DEPARTMENT OF THE ARMY
U.S. ARMY CONTRACTING COMMAND – NEW JERSEY
PICATINNY ARSENAL, NEW JERSEY 07806-5000

REPLY TO
ATTENTION OF

01 July 2020

Army Contracting Command – New Jersey
ACC-NJ, Building 9
Picatinny Arsenal, NJ 07806

SUBJECT: Technical Direction Letter for Medical CRBN Defense Consortium (MCDC), Request for Prototype Proposals (RPP) 20-05, Objective Area TRE-20-05, entitled "Development of EIDD-2749 and Supplemental Candidates for Alphavirus, Arenavirus and Other Biodefense Threats" (Emory University)

REF: Request for Updated Proposal, MCDC OTA, W15QKN-16-9-1002, RPP 20-05, Objective TRE-20-05, dated 08 June 2020

Advanced Technology International
ATTN: (b) (6), Sr. Contracts Manager
315 Sigma Drive
Summerville, SC 29486

Dear (b) (6),

The Army Contracting Command – New Jersey (ACC-NJ), in supporting the Joint Project Manager – Medical Countermeasure Systems (JPM-MCS), issued MCDC RPP 20-05 on 14 April 2020. Members of the MCDC submitted proposals in accordance with this RPP. The Government received and evaluated all proposal(s) submitted and a Basis of Selection has been executed. The Government requests that a Firm Fixed Price Project Agreement be issued to Emory to award this proposal under Other Transaction Agreement W15QKN-16-9-1002, to be performed in accordance with the attached Government Statement of Work (SOW).

Based upon the acceptable update of Emory's proposal for "Development of EIDD-2749 and Supplemental Candidates for Alphavirus, Arenavirus and Other Biodefense Threats" and 1) The Project Agreement Recipient's concurrence with the requirements included in the Government SOW; 2) An acceptable milestone schedule that meets SOW requirements, and; 3) The Cost Proposal that has been analyzed and negotiated final by the Government, you are hereby directed to issue a Project Agreement to Emory for the subject project. The total project value has been determined fair and reasonable and Emory's proposal has been selected IAW the above referenced Basis of Selection.

The total approved cost to the Government for this effort is not to exceed (b) (4) The break-out of the costs is as follows: $11,192,009.00 to perform project efforts included in the SOW and (b) (4) for the Consortium Management Firm Administrative Cost and Fee. The effort currently has (b) (4) of available funding, comprised of $1,278,832.78 for the Project

Agreement and (b) (4) for the Consortium Management Firm Administrative Cost and Fee of (b) (4)

This Project Agreement is anticipated to be incrementally funded. The Government reserves the right to award future milestones/fund additional months of project tasks. If the Government decides to do so, the MCDC member will be notified via ATI. The Government's liability will never exceed the current amount of funding obligated under the Project Agreement. The Project Agreement Holder shall notify ATI when they are approaching 75% of current funding obligated in incurred costs by written notice.

The prime contractor is considered a small business, nontraditional defense contractor, or nonprofit research institution and determined to be providing a significant contribution. The affirmation of business status certifications submitted as part of the proposal are hereby incorporated into the agreement. The contractor shall notify the MCDC CMF of any deviation from the final proposed affirmation of business status certifications that would affect the contributions of the small business, nontraditional defense contractor, or nonprofit research institution as proposed.

In accordance with 10.U.S.C. 2371b(f), and upon a determination that the prototype project for this transaction has been successfully completed, this competitively awarded prototype OTA may result in the award of a follow-on production contract or transaction without the use of competitive procedures.

Points of Contact:

Agreements Specialist:
(b) (6)
E-mail: (b) (6)
Phone: (b) (6)

Agreements Officer:
(b) (6)
E-mail: (b) (6)
Phone: (b) (6)

Regards,

(b) (6)

Agreements Officer
Signed by: (b) (6)

Attachments:
Attachment 1: Encl 3_Statement of Work MCDC2005-005 7-1-2020 Changes Tracked

Statement of Work
for
Development of EIDD-2801 and Supplemental Candidate Prototypes

RPP #: 20-05
Project Identifier: MCDC2005-005
Consortium Member: Emory University
Title of Proposal: Identification and Development of Broadly Active Antiviral Countermeasures for Alphavirus, Arenavirus, and Other Biodefense Threats
Requiring Activity: Defense Threat Reduction Agency (DTRA), Vaccines/Therapeutics Division (CBM)

