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

Special Instructions 019 Issuance for Easy Broad Agency Announcement (EZ-BAA) BAA-20-100-SOL-0002

The purpose of these Special Instructions is the following:

1) Revise the descriptions of the following Areas of Interest (AOIs):

   AOI #12: Mitigating Long-term Effects (MILE) of Respiratory Distress

2) Update the closing dates for abstract submissions for the following AOIs:

   AOI #2: Infection Severity and Solving Sepsis
   AOI #5: ReDirect
   AOI #12: Mitigating Long-term Effects (MILE) of Respiratory Distress

I. INTRODUCTION AND OVERVIEW INFORMATION

A. Development Opportunity Objective:

Under these Special Instructions, DRIVe is doing the following:

1) Revise the descriptions of the following Areas of Interest (AOIs):

AOI #12: Mitigating Long-term Effects (MILE) of Respiratory Distress

2) Update the closing dates for abstract submissions for the following AOIs:

AOI #2: Infection Severity and Solving Sepsis
AOI #5: ReDirect
AOI #12: Mitigating Long-term Effects (MILE) of Respiratory Distress

Under these revised and new AOIs, we are seeking abstract submissions for the following:

AOI #12: Mitigating Long-term Effects (MILE) of Respiratory Distress

Lung injury or respiratory distress caused by infectious agents as seen in complications from common pathogens (e.g., influenza, pneumococcus), pandemics (SARS-CoV-2), or result of insult (e.g., radiation injury, chemical inhalation) can lead to hospitalizations and severe outcomes, including sepsis and acute respiratory distress syndrome (ARDS). These conditions can have long term consequences that linger beyond the initial recovery (i.e., discharge from the hospital) as currently observed with post-acute sequelae SARS-CoV-2 infection (PASC). Therapeutic approaches are needed to improve long-term outcomes.

Interventional strategies primarily focus on the acute phase to the respiratory distress with the goal of recovery from critical care or mitigation of the infectious agent. However, many survivors of severe respiratory injury subsequently face the difficult challenge of long-term recovery. Long-term health consequences, risk of health deterioration, or even mortality for previously hospitalized pneumonia, sepsis or ICU patients is well documented. For example, many COVID-19 patients requiring mechanical ventilation subsequently develop long-term sequelae, and both sepsis and ARDS survivors are disproportionately afflicted by sequelae of mental, physical, social, and functional impairments for years following their initial hospitalization. Interventional therapies are needed for administration either early in the course of disease (i.e., acute phase) or during the recovery phase to mitigate long-term symptoms and prevent hospital readmissions.

DRIVe is interested in host-directed therapeutic product candidates, including therapies and medical devices, as threat agnostic approaches to aid in mitigating long-term outcomes. These therapeutic product candidates may be implemented early in the progression of acute lung injury or can be administered once an individual has resolved from the acute phase of illness to specifically reduce the long-term morbidity and mortality resulting from the initial injury or infectious insult. Of specific interest are candidates already in development for treating lung injury or another acute indication that can be adapted to include additional clinical research and analytics beyond their original primary or secondary endpoint(s) to explore impact on long-

term outcomes as additional parameters. In addition, this topic has expanded interest in host-directed therapeutic approaches that can be administered during the recovery phase of illness to mitigate the long -term sequalae. Analyses should assess the potential of the treatment to restore or maintain baseline health characteristics or to reduce hospital readmission. To be responsive to this topic, product candidates must have safely completed a Phase I clinical trial with the FDA.

