PharmAthene

RypVax™ – RECOMBINANT PLAGUE VACCINE FOR THE PREVENTION AND TREATMENT OF PNEUMONIC PLAGUE

Plague Background

The Centers for Disease Control and Prevention classifies *Yersinia pestis (Y. pestis)* as a Category A bioterrorism agent, the highest threat category ranked by the CDC. Plague is a disease caused by the bacterium *Y. pestis* found endemically in rodents and flea populations in certain parts of the world. The World Health Organization reports an estimated 1,000 to 3,000 human cases of plague worldwide every year. More than a dozen cases occur annually in the western United States, most often in rural and semi-rural areas. There are two primary forms of the disease, bubonic and pneumonic. The majority of cases are of the bubonic form which is transmitted through the bite of an infected flea or upon exposure to infected material through a break in the skin. Symptoms include swollen, tender lymph glands called buboes. If bubonic plague is not treated the bacteria can spread through the bloodstream and infect the lungs, causing a secondary case of pneumonic plague. Pneumonic plague affects the lungs and can be transmitted from person to person when an individual breathes in *Y. pestis* particles in through the air. Naturally occurring pneumonic plague is uncommon, although small outbreaks do occur.

The Bioterror Threat

Y. pestis used in an aerosol attack could cause an outbreak of the pneumonic form of plague shortly after infection. Once pneumonic disease is established in a human host, the bacteria can be readily transmitted between individuals. The extended time between exposure to the bacteria and diagnosis increases the opportunity to transmit the bacteria over a vast area, making containment a challenge. Creating a bioweapon carrying *Y. pestis* is highly feasible as the bacterium occurs readily in nature and could easily be isolated and grown in quantity in a laboratory.

Current Standard of Care

To prevent a high risk of death, particularly for pneumonic plague, antibiotics must be given within 24 hours of the first symptoms. However, given the rapid onset of the disease and the difficulty diagnosing pneumonic plague, it can rapidly prove fatal in untreated individuals or in a situation where treatment is delayed. Currently, there is no available vaccine and there is a clear need for this medical countermeasure.

Key Characteristics

RypVax™ is a recombinant plague vaccine comprising separate recombinant F1 (rF1) and V (rV) antigens produced in *Escherishia coli*. The purified antigens are adsorbed onto an Alhydrogel adjuvant and filled into single-use glass vials. Antibodies to rF1 have been shown to be protective against bubonic plague while antibodies to rV have been shown to enhance protection against inhalation plague. As this vaccine combines both antigens it is expected to protect against both forms of the disease.

The vaccine is intended to be used to protect individuals before exposure to the *Y. pestis*. In the warfighter vaccination is anticipated to take place before deployment. It is expected that two or three doses, given several weeks apart, will be sufficient to induce protective immunity followed by an annual booster shot.

Development Timeline

The vaccine has successfully completed three Phase I clinical studies. RypVax™ has been demonstrated to be safe and well-tolerated and has elicited an immune response. In preclinical animal models of disease, subjects have been fully protected against a lethal aerosol challenge by the vaccine.

The manufacturing process for this product is currently at full commercial scale.

In 2004, PharmAthene UK was awarded a multi-year contract, valued at up to $50 million, from National Institute of Allergy and Infectious Diseases (NIAID) for the advanced development of the plague vaccine and approximately $36 million in funding from a Partnering Arrangement between the US, UK and Canadian governments to support the development of the plague vaccine for military use. Prior to this, the product had been developed by the Defence Science and Technology Laboratory (Dstl). PharmAthene has obtained an exclusive licence to the product from Dstl.