible, for pharmaceutical, gene therapy, cell therapy, and/or physical interventions. • Identification of information systems requirements (e.g., QMS, eCRF, etc.) for regulatory submission and compliance
Product Development and Regulatory Science	• Detailed commercialization plan and TPP to be delivered by performers at time of full proposal. • For therapeutics, New Drug Application submission for lymphatic specific indications. • For medical devices, 510(k), De Novo, or other FDA submission process for physical interventions or novel drug delivery devices. • Successful initiation of clinical trials for safety and efficacy.
Accessibility Requirements	Performing teams must address health inequities with respect to cost and accessibility of care, sex as a biological variable, gender (social identity), protection regardless of socioeconomic status or ethnicity. Each performer team will have formed at least one Discovery Duo that participates in GLIDE's Justice, Equity, Diversity, and Inclusion (JEDI) taskforce, patient voice sessions, and Phase II equity symposium. In collaboration with GLIDE's PM, the JEDI taskforce will develop equity KPIs for each performer team. Required attendance ≥90% is expected and will be enforced by the PM.
Dissemination	Disseminate new technology, models, documents, and other findings to the public and stakeholders through appropriate collaborations with private and government organizations (i.e., patient advocacy groups, and academic institutions).
Attendance and Participation	A 90% mandatory attendance policy will have established accountability, a positive competitive yet collaborative environment, and encourage a collaborative value-added contribution to the program success.

2.3.1 TA1 Metrics

The overall program objectives for TA1 are listed in **Table A above**. The expected metrics per phase in TA1 are listed in **Table 1 below.**

Table 1. TA1: Restore Flow through Physical Interventions	
Phase I	
Concept Generation	Conception of physical interventions to address an obstruction and/or abnormal flow (lymphatic dysfunction) such as smart compression device, electromagnetic stimulation / neuromodulation, stent, shunt, artificial valve or vessel implant, balloon, or embolization. A. Identify lymphatic system friendly material for device (avoids clotting, inflammation, restenosis and/or obstruction) B. Non-invasive, minimally invasive, and/or adjunct to existing or standard procedures (e.g. lymph node dissections or biopsy). Performers are encouraged to utilize state-of-the-art computational approaches (AI/ML) to improve the efficacy of their proposed solution.
Prototype Design and Optimization	1. Demonstrate compliance with FDA design controls and quality systems. 2. Computational and in-silico modeling, as appropriate. 3. Risk assessment. Affordability target of the physical device post manufacturing as cost of goods (as appropriate) **Target** and *ideal* goals for cost of goods: • Class I: **$250** / *$75* • Class II: **$3,000** / *$1,800* • Class III: **$8,000** / *$5,500*

Bench Tests	Evaluate design efficacy and performance via:
	• Material and stress testing (fatigue, wear, tensile, strength, etc.).
	  ○ Must meet current state of the art metrics for comparable interventions.
	• Ex-vivo and in-vitro testing with animal or human tissue (cytotoxicity, hemocompatibility, etc.).
	  ○ Must meet current state of the art metrics for comparable interventions.

End of Phase I Deliverables	1. Commercialization Plan due covering market analysis, regulatory, reimbursement, manufacturing, and intellectual property (IP) strategy (≤8 pages). 2. Functional early prototype of device and pilot data of approach. 3. Complete relevant IACUC protocols for Phase II. 4. Confirm all relevant information subsystems, data repositories, etc. are in place. 5. Performance, subsystem testing, quality, and integration reports (for devices or new methods/processes). 6. 513(g) or relevant FDA pre-submission for device classification. 7. Progress report on retirement of key risks and key success metrics (e.g., biocompatibility, delivery optimization, system costs, results of assays, benchmark performance, etc.).
Downselection Decision Criteria	Performers must meet all agreed upon efficacy targets and successfully submit all end of Phase I deliverables. Continuation into Phase II will be determined by ARPA-H and will be based on technical progress made in prior phases and available funding.

Phase II	
Bio-compatibility (in-vitro and in-vivo studies)	As appropriate, performers should study the efficacy and safety of their proposed physical intervention in: • Cell culture models (e.g. lymphatic endothelial cells and relevant immune populations) • Small and/or large animal models <u>Efficacy targets (**minimal**/*optimal* target)</u>: Performers must: 1. Define a target (normal or therapeutic) range of ≥ 1 lymphatic function in their disease indications and propose to restore function to that target range for <u>at least 3 months following intervention</u>. Targets should be specific, measurable, and represent transformative improvements in line with the guidance below: • Lymphatic transport (% clearance) or lymph drainage speed (cm/s): o Guidance: ▪ > **50%** / *75%* improvement compared to disease state. o Ex. Mouse tail Lymphedema (LE) model: Lymphatic tracer remaining at injection site after 48 hours. ▪ Target: Normal clearance: <40% residual tracer ▪ LE clearance: >60% residual tracer • Lymphatic Pressure (mm Hg): o Guidance: ▪ > **40%** / *60%* improvement compared to disease state. o Ex. Swine model of Tricuspid Regurgitation (TR): ▪ Target: Healthy TD pressure: ~8 mm Hg ▪ TR TD pressure: ~14 mm Hg • Lymphatic Vessel (LV) Contractility (contractions/min) o Guidance: ▪ > **75%** / *100%* improvement over disease state. o Ex. Mouse tail LE model: ▪ Target: Normal frequency: >3 contractions/min ▪ LE Frequency: <1.8 contractions/min • Volume Displacement (ml) o Guidance: > **20%** / *40%* reduction in volume compared to the disease state. o Ex. Mouse tail LE model: ▪ Target: Normal Tail Width: 3.8mm ▪ LE Tail Width: 4.7mm 2. Include additional **<u>minimal</u>** <u>and *optimal targets*</u> with respect to the claim or indication of use. For example: • Edema/Volume (ml/cm^3): o Guidance: ▪ > **20%** / *40%* reduction in volume compared to the disease state. o Ex. Mouse tail LE model: ▪ Target: Normal Tail Width: 3.8mm ▪ LE Tail Width: 4.7mm • Skin Thickness (μm or mm): o Guidance: ▪ > **50%** / *70%* reduction compared to disease state. o Ex. Mouse tail LE model: ▪ Target: Normal Dermal Thickness: 350μm ▪ LE Dermal Thickness: 650μm

	3. Submit a TPP inclusive of these metrics for each indication with full proposal. This will be reviewed and updated with the PM throughout the program.
	The TPP must aim to achieve the additional outcomes below:
	• No or low rates of adverse events (AE) in initial 3 months.
	  o **Minimal Target**: <5% of animals develop significant clotting, severe inflammation, restenosis and/or obstruction.
	  o *Optimal Target*: <5% of animals develop any observable AE
	• High technical/procedural success rate (**>95%** / *>99%*)

Risk Reduction	Adjust and refine design to achieve safety and efficacy targets while overcoming barriers to commercialization and adoption. For example:
	
	Minimal/*optimal* targets:
	
	• Affordability (cost of goods):
	  o Class I: **$250** / *$75*
	  o Class II: **$3,000** / *$1,800*
	  o Class III: **$8,000** / *$5,500*
	• Accessibility: Available at **community** / *rural hospitals* and healthcare centers
	• Ease of use: An experienced surgeon/user should be competent in the intervention with **≤ 2 weeks** (*≤5 days*) of training.
	
	If appropriate, further validate AI/ML approaches used for detection or functional measurement with additional testing and training sets.

End of Phase II Deliverables	1. Submit a revised commercialization plan (≤12 pages). Increased focus on:
	  a. Institutional Review Board (IRB) engagement strategy
	  b. Scale-up strategy for device manufacturing.
	2. Clinical Trial Protocol
	3. Summary report of preclinical investigation to show safety and efficacy.
	4. Second progress reports on key metrics (proof points, safety, scalability) and retirement of key risks.
	5. Investigational Device Exemption (IDE) or other relevant FDA approval for human clinical testing for safety and/or efficacy.