1.0 INTRODUCTION, SCOPE, AND OBJECTIVES

1.1 Introduction

Ribonucleic Acid (RNA) viruses are the most common cause of human illness, and at any given time are responsible for 80% of the viral disease burden worldwide. They are also the major contributors to the pool of emerging and re-emerging infectious diseases in humans. Riboviruses of the genus *Alphavirus* (family *Togaviridae*), *Mammarenavirus* (family *Arenaviridae)* and (b) (4) can cause significant morbidity and mortality in humans. Eastern Equine Encephalitis (EEE), Western Equine Encephalitis (WEE), and Venezuelan Equine Encephalitis (VEE) viruses are enveloped, plus-strand alphaviruses, that under natural conditions are transmitted to humans through mosquito bites. Although the frequency of severe disease in the United States associated with natural outbreaks, is generally low, all three (3) viruses are classified as Category B pathogens by the Centers for Disease Control (CDC) and National Institute of Allergy and Infectious Diseases (NIAID). The viruses are of significant public health concern, since they are potential agents of bioterrorism that can be delivered by the aerosol route. VEEV in particular has been deemed a significant biothreat, owing to its ability to rapidly produce Central Nervous System (CNS) infections after aerosol exposure, with high levels of morbidity and mortality. Arenaviruses, such as Lassa Fever Virus (LASV) and Junin Virus (JUNV), are enveloped, negative-strand viruses that cause hemorrhagic disease with significant morbidity in humans. Arenaviruses are zoonotic pathogens with each virus maintained in a specific rodent host species. Mucosal exposure to aerosolized infectious rodent excreta and direct contact of skin with infectious materials from rodents, are the primary routes humans are infected with arenaviruses. The NIAID and the CDC have classified Arenaviruses as Category A priority pathogens for posing a significant threat to public health and biodefense. Furthermore, LASV remains the only imported arenavirus to the United States documented, and has been identified by the World Health Organization (WHO) as highly likely to cause a future epidemic. Currently, there is no Food and Drug Administration (FDA) approved vaccine for the prevention of arenavirus infections, with treatment limited to supportive care and use of the non-specific antiviral drug, ribavirin.

(b) (4)

(b) (4) [redacted]

1.2 Scope

In order to address this ongoing need, this scope of work will include all tasks to allow for the identification and development of broadly active, small molecule therapeutic countermeasures for Department of Defense (DoD) specified viral biothreats. The program is designed to advance the ribonucleoside analog EIDD-2749, or a prodrug thereof, through completion of 7-day Dose Range Finding (DRF) toxicology/toxicokinetic studies in two (2) species, as a treatment for alphaviruses and arenavirus (with emphasis on Lassa Fever) infections, as well as for other biodefense threats, (b) (4) [redacted] In addition, a second structurally unique, broadly active antiviral backup compound, will be identified and developed to the same stage, with a similar or complimentary scope of activity within the period of performance. (b) (4) [redacted]

1.3 Objective

The objective of the prototype project is to develop the broadly active ribonucleoside analog EIDD-2749, or a prodrug, as a backup to EIDD-2801, for the treatment of targeted infections, such as VEEV. The molecule will be evaluated in murine models of VEEV infection, and will be advanced through dose ranging toxicology and pharmacokinetic/distribution studies. In addition, EIDD-2749 is active against Arenaviruses (b) (4) [redacted], and consequently will be evaluated in proof-of-concept prophylaxis and treatment studies in guinea pig models of LASV and JUNV infection, (b) (4) [redacted]. A medicinal chemistry program will be run in parallel to identify a second backup lead compound, in the event that early efficacy studies, toxicological findings, or pharmacokinetic/pharmacodynamic data, reveal EIDD-2749 to be suboptimal or unsuitable as a clinical candidate for the treatment of VEEV, LASV, or JUNV. The overall approach to be used is 'mechanism of action' based. It is focused on targeting the RNA-dependent RNA polymerases encoded by riboviruses, and interrupting the synthesis of viral genomic and/or mRNA. Medicinal chemistry efforts will focus on designing new RNA mutagenic ribonucleoside analogs, RNA chain terminating ribonucleoside analogs, and non-competitive ribonucleotide-5'-triphosphate mimics, to intercept RNA viral replication. All compounds designed and synthesized under the proposed project, as an optional task, will be evaluated against (b) (4) [redacted]. EIDD-2749 was initially discovered at the Emory Institute for Drug Development (EIDD) under DTRA Contract HDTRA1-15-C-0075.

This is a prototype project because Emory will develop EIDD-2749, or a prodrug thereof, to Preclinical Development Candidate status, as well as a second Preclinical Development Candidate, in order to evaluate the technical feasibility of using the candidates as an effective treatment for VEEV, LASV, JUNV, (b) (4)

In accordance with 10.U.S.C. §2371b(f), and upon a determination that the prototype project for this transaction has been successfully completed, this competitively awarded prototype OTA may result in the award of a follow-on production contract or transaction without the use of competitive procedures. This prototype project will be successfully completed if the contractor meets the key technical goals of the project, as listed within this document, meets the success metrics established by this agreement or, at the accomplishment of particularly favorable or unexpected results that justifies transition to production.

If there is a conflict between the Project Agreement and the Base Agreement, the Project Agreement language will supersede and control the relationship of the parties.

