OBJECTIVE: PLEASE NOTE - DHA Topic DHA201-002 has been approved by SBA to exceed Phase II guideline amounts. Upon completion of the Phase I effort, proposers may be selected for a Phase II award, with a ceiling not to exceed $3,000,000.

To provide a radioprotector medical countermeasure (MCM) to the Joint Force with effective prophylactics to recover from and survive Acute Radiation Syndrome (ARS) resulting from ionizing radiation exposure. In concert with resuscitative intervention and supportive care, MCMs would improve survival and reduce recovery times for the individual contributing to a higher level of unit readiness.

DESCRIPTION: The current Joint Force requires Medical Counter Measures (MCMs) against threats to sustain the full range of military operations. The Joint Force must effectively protect the maximum number of personnel against the greatest number of hazards as far forward as possible, and sustain the casualty from the point of exposure to the point of definitive care. These MCMs will be administered at the lowest echelon of health care possible. They will work in concert with other medical products to lessen performance degradation and increase survival for the individual contributing to a higher level of unit readiness.

The Department of Defense requires MCMs for Acute Radiation Syndrome (ARS) that are safe and effective prophylaxes and therapeutics. To be effective, any prophylaxes must be available to Joint Force personnel prior to ionizing radiation (IR) exposure. It will reduce the likelihood of developing severe adverse health effects associated with ARS to increase survival. Prophylaxes would be administered to the Joint Force prior to operating in a known, high risk Ionizing Radiation (IR) environment.

ARS encompasses a spectrum of pathophysiologic changes caused by exposure to high doses of penetrating radiation in a relatively short time period. Injuries sustained depend on the dose and extent of radiation exposure (e.g., whole- or partial-body). Radiation exposures exceeding 2 Gray (Gy) in adults can result in the depletion of hematopoietic stem cells and cellular progenitors in the bone marrow, which may lead to severe neutropenia, thrombocytopenia, and death from infection or hemorrhage. Higher radiation doses can cause gastrointestinal (GI) complications, including mucosal barrier breakdown, bacterial translocation, and loss of GI structural integrity, which can lead to rapid death. Individuals who survive ARS may suffer from the delayed effects of acute radiation exposure (DEARE), which can include pulmonary, renal, cardiovascular, immunological, and cutaneous complications occurring weeks to months after radiation exposure.

There are three FDA-approved post-exposure therapeutic drugs to treat the hematopoietic subsyndrome of ARS. There are no FDA-approved prophylactic MCMs for IR exposures resulting in ARS. Future pharmaceuticals will be used in concert with the most appropriate and cost effective mix of existing protocols for treating radiation injuries and could be used at any role of care. Together, future pharmaceuticals and existing medical management protocols (e.g., supportive care, antioxidants, antiemetics, antibiotics, colony stimulating factors, blood/bone marrow transplants, isolation) will provide the means to effectively treat the maximum number of personnel.

For the purpose of this effort, the terms “MCM(s)” and “drug(s)” will include drugs, biologics, and cellular therapies. The objective of a prophylactic MCM is to reduce the likelihood of developing severe adverse health effects associated with ARS to increase survival. The prophylactic MCM must work in concert with other medical products to lessen performance degradation and increase survival for an individual contributing to a higher level of unit readiness. A prophylactic MCM will need to be given pre-exposure, pre-symptomatic and be administered at the lowest echelon of health care possible to the Joint Force (age range of 18 - 62 years) prior to operating in a known, high risk irradiated environment. To achieve this effect the method of administration must be tailored to optimize ease of administration in an operational environment.

PHASE I: Offerors must propose proof-of-concept experiments to demonstrate the efficacy of proposed ARS prophylactic MCM against a relevant susceptible cell populations such as hematopoietic progenitors. Demonstration of efficacy in some form of an in vivo model is also acceptable, but not required for Phase I. Technologies of interest include, but are not limited to, drugs, but can include biologics
or cellular therapies. Exit criteria for successful completion of Phase I research would be the demonstration of efficacy at the LD70/30 or greater radiation dose levels. The LD70/30 represents a radiation dose that would result in 70% mortality over 30 days in vehicle treated mice. Information garnered from Phase I experiments may be more qualitative than quantitative.

PHASE II: With successful completion of Phase I experiments, Phase II would further evaluate the medical countermeasure (MCM) in a small animal study. A Phase II effort will test effective prophylactic ARS MCMs at the LD70/30 dose level or greater in an appropriate animal model. In these studies, the MCM would be administered to animals prior to radiation exposure. The animal model should be of sufficient size and scope to demonstrate a statistically significant increase in survival in animals receiving the MCM. The SBIR Phase II studies shall include experiments of a manner that facilitates the collection of non-clinical GLP pharmacokinetic (PK) and pharmacodynamic (PD) data. The PK and PD information will be of paramount importance to inform subsequent Phase III studies. Optimized formulation studies involving development of a preparation of the drug should be conducted during this phase II effort. Responders to this SBIR should provide a test plan for in vivo evaluation prior to the start of Phase II studies.

PHASE III DUAL-USE APPLICATIONS: Phase III studies would further refine the animal model and the compound/drug dosing regimen. The goal would be to work toward FDA approval of a MCM for one or more radioprotector MCMs against ARS. The studies in Phase III should support FDA approval/licensure to include entry into clinical studies, cGMP manufacturing scale up, and pivotal efficacy studies. FDA licensure/approval is not necessary for the project to be deemed successful. One means for the offeror to document progress is through a Technology Readiness Assessment (TRA) of the technology using the harmonized Quantitative Technology Readiness Level (QTRL) guidance document as described by the Public Health Emergency Medical Countermeasures Enterprise (PHEMCE). A second means for demonstrating success is the establishment of funding and partnering with commercial companies (if necessary) to facilitate bringing the product to market.

Successful radioprotector MCM products directed against ARS will clearly have use by other government agencies, hospitals/ emergency departments, first responders, and others providing responses to nuclear and radiation dispersal incidents.

REFERENCES:

KEYWORDS: Radioprotectors, Prophylaxes, Medical Countermeasures (MCM), Acute Radiation Syndrome (ARS), Ionizing Radiation (IR), Sub-syndromes