Special Notice (SN) ARPA-H-SN-24-110
Proposers' Day Announcement for Advanced Research Projects Agency for Health (ARPA-H)/Health Science Futures (HSF) Office
Opportunity: Platform Optimizing SynBio for Early Intervention and Detection in ONcology - POSEIDON

I. KEY INFORMATION

Proposers' Day	September 4, 2024: 9:00AM to 4:00PM ET
Location	Baltimore, MD
Website for registration	https://solutions.arpa-h.gov/POSEIDON/
Registration opens	August 1, 2024, at 12:00PM ET
Registration closes	August 27, 2024, at 12:00PM ET or when capacity is reached, whichever comes first
Technical Point of Contact	Ross Uhrich, DMD, MBA, Program Manager, ARPA-H / HSF Office
Program email	POSEIDON@ARPA-H.gov
Program Solicitation	ARPA-H-SOL-24-109 (Anticipated in August 2024)

II. INTRODUCTION

This Special Notice is intended to alert the scientific community to a newly approved ARPA-H Program and notify potential proposers of an associated Proposers' Day (PD). Under the cognizance of HSF, ARPA-H intends to release an Innovative Solutions Opening (ISO) for the POSEIDON Program by mid-August (ARPA-H-SOL-24-109) to SAM.gov.

Potential proposers are encouraged to attend the optional Proposers' Day. While not mandatory, ARPA-H is hosting the POSEIDON PD to achieve the following objectives:

- Provide information about the Program to potential proposers, including details about the overall Program goals, and forthcoming ISO.
- Share the intended scope, timeline, and scale of POSEIDON and how proposers, in collaboration with the ARPA-H team and resources, can accomplish the collective mission of accelerating equitable healthcare outcomes for all Americans.
- Provide a venue to foster potential collaborations and teaming opportunities. Note: ARPA-H anticipates teaming will be required to accomplish the timelines of POSEIDON.

Attendance at this event is **not** a requirement for submission of Solutions in response to the ISO. However, the event has been designed to maximize benefits for potential proposers, including teaming and collaboration opportunities available to participants.

ARPA-H will collect participant questions throughout the event and publish answers on a publicly available Frequently Asked Questions (FAQ) site. Information relayed during the PD will be made available on the HSF Office section of the ARPA-H Opportunities page: POSEIDON website as well as SAM.gov.

Advance Registration is required. Registration requests will only be accepted from the potential proposer community, and at the discretion of ARPA-H. Registration does not guarantee acceptance to attend. Due to limited space, participation will be limited to Principal Investigators (PI) from academic institutions and Executives/scientific leaders across the oncology, biopharma, biotech, medtech, and health technology sectors. No single academic lab or commercial entity may register more than 3 participants. Participation is not intended for patients, patient advocates, press, or a general interest audience. Accepted attendees will be notified via email and will also be provided further details about the event at that time.

III. POSEIDON – PROGRAM INFORMATION

The following is a brief description of the POSEIDON Program. Full programmatic details will be provided in the ISO.

POSEIDON – Revolutionizing Multi-Cancer Early Detection

POSEIDON envisions a future where all cancers are detected early, while they are still localized, and curative treatment is far more likely. To achieve this goal, POSEIDON aims to develop first-in-class, at-home, over the counter, synthetic-sensor-based Multi-Cancer-Early Detection (MCED) tests for Stage I detection of 30+ solid tumors using breath or urine samples. Detecting these 30+ tumors at Stage 1 would save millions of lives and eliminate the economic burden of late-stage cancer care. POSEIDON leverages a human-centered design approach that combines cutting-edge synthetic biology approaches for smart sensor and synthetic reporter designs (TA1) with innovative engineering solutions for at-home systemic sensor administration, multiplexed reporter detection and full integration into clinical practice with digitally enabled care (TA2) to deliver the most sensitive, accurate, cost-effective, and accessible 30+ MCED test to all Americans.

Cancer is difficult to detect early when it is most curable and before it progresses to later stages. Cancer is the second leading cause of death in the U.S. and the leading cause of death for those under 65 years old and cancer diagnoses for people under 50 have increased by 13% between 2000 and 2019. The National Cancer Institute (NCI) estimates more than two million new cases of cancer diagnoses in 2024, and nearly 60% of diagnosed cancers do not have a recommended screening test. Over the next 30 years, more than 40 million Americans are projected to be diagnosed with late-stage cancer, accounting for 44% of all new cancer diagnoses in the U.S. However, there are currently recommended screening tests for only 4 cancers. Further, MCED tests currently in development rely on endogenous, tumor-shed biomarkers, which have been ineffective in accurately detecting stage-1 tumors. As a result, late-stage diagnoses continue to be a key driver of cancer mortality and patient-related economic burden due to higher treatment costs. Innovative and revolutionary solutions are urgently required to generate over-the-counter tests that can

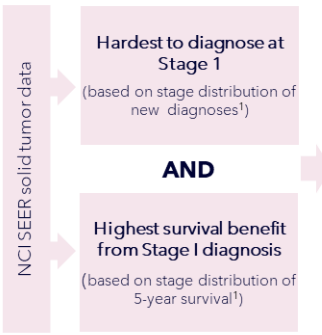
accessibly and reliably detect Stage I cancers, saving millions of lives.