2.0 APPLICABLE REFERENCES

1. Product Development Under the Animal Rule: Guidance for Industry, FDA, October 2015.
2. Expanded Access to Investigational Drugs for Treatment Use – Questions and Answers: Guidance for Industry, FDA, June 2016 (Updated October 2017).
3. Urakova, N.; Kuznetsova, V.; Sokratian, A.; Frolova, E. I.; Frolov, I.; Crossman, D. K.; Crowley, M. R.; Guthrie, D. B.; Kolykhalov, A. A.; Lockwood, M. A.; Natchus, M. G.; Painter, G. R.; Painter, G. R., β-d-N(4)-Hydroxycytidine Is a Potent Anti-alphavirus Compound That Induces a High Level of Mutations in the Viral Genome. *J Virol* **2018,** *92* (3).
4. (b) (4)
5. Painter, G. R.; Bowen, R. A.; Bluemling, G. R.; DeBergh, J.; Edpuganti, V.; Gruddanti, P. R.; Guthrie, D. B.; Hager, M.; Kuiper, D. L.; Lockwood, M. A.; Mitchell, D. G.; Natchus, M. G.; Sticher, Z. M.; Kolykhalov, A. A., The prophylactic and therapeutic activity of a broadly active ribonucleoside analog in a murine model of intranasal venezuelan equine encephalitis virus infection. *Antiviral Res.* **2019,** *171*, 104597.
6. Sticher, Z. M.; Lu, G.; Mitchell, D. G.; Marlow, J.; Moellering, L.; Bluemling, G. R.; Guthrie, D. B.; Natchus, M. G.; Painter, G. R.; Kolykhalov, A. A., Analysis of the Potential for N⁴-Hydroxycytidine to Inhibit Mitochondrial Replication and Function. *Antimicrobial Agents and Chemotherapy* **2019**, AAC.01719-19.
7. (b) (4)

(b) (4) [redacted]

3.0 REQUIREMENTS

3.1 Phase 1

3.1.1 Milestones (Go/No Go) for Phase 1

1. Establish uptake and distribution profile of EIDD-2749.
2. Confirm efficacy of EIDD-2749 in a mouse model of VEEV infection and in a guinea pig model, arenavirus infection (LASV and JUNV).
3. Establish one to two (1-2) unique chemotypes active against two (2) or more viruses.

3.1.2 Tasks and Deliverables for Phase 1

4. The awardee shall synthesize and evaluate in vitro antiviral efficacy and cytotoxicity, anabolic profile, Pharmacokinetic (PK) and tolerability of new EIDD-2749 prodrugs and analogs, as well as new structurally unique prodrugs and analogs.
5. The awardee shall establish the distribution profile of EIDD-2749 in mice, in preparation for establishing a pharmacodynamic profile.
6. The awardee shall determine efficacy of EIDD-2749 in mouse models of VEEV (b) (4) [redacted], and in guinea pig models of LASV and JUNV infections.
7. The awardee shall characterize the Mechanism of Action (MOA) and resistance profile of EIDD-2749.

3.2 Phase 2

3.2.1 Milestones (Go/No Go) for Phase 2

8. Identify EIDD-2749, or a prodrug thereof, that meets the criteria for Late Lead.
9. Identify a backup to EIDD-2749 that meets the criteria for Early Lead status.

3.2.2 Tasks and Deliverables for Phase 2

10. The awardee shall synthesize and evaluate in vitro antiviral efficacy and cytotoxicity, anabolic profile, PK and tolerability of new EIDD-2749 prodrugs and analogs.
11. The awardee shall complete the scale up synthesis of Lead 1 to support all Option Period 1 and 2 tasks.
12. The awardee shall determine the MOA and resistance profile of Lead 1.
13. The awardee shall determine the in vitro toxicity of EIDD-2749 and key prodrugs and analogs.
14. The awardee shall determine efficacy in mouse models of VEEV (b) (4) [redacted], and in guinea pig models of JUNV and LASV infections.
15. The awardee shall synthesize and evaluate in vitro antiviral efficacy and cytotoxicity, anabolic profile, PK and tolerability of analogs and prodrugs that are structurally unique to EIDD-2749, in order to identify a second lead.

3.3 Phase 3

3.3.1 Milestones (Go/No Go) for Phase 3

16. Identify EIDD-2749, or a prodrug thereof, that meets the criteria for Preclinical Development Candidate status.
17. Identify an analog or prodrug structurally unique to EIDD-2749, that meets the criteria for Late Lead status.

3.3.2 Tasks and Deliverables for Phase 3

18. The awardee shall determine the pharmacokinetic and tissue distribution profile of Lead 1 in Non-Human Primates (NHP).
19. The awardee shall characterize Lead 1 in a 7-day tolerability study in NHPs.
20. The awardee shall determine the pharmacokinetic and tissue distribution profile of Lead 1 in rats and dogs.
21. The awardee shall evaluate Lead 1 in 7-day DRF toxicology studies in rats and dogs.
22. The awardee shall complete the development of a scale-up synthesis of Lead 2.
23. The awardee shall characterize the MOA and resistance profile of Lead 2.
24. The awardee shall synthesize and evaluate in vitro antiviral efficacy and cytotoxicity, anabolic profile, PK and tolerability of new prodrugs and analogs of one to two (1-2) unique chemotypes, in order to identify Lead 2.

3.4 Phase 4

3.4.1 Milestones (Go/No Go) for Phase 4

25. Identify an analog or prodrug structurally unique to EIDD-2749, that meets the criteria for Preclinical Development Candidate status.

