Proposal Number: MTEC-20-09-COVID-19-065
Organization: (b) (4)
Title: Treatment and Prevention of Acute Respiratory Distress Syndrome (ARDS) in Patients with COVID-19 (b) (4)
ACURO approval needed: No
HRPO approval needed: Yes
EGS#: MT20009.065
(b) (4) **will provide all FDA communications and documents related to this award for review if requested by SOTR, HRPO and ORP.**

Introduction/Background:
Providing a pharmacologic therapeutic to accelerate recovery in patients with COVID-19 and prevent progression to moderate-to-severe ARDS would overcome many of the challenges facing lack of hospital beds, ventilators and trained personnel including in the military setting. Preclinical models, large human observational studies, and human genetic studies from leading groups worldwide have converged on the concept that a vascular endothelial receptor, Tie2, may play a pivotal role in the defense against microvascular breach in ARDS. (b) (4) will exhibit an acceptable safety profile and show efficacy for treatment and prevention of COVID-19 associated ARDS and be a life-saving therapeutic for service members in the field suffering from the devasting respiratory effects of COVID-19.

Scope:
(b) (4) will exhibit an acceptable safety profile and show efficacy for treatment of COVID-19 by promoting earlier recovery and preventing progression to moderate to severe ARDS via pleiotropic actions to (a) restore vascular barriers; (b) blunt inflammation; (c) enhance endothelial cell viability; (d) reduce pulmonary vascular resistance; (e) attenuate *in situ* thrombosis; and (f) promote lymphatic function for the clearance of lung edema. (b) (4)
(b) (4)
in patients with moderate to severe COVID-19 not yet requiring mechanical ventilation.

Project Objectives:
1. Safe and efficacious dose for treatment of warfighters with moderate to severe COVID-19 to prevent progression to ARDS and promote earlier recovery
2. Submit to FDA emergency use authorization
3. (b) (4) for emergent use

Major milestones (deliverables):
1. Demonstrate safe and efficacious dose of patients with ARDS due to COVID-19
2. Receive FDA authorization for emergent use or advance to Phase 3
3. (b) (4)

Task 1: Study Development (100% complete)

Time: Approximately 14 days
Deliverable: Research Protocol

Task 2: IRB submission and approval (using central IRB)

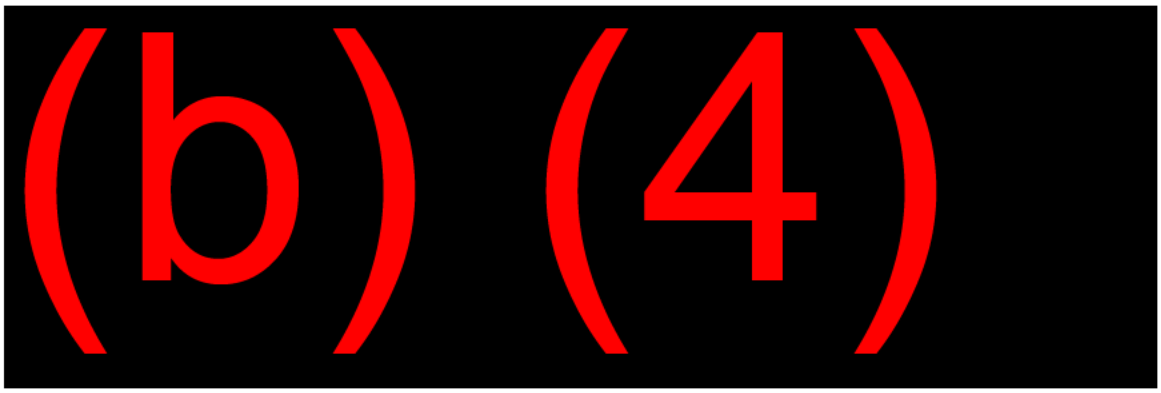
Time: approximately 14 days
Deliverable: IRB approval

Task 1 and Task 2 Requirements:
To develop research protocol, submit IND and receive IRB approval, internationally renowned ARDS researchers (b) (4), (b) (6) will serve as advisors to the program. All work will be completed in the United States, with no international sites. (b) (4) (b) (4), (b) (6) will lead communication with the US Food and Drug Administration (FDA). (b) (4) (b) (4), (b) (6) will serve as the lead scientific advisor. The program's steering committee, consisting of an internationally renowned team of ARDS researchers, cardiologists, immunologists and experts in vascular biology as it relates to Tie2 will provide clinical and scientific support for the (b) (4) to treat patients suffering from ARDS due to COVID-19. This team includes (b) (4) (b) (4) (b) (4) Based on the protocol, the selected CRO will develop electronic case report forms (eCRFs).

All sites will use a common protocol and eCRFs maintained by (b) (4) in conjunction with the selected CRO and approved by a central IRB. Coordinators and investigators at all enrolling sites will be given access to these electronic CRF's for data entry. After data entry into the CRF, blinded data will be immediately available to key study personnel for monitoring and ongoing safety analysis. (b) (4) and the selected CRO will be charged with maintaining the protocol and case report form, training all sites on execution of the protocol, monitoring and cleaning the data, maintaining IRB approval, reporting adverse events, and analyzing the final data. Investigators and coordinators at each site will be charged with executing the trial locally.

A qualified medical monitor and (b) (4) /CRO clinical operations personnel will be on call at all times when the Phase 2 trial is active for site personnel to contact with questions. Collection kits for biological specimens will be provided by a central laboratory to each of the enrolling sites. Specimens will be collected by research personnel at each enrolling site, temporarily stored locally, and then shipped to the program's central. Specimens will be analyzed in the central laboratory and results entered into the CRF.