Downselection Decision Criteria	Performers must meet all agreed upon efficacy targets and successfully submit all end of Phase II deliverables. Continuation into Phase III will be determined by ARPA-H and will be based on technical progress made in prior phases and available funding.
Phase III	

Early Feasibility Studies (Safety)	Study Targets (**minimal**/optimal target):
	
	• Study Size: >**10** / 25 participants.
	• Technical success: **>95%** / >99%
	• No or low rates of adverse events (AE) in first six months:
	  o **Minimal: <5% rate of Grade II or higher AEs**
	  o Optimal: <1% rate of Grade II or higher AEs

Pivotal Studies (Safety and efficacy)	Efficacy targets (**minimal**/*optimal* target): Performers must: 1. Define a target (normal or therapeutic) range of ≥ 1 lymphatic function in their disease indications and propose to restore function to that target range for at least 1 year following

	intervention. Targets should be specific, measurable, and represent transformative improvements in line with the guidance below:
	• Lymphatic transport (% clearance) or lymph drainage speed (cm/s):
	  o Guidance:
	  ▪ > **50%** / *75%* improvement compared to disease state.
	  o Ex. Breast Cancer Related Lymphedema (BCRL)
	  ▪ Normal lymph transport speed: >0.15cm/s
	  ▪ BCRL lymph transport speed: <0.05cm/s
	• Lymphatic Pressure (mm Hg):
	  o Guidance:
	  ▪ > **40%** / *60%* improvement compared to disease state.
	  o Ex. Congenital heart defects:
	  ▪ Control TD Pressure: <10 mm Hg
	  ▪ CHF TD Pressure: >16 mm Hg
	
	• LV Contractility (contractions/min)
	  o Guidance:
	  ▪ > **75%** / *100%* improvement over disease state.
	  o Ex. Arm LE:
	  ▪ Normal Frequency: ~1.3 **contractions/min**
	  ▪ Arm LE Frequency: <0.5 contractions/min
	2. Include additional **minimal** and *optimal* targets with respect to the claim or indication of use. For example:
	• Edema/Volume (mL/cm^3):
	  o Guidance:
	  ▪ > **20%** / *40%* reduction in volume compared to the disease state.
	  o Ex. Arm Lymphedema:
	  ▪ Target: Normal Arm Volume: ~2100ml
	  ▪ Arm LE Volume: >2500ml
	• Skin Thickness (µm or mm):
	  o Guidance:
	  ▪ > **50%** / *70%* reduction compared to disease state.
	  o Ex. Arm Lymphedema:
	  ▪ Target: Normal Skin Thickness: <20mm
	  ▪ LE Skin Thickness: >60mm
	3. Submit a TPP inclusive of these metrics for each indication with full proposal. This will be reviewed and updated with the PM throughout the program.
	
	The TPP must aim to achieve the additional outcomes below:
	• Study Size: >**100** / *200* participants (will be based on FDA discussions and class of device)
	• No or low rates of adverse events (AE) in initial 3 months.
	  o **Minimal target:** <5% rate of Grade II or higher AEs
	  o *Optimal target*: <1% rate of Grade II or higher
	• High technical/procedural success rate (**>95%** / *>99%*)

End of Phase III Deliverables	1. Evaluation of product by stakeholders.
	2. ARPA-H Exit Plan - Final design review and report:
	  a. Detailed demonstration of final product ready for clinical trial testing.
	  b. Cost and scalability assessment.
	  c. Evaluation by potential stakeholders including providers, patients, and scientists.
	  d. Safety and effectiveness report.
	  e. Strategy to secure external funding.
	3. Draft of submission paperwork for FDA approval.

Transition and Adoption	Successfully transition to external funding for further clinical trials, scale up technology adoption. Develop workshops and showcases of technology for key stakeholders.

2.3.2 TA2 Metrics

The overall program objectives for TA2 are listed in **Table A**. The expected metrics per phase in TA2 are listed in **Table 2 below.**

Table 2. TA2: Normalize Function through Targeted Pharmacologic, Gene & Cell Therapy	
Phase I	
Therapeutic Identification	Utilize high throughput lymphatic-relevant screens and state-of-the-art computational approaches, and/or AI-assisted rational drug design, to identify optimal molecular targets and compound modifications to achieve lymphatic normalization (**minimal**/*optimal* target). • Small Molecule: ≥**10** to *20* viable lead candidates • Biologics: ≥**3** to *10* viable lead candidates • Cell/Gene Therapies: ≥**3** to *5* candidates Viable candidates defined as possible targeted therapeutic solutions capable of achieving >90% specificity and >90% selectivity, with efficacy targets outlined below in Preliminary PK/PD & non-GLP Toxicology. **For Gene and Cell Therapy Solutions:** achieve >**50%** target cell penetration / *>70-100% targeted cell penetration,* >**50%** editing efficiency / *> 70-100% editing efficiency*, **1:1000** detection limit / *not detected at 1:1000 level of cellular assay for off-target effects and chromosomal abnormalities.* All metrics must align to the corresponding observed lymphatic phenotype targets.
Delivery Optimization	Design or implement a delivery methodology that delivers the therapeutic compound to the LS in the first 12 hours post-delivery. **Minimal target: >30% delivery to Lymphatic System;** *Optimal target: 45% delivery to LS*

Preliminary PK/PD & non-GLP Toxicology	Appropriate studies (*in-vitro*, *ex-vivo*, and small animal subjects) to assess efficacy.
	• Dosing/Toxicology studies
	• PK/PD Studies
	
	<u>Efficacy targets (**minimal**/*optimal* target)</u>:
	
	Performers must:
	
	1. Define a target (normal or therapeutic) range of ≥ 2 lymphatic function in their disease indications and propose to restore normal function to that target range <u>within 2 weeks following treatment</u>. Targets should be specific, measurable, and represent transformative improvements in line with the guidance below:
	• LV density (LVs/unit area) or lymphatic vascular area (mm^2):
	  ○ Guidance:
	  ▪ > **100%** / *200%* improvement compared to disease state.
	  ○ Ex. Mouse ulcerative colitis (UC) model:
	  ▪ Target: Therapeutic LV density: ~48 LVs/mm^2
	  ▪ UC LV density: 25 LVs/mm^2

	• Lymphatic transport (% clearance) or lymph drainage speed (cm/s):
	  o Guidance:
	  ▪ > **50%** / *75%* improvement compared to disease state.
	  o Ex. Mouse tail LE model: Lymphatic tracer remaining at injection site after 48 hours.
	  ▪ Target: Normal clearance: <40% residual tracer
	  ▪ LE clearance: >60% residual tracer
	
	• Lymphatic Pressure (mm Hg):
	  o Guidance:
	  ▪ > **40%** / *60%* improvement compared to disease state.
	  o Ex. Rat tail lymphatics:
	  ▪ Target: Normal max pressure generation: >30 mm Hg
	  ▪ Impaired max pressure generation: <20 mm Hg
	• LV Contractility (contractions/min)
	  o Guidance:
	  ▪ > **75%** / *100%* improvement over disease state.
	  o Ex. Mouse tail LE model:
	  ▪ Target: Normal frequency: >3 contractions/min
	  ▪ LE Frequency: <1.8 contractions/min
	2. Include additional **minimal** and *optimal* targets with respect to the claim or indication of use. For example:
	• Edema/Volume (ml/cm^3):
	  o Guidance:
	  ▪ > **20%** / *40%* reduction in volume compared to the disease state.
	  o Ex. Mouse tail LE model:
	  ▪ Target: Normal Tail Width: 3.8mm
	  ▪ LE Tail Width: 4.7mm
	• Skin Thickness (μm or mm):
	  o Guidance:
	  ▪ > **50%** / *70%* reduction compared to disease state.
	  o Ex. Mouse tail LE model:
	  ▪ Target: Normal Dermal Thickness: 350μm
	  ▪ LE Dermal Thickness: 650μm
	3. Submit a TPP inclusive of these metrics for each indication with full proposal. This will be reviewed and updated with the PM throughout the program.
	
	The TPP must aim to achieve the additional outcomes below:
	• Appropriate benefit-risk profile:
	  o **Minimal Target**: <10% Grade 3 or higher adverse events
	  o *Optimal Target*: <3% Grade 3 of adverse events

End of Phase I Deliverables	Recognize key regulatory risks, including required companion diagnostics, additional experimental assays, and validation in future. 1. Commercialization Plan due covering regulatory, reimbursement, manufacturing, and IP strategy (≤8 pgs.). 2. Confirm all information subsystems in place. 3. Assay validation reports. 4. Complete pre-IND meeting. 5. Progress reports on retirement of key risks and key success metrics (e.g., pharmacokinetic parameters, delivery optimization, costs, results of assays, benchmark performance, etc.).