3.4.2 Tasks and Deliverables for Phase 4

26. The awardee shall complete scale-up synthesis of Lead 2 to support Option Period 3 tasks.
27. The awardee shall determine the pharmacokinetic and tissue distribution profile of Lead 2 in NHPs.
28. The awardee shall characterize Lead 2 in a 7-day tolerability study in NHPs.
29. The awardee shall determine the pharmacokinetic and tissue distribution profile of Lead 2 in rats and dogs.
30. The awardee shall evaluate Lead 2 in 7-day DRF toxicology studies in rats and dogs.
31. The awardee shall determine the efficacy profile of new compounds in mouse models of VEEV, guinea pig models of LASV and JUNV, (b) (4)

3.5 Specific Tasks for Phase 1

32. The awardee shall synthesize the EIDD-2749, EIDD-2749 prodrugs and analogs, analogs and prodrugs structurally unique to EIDD-2749, and bioanalytical standards, and evaluate them for cellular efficacy and cytotoxicity, cellular uptake and metabolism, and plasma and microsome stability.
33. The awardee shall evaluate EIDD-2749, EIDD-2749 prodrugs and analogs, and structurally unique analogs and prodrugs in non-Good Laboratory Practice (GLP) in vitro toxicity studies, including AMES and mitochondrial toxicity studies, as well as determine selectivity against host DNA polymerases.
34. The awardee shall conduct single ascending-dose PK and distribution studies in mice and guinea pigs, in order to support in vivo 10-day tolerability and efficacy studies.
35. The awardee shall serial passage LASV and JUNV in the presence of EIDD-2749, in order to select escape mutants and establish resistance profiles of the selected viruses.
36. (b) (4)

37. The awardee shall develop a LASV polymerase assay, in order to determine mechanism of action and for use as a screening assay to determine intrinsic activity.
38. The awardee shall conduct multiple ascending dose and repeat dose studies, evaluating EIDD-2749 in the systemic mouse model of VEEV infection, in order to establish efficacy and safety.
39. (b) (4) [redacted]
40. The awardee shall adapt the LASV vaccine guinea pig model, in order to evaluate small molecule therapeutics.
41. The awardee shall conduct multiple ascending dose and repeat dose studies, evaluating EIDD-2749 in the guinea pig models of LASV and JUNV infections, in order to establish efficacy and safety.

3.6 Specific Tasks for Phase 2

42. The awardee shall synthesize EIDD-2749 prodrugs and analogs, as well as structurally unique analogs and prodrugs, and their bioanalytical standards, and evaluate them for cellular efficacy and cytotoxicity, cellular uptake and metabolism, and plasma and microsome stability.
43. The awardee shall evaluate EIDD-2749 prodrugs and analogs, and structurally unique analogs and prodrugs in non-GLP in vitro toxicity studies, including AMES and mitochondrial toxicity studies, as well as determine selectivity against host DNA polymerases.
44. The awardee shall conduct single ascending-dose PK and distribution studies in mice and guinea pigs, in order to support in vivo 10-day tolerability and efficacy studies.
45. The awardee shall serial passage LASV and JUNV in the presence of Lead 1, in order to select escape mutants and establish resistance profiles of the selected viruses.
46. (b) (4) [redacted]
47. The awardee shall screen new compounds utilizing the LASV polymerase assay, in order to determine mechanism of action and to establish activity.
48. The awardee shall conduct multiple ascending dose and repeat dose studies, evaluating Lead 1 in the systemic mouse model of VEEV infection, in order to establish efficacy and safety.
49. (b) (4) [redacted]
50. The awardee shall conduct multiple ascending dose and repeat dose studies, evaluating Lead 1 in the guinea pig models of LASV and JUNV infections, in order to establish efficacy and safety.

3.7 Specific Tasks for Phase 3

51. The awardee shall synthesize structurally unique analogs and prodrugs, and their bioanalytical standards, and evaluate them for cellular efficacy and cytotoxicity, cellular uptake and metabolism, and plasma and microsome stability.
52. The awardee shall develop a scale-up synthesis and conduct pre-formulation studies on the lead 2.
53. The awardee shall evaluate the Lead 2 in non-GLP in vitro toxicity studies, including hERG binding, chromosome aberration studies, pharmacologic toxicity panel, P-gp assay, and CYP-450 profiling, as well as determine selectivity against host DNA polymerases.

54. The awardee shall serial passage LASV and JUNV in the presence of Lead 2, in order to select escape mutants and establish resistance profiles of the selected viruses.
55. (b) (4) [redacted]
56. The awardee shall conduct multiple ascending dose and repeat dose studies, evaluating Lead 2 systemic mouse model of VEEV infection, in order to establish efficacy and safety.
57. (b) (4) [redacted]
58. The awardee shall conduct multiple ascending dose and repeat dose studies, evaluating Lead 2 in the guinea pig models of LASV and JUNV infections, in order to establish efficacy and safety.
59. The awardee shall conduct single ascending-dose PK and distribution studies on the Lead 1 in rats, dogs, and NHPs, in order to support future in vivo tolerability and toxicity studies.
60. The awardee shall evaluate the Lead 1 in NHP in a 7-day tolerability study.
61. The awardee shall conduct a 7-day, non-GLP dose-ranging toxicology/toxicokinetic study in rats on Lead 1, in order to define the No Observed Effect Level (NOEL), No Observed Adverse Effect Level (NOAEL), and Maximum Tolerated Dose (MTD), to support pivotal animal toxicology studies.
62. The awardee shall conduct a 7-day, non-GLP dose-ranging toxicology/toxicokinetic study in dogs on Lead 1, in order to define the NOEL, NOAEL, and MTD, to support pivotal animal toxicology studies.

