PROJECT DESCRIPTION/STATEMENT OF OBJECTIVES

2.1 OBJECTIVE AREA – Treatment (RPP#TBD) Broad-spectrum Therapeutics

2.1.1 OBJECTIVE OF THE PROJECT:

DTRA, RD-CBM-Therapeutics intends to develop prototype Medical Countermeasures (MCMs) to address therapeutic indications of Warfighter exposure to viral and bacterial biothreat agents. This effort will execute all of the necessary partnerships, implement necessary quality assurance and project management systems to enable the discovery and development of a prototype MCM.

2.1.2 STATEMENT OF OBJECTIVES (SOO):

The Joint Science and Technology Office (JSTO) intends to develop threat-agnostic prototype MCMs to address the therapeutic indications of Warfighter exposure to viral and bacterial biothreat agents. This effort will execute all of the necessary partnerships, implement necessary quality assurance and project management systems to enable the discovery and development of a prototype MCM. Enhanced White Papers (EWP) and its accompanying draft Statement of Work needs to indicate whether it is proposing a solution to Thrust Area 1, Thrust Area 2, or Thrust Areas 1 & 2 (e.g., direct acting and host-directed combination approach). The Project Agreement Holder's proposal will include a Statement of Work (SOW) template provided in Enclosure 2 that describes all activities proposed to meet the objectives of the chosen Thrust Area(s). Stated again, it is imperative that the prospective Project Agreement Holder states whether its proposal is for solutions to the objectives of Thrust 1, Thrust 2, or the combination of Thrust 1 and 2 in their entirety. Based on that, the Government will evaluate solutions either against Thrust 1 or Thrust 2 independently, or the consolidated solutions including both Thrust 1 and Thrust 2.

1) **Direct Acting MCM Thrust Area 1:** The targeted biothreats in this solicitation are for the following viral families (not in order of priority): Filoviridae, Togaviridae, Paramyxoviridae, Hantaviridae, and Arenaviridae. Screening and evaluation for compounds against any other traditional, emerging, or endemic viruses will be also considered. Prioritization is on oral, broad-spectrum, and combination therapies. Candidate MCMs that are not broad-spectrum (inter- or intra-family) will not be considered. Repurposed commercial candidates and approved compounds are also sought. Both aerosol and non-aerosol routes of exposure will be considered. Platform technologies to improve bioavailability and targeted tissues may be considered. All other concepts for MCM and platform development are welcomed but will likely be rated at a lower priority unless they propose significant advancements beyond state-of-the-art. Project Agreement Holders are encouraged to collaborate with OTA MCDC Consortium members for animal model testing.

2) **Host-Directed Therapies Thrust Area 2**: MCMs in this solicitation must be broad-spectrum (inter- or intra-family) and threat-agnostic. Therapeutic targets may include, but are not limited to, host pathways involved in biothreat-induced acute respiratory distress syndrome (ARDS), meningoencephalitis, and sepsis. The Project Agreement Holder shall demonstrate broad-spectrum efficacy for either viral or bacterial threats or with suitability

for both types of threats. Example pathogens include bacterial species such as *Bacillus anthracis, Francisella tularensis, Burkholderia pseudomallei,* and *Yersinia pestis,* and viral families Filoviridae, Togaviridae, Paramyxoviridae, Hantaviridae, and Arenaviridae. Screening and evaluation for MCMs against any other traditional, emerging, or endemic bacterial and viral threats will be considered if they cause sepsis, ARDS, and/or additional pathogen-induced syndromes, or involve MCMs that target host signaling pathways or those necessary for metabolism and lifecycle events; epigenetic and post-translational modifications in the host; modulation of host immune response; cell-based therapies and cytokine therapies; and other novel approaches. Preferred combination therapies will use FDA approved products re-labeled for biodefense disease indications since they represent low-hanging fruit and host-directed therapies may improve efficacy of the approved treatment in humans or reduce incidence of drug failure due to emergence of resistant pathogens. Other FDA approved or advanced development molecules (completed Phase 1 clinical trials) would be considered more favorable than low maturity molecules for use in combinations with host-directed therapeutic candidates. Project Agreement Holders are encouraged to collaborate with OTA MCDC Consortium members for animal model testing. Proposals that that can demonstrate target/pathway validation through use of multi-system approaches e.g. *in vitro* and animal models to human via microphysiological system, organ-on-a-chip, organoid, or similar assay(s) are best.

Performance Objectives (required results)

a. **Project Objectives:** Any activities from discovery up to Phase 1 clinical trials are welcomed with this solicitation (TRL1-6). A traditional drug development plan is anticipated but unique programmatic approaches are also of interest and are needed for combination therapies. The intent is to offer multiple awards for promising candidates ending with proof-of-concept small animal evaluation. However, more advanced candidates that have been evaluated through Phase 1 clinical trials and beyond are also invited. Proposals divided into two periods may be of benefit given a 36-month total Period of Performance (PoP), though any structure may be acceptable. Proposals shall include decision gates with rational for follow-on work to proceed.

b. **Regulatory Objectives:** If the proposal posits an advanced candidate, then pre-IND meetings and a pre-IND briefing package is anticipated to gain FDA concurrence on the preclinical strategy and plans.