Downselection Decision Criteria	Performers must meet all efficacy targets and successfully submit all end of Phase I deliverables. Continuation into Phase II will be determined by ARPA-H and will be based on technical progress made in prior phases and available funding.
Phase II	
IND Enabling GLP Toxicology & Nonclinical Studies	Ensure GLP compliant study therapy in an appropriate IND enabling model (≥24 animals) for safety and efficacy to support IND submission. (reminder to consider sex as a biological variable) • Dosing/Toxicology studies • PK/PD Studies <u>Efficacy targets (**minimal**/*optimal* target)</u>: Performers must: 1. Define a target (normal or therapeutic) range of ≥ 2 lymphatic function in their disease indications and propose to restore function to that target range <u>within 2 weeks following treatment</u>. Targets should be specific, measurable, and represent transformative improvements in line with the guidance below: • LV density (LVs/unit area) or lymphatic vascular area (mm^2): o Guidance: ▪ > **100%** / *200%* improvement compared to disease state. o Ex. Porcine LE model: ▪ Target: Therapeutic LV density: >20 LVs/mm^2 ▪ LE LV density: < 3 LVs/mm^2 • Lymphatic transport (% clearance) or lymph drainage speed (cm/s): o Guidance: ▪ > **50%** / *75%* improvement compared to disease state. o Ex. Sheep lymphadenectomy: Transport of radiolabeled BSA from LS to plasma. ▪ Target: Normal transport: >50% transported ▪ Injured transport: <15% transported • Lymphatic Pressure (mm Hg): o Guidance: ▪ > **40%** / *60%* improvement compared to disease state. o Ex. Swine model of Tricuspid Regurgitation (TR): ▪ Target: Healthy TD pressure: ~8 mm Hg ▪ TR TD pressure: ~14 mm Hg • LV Contractility (contractions/min) o Guidance: ▪ > **75%** / *100%* improvement over disease state. o Ex. Sheep lymphatic insult model: ▪ Target: Normal frequency: 4 contractions/min ▪ Dysfunction Frequency: <2 contractions/min 2. Include additional <u>**minimal** and *optimal* targets</u> with respect to the claim or indication of use. For example: • Edema/Volume (mL/cm^3): o Guidance: ▪ > **20%** / *40%* reduction in volume compared to the disease state. o Ex. Sheep lymphadenectomy: ▪ Target: 35% circumference reduction • Fibrosis - Collagen Content (%): o Guidance:

	▪ > **30%** / *50%* reduction compared to disease state. o Ex. Sheep Pulmonary Fibrosis model: ▪ Target: Normal Collagen: 4.5% ▪ PF Collagen: 7.5% • Bioimpedance (BI) Ratio: o Guidance: ▪ > **5%** / *10%* improvement compared to disease state. o Ex. Porcine LE model: ▪ Target: Normal BI Ratio: 0.98 ▪ LE BI Ratio: >1.07 3. Submit a TPP inclusive of these metrics for each indication with full proposal. This will be reviewed and updated with the PM throughout the program. The TPP must aim to achieve the additional outcomes below: • Appropriate benefit-risk profile: o **Minimal Target**: <10% Grade 3 or higher adverse events o *Optimal Target*: <3% Grade 3 of adverse events
Manufacturing	• GLP compliant product production. • Ensure scalable cGMP pathway determined with informed decision based on discussion with FDA and consultants.
Affordability	Target cost to patient (**minimal**/*optimal* target*)*: <**$100**/*$75* month for management <**$10,000**/*$5,000* to cure
Stability	Minimal Target: Therapeutic should be stable for 1.5 years. Optimal Target: Therapeutic should be stable for 2 years at temperatures ≥ -20°C.
End of Phase II Deliverables	1. Submit a revised commercialization plan (≤12 pages). Increased focus on: a) IRB engagement strategy b) Scale-up strategy for device manufacturing. 2. Clinical Trial Protocol 3. Subsystem testing, quality, and integration reports (for devices or new methods/processes). 4. Second progress reports due on retirement of key risks and outlining key success metrics. 5. Complete IND approval.
Downselection Decision Criteria	Performers must meet all efficacy targets and successfully submit all end of Phase II deliverables. Continuation into Phase III will be determined by ARPA-H and will be based on technical progress made in prior phases and available funding
Phase III	
Phase 0 Clinical Trial *(optional)*	• Establish preliminary demonstration of safety, target engagement and modulation. • Assess bioavailability and biodistribution. • Prioritize promising drug candidates. • Inform dose range for Phase I clinical trial.

Phase I Clinical Trial	• Complete Phase I clinical trial with 25+ participants to assess safety at the therapeutic doses. • Adhere to FDA guidelines on Diversity in Clinical Trials. • Submit Clinical Study Report.
Preparation for Phase II Clinical Trial	• Complete and submit IRB paperwork. • Develop and implement a recruitment plan for Phase II clinical trials. • Ensure sufficient cGMP compliant product supply.
End of Phase III Deliverables	Final report including: 1. Detailed demonstration of deliverable product. 2. Cost and scalability assessment. 3. Evaluation by potential stakeholders including providers, patients, and scientists. 4. Safety and effectiveness report. 5. ARPA-H exit plan.
Transition and Adoption	Successfully transition to the clinic or larger commercial entities. Develop workshops and showcases of technology for key stakeholders.

2.4 GENERAL REQUIREMENTS

2.4.1 PROPOSING TEAMS

Proposals are expected to involve teams with the expertise needed to collectively achieve the goals of the proposed TA(s) specific content. Communications, networking, and team formation are the sole responsibility of the proposer. Proposers must submit a single, integrated proposal led by a Principal Investigator (PI), under a single prime awardee that addresses all program phases as applicable. Teaming (that considers accessibility across geographies) is highly encouraged to accomplish the transformational goals set forth in the GLIDE program.

Proposers may only submit one proposal as the prime proposer. See Section 3.1 in terms of what constitutes a proposer. The Government's expectation is that all key members of the performer team will be onboard within 60 days of the award.

At minimum, each Performer Team must include the following individuals:

- **Lead Principal Investigator (PI)**
  The lead PI is responsible for overseeing and directing the project design, implementation, and reporting of results. Further the PI is responsible for organizing the performer team and ensuring compliance with GLIDE requirements.
- **Project Manager** Proposers must include a Project Manager who coordinates efforts across the team, ensuring compliance with timelines and programmatic goals. The Project Manager will assist the lead PI in day-to-day project operations and execution as well as financial management and reporting.
- **Product Development Lead (PDL)**
  The Product Development Lead is an individual with the background necessary to manage the commercialization and regulatory efforts. This includes oversight of the "product development team"; regulatory, reimbursement, and commercialization experts who can act as either consultants or subcontractors. While the Government may

offer to augment the proposers' team with additional commercialization experts post award (e.g., Regulatory Consultants), the Proposer must propose a team independently capable of meeting GLIDE's translational/commercialization goals.

- **Discovery Duo Program**
  The Discovery Duo program is designed to further engage the patient community in our research efforts by pairing a patient or parent ambassador with an early-stage scientific investigator who is within the first 10 years of receiving their advanced research degree. The early-stage investigator is designated as the performer's JEDI representative for the performing team. The background or expertise of the Discovery Duo should align with the technology and disease area of the performing team's proposal. Discovery Duos will be expected to meet regularly (at least quarterly) and work directly with the lead PI and PDL, and who in turn will provide oversight and guidance with respect to inclusion, affordability, and accessibility considerations. GLIDE's PM will ensure that the Duos across the GLIDE program represent the patient's experiences across the range of lymphatic diseases being studied.

  The goal of the Discovery Duo program is to center the "patient experience", encouraging researchers and clinicians to be advocates for lymphatic disease and empowering patients and patient ambassadors with a better understanding of the research process. The partnership will bidirectionally inform and motivate each other while engaging the patient community. Researchers and clinicians will engage with people who live with LD or a common chronic disease with underlying lymphatic dysfunction; patient ambassadors will have the ability to contribute to the scientific process informed by their Duo research partner.

  As key members of GLIDE's JEDI taskforce (see Section 2.4.2), the Discovery Duo will help to ensure that affordability, accessibility, and user experience is centered in the program. These Duos are tasked with conducting patient centered customer discovery, termed Patient Voice Sessions, which should include meetings with specialized hospital settings, patient advocacy organizations, medical associations, undergraduate and graduate healthcare institutions and more. Each Duo is responsible for outlining their own approach and timeline to complete at least 50 Patient Voice Sessions by the end of Phase I in preparation for the Accessibility Workshop in Phase II. Ultimately, Discovery Duos will integrate their findings into their program's structure through direct involvement with activities such as in study design, the study review, ensuring accessibility, affordability of new technologies, stakeholder education, data sharing, and informed consent in clinical trials. The proposals must allocate funding for both members of the Discovery Duo and to include expenses related to these efforts (such as travel expenses) in the program budget. GLIDE requires this stipend to be, at minimum, $5,000/each per year of the Period of Performance (i.e., minimum of $10,000 per Duo).

  Patient involvement and community-engaged research are critical to the process of developing technologies supported by the GLIDE program. To facilitate connections between patient groups and GLIDE technical proposers, we have created a patient engagement page where individuals can share their profiles and learn more about Discovery Duo partners.

2.4.2 GLIDE PROGRAM MEETINGS AND ATTENDANCE

- **Monthly Status Reports (MSR) with PM/GLIDE Team** – Each team lead performer and project manager (if team has one) will be required to meet with the PM/GLIDE Team monthly (estimated as 1 hour each meeting.) for update and reviews. Status reports outlining technical and financial updates will be required at monthly meetings with the PM.

- **Meeting of the Minds (M&M)** – In an effort to promote collaboration and learnings from all, the lead PI, Discovery Duo, PDL, and the Project Manager from each performer team must meet semiannually throughout the GLIDE program at a virtual Meeting of the Minds (M&M) where discovery and technology will be discussed among all performers of the GLIDE program. Additional members of each performing team are welcome to join M&M.

