

Science of the Skin and Respiratory Tract, and Related Countermeasures Pertinent to
Chemical/Biological Defense

PUL-042 – A Novel, Broad Spectrum, Immune Stimulant to Prevent Infection and Mortality from a Broad Range of Respiratory Infections

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A broad array of medical countermeasures (MCMs) for infections of the respiratory tract have been proposed and introduced, but significant threats still remain. Military and civilian populations are at an added risk against conflict and terrorism, requiring improved mitigation and treatment options. Opportunistic infections and multi-drug resistance infections are increasing, presenting additional unique challenges. These threats can also be contagious respiratory illnesses that lead to hospitalization or death. While vaccines offer some pre-exposure protection, they are limited to specific strains and are difficult to manufacture and distribute quickly, offering only a limited response.

When the respiratory tract is exposed to virulent pathogens, a microscopic arms race ensues. Time for treatment is critical. Pulmotect is developing a clinical stage drug, PUL-042, for prevention and treatment of infection by inhaled pathogens that is complimentary to vaccine, anti-viral, and antibiotic approaches. The drug has immediate activity to boost the host's immune system to fight off a broad range of infections, often leading to death of the pathogen on contact with the airways.

PUL-042 is a novel, first-in-class immunomodulatory agent consisting of two stable Toll-Like Receptor (TLR) agonists that are synthetic molecules that can be mass-produced. The mechanism of action exploits a phenomenon of stimulated antimicrobial resistance in the respiratory epithelia by locally activating the lung's innate immune defenses. The host-based resistance mechanism is initiated in seconds and is pathogen agnostic, showing activity against viral, bacterial and fungal pathogens.

Both *in vitro* and live lethal challenge models have been used to demonstrate the breadth and strength of PUL-042. The drug has been shown to maintain activity with multiple doses and provide activity for up to 4 weeks. In addition, PUL-042 synergizes with current licensed products to enhance efficacy and expand treatment windows.

PUL-042 is a clinical stage drug with two active INDs and two Phase I clinical trials completed that characterized the safety and tolerability profile in humans. Three current indications are being pursued for this technology that are synergistic with each other and will help accelerate this technology into the hands of end users: 1) immunocompromised cancer patients at risk of pneumonia, in collaboration with researchers at MD Anderson Cancer Center; 2) COPD patients that suffer from exacerbations that are often caused by respiratory infections; and 3) use as a broad spectrum resource to better combat severe and pandemic flu.