Office of Biomedical Advanced Research and Development Authority
Division of Research, Innovation & Ventures (DRIVe)
Easy Broad Agency Announcement EZBAA-22-100-SOL-00003

The purpose of Amendment #025 is the following:

1) Reopen the following Area of Interest (AOI):

AOI #24: RePAIR

2) Revise the following Area of Interest (AOI):

AOI #24: RePAIR

INTRODUCTION AND OVERVIEWINFORMATION

A. Development Opportunity Objective:

Under this Amendment, DRIVe is doing the following:

1) Reopening the following research Area of Interest (AOI):

AOI #24: RePAIR

2) Revising the following research Area of Interest (AOI):

AOI #24: RePAIR

Repurposing and **A**dvancing **I**nnovations Against **R**ad/Nuc Threats (**REPAIR**)

Exposure to ionizing radiation can result in a spectrum of injuries known as Acute Radiation Syndrome (ARS). Due to multiple organ involvement, medical countermeasures (MCM) that treat the systemic nature of the injury or multi-organ pathologies are needed. These MCMs need to be effective when given 24 hours or later post-exposure to be consistent with current deployment expectations. Optimally, MCMs would be commercially available products that are familiar to end users, as well as be potentially available at multiple points of care such as pharmacies and hospitals. This availability ensures MCMs are immediately accessible when and where they are needed, while additional resources are being deployed from stockpiles.

BARDA's goal for REPAIR is to repurpose existing FDA-approved and clinical-stage investigational therapeutics through label expansion (e.g. additional clinical indications after initial approval or if investigational, in addition to proposed commercial clinical indication(s)) as potential MCMs for radiological and nuclear events to expand treatment options as well as support the concept of pre-deployed MCMs. It is expected that the data collected to reach these stages of clinical development would aid development of the MCM indication under FDA's Animal Rule and therefore, must include a well-defined mechanism of action (MOA) anticipated to be relevant for ARS, clinical safety data, and stage appropriate manufacturing.

BARDA is seeking abstracts that propose the repurposing, through label expansion, of therapeutics as MCMs to treat ARS. ***Candidate MCMs should either be FDA approved or in a Phase 2 clinical trial or later, having successfully completed their Phase 1 trial for their commercial indication(s), with a defined MOA anticipated to show benefit for ARS.***

This Program is focused on repurposing therapeutics through label expansion by targeting one or more of the following primary MOAs:

Direct Effects:

Cell Death: Development of MCMs to counteract loss of tissue/organ cellularity resulting from exposure to ionizing radiation. These treatments should either aim to maintain cellular populations, or replenish or preserve stem/progenitor cell population. The MOA should not act

on myeloid lineage progenitors.

Indirect Effects:

Vascular Injury: Development of MCMs that treat vascular injury by targeting the vascular endothelium and either prevent or repair injury to blood vessels caused by exposure to ionizing radiation.

Bleeding/Coagulation: Development of MCMs that can address blood loss (including hemorrhage), restore hemostasis, and/or target the coagulation cascade. Candidates should have an MOA distinct from increasing thrombopoietin or binding to the thrombopoietin receptor.

Ischemia: Development of MCMs to treat and/or prevent hypoxia and facilitate tissue oxygenation caused by exposure to ionizing radiation.

The end goal of this Area of Interest (AOI) is to support the collection of proof-of-concept and/or enabling data to support ARS MCM development for FDA-approved and clinical-stage therapeutics. These data should be generated in relevant nonclinical models that support the MCM regulatory strategy.

To be considered responsive under this AOI, respondents should have the following:

- A drug that is a candidate for repurposing as an MCM by label expansion with an MOA targeting cell death, vascular injury, bleeding/hemostasis, or ischemia associated with ARS.
- A drug that is FDA-approved or in Phase 2 clinical trial(s) or later, and have established an initial safety profile from a Phase 1 clinical trial(s); evidenced by a clinical study report(s).
- Ideally, the developed commercial formulation should be the same as the MCM formulation.
- A clear rationale, based on the drug's established MOA, as to why the candidate should be effective as a post-exposure therapy to treat ARS.
- Outline of appropriate facilities (or description of subcontractors or other partners).
- Freedom to operate for other indications using the proposed drug.

Out of scope (nonresponsive):
-Evaluation of MCMs which already have an indication for the hematopoietic sub-syndrome of ARS.
-Administration of the drug prior to exposure to ionizing radiation; i.e., prophylaxis.
-Drugs that do not have a defined MOA and relevant pharmacodynamic markers.
-Evaluation of MCMs outside the context of injuries resulting from a nuclear detonation.
-Projects that propose drugs that will *only* be developed as MCMs (even those targeting more than one threat)

B. Eligible Respondents & Scope Parameters:

This Amendment is open to all responsible sources as described in the EZ-BAA. Abstract submissions that do not conform to the requirements outlined in the EZ-BAA may be considered non-responsive and will not be reviewed. An entity must have an active

registration with https://sam.gov at the time of submission to be reviewed. If not, the abstract submission will not be reviewed and will be rejected. Please do not attempt to submit an abstract if your registration is not active in https://sam.gov.

IMPORTANT NOTE: Interested vendors are strongly encouraged to request and schedule a pre-submission call before submitting an abstract. This request should include the project title, key project staff, and a brief description of the proposed project. Please submit the requests to the following:

AOI #24: RePAIR (repair@hhs.gov)

The closing date for abstract submissions for these AOIs is listed below.

Area of Interest	Closing Date for Abstract Submissions
#24	12:00pm ET on May 15, 2024

Note: To streamline the EZ-BAA, all Areas of Interest will be open for a few months at a time following a staggered approach. This is being done to encourage high-quality submissions earlier in the fiscal year allowing adequate review time. Depending on programmatic need and funding availability, Areas of Interest may be reopened for another period of time.

C. Number of Awards:

Multiple awards are anticipated and are dependent upon the program priorities, scientific/technical merit of abstract submissions, how well the abstract submissions fit within the goals of the AOI, and the availability of funding. The program funding is subject to change based on the Government's discretion.

Funding is limited, so we encourage any interested vendors to reach out to the respective program as soon as possible before submitting an abstract.

D. Amendment Application Process:

This Amendment will follow the same submission process and review procedures as those established under this EZ-BAA, unless otherwise noted. For complete details, please read the EZ-BAA in its entirety along with all amendments.

IMPORTANT NOTE: Respondents who are awarded a contract under each of these AOIs will be required to share any collected, de-identified data to advance the field and knowledge. Interested Respondents are strongly encouraged to commercialize their technology and algorithms, however, note that consistent with BARDA's mission and federal standards, data collected through the use of government funding will be delivered to BARDA for government usage pursuant to applicable regulations and law.