- **GLIDE's Innovative Technology Workshop** – During Phase I, GLIDE will host an internal, in-person, workshop (site to be determined (TBD)) where all performers will present progress and updates on their technology and will have the opportunity to meet FDA, National Institutes of Health (NIH), and Department of Defense (DoD) representatives. Further, this workshop will provide the opportunity for those members of the GLIDE program to interact with members of the Lymphatic Imaging, Genomic, and pHenotyping Technologies (LIGHT) program.

- **JEDI Taskforce Meetings and Accessibility Workshop**
  The JEDI Taskforce will meet within the first quarter of each of the three phases. The JEDI Taskforce meetings will be mandatory for all Discovery Duos and PDLs for each performer team (however other members of the GLIDE performer teams are welcome to attend upon approval from the PM). The learnings and findings from the JEDI Taskforce meetings will inform the Accessibility Workshop.

  During the first 12 months of Phase II, the JEDI Taskforce will hold an Accessibility Workshop to establish KPIs and to which all performers will be invited to attend to share the findings from the JEDI Taskforce Meetings. The KPIs developed in this workshop will provide additional considerations to ensure the technology is tolerable and commercially viability. The lead PI, Discovery Duos, the PDL, and the project manager of each performer team are required to attend the Accessibility Workshop.

- **Attendance**
  Attendance at all meetings will be recorded and expected to be no less than 90% annually. This policy establishes accountability, a competitive-yet-collaborative environment, and collaborative value-added contribution to the program's success. Each team will also be required to meet with the PM at least monthly to review progress, metrics, and milestones.

Invited Guests from NIH and the National Commission of Lymphatic Diseases (NCLD), FDA and other government agencies may be invited to GLIDE in person and virtual meetings,

workshops and Accessibility Taskforce meetings with the intended purpose of gathering insight into possible transition partners, commercialization strategies, and regulatory hurdles.

DIVERSITY IN CLINICAL TRIAL POPULATIONS FOR GLIDE PHASE III

While following the guidelines outlined by FDA on clinical trials, ARPA-H is also committed to equitable healthcare access irrespective of age, race, ethnicity, gender/gender identity, sexual orientation, disability, geography, employment, insurance, and socioeconomic status. Lymphatic dysfunction does not discriminate by age, sex, gender, socioeconomic status, religion, or ethnicity. GLIDE will ensure that all performers follow the FDA's guidance titled Diversity Action Plans to Improve Enrollment of Participants from Underrepresented Populations in Clinical Studies and that participants in clinical trials supported by GLIDE mirror the proportions of the US population that live with the disease (±5%).

2.4.3 ACCESSIBILITY REQUIREMENTS

Lymphatic disease spares no one and knows no borders. GLIDE will ask lead PIs from each team to prioritize diversity, adopting intentional inclusion practices, addressing systemic inequities, and ensuring inclusivity, including a wide range of voices within core research teams. ARPA-H is committed to accessibility inclusive of diverse and underrepresented scientists, clinicians, students, and patients. In an intentional effort to build capacity for research/innovation among underrepresented communities, GLIDE proposers are highly encouraged to involve qualified early investigators, graduate students, and undergraduates inviting them as team members or offering research opportunities that they may not otherwise have to explore the field of lymphatic medicine. Such creative solutions may include availability of scholarships, internships, and stipends for summer research projects.

Further, ARPA-H is committed to equitable health care access irrespective of age, race, ethnicity, gender/gender identify, sexual orientation, disability, geography, employment, insurance, and socioeconomic status. With support from a trained Accessibility Advisor retained by ARPA-H, all conforming proposals and performers will be reviewed throughout the program to ensure that metrics and milestones prioritize end-user needs regarding affordability and accessibility.

Overview of Accessibility Responsibilities as a GLIDE performer:

All proposers must describe how they will engage specific stakeholder groups (e.g., patients, caregivers and community organizations) to maximize health accessibility. **All proposers must articulate how they will incorporate accessibility considerations** (e.g., diverse user demographics) into design, development, and testing of prototypes to ensure equal access and mitigation of bias.

Performers who may collect patient data in support of research deliverables must collect data elements that enable assessment of health accessibility and disparity indices (e.g., race, ethnicity, sex, foreign-born, rural, geographic and other demographic data). **Performers must designate one Discovery Duo member (preferably an early investigator or postdoctoral student) as the primary point of contact for accessibility activities** and considerations, then remain responsive to communication and coordination with GLIDE's team.

Performers involved in the handling of personalized and/or identified demographics or health

data must ensure appropriate privacy and security standards are met. All proposers should outline anticipated risks and potential ramifications of not meeting accessibility goals. The ARPA-H Accessibility Advisor will be involved in reviewing all milestone reports and evaluations and will advise on how accessibility issues can be strengthened throughout the program.

GLIDE's JEDI Taskforce

The GLIDE program will develop the *JEDI Taskforce*. Under the guidance of expertise from ARPA-H, each performer team's Discovery Duo and PDL must serve as members on the JEDI Taskforce. Performers can recommend additional members, such as community hospital administrators or representatives of patient advocacy organizations, to join the taskforce with PM approval.

The JEDI Taskforce's mission will be to ensure accessibility, diversity, inclusion, and justice in the form of accessibility and affordability as well as advocacy and stakeholder education among all teams under GLIDE.

Responsibilities of JEDI Taskforce:

- Attend PM team meetings, workshops, participate in "Patient Voice Sessions."
- Advocate for insurance, accessibility, clinical trial accessibility, and central data sharing.
- Work with the Customer Experience Network and Investor Catalyst Network Hubs providing a patient perspective.
- Attend an Accessibility workshop in collaboration with the LIGHT Program and the PM's portfolio of programs within the first 3 years of the GLIDE program.
    - **Goal** - Define accessibility Key Performer Indicators (KPI) 's for the taskforce. Resulting in a Road Map to accessibility report.
    - Disseminate Road Map to accessibility Report across the United States (i.e., hospitals, clinics, patient advocacy organizations, Centers for Medicare and Medicaid Services (CMS), Centers for Disease Control and Prevention (CDC), NIH and the National Lymphatic Commission, private insurers, FDA, Centers of Excellence, professional societies).

Figure 2: Justice, Equity, Diversity and Inclusion - JEDI Taskforce Goals

JEDI Taskforce Goals

Challenge: Lack of patient input in design and development of lymphatic medical technologies

Goal: Involve patient in the design process early via Discovery Duo Program

Lymphatic dysfunction does not discriminate

Challenge	Solution
1. Access to care, inclusion, affordability	1. Built within the Target Product Profiles
2. Isolated and siloed research	2. Bridge LIGHT & GLIDE
3. Insurance coverage, coding	3. Data collection for evidence
4. Isolated patients and providers	4. Interviews, community health fairs, visit MSI, underserved/rural communities, med student engagement
5. Bridging the Valley of Death for LD technology	5. Involve VCs, IC Hub to LIGHT/GLIDE workshops
6. Duplication of efforts with National Commission on Lymphatic Disease	6. Promote collaboration with federal stakeholders, FFRDCs – invitation to attend LIGHT/GLIDE workshops

Final Product: An Accessibility Roadmap used by all stakeholders in the Lymphatic Ecosystem

- Ensures research to include benchmarks for inclusion, affordability and accessibility considerations.

Stakeholder Education and Dissemination

GLIDE recognizes the importance of stakeholder education and dissemination to ensure that the community embraces the new innovative technology developed by this program. As such, GLIDE intentionally has incorporated opportunities for its performers to educate the next generation of researchers and providers, cultivating a newly created ecosystem of lymphatic medicine. Each PI is required to give at least one lecture centered on lymphatics per year during the GLIDE program. The lectures should be coordinated with and approved by the Program Manager, and directed to either a medical school, graduate, undergraduate school audience (preferably of underserved or rural academic centers), and/or patient advocacy group or professional society. Further, GLIDE will encourage collaborative efforts of the performer teams with the ARPANET-H Hub and spoke system. This may include formative user

studies offering a diverse array of stakeholders, customer discovery to inform product design and patient voice sessions including interactions with the FDA to include patient-led research.

The interactions and communications of the performing teams with various professional societies, advocacy groups, and students will strengthen and intentionally build formative educational opportunities and capacity among the lymphatic community engaging all stakeholder and consumer communities and therefore yielding more inclusive technologies and management of disease.

3. ELIGIBILITY INFORMATION

3.1 ELIGIBLE PROPOSERS

All responsible sources capable of satisfying the Government's needs may submit a proposal to this ISO.

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 organization. ARPA-H encourages organizations to submit their research ideas notwithstanding this perceived limitation. Any proposal received will be fairly considered for award and, if it is 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 will have unique capabilities that are not available to proposing teams through any other resource. Accordingly, the following principles will apply to this solicitation.

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

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

- If a potential prime performer 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.

3.1.2 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.

3.2 SYSTEM FOR AWARD MANAGEMENT (SAM)

All proposers must have an active registration in SAM.gov in order 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 or a current award from ARPA-H is held.

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.