Project Management Objectives: The Project Agreement Holder will propose a kick-off meeting, monthly meetings, forecasts of expenditures; monthly, quarterly and annual technical reports; and quarterly Integrated Master Schedule (IMS) updates to support the Government assessment of technical and schedule performance. At the end of the effort, the Project Agreement Holder will propose to provide a detailed final technical and business report. This effort will provide deliverables (data and corresponding documentation) sufficient to file an IND(s) for the proposed medical countermeasure(s)

against biodefense pathogen indication. The Project Agreement Holders' proposal will describe and include all costs required to perform all activities proposed.

Logistics Objectives: N/A

Performance Requirements: TRL 1-6 activities will be considered in scope for this solicitation. The prioritization of characteristics sought are oral, broad-spectrum, and repurposed.

Operational constraints/Limitations/Restrictions: N/A

2.1.3 PERIOD AND PLACE OF PERFORMANCE:

The anticipated Period of Performance for this effort is up to three (3) years from date of award but longer efforts may be considered. Specific dates to be negotiated. It is anticipated that the primary place of performance will be the Project Agreement Holders' facilities, however this aspect can be negotiated as part of each Project Agreement Holders' submission.

The Project Agreement Holder shall submit all deliverable report submissions to the Agreement Officer's Representative (AOR) in the applicable format. The format and content of these deliverables is to be negotiated. Data Deliverables may include but are not limited to:

2.1.4.1 DATA DELIVERABLE(S)

2.1.4.1.1 Meeting/Teleconference Agendas and Minutes.

The Project Agreement Holder shall provide an agenda, slides, and all supporting documentation prior to the scheduled meeting. The frequency of the meetings will be monthly.

2.1.4.1.2 Study Reports and Animal Study Protocols

The Project Agreement Holder shall provide draft and final versions of documents that describe animal studies (study protocols) and study reports (executive summary, rational, objectives, methods, raw and analyzed data, results, discussion/conclusions and corresponding documentation) sufficient to file an IND(s) for the proposed medical countermeasure(s). Submissions of draft and final documents to the government will have 15 days for animal protocols and 30 days for reports to respond with any comments and the performer will have an additional 2 weeks to revise the deliverable or respond to those comments. Project Agreement Holders are reminded that all testing in animals (toxicology or efficacy) will need to be reviewed and approved by the ACURO processes after all institutional reviews. The schedule will need to reflect these activities, including 4 months advanced review before approval of new animal protocols or shorter timelines for protocol amendments.

2.1.4.1.3 Quarterly Financial Status and Progress Report

The Project Agreement Holder shall include an expenditure forecast for each reporting period and include both the monthly planned accrual, as well as the cumulative total. The schedule update shall include the explanation for any changes on the schedule, drivers for the change, as applicable. The progress report should also address any concerns the Project Agreement Holder might have that would impact performance, schedule, or cost planned for the effort.

The Project Agreement Holder shall report risk matrix format to include risk mitigation strategies. Submission shall be 15 calendar days after the end of each month of performance. The Government will have 30 business days to respond to the report with any comments and the Project Agreement Holder will have an additional 2 weeks to revise the deliverable or respond to those comments.

2.1.4.1.4 Annual Report.

The annual report shall narrate a complete summary of the project execution and associated results obtained to include project results and accomplishments, issues encountered and recommended solutions. The report shall also address tasks that were not completed, reasons for non-completion, and a plan to accomplish the tasks or alternative approach to accomplish project goals, and as needed, an updated Statement of Work. Submission within 15 calendar days of the anniversary date of award per annum. The Government will have 30 days to respond to the report with any comments and the performer will have an additional 2 weeks to revise the deliverable or respond to those comments.

2.1.4.1.5 Final Report.

A Final Report shall be submitted at the end of the project, regardless of whether any or all of the phases are completed. This report takes the place of the last annual report due. (A Financial Report is still required.) The report shall narrate a complete summary of the project performance and associated results obtained. The report shall document any outstanding problems and their potential solution, as well as any problems solved during the course of the project, along with the solution to the solved problems. The report shall address whether the Technology Readiness Level (TRL) has been advanced, and if so, provide the TRL level along with supporting details as to its advancement.

2.1.4.1.6 Master Government Property – Physical Inventory.

During performance of the contract, the Project Agreement Holder may purchase material or equipment using government funds [Contractor Acquired Property (CAP)] if approved by the Agreements Officer. The Project Agreement Holder shall perform, record, and disclose physical inventory results of all CAP in its possession.