Task #3: To conduct a Phase 2 clinical trial of (b) (4) for the treatment of ARDS in patients with COVID-19. Phase 2 trials will be conducted at 10 clinical sites



Time: 6 months
Deliverable: Safety and Efficacy in Treatment of ARDS in COVID-19 patients

Task #4: Data Readout

Time: 4 weeks
Deliverables: Date readout and analysis

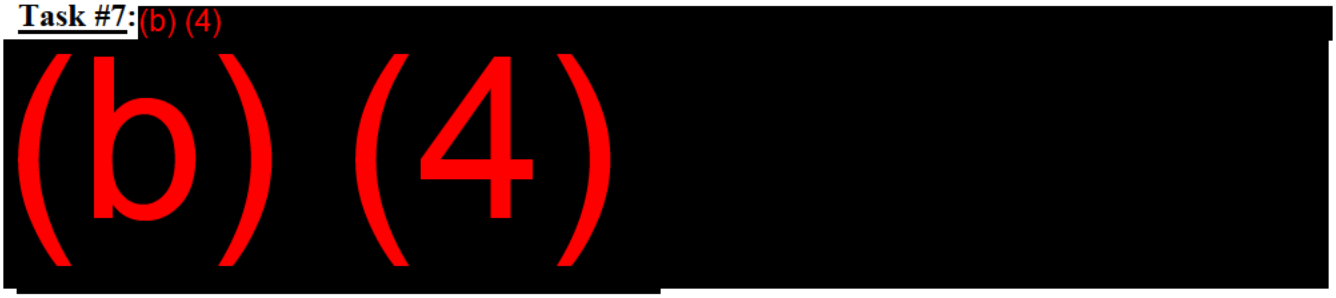
Task #5: Request to the FDA for approval of (b) (4) under the Coronavirus Treatment Acceleration Program (CTAP) or development of Phase 3 protocol for registration study starting January 2021.

Time: 4 weeks
Deliverables: Request to FDA

Task #6: Prepare for Phase III

Time: 4 weeks
Deliverable: Type C meeting with the FDA

Task #7: (b) (4)



Time: 4 weeks to develop plan
Deliverable: Plans for large scale manufacturing

Period of Performance Summary:

Milestones		Period of Performance - 8 months								Notes
		M1	M2	M3	M4	M5	M6	M7	M8	
IND Submitted										Complete
Task #1	Study Development	Task #1								Ongoing
Task #2	IRB Approval	Task #2								TBD
Drug Supply for Studies										Complete
(b) (4)										
Task #4	Data Readout								Task #4	
Task #5	Request FDA Emergent Use Approval								Task #5	
Task #6	Prepare for Phase III								Task #6	
Task #7	Manufacture Drug for Emergent Use								Task #7	

Preferred Payment Method: Cost Reimbursement Milestones (with ceiling).

Payment Schedule: Cost reimbursement requests will be made at the end of each month with an invoice. We anticipate a relatively even distribution of patients but our clinical sites might have the capacity and opportunity to enroll and complete more patients than expected whereby our initial invoices might be higher (or lower).

Milestone	Milestone Event	Due Date	MTEC Amount	Aerpio Cost Share	Total
1	IND approval, IRB approval, CRO Execution of Work Order and submission of HRPO	7/15/2020	(b) (4)		$(b) (4)
2	1st Investigator / Site Pass Through	7/15/2020	(b) (4)		$(b) (4)
3	Quarterly Report 1 (June, Technical and Business Reports)	7/25/2020	0	0	0
4	CRO First Patient Enrolled	8/15/2020	(b) (4)	(b) (4)	$(b) (4)
5	2nd Investigator / Site Pass Through	8/15/2020	(b) (4)	(b) (4)	$(b) (4)
6	CRO 25% Patients Enrolled	9/15/2020		(b) (4)	$(b) (4)
7	3rd Investigator / Site Pass Through	9/15/2020	(b) (4)	(b) (4)	$(b) (4)
8	CRO 50 % Patients Enrolled	10/15/2020	(b) (4)	(b) (4)	$(b) (4)
9	4th Investigator / Site Pass Through	10/15/2020	(b) (4)	(b) (4)	$(b) (4)
10	Quarterly Report 2 (July – Sept. Technical and Business Reports)	10/25/2020	0	0	0
11	CRO 100% Patients Enrolled	11/15/2020	(b) (4)	(b) (4)	$(b) (4)
12	5th Investigator / Site Pass Through	11/15/2020	(b) (4)	(b) (4)	$(b) (4)
13	6th Investigator / Site Pass Through	12/15/2020	(b) (4)	(b) (4)	$(b) (4)
14	CRO Final Database Lock	1/15/2021	(b) (4)	(b) (4)	$(b) (4)

15	7th Investigator / Site Pass Through	1/15/2021	(b) (4)	(b) (4)	$(b) (4)
16	CRO Clinical Study Report	1/31/2021	(b) (4)	(b) (4)	$(b) (4)
17	8th Investigator / Site Pass Through	2/15/2021	(b) (4)	(b) (4)	$(b) (4)
18	Final Reports (Technical and Business Reports)	2/25/2021	0	0	0
	Total		(b) (4)	(b) (4)	$7,903,574

Data Rights:

The Offeror shall comply with the terms and conditions defined in the Base Agreement regarding Data Rights. It is anticipated that anything delivered under this proposed effort would be delivered to the Government with Government purpose data rights or unlimited data rights. If this is not the intent, then the proposal should discuss data rights associated with each item, and possible approaches for the Government to gain Government purpose data rights or unlimited data rights as referenced in the Base Agreement. Rights in technical data in each Research Project Award shall be determined in accordance with the provisions of MTEC Base Agreement. If applicable, complete the below table for any items to be furnished to the Government with restrictions.

Please indicate your assertion: Unlimited Data Rights.