POSEIDON aims to create a future in which any adult can take a simple, over-the-counter test to screen for and detect 30+ cancers at Stage I, when they are still localized, to drastically improve the chances of curative treatment and survival, POSEIDON's MCED tests will overcome the inherent limitations of native biomarkers by using engineered sensors and synthetic reporters. Access to low-cost, simple-to use at-home screening tests that do not require a doctor's visit or laboratory testing will prevent late-stage diagnoses, increase cancer survival rates, reduce cancer economic burden, and improve the lives of people impacted by cancer.

Technical Approach

POSEIDON will develop low-cost, simple-to-operate MCED tests that use synthetic biology (SynBio) based sensors and biomarkers that can detect 30+ solid tumors with unmatched sensitivity and specificity. Sensors will be engineered for systemic administration at home, without a healthcare professional or a hospital visit. Synthetic reporters will be engineered for multiplexed detection in the urine or breath (in separate tests) without the need for laboratory testing, using a low-cost device with telemedicine and Electronic Health Record integration.

Each performer team will be required to build up to two MCED tests, one designed for breath-based detection and/or one for urine-based detection. Each test must target 30+ solid tumor types, which include 25 solid cancer types that are required by the program and at least 5 additional ones selected from a second list of 19 solid tumors (Table 1).



	25 required by the program		≥5 selected by performers
1	Gallbladder	1	Anus, Anal Canal & Anorectum
2	Stomach	2	Corpus and Uterus
3	Pancreas	3	Urinary Bladder
4	Adenocarcinoma of the Lung and Bronchus	4	Diffuse and Anaplastic Astrocytoma
5	Large Cell Carcinoma of the Lung and Bronchus	5	Small Intestine
6	Adenocarcinoma of the Esophagus	6	Bones and Joints
7	Gum and other mouth	7	Melanoma of the Skin
8	Cervix Uteri	8	HR-/HER2+ Breast Cancer
9	Larynx	9	Kidney
10	Ovary	10	HR+/HER2+ Breast Cancer
11	Floor of Mouth	11	Eye and Orbit
12	Vagina/Vulva	12	Other Glioma of the Brain/Other Nervous System
13	Renal Pelvis	13	HR+/HER2- Breast Cancer
14	Small Cell Carcinoma of the Lung and Bronchus	14	Meningioma of the Brain/Other Nervous System
15	Squamous Cell Carcinoma of the Lung and Bronchus	15	Papillary Subtype of the Thyroid
16	Salivary Gland	16	Prostate
17	Liver and Intrahepatic Bile Duct	17	Glioblastoma of the Brain/Other Nervous System
18	Mesothelioma	18	Follicular Subtype of the Thyroid
19	Colorectal	19	Testis
20	Squamous Cell Carcinoma of the Esophagus		
21	Tongue		
22	Oropharynx & Tonsil		
23	HR-/HER2- Breast Cancer		
24	Lip		
25	Soft Tissue including Heart		

Table 1. POSEIDON cancers

POSEIDON's vision builds upon two key disciplines: 1) Synthetic biology, which allows for engineering of cell-free and cell-based circuits with sophisticated sensing, signal analysis, and signal output functions, and 2) multi-omic tumor profiling efforts, which combine genomics, transcriptomics, epigenomics, proteomics, volatilomics, and metabolomics to decipher features of tumor molecular landscapes. The program seeks to

functionalize tumor-specific and/or pan-cancer molecular signatures via synthetic biology circuits engineered to sense and respond by releasing synthetic reporters that distinguish between cancers. To build a revolutionary 30+ MCED test, these sensors will be combined into a single library for one-time administration and downstream clinical implementation. To accomplish these goals, POSEIDON is structured into two (2) technical areas (TAs) and three (3) "phases" that cover discovery and development, IND-enabling nonclinical studies and clinical testing.