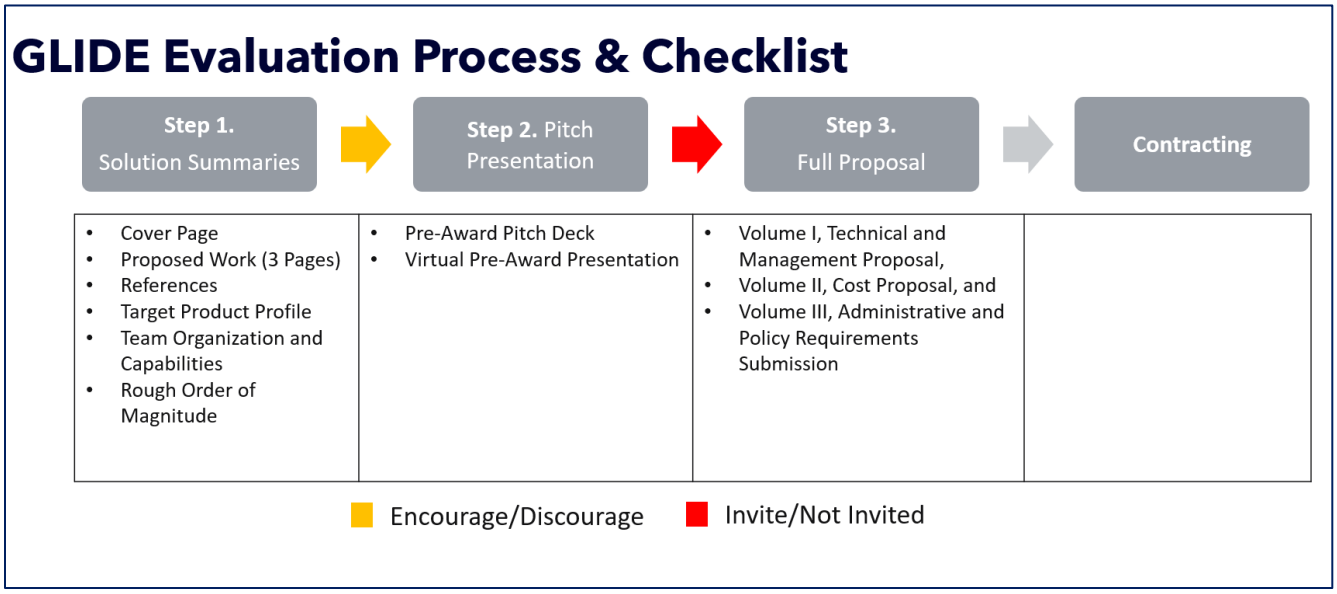
4. GLIDE SUBMISSION AND EVALUATION PROCESS

4.1 SUBMISSION PROCESS OVERVIEW

Proposals to GLIDE will be reviewed in three steps that consists of the following:

- ✓ **Step 1:** Submit Solution Summary (Proposers are encouraged / discouraged to move to Step 2)
- ✓ **Step 2:** Submit Pre-Award Pitch Presentation and schedule the virtual oral presentation.
- ✓ **Step 3:** Submit Full Proposals, if invited.

Figure 3. Evaluation Process and Requirement



4.2 SOLUTION SUMMARY SUBMISSIONS

Solution Summary submissions are required. See Appendix A for the required Solution Summary format.

4.3 PRE-AWARD PITCH PRESENTATION SUBMISSIONS

ARPA-H will respond to conforming solution summaries encouraging or discouraging proposers to submit a pitch deck for virtual oral presentations. See Appendix B for the required GLIDE Pre-Award Pitch Presentation format.

4.4 FULL PROPOSAL SUBMISSIONS

Full proposal submissions are by invitation only. See Appendix C for the required Full Proposal format.

4.5 SUBMISSION INFORMATION

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

All solution summaries, pre-award pitch presentations 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), Appendix B (Pre-Award Pitch Presentation Format and Instructions) and Appendix C (Full Proposal Format and Instructions).

Proposers are responsible for submitting all solution summaries, pre-award pitch presentations, and full proposals via the ARPA-H Solution Submission Portal and ensuring receipt by the date and time specified in the ISO or as communicated through feedback letters. 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. Plan 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.

4.6 SOLUTION SUMMARY, PRE-AWARD PITCH PRESENTATION AND FULL PROPOSAL SUBMISSION DEADLINES

The closing date of this solicitation, as established in Section 1, is the date Solution Summaries are due.

The pre-award pitch submission deadline will be provided to proposers at the time of Solution Summary feedback (i.e., encourage/discourage submission of the pre-award pitch presentation). See Appendix B (Pre-award pitch presentation required format).

The full proposal submission deadline will be provided to the proposers at the time of the pre-award pitch presentation feedback (i.e., invited/not invited to submit full proposal). See Appendix C (Full Proposal Format and Instructions) for required full proposal format. Proposal packages must include Volumes I-III.

4.7 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.

5. SOLUTION SUMMARY AND PRE-AWARD PITCH PRESENTATION REVIEW, AND EVALUATION OF FULL PROPOSALS

5.1 CONFORMING SOLUTION SUMMARY, PRE-AWARD PITCH PRESENTATIONS, AND FULL PROPOSAL SUBMISSIONS

Conforming submissions contain all requirements detailed in this ISO. Solution summaries, pre-award pitch presentations, or full proposals that fail to include required information may be deemed non-conforming and may be removed from further consideration. Non-conforming submissions may be rejected without further review. A solution summary, pre-award pitch presentation, or full proposal will 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 GLIDE Program.
- The proposers meet the eligibility requirements.
- The solution summary/pitch deck/full proposal meets the submission requirements.
- The solution summary/pitch deck/full proposal meets the content and formatting requirements in the attached instructions.

- The proposer's concept has not already received funding or been selected for award negotiations for another funding opportunity (whether from ARPA-H or another Government agency).

Non-conforming solution summary, pre-award pitch decks, and full proposal submissions may be removed from consideration. Proposers will be notified of non-conforming determinations via email correspondence.

5.2 STEP 1: SOLUTION SUMMARY REVIEW PROCESS

ARPA-H will review and respond to all proposers submitting solution summaries. At a minimum, the response will indicate whether a proposer is encouraged or discouraged from moving on to Step 2: Submitting a pitch deck for oral presentation. Conforming solution summaries will be reviewed and encourage or discourage feedback will be provided based on ARPA-H's interest in the concept submitted. Feedback will be provided to the administrative and technical points of contacts noted on the solution summary cover page.

5.3 STEP 2: PRE-AWARD PITCH PRESENTATION PROCESS

ARPA-H will review and respond to all proposers submitting a pre-award pitch deck and completing a virtual oral presentation. At a minimum, the response will provide the Government's invitation to submit a full proposal or not. Feedback will be provided to the administrative and technical points of contacts noted on the pitch deck cover page.

5.4 STEP 3: FULL PROPOSAL REVIEW PROCESS

ARPA-H will review and respond to all proposers submitting a full proposal. Feedback will be provided to the administrative and technical points of contacts noted on the full proposal cover page.

5.5 EVALUATION CRITERIA FOR STEPS 2-3 AND AWARD

Pre-award pitch presentations and full proposals will be evaluated using the following evaluation criteria listed in descending order of importance.

5.5.1 CRITERIA 1: OVERALL SCIENTIFIC AND 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 the award. The proposal identifies major technical risks and planned mitigation efforts are clearly defined and feasible. In addition, the evaluation may take into consideration the extent to which the proposed IP rights structure will potentially impact the Government's ability to transition technology.

5.5.2 CRITERIA 2: PROPOSER'S CAPABILITIES AND/OR RELATED EXPERIENCE

Factors considered may include: 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; and similar efforts completed/ongoing by the proposer in this area are fully described including identification of other Government entities (see Section

3.1.1).

In terms of capability, the Government shall assess the Volume III bio-sketches provided for the performer team members including the PI, Project Manager, the Discovery Duo team (Early Investigator and Patient/Parent/Caregiver Ambassador), Regulatory expert (PDL), Commercialization experts, and any other key personnel on the project team as requested by ARPA-H.

5.5.3 CRITERIA 3: POTENTIAL CONTRIBUTION TO RELEVANCE TO THE ARPA-H MISSION AND USER EXPERIENCE

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 currently 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. Further, the proposed solution contemplates the end user first by understanding for whom the solution solves. For example, who will use this? Second, the solution meets the needs of the end user whether patients, providers, health systems, or payers. For example, how would this solution fit inside the clinical workflow? Or how will this be accessible to users in all geographies, and at an affordable cost?

5.5.4 CRITERIA 4: PRICE ANALYSIS

All solution summaries and proposals will be evaluated to determine the reasonableness of the estimated budget proposed to accomplish the work in the Statement of Work (SOW). Cost realism analysis may be performed to ensure proposed costs are realistic for the technical and management approach, accurately reflect the technical goals and objectives of the solicitation, the proposed costs are consistent with the proposer's scope of work and reflect a sufficient understanding of the costs and level of effort needed to successfully accomplish the proposed technical approach. The costs for the prime proposer and proposed sub-awardees should be substantiated by the details provided in the proposal (e.g., the type and number of labor hours proposed per task, the types and quantities of materials, equipment and fabrication costs, travel and any other applicable costs including the basis for the estimates).