2.1.4.1.7 Patents – Reporting of Subject Inventions.

In accordance with terms and conditions of the MCDC Base OTA.

2.1.4.1.8 Regulatory Documentation and Technical Data Packages.

The Project Agreement Holder shall give the USG a right of reference to all regulatory filings executed under this agreement. The Project Agreement Holder is responsible for submitting all documentation in support of the pre-Investigational New Drug (IND), IND, and/or pre-Emergency Use Authorization (EUA) filings to the FDA. The Project Agreement Holder shall provide the Government copies of all technical data generated by the Project Agreement Holder prior to and during performance of the agreement, necessary to pursue FDA approval of pre-IND, IND, or pre-EUA, and notify the Government of FDA decisions. All written communications to and/or from the FDA will be provided to the Government. The IND shall be prepared for the submission to the FDA and provided to the Government in the appropriate format (eCTD, SEND, &/or SEND-AR).

The Project Agreement Holder shall submit all pre-IND, IND, and/or pre-EUA report submission to the Agreement Officer's Representative (AOR) in the applicable FDA format.

The Project Agreement Holder shall report all written communications to and/or from the FDA as it takes place. The Project Agreement Holder shall courtesy copy the AOR on all email traffic to the FDA and will forward all emails received from the FDA to the AOR. Meeting minutes will be forwarded to the AOR within 7 calendar days of the meeting or teleconference. Please note, Government review/approval will not impede submission of documents to FDA by the Project Agreement Holder.

2.1.4.1.9 Miscellaneous Data Submissions.

Required submissions include but are not limited to Point Papers, Briefings, TPP, PDP, Regulatory Strategy, Technology Transfer Report and Gap Analysis, Formulation Development, Feasibility and Optimization Reports, ACURO (animal study) approvals, OHRO (human study) approvals, Technical Presentations and Publications. Also, any formal technical reports that have been prepared for eventual submission to FDA or other regulatory agencies. This is to include reports on Pharmaceutical Development, Manufacturing Development, Manufacturing Validation, Analytical Development and Validation, Drug Substance and Product Stability and the like. The Project Agreement Holder shall also submit completed batch records, certificates of analysis and related documentation, as applicable.

2.1.4.1.10 Work Breakdown Structure (WBS).

Four-level WBS with costs and schedule (top level is program, level 2 is phase, level 3 are major tasks, level 4 are subordinate tasks). For lowest task level, show breakdown for labor, material, and other indirect costs.

WBS shall be updated annually or 30 calendar days after a scope modification. Government review/approval is 15 calendar days after receipt of first submittal. Provide changes to draft within 10 calendar days of such request. Provide final document within 10 calendar days after approval of changes is received.

2.1.4.1.11 Expenditure Forecast

The Contractor shall submit the first expenditure forecast within 30 days after award. Subsequent update reports are due by 15 January of each year or whenever the original estimates vary by more than 20% from the original submission. An updated forecast shall be submitted within 30 days of any contractual modifications that change the period of performance or the cost of the contract. Report shall forecast by month and shall include both the monthly planned accrual, as well as the cumulative total.

2.1.4.1.12 Integrated Master Schedule (IMS)

The IMS at a minimum will include and correlate to all activities described in the SOW and the WBS. The IMS will include detail to provide both the Project Agreement Holder and the Government the ability to track project progress. The IMS should reflect all lead times required for statutory and regulatory approvals. Project Agreement Holders are reminded that all testing in

animals (toxicology or efficacy) will need to be reviewed and approved by the ACURO processes after all institutional reviews. The schedule will need to reflect these activities, including 4 months advanced review before approval of new animal protocols or shorter timelines for protocol amendments.

Note: Technical data deliverables described herein shall be delivered to the Government with Government Purpose Rights.

2.1.4.2 PROTOTYPE DELIVERABLE(S): The prototype delivered will be a medical countermeasure that has advanced to a higher TRL.

2.1.5 SPECIAL REQUIREMENTS: N/A

2.1.5.1 Export Control: N/A

2.1.5.2 Security and Classified Data: All data will be considered Unclassified

2.1.5.3 Acceptance of Deliverables: The Government will provide acceptance of all data deliverables within 15 days of delivery. The Government will provide acceptance of all prototype deliverables within 15 days of delivery**.**

2.1.5.4 Travel: Travel for IPT meetings, face-to-face meetings with the FDA, or other non-directed meetings considered necessary is allowed. Include the number of trips, trip destination, and number of contractor personnel allowed, and estimated dates.

2.1.6 GOVERNMENT FURNISHED PROPERTY/SERVICE: N/A

2.1.7 FUNDING CONFIDENCE LEVEL and PROJECT AWARD MONTH or FY QUARTER:

CL-1 Highly Confident funds will be available

This effort is anticipated for award: 2Q FY25

Thrust Area 1

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2.1.9.2 Requiring Activity:
DTRA Joint Science and Technology Office (CBM)