Submissions should consider the following:

- Include appropriate quantitative endpoints that reflect impact to longer-term (>3 months) health deterioration after recovery from the initial acute phase of illness. Potential long-term effects include, but are not limited to, physical stamina, cognitive function, mortality, hospital readmission, and should be compared to an untreated population following the same course of illness/infection.
- Patient enrollment and treatment should be limited to subjects who initially experienced or who are currently experiencing a primary event or hospitalization due to respiratory distress or lung injury. Priority will be given to products that have already demonstrated some efficacy against primary indication (e.g., acute phase of lung injury). Interventional agents may either be administered during the initial hospital stay to demonstrate the long-term benefit or during the recovery period
- Include a rationale to support how the potential mechanism of action of the therapeutic may impact patient post-discharge health.
- Although not required, approaches able to predict or stratify patients that will be responsive to therapy and exhibit long term benefit, like endotyping, are of interest. (please also see "AOI # 13: Endotyping for Host-Directed Therapeutics").
- Provide clear intended use statement for product in terms of population of interest, stage of lung injury for treatment, timing, and route of administration targeted indication for the long-term consequences, and clinical setting for administration.
- Clinical studies should take into consideration the need to represent diverse populations and must be equitable in terms of enrollment, including diversity amongst race, ethnicity, and biological sex.
- Address how the proposed study is different from or expands existing clinical trials of the candidate therapeutic.
- Address appropriate route(s) of administration as relevant to drug candidate dose and clinical setting, especially if will be administer in recovery stage of illness (i.e., at-home, SNF, etc.).
- Only technologies focused on host-directed therapeutics or clinical management approaches will be considered. BARDA has existing programs for pathogen-targeted approaches outside of this AOI.
- Research should be considered translational science. Early stage or fundamental research will not be considered at this time.
- The investigational drug must have an IND filed and be on a clear path to achieving regulatory NDA or BLA with the FDA and information on regulatory approach and guidance to date should be provided.
- Submissions should provide evidence of pre-established agreements with proposed partners (i.e., CROs, clinical sites, subcontractors) for relevant clinical studies, GMP manufacturers of product, etc.
- Submissions should include consideration of a commercialization strategy outside of the work proposed to this announcement. This may include other ongoing relevant research;

establishment of partnerships with appropriate manufacturers; addressing the ability to scale, deploy, and distribute the product; intellectual property; and modeling the cost per unit, or reimbursement strategy.

Out of Scope Topics:

- Pathogen-based or pathogen targeted products.
- Supportive care technologies that do not specifically improve clinical outcomes for patients.
- Exploratory research with no near-term translational application.
- Studies only targeting long-term outcomes of respiratory distress from chronic conditions (e.g., asthma, COPD).
- Product candidates that are intended for administration after the acute phase of injury (i.e., post-discharge).

B. Eligible Respondents & Scope Parameters:

These Special Instructions are 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 #2: Infection Severity and Solving Sepsis (solvingsepsis@hhs.gov)
AOI #5: ReDirect (chemrepo@hhs.gov)
AOI #8: Bringing Laboratory Testing to the Home (homediagnostics@hhs.gov)
AOI #9: Digital Health Tools for Pandemic Preparedness (digitalhealth@hhs.gov)
AOI #11a: Home-based, Over-the-Counter Diagnostics for the Detection of SARS-CoV-2 (COVID19_homeDx@hhs.gov)
AOI #11b: Enabling Technologies to Support Home-Based Diagnostics for SARS-CoV-2 Acute Infection (COVID19_homeDx@hhs.gov)
AOI #12: Mitigating Long-term Effects (MILE) of Respiratory Distress (HostTx@hhs.gov)
AOI #13: Endotyping for Host-Directed Therapeutics (HostTx@hhs.gov)

The table below indicates the closing dates for abstract submissions for each AOI, unless otherwise extended:

Area of Interest	Closing Date for Abstract Submissions
#11a, #11b	12:00pm ET on 29 April 2022
#2, #12, and #13	12:00pm ET on 29 July 2022
#5	12:00pm ET on 30 September 2022
#8 and #9	12:00pm ET on 03 February 2023

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.

Additionally, awarded contracts expected to be made under the EZ-BAA will be less than $750,000 in total Government funding. 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. Special Instructions Application Process:

These Special Instructions will follow the same submission process and review procedures as those established under the EZ-BAA. For complete details, please read the EZ-BAA in its entirety. DRIVe takes the protection of Respondent information very seriously to ensure that information is safeguarded in full compliance with all applicable regulations and law.

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 encouraged to commercialize their technology and algorithms but data collected through the use of Government funding will be made available through full Government purpose rights.