3.8 Specific Tasks for Phase 4

63. The awardee shall complete scale-up synthesis of Lead 2, in order to support Option Period 3 tasks.
64. The awardee shall characterize the MOA and resistance profile of Lead 2.
65. The awardee shall evaluate the lead 2 in non-GLP in vitro toxicity studies, including hERG binding, chromosome aberration studies, pharmacologic toxicity panel, P-gp assay, and CYP-450 profiling, as well as determine selectivity against host DNA polymerases.
66. The awardee shall conduct single ascending-dose PK and distribution studies on the Lead 2 in rats, dogs, and NHPs, in order to support future in vivo tolerability and toxicity studies.
67. The awardee shall evaluate the Lead 2 in NHP in a 7-day tolerability study.
68. The awardee shall conduct a 7-day, non-GLP dose-ranging toxicology/toxicokinetic study in rats on Lead 2, in order to define the NOEL, NOAEL, and MTD, to support pivotal animal toxicology studies.
69. The awardee shall conduct a 7-day, non-GLP dose-ranging toxicology/toxicokinetic study in dogs on Lead 2, in order to define the NOEL, NOAEL, and MTD, to support pivotal animal toxicology studies.

4.0 DELIVERABLES

Del. #	Deliverable Description	Due Date	Milestone Reference	SOW Reference	Government Role	Data Rights

1	EIDD-2749 PK and Distribution Report	03/30/2021	1	3.5	N/A	Government Purpose Rights
2	EIDD-2749 In Vivo Efficacy	06/30/2021	2	3.5	N/A	Government Purpose Rights
3	EIDD-2749 MOA and Resistance Profile Report	06/30/2021	2	3.5	N/A	Government Purpose Rights
4	New Compound Summary Report	12/31/2020 06/30/2021	3	3.5	N/A	Government Purpose Rights
5	New EIDD-2749 Analog and Prodrug Summary Report	9/30/2021 03/30/2022	8	3.6	N/A	Government Purpose Rights
6	Lead 1 Material Synthesis	06/30/2022	8	3.6	N/A	Government Purpose Rights
7	New Compound Summary Report	12/31/2021 06/30/2022	9	3.6	N/A	Government Purpose Rights
8	In Vivo Efficacy Reports	09/30/2021 12/31/2021 06/30/2022	8	3.6	N/A	Government Purpose Rights
9	MOA and Resistance Report for Lead 1	06/30/2022	8	3.6	N/A	Government Purpose Rights
10	In Vitro Toxicity Report	06/30/2022	8	3.6	N/A	Government Purpose Rights
11	New Compound Summary Report	012/31/202 2 06/30/2023	17	3.7	N/A	Government Purpose Rights
12	Lead 1 PK Distribution Profile Reports	03/30/2023	16	3.7	N/A	Government Purpose Rights
13	NHP Tolerability Report for Lead 1	03/30/2023	16	3.7	N/A	Government Purpose Rights

14	Lead 1 DRF Rat and Dog Reports	06/30/2023	16	3.7	N/A	Government Purpose Rights
15	Lead 2 MOA and Resistance Profile Report	06/30/2023	17	3.7	N/A	Government Purpose Rights
16	Lead 2 Scale-Up Synthesis Developed	06/30/2023	17	3.7	N/A	Government Purpose Rights
17	Completion of Lead 2 Scale-Up Synthesis	03/30/2024	25	3.8	N/A	Government Purpose Rights
18	Lead 2 PK Distribution Profile Reports	03/30/2024	25	3.8	N/A	Government Purpose Rights
19	NHP Tolerability Report for Lead 2	03/30/2024	25	3.8	N/A	Government Purpose Rights
20	Lead 2 DRF Rat and Dog Reports	06/30/2024	25	3.8	N/A	Government Purpose Rights
21	Quarterly Technical and Business Reports	03/31, 06/30, 12/31 (2020-2024)	-	-	N/A	Government Purpose Rights
22	Annual Technical and Business Reports	09/30/2020 09/30/2021 09/30/2022 09/30/2023	-	-	N/A	Government Purpose Rights
23	Final Technical and Business Report	06/30/2024	-	-	N/A	Government Purpose Rights

5.0 MILESTONE PAYMENT SCHEDULE

Milestone #	Milestone Description (Deliverable Reference)	Due Date	Total Program Funds
1	Summary report of resistance to EIDD-2749 (Ref 3.1, 3.5)	09/30/2020	

