



## Request for Project Information (RPI)

### “Candidate Drug Treatment for Traumatic Brain Injury for Phase 2 Clinical Trials”

The Medical Technology Enterprise Consortium (MTEC) is excited to post this announcement for a Request for Project Information (RPI) focused on **Traumatic Brain Injury Drug Treatment (TBI DT) – to rapidly conduct Phase 2 clinical trials on traumatic brain injury (TBI) drug candidates and identify at least one TBI drug candidate for advancement into a Phase 3 clinical trial.** The end goal of the TBI DT program is a commercially-available TBI drug that is approved by the U.S. Food and Drug Administration (FDA) to treat moderate to severe TBI (i.e., patients presenting with a Glasgow Coma Scale (GCS) score of  $\leq 12$ , or 13-15 with evidence of intracranial injury on imaging (CT or MRI) referable to trauma).

This RPI contains background material and guidance for the preparation of Project Information Papers to MTEC.

#### *Background:*

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Treating TBI remains one of the top priorities for the Department of Defense (DoD). The DoD and the military services require solutions to fill the capability gap to treat moderate to severe TBI as close to point of injury as possible to mitigate brain injury and improve short- and long-term outcomes. The current standard of care for TBI remains supportive in nature, based on management of symptoms, with no drug therapies that address the brain injury, resulting in increased long-term mortality and reduced life expectancy. Estimated economic costs of care for TBI in the U.S. are  $> \$75B$  per year according to the Centers for Disease Control and Prevention (CDC). Therefore, it is important to develop a therapy that will decrease lost duty time and mitigate the life-long disability and rehabilitation costs associated with moderate to severe TBI.

Despite numerous clinical trials of potential therapies, there are currently no drugs approved by the FDA for the treatment of acute TBI. The lack of success of clinical trials for TBI is complex and includes the need for optimization of therapeutic dosing, poor patient stratification, lack of biomarkers for mechanism of action, and inadequate data to inform confirmatory Phase 3 clinical trials.

Through MTEC, the DoD U.S. Army Medical Material Development Activity (USAMMDA) has recently made an award and established a contractual relationship with a competent and experienced TBI Clinical Trial Network to enable the rapid clinical testing of several TBI drug candidates. The intent of this prior award was to establish an experienced and funded infrastructure that could be made available to drug sponsors/industry partners for

the evaluation of candidate TBI therapeutics in Phase 2 clinical trials. The awarded Network brings 18 potential clinical sites and staff that are very familiar with TBI diagnosis, studies and treatment.

The already awarded TBI Clinical Trial Network is now poised and ready to collaborate with several drug sponsors/industry partners to design and execute focused Phase 2 clinical trials on TBI drug candidates, with the goal to reduce the overall risk of future investment in a Phase 3 clinical trial for TBI.

**The benefit to drug sponsors/industry partners is the ability to leverage this experienced TBI Clinical Trial Network which has already been centrally funded by DoD. This enables drug sponsors/industry partners access to Phase 2 clinical trials with relatively low cost, where drug sponsors/industry partners will partner with the DoD and the TBI Clinical Trial Network to provide the drug and their subject matter expertise (i.e., other costs related to the Phase 2 Clinical Trials are already funded by the DoD). This Network approach should lead to faster, more complete, and relatively low-cost completion of Phase 2 clinical trials.**

The desired end goal is to demonstrate efficacy of at least one TBI drug in Phase 2 clinical trials and recommend its continued development toward FDA regulatory clearance.

***Objective:***

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This RPI is part of the second step of this process by identifying TBI drug candidates that would be sufficiently mature and robust to warrant Phase 2 clinical studies by the TBI Clinical Trial Network.

TBI drug candidates must target a moderate to severe TBI indication, be currently in or have already completed Phase 1 trials (at a minimum), be ready for Phase 2 clinical trials, or have completed Phases 1-3 for other TBI-related indications.

The broad classes of compounds that the program will consider for evaluation in Phase 2 clinical trials by the TBI Clinical Trial Network are:

- (1) **Novel compounds under development by pharmaceutical/biotechnology/academic investigators:** Neurotrauma investigators are developing a wide range of novel chemical entities that show promise in experimental models of TBI.
- (2) **Repurposed drugs:** Pharmaceuticals that are FDA-approved and in clinical use for other medical conditions, and have substantial preclinical data and clinical observations supporting their role in neuroprotection and neuroplasticity.
- (3) **Nutraceuticals:** Several nutraceuticals show potential, either as neuroprotective agents or promoters of neuroregeneration. Compounds in wide use as dietary supplements are regulated by FDA using standards that differ from those applied to drugs.

