Office of Biomedical Advanced Research and Development Authority (BARDA) Division of Research, Innovation & Ventures (DRIVe)

Amendment 015 Issuance for Easy Broad Agency Announcement (EZ-BAA) BAA-22-100-SOL-00003

The purpose of this Amendment is the following:

1) Update the closing date for the following Area of Interest (AOI):

   AOI #22: ReBoot

2) Update the closing date for the following Area of Interest (AOI):

   AOI #25: FASTx

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

   AOI #22: ReBoot

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

   AOI #25: FASTx

INTRODUCTION AND OVERVIEWINFORMATION

A. Development Opportunity Objective:

Under this Amendment, DRIVe is doing the following:

1) Updating the closing date for the following research Area of Interest (AOI):

AOI #22: ReBoot

2) Updating the closing date for the following research Area of Interest (AOI):

AOI #25: FASTx

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

AOI #22: ReBoot

We are seeking abstract submissions for the following AOI:

AOI #22: ReBooT

Antiviral therapeutics have the potential to impact multiple viruses that utilize conserved mechanisms of action for infection, require specific host proteins for infection, or share conserved viral proteins. Typically, antivirals are advanced for one indication, but they may have efficacy against other related pathogens. As the commercial market for products targeting filoviruses is small and evaluation of candidates requires access to BSL4 facilities, product developers have limited incentive to test candidate products against filoviruses. Under the ReBooT program, the Antivirals and Antitoxins (AVAT) branch aims to support the testing and evaluation of candidate therapeutics that have been developed past Phase 1 clinical trials for another indication, but which have a mechanism of action likely to be effective against filoviruses (including but not limited to Ebola virus, Sudan virus, and Marburg virus). Products could then be considered for additional funding through the EZ-BAA+ mechanism or under the BARDA Broad Area Announcement (BAA-22-100-SOL-00003).

The ReBooT program will primarily support preclinical efficacy studies (i.e. efficacy in animal models of filovirus disease). Proposals for preclinical studies should clearly delineate the proposed study design; laboratory partners, if required; outcome measures; and proposed threshold for study success, which could guide go/no go decisions for follow on funding. Proposals focusing on chemistry manufacturing and controls (CMC) activities, safety/toxicity, or other studies that will facilitate evaluation of the product as a viable candidate to treat filovirus infection will also be considered.

<u>To be considered responsive under this AOI, respondents should propose evaluation of products meeting the following requirements:</u>

1. Direct-acting antivirals or host-directed countermeasures that are anticipated to improve morbidity or mortality associated with filovirus infection
    a. Product may be proposed as a monotherapy or in combination with late stage or licensed products; and

2. In vitro data against filoviruses and/or in vivo efficacy data in appropriate small animal models of filovirus disease and/or a mechanism of action that is anticipated to have efficacy against filoviruses; and
3. Known and acceptable safety and toxicology profiles evidenced by Phase I results in the United States OR licensed in the US for another clinical indication and with the potential to undergo label expansion; and
4. Freedom to operate for other indications.

Factors increasing competitiveness of a proposal:

- Product has anticipated efficacy against multiple species or genera of viruses
- Product may be administered effectively through multiple routes of administration, including oral
- Product requires room temperature storage or otherwise has limited cold chain requirements

Out of scope products/proposals:

- Drugs with Phase I failures or withdrawn from market for safety reasons as well as drugs with black box labels
- Development of AI/ML
- Vaccines

Future amendments to this AOI may expand the scope of interest to other RNA viruses of pandemic potential.

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

AOI #25: FASTx

We are seeking abstract submissions for the following AOI:

AOI #25 : Early stage therapeutic platform development for Flexible and Strategic Therapeutics (FASTx)

Antiviral therapeutics are essential to reduce disease burden and improve clinical outcomes during outbreak response. However, emerging outbreaks are difficult to predict, and viral mutation can render medical countermeasures (MCMs) like monoclonal antibodies (mAbs) and small molecules that target viral proteins ineffective. Development of new antivirals often cannot keep pace with spontaneously emerging and rapidly evolving biological threats. Therefore, BARDA aims to support cost-effective, quickly adaptable therapeutic platforms to advance its mission of preparedness and response to emerging biological threats that continue to occur with increasing frequency, scale, and diversity. For the purposes of this area of interest (AOI), "platforms" enable accelerated regulatory review of subsequent products by leveraging the **development, manufacturing, nonclinical, or clinical data from a prototype product**. Competitive platforms should have the capacity to target a diverse set of viral families. Pre- or post-exposure prophylaxis (PrEP or PEP) indications will be considered, but therapeutic (i.e. post-symptom onset) indications are preferred.

Platforms of interest include, but are not limited to, nucleic acid-expressed mAbs, single domain

antibodies, double-stranded RNA-mediated interference (RNAi), and clustered regular interspaced short palindromic repeat-associated proteins (CRISPR-Cas), which are anticipated to improve BARDA's ability to address public health emergencies. Nucleic acid-based antiviral platforms are of particular interest due to their potential for rapid adaptation to diverse threats based on pathogen sequence data alone.

Abstract submissions should include the following:

1. Identify specific technical gaps or challenges impacting the platform's performance that could be addressed to improve its utility. Propose technical solutions to address those challenges or test and evaluate an improved platform. Challenges may include, but are not limited to, the following:
    a. Delivery of the investigational candidate to target tissues
    b. Efficacy
    c. Formulation
    d. Manufacturability (speed, scale, cost, etc.)
    e. Safety and toxicity
    f. Thermostability

2. Minimum data required to use the platform to generate therapeutics against a newly identified viral threat (e.g., viral genome sequence vs. clinical samples, etc.).
3. Description of the applicability of the platform to both respiratory and systemic infections.
4. Description of the mechanism of action of products produced on the platform.
5. Any existing safety data and approaches to mitigate the risk of toxicity or off-target effects if applicable.
6. The current timeline from pathogen identification to Investigational New Drug (IND) filing, including key intermediate steps and timeline drivers. If the proposed technical improvements would impact the timeline to IND, a second optimal timeline to IND reflecting the proposed improvements is requested.
7. Current state of manufacturing capabilities, including geographic location and scale.

Priority targets:

- Filoviruses (Ebola, Sudan, and Marburg virus)
- Sarbecoviruses (SARS-CoV-2 and SARS-CoV) (see note below for SARS-CoV-2)
- Orthomyxoviruses (influenza)
- Variola virus (smallpox)
- Botulinum neurotoxins

Guidance for submissions advancing the development of a candidate therapeutic for SARS-CoV-2:

Support for SARS-CoV-2 is dependent on specific funding availability. Offerors are strongly encouraged to reach out to FASTx@hhs.gov prior to abstract submission so as to receive feedback on their planned submission. Submissions should include all available efficacy data against the latest viral variants

Topics that are out of scope for this AOI include:

1. Vaccine platforms
2. Host directed therapeutics
3. Broad acting antivirals

4. Monoclonal antibody approaches
5. CHO-based manufacturing
6. Artificial Intelligence/Machine Learning platforms

We strongly encourage all interested parties to reach out via email to FASTx@hhs.gov with a description of the therapeutic platform and the intended viral target(s) prior to abstract submission. We will schedule a market research call with you to further discuss your technology and the EZ-BAA submission process.

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. In particular, 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 #22: ReBoot (reboot@hhs.gov)
AOI #25: FASTx (FASTx@hhs.gov)

The closing date for abstract submissions for these AOIs, unless otherwise extended will be:

Area of Interest	Closing Date for Abstract Submissions
#22, #25	12:00pm ET on March 1, 2024

Note: In an effort 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 in an effort 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 in an effort 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.