Milestone #	Milestone Description (Deliverable Reference)	Due Date	Total Program Funds
2	Summary report on development of polymerase assay (Ref 3.1, 3.5)	09/30/2020	
3	EIDD-2749 compound report: Scale up synthesis of EIDD-2749 and bioanalytical standards (Ref 3.1, 3.5)	09/30/2020	
4	New compound summary report: Chemistry, cellular efficacy, cytotox, uptake and metabolism (Ref 3.1, 3.5)	09/30/2020	
5	Q1 Annual Report (budget is for entire quarter milestones)	09/30/2020	(b) (4)
6	New compound summary report: Chemistry, cellular efficacy, stability, cytotox, uptake and metabolism (Ref 3.1, 3.5)	12/31/2020	
7	New compound in vivo summary report: PK, distribution, tolerability in mice (Ref 3.1, 3.5)	12/31/2020	
8	Final report on resistance to EIDD-2749 (Ref 3.1, 3.5)	12/31/2020	
9	Study report: Arenavirus replicase assay (Ref 3.1, 3.5)	12/31/2020	
10	Guinea pig LASV model (Ref 3.1, 3.5)	12/31/2020	
11	In vivo efficacy report: mouse model of VEEV and guinea pig models of LASV and JUNV (Ref 3.1, 3.5)	12/31/2020	
12	Q2 Quarterly Report (budget is for entire quarter milestones)	12/31/2020	(b) (4)
13	New compound summary report: Chemistry, cellular efficacy, stability, cytotox, uptake and metabolism (Ref 3.1, 3.5)	03/31/2021	
14	New compound summary report: Guinea pig PK and distribution (Ref 3.1, 3.5)	03/31/2021	
15	Summary report on EIDD-2749 escape mutants (Ref 3.1, 3.5)	03/31/2021	
16	Summary report of new compound activity in Arenavirus replicase assay (Ref 3.1, 3.5)	03/31/2021	
17	In vivo efficacy report: Mouse models of VEEV (b) (4), and guinea pig models of LASV and JUNV (Ref 3.1, 3.5)	03/31/2021	

Milestone #	Milestone Description (Deliverable Reference)	Due Date	Total Program Funds
18	Q3 Quarterly Report (budget is for entire quarter milestones)	03/31/2021	(b) (4)
19	New compound summary report: Chemistry, cellular efficacy, stability, cytotox, uptake and metabolism (Ref 3.1, 3.5)	06/30/2021	
20	New compound in vitro toxicity summary report: AMES, mitochondrial toxicity, human DNA polymerases (Ref 3.1, 3.5)	06/30/2021	
21	Final report on EIDD-2749 escape mutants (Ref 3.1, 3.5)	06/30/2021	
22	Summary report of new compound activity in Arenavirus replicase assay (Ref 3.1, 3.5)	06/30/2021	
23	In vivo efficacy report: Mouse models of VEEV (b) (4), and guinea pig models of LASV and JUNV (Ref 3.1, 3.5)	06/30/2021	
24	Quarterly Report (budget is for entire quarter milestones)	06/30/2021	(b) (4)
25	New compound summary report: Chemistry, cellular efficacy, stability, cytotox, uptake and metabolism (Ref 3.2, 3.6)	09/30/2021	
26	Lead 1 report: Scale up synthesis of lead and bioanalytical standards (Ref 3.2, 3.6)	09/30/2021	
27	Summary report of resistance to Lead 1 (Ref 3.2, 3.6)	09/30/2021	
28	Summary report of new compound activity in Arenavirus replicase assay (Ref 3.2, 3.6)	09/30/2021	
29	In vivo efficacy report: guinea pig models of LASV (Ref 3.2, 3.6)	09/30/2021	
30	Annual Report (budget is for entire quarter milestones)	09/30/2021	(b) (4)
31	New compound summary report: Chemistry, cellular efficacy, stability, cytotox, uptake and metabolism (Ref 3.2, 3.6)	12/31/2021	
32	New compound in vivo summary report: PK, distribution, tolerability in mice (Ref 3.2, 3.6)	12/31/2021	

Milestone #	Milestone Description (Deliverable Reference)	Due Date	Total Program Funds
33	Final report on resistance to Lead 1 (Ref 3.2, 3.6)	12/31/2021	
34	Summary report of new compound activity in Arenavirus replicase assay (Ref 3.2, 3.6)	12/31/2021	
35	Q6 Quarterly Report (budget is for entire quarter milestones)	12/31/2021	(b) (4)
36	New compound summary report: Chemistry, cellular efficacy, stability, cytotox, uptake and metabolism (Ref 3.2, 3.6)	03/30/2022	
37	Summary report on Lead 1 escape mutants (Ref 3.2, 3.6)	03/30/2022	
38	Summary report of new compound activity in Arenavirus replicase assay (Ref 3.2, 3.6)	03/30/2022	
39	In vivo efficacy report: Mouse models of VEEV (b) (4), and guinea pig models of LASV and JUNV (Ref 3.2, 3.6)	03/30/2022	
40	Q7 Quarterly Report (budget is for entire quarter milestones)	03/31/2022	(b) (4)
41	New compound summary report: Chemistry, cellular efficacy, stability, cytotox, uptake and metabolism (Ref 3.2, 3.6)	06/30/2022	
42	New compound in vitro toxicity summary report: AMES, mitochondrial toxicity, human DNA polymerases (Ref 3.2, 3.6)	06/30/2022	
43	Final report on Lead 1 escape mutants (Ref 3.2, 3.6)	06/30/2022	
44	Summary report of new compound activity in Arenavirus replicase assay (Ref 3.2, 3.6)	06/30/2022	
45	In vivo efficacy report: Mouse models of VEEV (b) (4), and guinea pig models of LASV and JUNV (Ref 3.2, 3.6)	06/30/2022	
46	Quarterly Report (budget is for entire quarter milestones)	06/30/2022	(b) (4)
47	New compound summary report: Chemistry, cellular efficacy, stability, cytotox, uptake and metabolism (Ref 3.3, 3.7)	09/30/2022	

