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

Amendment 003 Issuance for Easy Broad Agency Announcement (EZ-BAA) BAA-22-100-SOL-00003

The purpose of this Amendment is the following:

1) Revise the following Areas of Interest (AOI):

AOI #19: Healing Lungs

INTRODUCTION AND OVERVIEWINFORMATION

A. Development Opportunity Objective:

Under this Amendment, DRIVe is doing the following:

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

AOI #19: Healing Lungs

We are seeking abstract submissions for the following revised AOI:

AOI #19: Healing Lungs

Acute respiratory distress syndrome (ARDS) is a serious lung condition caused by multiple factors, including viral and bacterial infections, exposure to toxic radiation or chemicals, smoke inhalation, as well as trauma and severe chest injury. ARDS is characterized by an acute and diffuse lung inflammation associated with alveolar fluid accumulation and surfactant dysfunction, which results in improper lung function, leading to low blood oxygen and, in severe cases, causing lung tissue scarring and permanent respiratory impairment. Mechanical ventilation, which is currently the first-line intervention for ARDS patients, often results in further lung injury. Patients who do not respond to mechanical ventilation are more and more frequently placed on veno-venous extracorporeal membrane oxygenation (VV-ECMO), an intervention that remains labor-intensive, and costly, requiring highly specialized personnel, and prone to risks and complications. The Division of Research, Innovation, and Ventures (DRIVe) is interested in developing novel technologies to sustain healthy oxygenation levels in ARDS patients, as they heal naturally or await lung transplant, all the while preventing further tissue injury to already damaged lungs, and in advancing solutions for patients refractory to mechanical ventilation. DRIVe is seeking two types of novel technological solutions for severe ARDS patients: 1) non-ECMO methods of oxygen delivery (e.g., synthetic and mammalian cell-derived oxygen carriers) that may offer alternative options to severe ARDS management and 2) innovations that simplify the implementation and operation of VV-ECMO, improve its safety profile, and potentially enhance its availability outside of specialized ECMO centers.

DRIVe is interested in the following two focus areas, which cover oxygen carrier injectable products and VV-ECMO:

Alternative methods for oxygen delivery and/or carbon dioxide removal:

DRIVe is interested in compounds or products that provide sufficient respiratory support to maintain patient oxygen saturation levels at 95% and above, are non-alloimmunizing, and can demonstrate an oxygen-carrying capacity similar to that of human hemoglobin (i.e., ~1.34 ml oxygen per gram). DRIVe seeks to develop technologies that allow repeated administration of oxygen and demonstrate reduced toxicity at effective dosage compared to current generation hemoglobin-based products and perfluorochemical emulsions. Responsive proposals shall discuss biocompatibility assessment and include an evaluation of the oxygen carrier efficacy and

toxicity in an animal model recapitulating severe ARDS presentation in humans (i.e., PaO2/FiO2<100 mmHg). DRIVe is also interested in injectable compounds or products that provide sufficient respiratory support to maintain arterial carbon dioxide levels at 35-45 mmHg and/or prevent severe hypercarbia.

Solutions of interest include, but are not limited to:

a. Perfluorocarbon (PFC)-based carriers, polymer-based hollow microparticles (PHMs), lipid-coated microbubbles (LOMs), synthetic or cell-based hemoglobin-based oxygen carriers (HBOC), and others

b. Carriers that can support respiration without contribution from the lungs to enable lung tissue healing

VV-ECMO:

1. **Maintaining balance between pro- and anticoagulant states in ECMO patients**: DRIVe is pursuing innovative technologies that maintain blood flow inside the circuit yet prevent pathological thrombosis and hemorrhage and reduce the need for systemic anticoagulation or allow for ECMO to be administered anticoagulant-free ideally for a minimum of 16 days. Responsive proposals shall include plans to evaluate the biocompatibility and anti-clotting properties of proposed technological solutions. Applicants should aim to conduct *in vivo* tests preferably for 16 days or longer, during which no clots or internal hemorrhage should occur and no embolic complications or adverse events resulting from clot formation should be recorded. The evaluation of proposed solutions will include an assessment of the hemostatic state and coagulation profile using a test panel composed of TEG, ACT, aPTT, PT, antithrombin III, von Willebrand factor, D-dimer, platelet, and fibrinogen concentration. Solutions should aim to maintain tests values within 10% of baseline for the duration of the study. Projects seeking to develop systemic anticoagulant drugs are out of scope. Approaches that focus on dissolving existing clots will not be considered.

Solutions of interest include, but are not limited to:

a. Novel coatings and modifications (e.g., solutions leveraging nitric oxide, tethered liquid perfluorocarbon, novel anticoagulant compound, or combinations of solutions) of the inner surface of circuit tubing and components such as the gas exchanger.

b. Novel design of circuit components (e.g., oxygenator, tubing junction connectors) that improve blood flow path control, limit blood/surface contact, and enhance gas exchange rate, as well as supportive adjunct technologies (e.g., ultrasound-based platforms)

c. Any approach that would combine technical innovations of several circuit components

2. **Approaches that make ECMO more compact and portable, easier to implement and operate:** DRIVe is interested in solutions that would ideally integrate the pump, oxygenator, and heat exchanger into a single miniaturized ECMO circuit component. However, submissions focused on miniaturizing one of these three components alone will also be considered. Responsive proposals shall include comparative studies evaluating the performance of miniaturized components against commercialized components and as part of a complete ECMO circuit. Teams of applicants are welcome to propose collaboration projects and submit their abstract together.

Proposed VV-ECMO solutions should ideally be compatible for use in combination with commercially available circuit components. VV-ECMO submissions shall provide evidence that the technology is ready for large animal testing and include an ovine or porcine ECMO model study using no less than 10 animals. Although large animal studies are preferred for both VV-ECMO topics, small animal studies that may be required for component miniaturization will be considered.

Submissions should address the following points:

• Detailed description of the technology and the innovation.
• Preliminary data that demonstrate the proposed approach is scientifically viable, feasible, and suitable for practical applications and product development. Applicants should provide a summary of their preliminary work in the abstract and additional details in attachments to their submission.
• Quantitative success metrics and plans to evaluate the safety and efficacy of the proposed solution as part of the project.
• Rationale for the choice of selected animal model, including a clear justification and evidence dictating the use of a large animal model rather than other models when appropriate. Applicants shall explain why a particular animal model is required at the stage of development reached by their technology.
• Regulatory and commercial strategies beyond the proposed study are strongly recommended.

Out-of-scope topics:

• Approaches relying on positive or negative air pressure systems and mechanical ventilation are out of scope. *Aerosol or gas inhalation formulations may be considered, however, if the proposed solution relies, at least in part, on a mechanism of action that enables gas exchange (i.e., compounds that deliver oxygen and/or remove carbon dioxide).*
• Therapeutic drugs that indirectly improve oxygenation by acting on the host response to lung injury or dysfunction are not responsive to this AOI.
• Platforms that have not reached, at minimum, a technology readiness level of 3 (TRL 3) and proposals for basic research projects that have not achieved preclinical proof of concept level of development will not be considered.

Additional considerations:

Awardees are encouraged, but not required, to share information and project progress with each other in quarterly meetings, and to consider testing their technology in combination with the innovations of others to assess their synergistic potential. All awarded projects will be reviewed quarterly by an internal review committee comprised of federal staff from BARDA and other federal entities.

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 #19: Healing Lungs (HealingLungs@hhs.gov)

The closing date for abstract submissions for this AOI, unless otherwise extended will be:

Area of Interest	Closing Date for Abstract Submissions
#19	12:00pm ET on February 3, 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.

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.