It is expected the effort will leverage all available relevant prior research to obtain the maximum benefit from the available funding. For efforts with a likelihood of commercial application, appropriate direct cost sharing may be a positive factor in the evaluation. ARPA-H recognizes that undue emphasis on cost may motivate proposers to offer low-risk ideas with minimum uncertainty and to staff the effort with junior personnel to assume a more competitive posture. ARPA-H discourages such cost strategies.

5.6 REVIEW, EVALUATION, AND SELECTION PROCESS FOR AWARD

It is the policy of ARPA-H to ensure impartial, equitable, comprehensive evaluations based on the evaluation criteria listed above and to select the proposals whose solutions are most advantageous to the Government.

ARPA-H will conduct a review of each conforming proposal. All proposal evaluations will be based solely on the evaluation criteria. A selection for award negotiations will be made to proposers whose full proposal is determined to be most advantageous by the Government.

NOTE: proposals will not be evaluated against each other during the scientific review process, but rather evaluated on their own individual merit to determine how well the submission meets the criteria stated in this ISO.

5.6.1 REVIEW AND EVALUATION TIMELINES

ARPA-H's intent is to review and evaluate Solution Summaries, the pre-award pitch presentations, and full proposals as soon as possible after the closing of the submission deadlines.

5.7 HANDLING OF SELECTION SENSITIVE INFORMATION

It is the policy of ARPA-H to protect all Solution Summaries, pitch decks, and full proposals as selection sensitive information and to disclose their contents only for the purpose of evaluation and/or 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 solution summaries and proposals may be solicited by ARPA-H from non-Government consultants/experts who are strictly bound by appropriate non-disclosure requirements. No submissions will be returned.

5.8 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. Proposals are expected to use innovative approaches that include novel technology, enabling revolutionary advances in medicine and healthcare. The ISO uses merit-based competitive procedures to the maximum extent practicable.

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

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

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

requirement for ARPA-H concurrence before publishing any information or results on the effort. At a minimum, all awards will include a requirement for performer teams to submit information for review to ARPA-H before publishing.

6. POLICY REQUIREMENTS AND MISCELLANEOUS OTHER INFORMATION

6.1 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.

6.1.1 AGENCY SUPPLEMENTAL OCI POLICY

In addition, ARPA-H restricts performers from concurrently providing professional support services, or similar support services and being a 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 (proposed sub-awardee, etc.) is providing professional support services to any ARPA-H office(s) under: (a) a current award or subaward; or (b) 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 C) 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.

6.1.2 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 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. ARPA-H strongly encourages IP rights to be aligned with open-source regimes. 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.

NOTE: IP rights assertions will be reviewed under Criterion 1.

6.3 HUMAN SUBJECTS RESEARCH

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

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

6.4 ANIMAL SUBJECTS 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) must comply with the laws, regulations, and policies on animal acquisition, transport, care, handling, and use as outlined in: (i) 9 CFR parts 1-4, U.S. Department of Agriculture rules that implement the Animal Welfare Act of 1966, as amended, (7 U.S.C. § 2131-2159); (ii) the Public Health Service Policy on Humane Care and Use of Laboratory Animals, which incorporates the "U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training," and "Guide for the Care and Use of Laboratory Animals" (8th Edition)."

Proposers must provide documentation of a current Animal Welfare Assurance (AWA) on file with the Office of Laboratory Animal Welfare (OLAW).

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

All animal use research must undergo review and approval by the local Institutional Animal Care Use Committee (IACUC) prior to incurring any costs related to the animal use research. For all proposed research anticipating animal use, proposals should briefly describe plans for IACUC review and approval.

6.5 ELECTRONIC INVOICING AND PAYMENTS

Performers will be required to submit invoices in a designated electronic payment system as described in the award document.

6.6 GOVERNMENT-FURNISHED PROPERTY/EQUIPMENT/INFORMATION

Government-furnished property/equipment/information may be provided to selected performers. Any instances of GFP/GFE will be specifically negotiated.

APPENDIX A: SOLUTION SUMMARY FORMAT AND INSTRUCTIONS

A. General Instructions

All Solution Summaries must use a font type not smaller than 11-point font. Smaller font may be used for figures, tables, and charts (but should be legible). Margins may be no less than 0.5" 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 3 total; and any Solution Summary submitted that exceeds 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 GLIDE program. Your 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) as a guide:

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.

Solicitation #	ARPA-H-SOL-24-111
Solution Summary Title	
Technical Approach (TA) Selection (TA1 or TA2 – must select only one)	
Technical Pathway Selection (Activator or Accelerator)	
Submitter Organization	
Type of Organization and website URL if applicable	**Choose all that apply:** Large Business, Small Disadvantaged Business, Other Small Business, HBCU, MI, Other Educational, or Other Nonprofit
Technical Point of Contact (POC)	Name: Mailing Address: Telephone:

	Email:
Administrative POC	Name: Mailing Address: Telephone: Email:
Total Estimated Budget	Total: $
Place(s) of Performance	
Other Team Members (sub-performers, including consultants) if any	Technical POC Name: Organization: Organization Type:
What is your rare disease indication?	
What is your chronic disease indication?	

C. Proposed Work

Clearly identify the problem(s) to be solved and the outcome(s) sought with the proposed technology concept. Explain the concept's potential to be disruptive compared to existing or emerging technologies including anything with pre-existing funding and how the proposed approach will go far beyond current commercial capabilities.

Describe the final deliverable(s) for the project, one or two key interim milestones, and the overall technical approach used to achieve project objectives. Describe the background, theory, simulation, modeling, experimental data, or other sound engineering and scientific practices or principles that support the proposed approach. Identify adoption challenges to be overcome for the proposed technology to be successful. Describe key technical risks.

D. Target Product Profile

Proposers must include a target product profile (TPP) for the proposed solution for each disease indication (minimum of 2 indications). The TPP 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 target product profile, with required key metrics for impact on lymphatic function and disease indications, are provided as attachments (See Attachment 1). No more than two pages per TPP.

E. Team Organization and Capabilities

Indicate the roles and responsibilities of the organizations and key personnel that comprise the Performer Team. Provide the name, position, and institution of each key team member; and describe in 1-2 sentences the skills and experience they bring to the team.

F. Rough Order of Magnitude (ROM)

Please include a basis of estimate (BOE) to support the proposed project budget as well as the

total project cost including cost sharing, if applicable. The BOE should also include a breakdown of the work by fully burdened labor (inclusive of fringe), subcontracts, materials, equipment, other direct costs (e.g., travel), indirect costs, profit, cost sharing, and any other relevant costs. Also, estimate the total number of labor hours anticipated per phase in the labor hours row. All subcontracts should total together in the subcontracts line. The below table may be used for this breakdown:

Categories	**Phase I Amount**	**Phase II Amount**	**Phase III Amount**	**Total**
Direct Labor (including fringe)				
Subcontracts				
Materials				
Equipment				
Travel				
Other Direct Costs				
Indirect Costs				
Profit/Fee				
Total				
Cost Sharing (if applicable/appropriate)				
Labor hours (in hours)				

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

NOTE: Delete all formatting and content instructions prior to submission.

APPENDIX B: PRE-AWARD PITCH PRESENTATION FORMAT AND INSTRUCTIONS

A. General Instructions.

All GLIDE pre-award pitch submissions must use the pitch deck slides provided on SAM.gov. See Attachment 2. Go to the ARPA-H Solution Submission Portal and follow the directions to submit your pre-award pitch presentation slide deck. Create a username and password and navigate to the pitch submission.

Be advised of the following important information:

- It is recommended that all proposers review and follow all pre-award pitch presentation slide deck instructions provided.
- Submissions will not be considered complete until all required files have been uploaded.
- Your pre-award pitch presentation submission will be set-up for you on pitch day. **No revisions post submission will be allowed.**

B. Pre-Award Pitch Presentation Format and Logistics

All GLIDE pre-award pitch oral presentations will be virtual. Two people from each team will be allowed to attend the presentation. All pitch presentations will be 30 minutes total including 20 minutes for your presentation and 10 minutes of questions and answers (Q&A). Proposers should consider all the ARPA-H Heilmeier Questions (HQs) (HQs 1-10) as a guide throughout the pitch slides where noted. There is a maximum of 2 slides per HQs. The pitch presentation should also include a Target Product Profile (TPP) for their proposed solution in TA1. Physical Devices or TA2. Pharmacologic, gene or cell therapies. Pictures, figures and diagrams are encouraged in place of text where relevant.

A link will be provided to proposers who submit a conforming pre-award pitch deck to schedule the virtual pitch presentation.