Milestone #	Milestone Description (Deliverable Reference)	Due Date	Total Program Funds
48	New compound in vitro toxicity summary report: AMES, mitochondrial toxicity, human DNA polymerases (Ref 3.3, 3.7)	09/30/2022	
49	Summary report of new compound activity in Arenavirus replicase assay (Ref 3.3, 3.7)	09/30/2022	
50	Annual Report (budget is for entire quarter milestones)	09/30/2022	(b) (4)
51	New compound summary report: Chemistry, cellular efficacy, stability, cytotox, uptake and metabolism (Ref 3.3, 3.7)	12/31/2022	
52	Lead 1 NHP PK, distribution, and tolerability report (Ref 3.3, 3.7)	12/31/2022	
53	Summary report of the analysis of escape mutants against Lead 2 (Ref 3.3, 3.7)	12/31/2022	
54	Summary report of drug interactions with lead compound (Ref 3.3, 3.7)	12/31/2022	
55	In vivo efficacy report: Mouse models of VEEV (b) (4), and guinea pig models of LASV and JUNV (Ref 3.3, 3.7)	12/31/2022	
56	Q10 Quarterly Report (budget is for entire quarter milestones)	12/31/2022	(b) (4)
57	New compound summary report: Chemistry, cellular efficacy, stability, cytotox, uptake and metabolism (Ref 3.3, 3.7)	03/30/2023	
58	Preclinical drug development summary report: Scale up optimization, pre-formulation, physiochemical properties determination, and major metabolite synthesis (Ref 3.3, 3.7)	03/30/2023	
59	New compound in vivo summary report: PK, distribution, tolerability in mice (Ref 3.3, 3.7)	03/30/2023	
60	Summary report of the analysis of escape mutants against Lead 2 (Ref 3.3, 3.7)	03/30/2023	
61	Final report of drug interactions with lead compound (Ref 3.3, 3.7)	03/30/2023	
62	In vivo efficacy report: Mouse models of EEEV and VEEV, and guinea pig models of LASV and JUNV (Ref 3.3, 3.7)	03/30/2023	

Milestone #	Milestone Description (Deliverable Reference)	Due Date	Total Program Funds
63	Q11Quarterly Report (budget is for entire quarter milestones)	03/31/2023	(b) (4)
64	New compound summary report: Chemistry, cellular efficacy, stability, cytotox, uptake and metabolism (Ref 3.3, 3.7)	06/30/2023	
65	Preclinical drug development final report: Scale up optimization, pre-formulation, physiochemical properties determination, and major metabolite synthesis (Ref 3.3, 3.7)	06/30/2023	
66	Lead 1 in vitro toxicity report: hERG, chromosome aberration test, S9 microsome metabolite ID, pharmacology toxicity panel, human DNA polymerases, P-gp substrate/inhibition assay, and CYP-450 profiling (Ref 3.3, 3.7)	06/30/2023	
67	Report for DRF toxicology in rats for Lead 1 (Ref 3.3, 3.7)	06/30/2023	
68	Report for DRF toxicology in dogs for Lead 1 (Ref 3.3, 3.7)	06/30/2023	
69	In vivo efficacy report: Mouse models of VEEV (b) (4), and guinea pig models of LASV and JUNV (Ref 3.3, 3.7)	06/30/2023	
70	Identify clinical development candidate (Ref 3.3, 3.7)	06/30/2023	
71	Quarterly Report (budget is for entire quarter milestones)	06/30/2023	(b) (4)
72	New compound summary report: Chemistry, cellular efficacy, stability, cytotox, uptake and metabolism (Ref 3.4, 3.8)	09/30/2023	
73	Lead 2 NHP PK, distribution, and tolerability report (Ref 3.4, 3.8)	09/30/2023	
74	Annual Report (budget is for entire quarter milestones)	09/30/2023	(b) (4)
75	New compound summary report: Chemistry, cellular efficacy, stability, cytotox, uptake and metabolism (Ref 3.4, 3.8)	12/31/2023	

