COMBATTING FUTURE BIOLOGICAL THREATS – HOST-DIRECTED INTERVENTIONS TO EMERGING THREATS FOR RAPID RESPONSE

Mitigating Severe Outcomes Of Disease Caused By Emerging Threats

Lindsay Odell U.S. Department of Health and Human Services, Administration for Strategic Preparedness and Response, Biomedical Advanced Research and Development Authority **Elaine Vo** U.S. Department of Health and Human Services, Administration for Strategic Preparedness and Response, Biomedical Advanced Research and Development Authority **Kimberly Sciarretta** U.S. Department of Health and Human Services, Administration for Strategic Preparedness and Response, Biomedical Advanced Research and Development Authority

Introduction:
Responding to emerging and unknown biological threats requires the ability to mitigate morbidity and mortality in a threat agnostic manner. To date, there are no therapeutics available to treat severe host dysregulation and organ dysfunction that occur with acute respiratory distress syndrome (ARDS) and sepsis. Such host dysregulation, and potential mortality, can arise as a result of complication to infectious diseases. Standard of care options for such critically ill patients are somewhat limited, and treatment is confounded by patient heterogeneity and pathophysiology of disease. There is a critical unmet need for threat agnostic therapeutics to prevent severe outcomes of disease as well as restore homeostasis to dysregulated organ systems for both civilians and the Joint Force. Approaches that take into account variation in host response, temporal stages of disease, and patient trajectories are needed. The Division of Research, Innovation, and Ventures (DRIVe) Host-Directed Therapeutics program within the Administration for Strategic Preparedness and Response, Biomedical Advanced Research and Development Authority is advancing innovative, precision medicine approaches to develop threat-agnostic, host-directed therapeutics that treat host dysregulation/restore homeostasis and can be used against current and emerging threats. Such medical countermeasures have the potential to directly benefit the Joint Force and civilian populations alike.

Methods/Approach:
The DRIVe Host-Directed Therapeutics program has partnered with companies to clinically evaluate host-directed therapies (e.g., immunomodulators) against ARDS and sepsis. The program is working with partners to explore the value of biomarkers to inform on patients that will most benefit from therapeutic intervention. The program also recognizes therapeutic repositioning and repurposing as an attractive approach for leveraging existing data as well as reducing timelines and costs for the development of host-directed therapeutics.

Results:
Current Host-Directed Therapeutic Program partners are evaluating host-directed therapeutic candidates, including immunomodulators, respiratory stimulants, and anti-coagulants early in clinical development for efficacy against ARDS, and they are collecting samples for biomarker analysis.

Conclusions/Impact:
The use of threat agnostic, host-directed therapeutics early in the response to an emerging biological threat will save lives and buy time while pathogen specific approaches are developed and employed. In addition, such approaches can be utilized with pathogen–targeted medical countermeasures to potentiate therapeutic effects and address the severe outcomes of infectious disease that may occur. DRIVe envisions working with our partners to validate patient stratification approaches to guide host-directed therapeutic interventions and restore homeostasis. Such an approach may help increase the success of host-directed therapeutics in development and advance threat-agnostic products to be pre-positioned for biological attack or disease epidemic.