***Industry Partners:***

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The DoD expects Project Information Papers to include drug sponsors/industry partner(s) committed to bringing the product to market. At a minimum, it is expected that drug sponsors/industry partners have already had formal communication with the FDA (e.g., pre-Investigational New Drug (IND) meeting) and have data sufficient to file an IND. **It is the DoD's desire that industry partners will manufacture and procure their TBI drugs (provide in-kind cost sharing, with sufficient clinical safety data to support Phase 2 clinical trials) in sufficient volumes to support rigorous Phase 2 testing.**

[\*\*In other words, the DoD/MTEC does not intend to provide funding directly to the drug sponsor/industry partner. The benefit to drug sponsors/industry partners is the ability to conduct a Phase 2 clinical trial by an experienced TBI Clinical Trial Network, which has already been centrally funded by DoD. This enables drug sponsors/industry partners access to Phase 2 clinical trials with relatively low cost, where drug sponsors/industry partners will partner with DoD and the TBI Clinical Trial Network to provide the drug and their subject matter expertise (i.e., almost all other costs related to the Phase 2 Clinical Trials are already funded by the DoD).]

The DoD will not exclude industry partners that are unable to manufacture or procure their TBI drugs, however, significant justification will be required. **Drug sponsors/industry partners of selected TBI drug candidates will be completely involved in the design and execution of the Phase 2 clinical trials to ensure that the studies are conducted in a manner that is agreed upon by all parties involved (i.e., drug sponsor/industry partner, DoD, the TBI Clinical Trial Network).**

[Note: Project Information Papers from internationally-based drug sponsors/industry partners are allowable.]

#### ***Data Sharing:***

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The DoD will provide oversight and negotiate for DoD interests in maximal data sharing in the spirit of sharing lessons learned across the breadth of the award. Accordingly, drug sponsors/industry partners will be expected to share data from the clinical trial for subsequent analysis and follow-on questions with the DoD in a manner that helps enable a successful outcome at the end of the award's delivery schedule.

#### ***Intellectual Property (IP):***

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In accordance with Army Directive 2018-26, standard government IP clauses will be applied so that the entities that provide TBI candidate drugs will retain their IP rights. Nondisclosure Agreements (NDAs) may be used in the planning phase to protect both Government and industry IP.

#### ***Requirements of the Project Information Paper (PIP):***

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The intent of this RPI is to solicit Project Information Papers that will serve as a Clinical Trial Synopsis as a means to assess TBI drug candidates intended to treat moderate to severe TBI (as defined above).

- Format

1. 4-page limit, exclusive of contact cover page and references
2. 12 point Arial font, smaller font may be used in figures and tables, but must be clearly legible
3. Single-spaced, single-sided, 8.5 inches x 11 inches.
4. Margins on all sides (top, bottom, left, and right) should be at least 0.5 inch
5. Project Information Paper should be in \*.pdf format

- Cover page with Submitter's name, organization, email address, and phone number and team member organizations and contact information

- Clinical Trial Synopsis [Please address the following technical requirements in your Project Information Paper]:

- Patient population targeted, the use of prognostic, predictive, and pharmacodynamics biomarkers, and proposed outcome measures
  - Strength of scientific rationale including mechanism of action, pre-clinical data to include peer reviewed publications and good laboratory practices (GLP) animal safety and toxicity studies
  - FDA-approved Investigational New Drug (IND) application for human TBI studies, if appropriate
  - Results of Phase 1 study in humans regarding toxicity/tolerability, and availability of PK and PD data for the compound relevant to dose selection
  - In cases of repurposed drugs, evidence of efficacy in human disease, results of Phase II and Phase III clinical trials
  - Known or potential drug interactions with drugs commonly used in neurological intensive care units
  - Current financial health and business plan to include funding/investment source partners (government/private) and investment status
  - Manufacturing and distribution capabilities and partnerships - Current stock of drug and placebo; weight, volumes, doses, and ability to produce under good manufacturing practices (GMP) conditions
  - Storage, transport, and distribution details of drug and placebo; production and dissemination; current operations and/or plans, temperature stability
  - Intellectual property and patent right assertions in U.S. and abroad
  - Experience - have submitters and/or their partners obtained FDA approval and marketed other solutions?
- *NOTE: A rough order magnitude (ROM) pricing is **NOT** required for this Project Information Paper since funding will neither come directly from MTEC nor DoD/USAMMDA to drug sponsors/industry partners.*

