MEDICAL PROPHYLAXIS TO MITIGATE CHEMICAL THREATS

Continuous Subcutaneous Infusion Of Sevalent Formulations Enabling Prophylactic Use Of Cbrn Medical Countermeasures

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BACKGROUND: Acetylcholinesterase reactivator therapies can be effective as nerve agent medical countermeasures (MCM). However, these drugs have limitations, including solubility, stability and volume constraints, and their pharmacokinetics are poorly suited to protecting individuals prior to exposure. The current standard of care oxime reactivator for nerve agent exposure is pralidoxime (2-PAM) chloride. Typical intramuscular injections of 2-PAM Cl result in therapeutic plasma level concentrations that peak at ~30 minutes with a half-life of ~3 hours. Multiple injections may be given following nerve agent exposure but are limited by autoinjector dose availability, volume constraints, and multiple injection toxicity concerns.
Bexson Biomedical has developed a novel, patented formulation technology (SEVALENTTM) that confers increased solubility and improved tissue compatibility to many small molecule therapies, allowing for their subcutaneous (SC) administration.
Bexson is in parallel developing a low-cost wearable SC infusion device (AKESO) that enables rapid, continuous, and autonomous delivery of these formulations without the need for burdensome IV administration or multiple intramuscular (IM) injections. These key advances may allow for new or repurposed prophylactic nerve agent MCMs.

PURPOSE: Bexson's mission is to address biomedical challenges by applying SEVALENT technology to novel and existing small molecule drugs, allowing for new routes of delivery, enhanced stability, and improved safety and efficacy profiles.

OBJECTIVE: The ultimate objective is the development of a deployable MCM utilizing multiple therapeutic drugs and Bexson's proprietary SEVALENT technology. These novel formulations will be amenable to continuous drug delivery via SC infusion, thereby enabling novel prophylactic use cases. Pharmacology, pharmacokinetic and pharmacodynamic data will be generated in pilot and GLP animal studies, enabling IND submission, human clinical trials, and eventual FDA approval.

RATIONALE: SC infusion is ideal for many drugs where rapid onset is required, steady-state blood levels are desirable, bioavailability is poor, and/or patients may be unconscious or GI-compromised. In the case of CB therapeutics, a continuous SC infusion that maintains steady state therapeutic threshold levels prior to exposure is a feasible strategy to achieve prophylaxis.

METHODS: SEVALENT formulations rely on a primary excipient, Sulfobutyl Ether-ß-Cyclodextrin, currently utilized in over 18 FDA-approved therapies.

PRELIMINARY RESULTS: Bexson has made over 45 formulations with SEVALENT to date, including antibiotics, antifungals, antivirals, pain therapies, opioid antagonists, and cancer drugs. SEVALENT formulations have been manufactured under cGMP conditions and have undergone GLP animal testing in preparation for clinical trials.

PRELIMINARY CONCLUSIONS: Bexson has teamed with the National Strategic Research Institute at the University of Nebraska (NSRI) to develop safe, effective, and deployable CBRN medical countermeasures. We have performed initial feasibility work on several molecules, including atropine, scopolamine, and several oximes, and conclude that a stable, multi-drug SEVALENT cocktail is possible with further support for development.

IMPACT TO JSTO MISSION AND JOINT FORCE: A multi-drug CBRN therapy in a wearable SC infusion pump could meet a significant unmet need for JSTO and the Warfighter by enabling long-lasting prophylactic protection against a variety of chemical threats.