APPENDIX C: FULL PROPOSAL FORMAT AND INSTRUCTIONS

Full proposals must follow the guidance in Appendix C. Conforming 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 GLIDE	
C. Technical Plan	
D. Management Plan	
E. Capabilities	
F. Commercialization Plan	
G. Statement of Work (SOW)	N/A, use provided template/format
H. Target Product Profiles	2 (maximum per TPP), use provided template/format
I. Schedule and Milestones	N/A use provided template/format
J. Data Management and Sharing Plan (DMSP)	N/A (estimated 2 pages)
K. References	N/A
Volume II, Cost Proposal	
Volume Element	Page Limit
Cover Page	1
A. Cost Proposal Spreadsheet(s), including for subcontractors 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	

B. OCI Affirmations and Disclosure	N/A, use provided template/format
C. National Security Disclosure and associated biosketches	
D. Novelty of Proposed Work	
E. Intellectual Property (IP)	
F. Human Subjects Research	
G. Animal Subjects Research	
H. Representations Regarding Unpaid Delinquent Tax Liability or a Felony Conviction Under any Federal Law	

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 11 point (Arial or non-serif 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 1-3 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-24-111
Full Proposal Title	
Technical Approach (TA) Selection (TA1 or TA2 – must select only one)	
Technical Pathway Selection (Activator or Accelerator)	
Rare Disease Indication	
Chronic Disease Indication	
Prime Awardee/entity submitting the proposal	
Unique Entity Identifier of primer proposer/awardee (UEI)	

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 or not a business qualifies as small.). Size standards may be found here: https://www.ecfr.gov/current/title-13/chapter-I/part-121#121.201
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 (sub-performers, including consultants) if applicable.	Technical POC Name: Organization: Organization Type:
Total funds requested from ARPA-H, and the amount of cost share (if any)	Total: $
Place(s) of Performance	

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

1. What is the proposed work attempting to accomplish or solve?
2. How is it done today? What are the limitations of present approaches?
    - *What is the competitive landscape?*
3. 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?*

4. 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?*
5. Who cares? If you succeed, what difference will it make?
6. 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.
7. How much will your project cost?
8. What are your milestones to check for success consistent with GLIDE metrics?
9. 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?*
10. How might this program be misperceived or misused (and how can we prevent that from happening)?

B. Solution Fit with GLIDE: Clearly describe what the team is trying to achieve and the difference it will make (qualitatively and quantitatively) if successful relative to GLIDE'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 any subcontractors and key personnel who will be doing the work. A PI for the project must be identified, along with a description of the team's organization, including the breakdown by TA. All teams are required to identify a Project Manager/Integrator 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 collaborators/subcontractors of the proposed effort. Include risk management approaches. Describe any formal teaming agreements required to execute this program.

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

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

G. Statement of Work (SOW): The SOW should provide a detailed task breakdown, citing specific tasks for each TA and their connection to the milestones and program metrics. Each Phase of the program should be separately defined. The SOW must not include proprietary information. Please note the technical proposal must stand on its own as the SOW cannot be used to supplement the 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 (prime awardee, sub-awardee(s), by name).
- A measurable milestone, i.e., a deliverable, demonstration, or other

event/activity that marks task completion. Include completion dates for all milestones. Include quantitative metrics.

- A definition of all deliverables (e.g., data, reports, software) to be provided to the Government in support of the proposed tasks/subtasks.

It is recommended the SOW be developed so that each TA and phase 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 1-3, 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-24-111
Full Proposal Title	
Technical Approach (TA) Selection (TA1 or TA2 – must select only one)	
Technical Pathway Selection (Activator or Accelerator)	
Rare Disease Indication	
Chronic Disease Indication	
Prime Awardee/entity submitting the proposal	
Unique Entity Identifier of primer proposer/awardee (UEI)	
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 or not a business qualifies as small.). Size standards may be found here: https://www.ecfr.gov/current/title-13/chapter-I/part-121#121.201
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 (sub-performers, including consultants) if applicable and type of organization for each	Technical POC Name: Organization: Organization Type:
Total proposed cost separated by base and option(s) (if any)	
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 120 days)	

A. Cost Proposal Spreadsheet: ARPA-H Standard Excel Cost Proposal Spreadsheet (See Attachment 3). All tabs and tables in the cost proposal spreadsheet should be developed in an editable format with calculation formulas intact to allow traceability of the cost proposal. The cost proposal spreadsheet must be used by the prime organization and all subcontractors at any tier.

While the prime proposer is ultimately responsible for submission of all required documents, subcontractor cost proposal spreadsheets may be submitted directly to the Government by the proposed subcontractor via email to GLIDE@ARPA-H.gov. Subcontractor proposals should include Interdivisional Work Transfer Agreements or

similar arrangements between the awardee and divisions within the same organization as the awardee.

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 in excess of the rate identified by the Office of Personnel Management for Executive Level II positions. Nor may the proposed and later negotiated salaries escalate in excess of 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.

III. Volume III, Administrative and Policy Requirements Submission

The Administrative and National Policy Requirements document must be completed in full and included as part of the Volume III proposal submission. **Do not delete any portion of this document.**

All pages shall be formatted for printing on 8-1/2 by 11-inch paper with 1-inch margins and font size not smaller than 11 point. Font sizes of 8 or 10 point may be used for figures, tables, and charts. There is no page limit for this document.

The Administrative and National Policy Requirements document must be in .pdf, .odx, .doc, or .docx formats. Submissions must be written in English.

Cover Page

Solicitation #	ARPA-H-SOL-24-111
Full Proposal Title	
Technical Approach (TA) Selection (TA1 or TA2 – must select only one)	
Technical Pathway Selection (Activator or Accelerator)	
Rare Disease Indication	
Chronic Disease Indication	
Prime Awardee/entity submitting the proposal	
Unique Entity Identifier of primer proposer/awardee (UEI)	
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 or not a business qualifies as small.). Size standards may be found here: https://www.ecfr.gov/current/title-13/chapter-I/part-121#121.201
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 (sub-performers, including consultants) if applicable and type of organization for each	Technical POC Name: Organization: Organization Type:
Total proposed cost separated by base and option(s) (if any)	
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 120 days)	

1. Team Member Identification

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

Prime				
Individual Name:	Organization:	Non-U.S. Organization: Non-U.S. Individual:	☐ Yes ☐ Yes	☐ No ☐ No
Subawardees/Consultants				
Individual Name:	Organization:	Non-U.S. Organization: Non-U.S. Individual:	☐ Yes ☐ Yes	☐ No ☐ No
Individual Name:	Organization:	Non-U.S. Organization: Non-U.S. Individual:	☐ Yes ☐ Yes	☐ No ☐ 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 (whether prime or subawardee or consultant) currently providing Systems Engineering Technical Assistance (SETA), Partnership Intermediary Agreement (PIA) or similar support to ARPA-H? ☐ No ☐ Yes

b. Did any of the proposed individual team members or their respective organizations (whether prime or subawardee or consultant) provide SETA, PIA, 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 (subawardee, consultant) 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 (whether prime or

subawardee or consultant)? ☐ No ☐ Yes

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

- Identification of applicable team member; and
- An OCI mitigation plan.]

3. Application for Federal Assistance SF-424 (R&R) (For Cooperative Agreements Only)

[Please provide a completed SF-424 (R&R) Application for Federal Assistance form.]

4. Research Security Disclosure

[Please provide a completed Research and Related Senior/Key Person Profile (Expanded) Form.] (for Cooperative Agreements only)

In addition, in accordance with National Security Presidential (NSPM)-33 and the associated White House Office of Science and Technology Policy Implementation Guidance[1], which requires certain individuals to disclose potential conflicts of interest (COI) and commitment (COC), PIs and other senior/key personnel[2] that will serve as prime and subawardees are required to complete the Current and Pending (other) Support Common Form as well as the Biographical Sketch Common Form. These forms must be included as attachments to the Research and Related Senior/Key Person Profile (Expanded) Form (for Cooperative Agreements) and can be found at: https://www.nsf.gov/bfa/dias/policy/nstc_disclosure.jsp].

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

i. Other organizational affiliations and employment
ii. Other positions and appointments[3]
iii. Participation in any foreign government-sponsored talent recruitment program(s)[4]

[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

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 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

funding, complimentary foreign travel, honorific titles, career advancement opportunities, promised future compensation, or other types of remuneration or consideration, including in-kind compensation.

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 (whether prime or subawardee or consultant) participate in any foreign government-sponsored talent recruitment program(s)? ☐ No ☐ Yes

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

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

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

5. Synthetic Nucleic Acids or Benchtop Nucleic Acid Synthesis Equipment

Does the proposed work include the potential to procure synthetic nucleic acids or benchtop nucleic acid synthesis equipment? This includes, but is not limited to, procuring synthetic DNA and RNA, as well as whole organism genomes (e.g., viruses, bacteria) containing any synthetic nucleic acid 200 nucleotides or greater, and benchtop equipment capable of synthesizing nucleic acids. ☐ No ☐ Yes

[If yes, see the OSTP Framework for Nucleic Acid Synthesis Screening for additional guidance, attestation requirements, and definitions of terms. The requirement to use the framework applies to all work performed under the award.]