*Evaluation of Project Information Papers:*

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All submissions will be evaluated for completeness and accuracy of information, and adherence to submission guidelines. The TBI Clinical Trial Network and DoD may consider appointment of external experts to advise on evaluation of Project Information Papers. The TBI Clinical Trial Network and DoD will review Project Information Papers and MTEC/DoD will communicate to the submitter of the Project Information Paper regarding the suitability of the proposed TBI drug candidate for further consideration.

#### *Financial Framework:*

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TBI drug sponsors/industry partners that are selected for evaluation in Phase 2 clinical trials will be requested to engage in and negotiate a contractual relationship with the TBI Clinical Trial Network and DoD for the execution of the clinical trial.

[NOTE: As stated above, it is the DoD's desire that industry partners will manufacture and procure their TBI drugs (provide in-kind cost sharing, with sufficient clinical safety data to support Phase 2 clinical trials) in sufficient volumes to support rigorous Phase 2 clinical testing. The DoD/MTEC does not intend to provide funding directly to the drug sponsor/industry partner. The benefit to drug sponsors/industry partners is the ability to conduct a Phase 2 clinical trial by an experienced TBI Clinical Trial Network, which has already been centrally funded by DoD. This enables drug sponsors/industry partners access to Phase 2 clinical trials with relatively low cost, where drug sponsors/industry partners will partner with the DoD and the TBI Clinical Trial Network to provide the drug (i.e., almost all other costs related to the Phase 2 Clinical Trials are already funded by the DoD).

#### *MTEC:*

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The MTEC mission is to assist the U.S. Army Medical Research and Development Command (USAMRDC) by providing cutting-edge technologies and supporting effective materiel life cycle management to transition medical solutions to industry that protect, treat, and optimize Warfighters' health and performance across the full spectrum of military operations. MTEC is a biomedical technology consortium collaborating with multiple government agencies under a 10-year renewable Other Transaction Agreement (OTA), Agreement No. W81XWH-15-9-0001, with the U.S. Army Medical Research Acquisition Activity (USAMRAA). MTEC is currently recruiting a broad and diverse membership that includes representatives from large businesses, small businesses, "non-traditional" government contractors, academic research institutions and not-for-profit organizations.

#### *Administrative Information:*

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Project Information Papers are due no later than **Wednesday, 4 September 2019 at 5:00 PM ET** using the MTEC submission format: <https://secure.ati.org/mtec/1911rpi.html>. This RPI will be posted to the MTEC website

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([www.mtec-sc.org](http://www.mtec-sc.org)) and FedBizOpps ([www.fbo.gov](http://www.fbo.gov)) to notify interested parties. **MTEC membership is NOT required for the submission of a Project Information Paper in response to this MTEC RPI.**

This RPI is focused on gathering sufficient information regarding TBI drug candidates for evaluation by the TBI Clinical Trial Network and DoD. The submitted Project Information Papers may generate questions about capabilities or risks that may be identified in your papers. In coordination with MTEC, the DOD reserves the right to interact directly with Offerors who submit Project Information Papers in response to this RPI. MTEC will communicate to the Offeror regarding the drug candidate's suitability for further consideration on or before Monday, 21 October 2019. Offerors with TBI drug candidates of interest will be invited to provide further information at individual presentations to be held on 17-18 December 2019 in Denver, CO.

For inquiries regarding this announcement, please direct your correspondence to the following contacts:

- Technical questions and Membership questions  
Dr. Lauren Palestrini, MTEC Director of Research, [Lauren.Palestrini@officer.mtec-sc.org](mailto:Lauren.Palestrini@officer.mtec-sc.org)
- Administrative questions  
Ms. Kathy Zolman, MTEC Interim Executive Director, [Kathy.zolman@ati.org](mailto:Kathy.zolman@ati.org)