Technical Area 1 (TA1): Sensor and synthetic reporter development for MCED

Focuses on the design, development and testing of sensors and synthetic reporters for breath- or urine-based detection of 30+ cancers. Technologies in this TA may include, but are not limited to, activity-based sensors with peptide, nucleic acid, other synthetic small molecule and/or macromolecule components, which may be coupled with biocompatible carriers to optimize safety, targeting and/or biodistribution. Sensor designs that include genetically encoded biomolecules, engineered live cells (prokaryotic or eukaryotic) and/or non-living artificial cells are also appropriate if they can meet the self-administration and at home screening requirements of POSEIDON MCED tests (see TA2 for additional information). Sensor designs may include innovative synthetic circuits, multi-layer logic gates, and positive and negative feedback loops to detect and respond to complex cancer-specific molecular signatures in the tumor microenvironment. They may leverage internal cellular processes including but not limited to transcription, translation, membrane transport, intracellular biosynthesis pathways, metabolite sensitive promoters and/or transcription factors and complex nucleic acid-based circuits They may also include signal amplification and multiplexed reporter detection strategies to improve sensitivity, specificity, and tissue of origin prediction.

Proposals must include TA1 and TA2. Sensors and synthetic reporters must be designed in parallel with the sensor administration and multiplexed detection modalities of the MCED kit from TA2 and must meet performance metrics specified for not only TA1 but also for TA2.

Technical Area 2 (TA2) – A Cancer Screening Kit for MCED.

Focuses on the design, development and testing of all hardware and software components for a low-cost, simple-to-operate device that integrates sensors and synthetic reporters from TA1 into an MCED kit for at-home screening. Each kit will include 1) a multiplexed detection modality that can display distinct, non-ambiguous outputs for 30+ cancer types as well as for negative and inconclusive results, 2) an at-home systemic administration method that does not compromise sensor performance, and 3) telemedicine and Electronic Health Record (EHR) System integration capabilities to allow digitally enabled care. Systemic sensor administration can be any modality that does not require a healthcare professional and/or a hospital visit (e.g., intranasal, oral, intramuscular, intradermal). Multiplexed detection modalities should be low-cost at scale and may include, but are not limited to, paper-based lateral flow enzymatic assays, semi-conducting single-walled

nanotube arrays, bio-/chemi-luminescent readouts, and/or integrated smartphone reader/imaging platforms.

Proposals must include TA1 and TA2. Sensor administration and multiplexed detection modalities must be designed, built, and tested in parallel with the sensors and synthetic reporters from TA1 and must meet performance metrics specified not only for TA2 but also for TA1.

Teams can submit proposals that cover these three TAs in one of the following permutations:

Technical Approach A: TA1 + TA2; urine-based test
Technical Approach B: TA1 + TA2; breath-based test
Technical Approach C: TA1 + TA2; breath-based test and urine-based test

Key Program Elements:

- As TA2 provides the framework in which the sensors and synthetic reporters from TA1 must function, and deliverables from TA1 and TA2 must coalesce as a single product ready for IND-enabling studies in Phase 2 and clinical testing in Phase 3 of the program, efforts across both TAs must be executed in parallel and closely coordinated.
- Delivering commercially viable end products that meet POSEIDON's human centered design principles is the single most important consideration for the program. As a result, the ISO will include commercialization, regulatory and accessibility metrics in addition to TA-specific technical objectives. A successful performer team will include organizations and team members with demonstrated expertise in each of these areas.
- Proposer teams are expected to establish a clear, feasible commercial and regulatory exit strategy to ensure that POSEIDON deliverables can quickly reach all Americans.
- ARPA-H anticipates that teaming will be necessary to accomplish the technical and non-technical requirements of the program and meet its aggressive timelines. Academic teams with strong expertise in TA1-relevant technologies are highly encouraged to team with commercial entities with prior experience in regulatory engagement and commercialization to ensure rapid translation of POSEIDON discoveries. More detailed information on teaming will be provided in the ISO.

Program Structure

The POSEIDON program is a 5-year effort that includes three sequential Phases covering key steps of the preclinical and clinical technology development pipeline.

- **POSEIDON Phase 1 is 36 months** and includes design, development and testing of sensors and synthetic reporters (TA1) and hardware and software components for a low-cost, simple to operate MCED test kit for at-home screening (TA2).
- **POSEIDON Phase 2 is 15 months** and includes IND-enabling, nonclinical ADME/PK (Absorption, Distribution, Metabolism, Excretion/Pharmacokinetic) studies to evaluate the safety and behavior of sensors.

- **POSEIDON Phase 3 is 9 months** and focuses on the first-in-human clinical testing of MCED kits for safety and efficacy in a Phase1b/2a clinical trial.