6. 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

7. Intellectual Property (IP)

[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 Restrictions	Summary of Intended Use in the Conduct of the Research	Basis for Assertion	Asserted Rights Category	Name of Person Asserting Restrictions

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.]

8. 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 XX of the ISO.]

9. Research and Related Other Project Information (For Cooperative Agreements Only)

[Please provide a completed Research and Related Other Project Information Form. The summary may be included with the Research and Related Other Project Information Form. Please note that Section Nos. 8 through 12 do not need to be completed.]

10. Project Abstract Summary (For Cooperative Agreements Only)

[Please provide a completed Project Abstract Summary Form. The summary may be included with the Research and Related Other Project Information Form.]

11. Human Subjects Research (HSR)

Does the proposed work involve Human Subject Research? ☐ No ☐ Yes

[If yes, please complete the HSR section of the Research and Related Other Project Information Form. Please also provide a completed PHS Human Subjects and Clinical Trials Information Form. Please also complete the below table for each organization, including team members and subawardees, performing HSR. Add row as needed.]

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

12. Animal Use Research (ASR)

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

[If yes, please complete the ASR section of the Research and Related Other Project Information Form. Please also provide a brief description of the plan for Institutional Animal Care and Use Committee (IACUC) review and approval. Please provide the Vertebrate Animals Section (VAS) worksheet in the format here: https://olaw.nih.gov/guidance/vertebrate-animal-section.htm), provided evidence of each applicable organization's Animal Welfare Assurance, and compete the below table for each organization, including team members and subawardees, performing ASR. Add rows as needed.]

Organization	Approved IACUC	Completed VAS	Animal Welfare

Performing ASR	Protocol (Y/N)	(Y/N)	Assurance Number

13. LOBBYING (FOR COOPERATIVE AGREEMENTS ONLY)

[Please provide a completed Certification Regarding Lobbying form. If paragraph (2) of the Certification Regarding Lobbying form is applicable, please provide a completed SF-LLL: Disclosure of Lobbying Activities form. The SF-LLL form may be provided as an attachment to the SF-424 (R&R)]

14. ASSURANCE OF COMPLIANCE WITH NON-DISCRIMINATION LAWS AND REGULATIONS (FOR COOPERATIVE AGREEMENTS ONLY)

[Please ensure an "Assurance of Compliance with Non-Discrimination Laws and Regulations" is on file with HHS and provide documentation confirming the assurance is on file.]

15. ASSURANCE OF COMPLIANCE WITH THE OFFICE OF RESEARCH INTEGRITY (ORI) (FOR COOPERATIVE AGREEMENTS ONLY)

[Please ensure an "Assurance of Compliance with the Office of Research Integrity" is on file with ORI and provide documentation confirming the assurance is on file.]

16. 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 and subcontract organizations 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 D: TARGET PRODUCT PROFILE GUIDELINES

The Target Product Profiles (TPP) for TA1. and TA2. located below provide specific guidance on the acceptable product specifications for products submitted to the GLIDE program.

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

TA1: Target Product Profile (TPP) Guidelines

Proposers must submit a TPP for each disease indication detailing the technologies capabilities. The template below outlines GLIDE's minimum expectations but should be expanded and tailored to fit the specific disease indications selected.

Product description/Therapeutic Modality		Physical Intervention (medical device, surgical tool, wearable, etc.)	
Product Target		**Minimal Acceptable Results**	**Optimal Results**
Primary Product Indication		Measurable improvement of lymphatic functions following intervention	Complete curative therapy for primary lymphatic diseases.
Patient Population*		A subset of patients with selected rare and chronic disease indications	All patients with selected rare and chronic disease indications
Procedure Frequency		Once every 5 years	Once
Delivery Mode		Minimally invasive or done at the time of other standard procedures (e.g.; lymph node dissections or biopsy)	Non- or minimally invasive
Quality of Life		>75% of patients experience a significant increase in QoL	>95% of patients experience a significant increase in QoL
Adverse Event Rate		<10% of patients develop adverse events (≥ Grade II)	<1% of patients develop adverse events (≥ Grade II)
Lymphatic Functional Efficacy Targets[1] (pick ≥1)	Lymphatic Transport	Define a healthy or therapeutic range which is expected to provide significant mitigation of symptoms.	Define a healthy or therapeutic range which is expected to be curative
	Lymphatic Pressure		
	Lymphatic Vessel Contractility		
	Volume/Displacement		
Disease Specific Efficacy Targets[2]	*Ex. Skin Thickness (Lymphedema)*		
	Ex. Stool Calprotectin Levels (IBD)		
	Ex. Lesion Size (Lymphatic Malformation)		
	Etc.		
Product Specificat.	*Ex. Product Dimensions*		

	Ex. Medical Device Class	*Define minimum targets needed for successful commercialization*	*Define stretch targets to maximize impact and patient health*
	Ex. Cost of Goods Manufactured (COGM)		
	Etc.		
Affordability and Accessibility	Device Cost (to purchaser)	Class I: $250; Class II: $3,000; Class III: $8,000	Class I: $250; Class II: $3,000; Class III: $8,000
	Procedure Cost (to patient)	< $1,300 (target out of pocket expense)	< $650 (target out of pocket expense)
	Ease of use	An experienced surgeon/user should be competent in the intervention with ≤ 2 weeks of training.	An experienced surgeon/user should be competent in the intervention with ≤ 5 days of training.
	Accessibility	Available at community hospitals and healthcare centers	Available at rural hospitals and healthcare centers

*The patient subset should include both males and females of varying age and race/ethnicity

Steps Required:

1. Define the *healthy* or *therapeutic range* of ≥2 lymphatic functions in their indication and propose to restore function to that target range.
2. Include additional *minimal and ideal results* specific to the claim and indication of use for the targeted disease. *Listed examples are not requirements or formal suggestions.*

TA2: Target Product Profile (TPP) Guidelines

Proposers must submit a TPP for each disease indication detailing the technologies capabilities. The template below outlines GLIDE's minimum expectations but should be expanded and tailored to fit the specific disease indications selected.

Product description/Therapeutic Modality		Pharmacologic, Gene, or Cell Therapy	
Product Target		**Minimal Acceptable Results**	**Optimal Results**
Primary Product Indication		Measurable improvement of lymphatic functions while on medication	Complete curative therapy of disease indications.
Patient Population*		Adults (may not include pregnant/lactating women), OR children and individuals with comorbidities for selected rare and chronic indications	Adults including pregnant and lactating women, AND children and individuals with comorbidities for selected rare and chronic indications
Treatment Duration		Chronic use	<6 months
Delivery Mode		All administrative routes that result in specific lymphatic targeting: Achieves >30% delivery to LS in first 12 hours.	Non- or minimally invasive administrative routes that result in specific lymphatic targeting (e.g. microneedle patch or lymph targeting oral formulations): Achieves >45% delivery to LS in first 12 hours.
Quality of Life		>75% of patients experience a significant increase in QoL	>95% of patients experience a significant increase in QoL
Adverse Event Rate		<10% of patients develop adverse events (≥ Grade III)	<3% of patients develop adverse events (≥ Grade III)
Lymphatic Functional Efficacy Targets[1] (pick ≥2)	Lymphatic Vessel Density/Vascular Area	Define a healthy or therapeutic range which is expected to provide significant mitigation of symptoms.	Define a healthy or therapeutic range which is expected to be curative
	Lymphatic Transport		
	Lymphatic Pressure		
	Lymphatic Vessel Contractility		

Disease Specific Efficacy Targets[2]	*Ex. Skin Thickness (Lymphedema)*		
	Ex. Stool Calprotectin Levels (IBD)		
	Ex. Lesion Size (Lymphatic Malformation)		
	Etc.		
Product Specific-ations[2]	*Ex. Cost of Goods Manufactured*	Define stretch targets to maximize impact and patient health	Define stretch targets to maximize impact and patient health
	Ex. Dosage Form		
	Etc.		
Affordability and Accessibility	Regimen	Oral: Daily Other (e.g. patches, intranasal): Daily Parenteral (e.g. IV/IM/SQ): Weekly In-clinic injection: Monthly	Oral: Weekly Other (e.g. patches, intranasal): Weekly Parenteral (e.g. IV/IM/SQ): Monthly In-clinic injection: Annually
	Drug Cost (to patient)	< $100/month for management; < $10,000 to cure	< $75/month for management; < $5,000 to cure
	Stability	Therapeutic should be stable for 1.5 years at temperatures ≥ -80C	Therapeutic should be stable for 2 years at temperatures ≥ -20C

*The patient subset should include both males and females of varying age and race/ethnicity

Steps Required:

1. Define the *healthy* or *therapeutic range* of ≥2 lymphatic functions in their indication and propose to restore function to that target range.
2. Include additional *minimal and ideal results* specific to the claim and indication of use for the targeted disease. *Listed examples are not requirements or formal suggestions.*