Milestone #	Milestone Description (Deliverable Reference)	Due Date	Total Program Funds
76	Lead 2 report: Scale up synthesis of lead and bioanalytical standards (Ref 3.4, 3.8)	12/31/2023	
77	Lead 2 in vitro toxicity report: hERG, chromosome aberration test, S9 microsome metabolite ID, pharmacology toxicity panel, human DNA polymerases, P-gp substrate/inhibition assay, and CYP-450 profiling (Ref 3.4, 3.8)	12/31/2023	
78	Lead 2 rat and dog PK and distribution reports (Ref 3.4, 3.8)	12/31/2023	
79	Lead 2 NHP tolerability report (Ref 3.4, 3.8)	12/31/2023	
80	In vivo efficacy report: Mouse models of VEEV (b) (4) , and guinea pig models of LASV and JUNV (Ref 3.4, 3.8)	12/31/2023	
81	Q14 Quarterly Report (budget is for entire quarter milestones)	12/31/2023	(b) (4)
82	New compound summary report: Chemistry, cellular efficacy, stability, cytotox, uptake and metabolism (Ref 3.4, 3.8)	03/30/2024	
83	In vivo efficacy report: Mouse models of VEEV (b) (4) , and guinea pig models of LASV and JUNV (Ref 3.4, 3.8)	03/30/2024	
84	Q15 Quarterly Report (budget is for entire quarter milestones)	03/31/2024	(b) (4)
85	New compound summary report: Chemistry, cellular efficacy, stability, cytotox, uptake and metabolism (Ref 3.4, 3.8)	06/30/2024	
86	Report for DRF toxicology in rats for Lead 2 (Ref 3.4, 3.8)	06/30/2024	
87	Report for DRF toxicology in dogs for Lead 2 (Ref 3.4, 3.8)	06/30/2024	
88	In vivo efficacy report: Mouse models of VEEV (b) (4) , and guinea pig models of LASV and JUNV (Ref 3.4, 3.8)	06/30/2024	
89	A4 Final Report (budget is for entire quarter milestones)	06/30/2024	(b) (4)
		Total (FFP):	**$11,192,009**
		Period of Performance:	**48 Months**

6.0 SHIPPING PROVISIONS

The contractor shall submit Quarterly, Annual, and Final Reports in accordance with the Base Agreement, to deliverables.mcdc.ati.org. All deliverables intended for the AOR shall be delivered in electronic format to the AOR and the Mail box below.

A copy of all data deliverables shall be sent to:

usarmy.detrick.dod-jpeo-cbrnd.mbx.otadeliverable@mail.mil.

7.0 INTELLECTUAL PROPERTY, DATA RIGHTS, AND COPYRIGHTS

The contractor shall comply with the terms and conditions defined in the MCDC Base Agreement. The table below identifies pre-existing technical data and computer software with restrictions that may be used during performance of this Agreement. The Government shall receive a Government Purpose Rights license to all technical data and computer software developed and delivered under this Agreement, except for the pre-existing technical data and computer software that was previously developed exclusively at private expense and identified in the table below. To the maximum extent practicable, segregable portions of deliverables that will be restricted shall be clearly identified and labeled. If, after award, the contractor wishes to use any other internally developed technical data or computer software, or any other pre-existing proprietary information not identified in the table below, then the contractor shall disclose its intent in writing to the MCDC CMF prior to its use, and shall receive written approval from the Agreements Officer prior to proceeding. All technical data and computer software developed or delivered under this Agreement shall have appropriate data rights markings in accordance with DFARS 252.227-7013(f) and 7014(f). The contractor asserts that all contractor owned or background patents that affect the Government's rights in the deliverables anticipated under this Agreement are identified in the table below.

Technical Data or Computer Software to be Furnished with Restrictions	Basis for Assertion	Asserted Rights	Name of Organization Asserting Restrictions	Deliverables Affected
Composition of Matter and Method of Use Claims in the cited patent applications.	Existing Data and Filings	EIDD-2749, including derivatives, prodrugs and methods of treating and preventing viral infection, is covered by U.S. Application No. 62/780,434, filed March 7, 2018 and PCT application, PCT/US2019/021168, filed March 7, 2019. These applications are assigned to Emory University.	Emory University	The data and compounds listed in the applications cited are the starting point for this program, so all deliverables in Table 1 could be potentially affected unless novel compounds emerge in this contract.

8.0 SECURITY

The security classification level for this effort is UNCLASSIFIED.

9.0 MISCELLANEOUS REQUIREMENTS (SAFETY, ENVIRONMENTAL, ETC.)

N/A

10.0 GOVERNMENT FURNISHED PROPERTY/MATERIAL/INFORMATION

N/A

11.0 AGREEMENTS OFFICER'S REPRESENTATIVE (AOR) AND ALTERNATE AOR CONTACT INFORMATION

AOR

NAME: (b) (6)
MAILING ADDRESS: (b) (6)
EMAIL: (b) (6)
PHONE: (b) (6)
AGENCY NAME/DIVISION/SECTION: DTRA RD-CBM

Alternate AOR

NAME: (b) (6)
MAILING ADDRESS: (b) (6)
EMAIL: (b) (6)
PHONE: (b) (6)
AGENCY NAME/DIVISION/SECTION: DTRA RD-CBM