Each POSEIDON phase includes ambitious yet realistic and measurable goals for performers to ensure the success of the program as well as regular checkpoints throughout the entire period of performance. Attendees of the Proposers' Day should consider the timeline, Program structure and metrics information in the forthcoming ISO within their teaming profiles.

IV: POSEIDON – PROPOSERS' DAY INFORMATION

Proposers' Day -Why Attend?

Attend sessions to learn about the funding opportunity, the Program, and the vision for the future of cancer care. Learn why, what, when, and how to apply. Learn from our ARPA-H team experts about Program expectations and requirements on technical success, contracting, regulatory engagement, commercialization, and accessibility. Take advantage of lightning talks to share the technical areas you and your organization can address. Use the networking and teaming opportunities to identify potential collaborators to complement your expertise.

Proposers' Day Structure and Goals

The overarching goal of POSEIDON's Proposers' Day is to present the ARPA-H vision for how POSEIDON aims to transform the field of cancer screening by developing first-in-class, next generation SynBio-based at home screening tests of unmatched sensitivity and specificity for Stage 1 detection. This event will also provide specific opportunities for prospective proposers to identify team members and start building collaborations.

Lightning Talks

Lightning Talks will be accepted on a first-come, first-served basis, and will require advanced registration on the POSEIDON Proposers' Day registration site. During registration, participants will be asked to select one (1) primary and up to two (2) secondary focus areas from the following choices:

1) Sensor/synthetic reporter design and building (TA1) **2)** Big cancer data for sensor design (TA1); **3)** Breath based detection; **4)** Urine based detection; **5)** Medical device development- hardware (TA2) ; **6)** Medical device development - software (TA2)

This information will be used to group lightning talks to facilitate connections between prospective performer teams. Participants will be granted five (5) minutes to present two (2) slides on their research as it relates to the intersection of their expertise and POSEIDON's technical areas. Accepted attendees will be provided instructions on how to submit their lightning talks slides, which must be shared with ARPA-H before registration closes.

Speed Networking

The Proposers' Day will include optional speed networking opportunities to allow further discussion between and among potential collaborators. Participants will be given 5 minutes to discuss their research and capabilities with another randomized attendee. Unstructured networking time to allow participants to interact based on complementary expertise and interests will also be included.

Teaming Profiles

Interested parties are also encouraged to submit a 'teaming profile' as part of their Proposers' Day registration, or separately via the Microsoft Forms link here. Teaming profiles will describe the technical competencies, team capabilities, team composition, research areas of interest, unique facilities and other capabilities, as they relate to the Program, and desired technical/other competencies sought from other potential team partners. The profile will include, at a minimum:

- Contact information, to include name, organization, email, telephone number, mailing address, and website.
- Brief description of the proposer's technical competencies* and relevant facilities.
- Desired technical, commercial and regulatory competencies* and facilities from other potential team members, if applicable

*Including the primary and secondary lightning talk focus area options in these sections is strongly recommended to streamline the process of identifying potential collaborators.

Specific content, communications, networking, and team formation are the sole responsibility of participants. ARPA-H does not endorse any participating organization or exercise any responsibility for improper dissemination of the team profiles.

Registration Information

POSEIDON Proposers' Day will be an **in-person only event**. Participants must register in advance through the registration website. **There is no registration fee for the POSEIDON Proposers' Day.** To allow sufficient time to organize lightning talks and networking events in a manner that will be most beneficial to all participants, registration will close one (1) week before the event. Individuals who are unable to register because the deadline has passed, or capacity has been reached for the PD will be added to a waitlist. After registration closes, any space that may open due to cancellations may be filled on a first-come, first-served basis from the waitlist. An online registration form and various other meeting details can be found at the registration website.

Adherence to attendance guidelines will be managed by POSEIDON Program staff. Upon entry to the meeting venue, all attendees will be required to present valid, Government issued photo identification.

All inquiries regarding the event should reference "POSEIDON Proposers' Day (ARPA-H-SN-24-110)" in the subject line of the email. Prior to submitting an e-mail inquiry, please check out the POSEIDON FAQs to see if your question is answered there.

V. DISCLAIMER

This SN is issued solely for information and potential new program planning purposes; the SN does not constitute a formal solicitation for solutions. Participation is voluntary and is not required to respond to subsequent ISOs (if any) or research solicitations (if any) on this topic. ARPA-H will not provide reimbursement for costs incurred in responding to this SN. Further, this announcement is not a request for solutions; any so sent will not be reviewed. Respondents are advised ARPA-H is under no obligation to acknowledge receipt of the information received or provide feedback to respondents with respect to any information submitted under this SN.