



## **SPARVAX™ - RECOMBINANT PROTECTIVE ANTIGEN (rPA) ANTHRAX VACCINE – NOVEL SECOND GENERATION VACCINE TECHNOLOGY**

### ***Bacillus anthracis* (Anthrax) Infection**

*Bacillus anthracis* is a spore forming, gram positive bacterium that has potential to be used as a weapon of bioterror when delivered in an aerosolized form. Following germination of the spores, the bacteria replicates and produces three toxins. Anthrax Protective Antigen (PA) initiates the onset of the illness by attaching to cells in the infected person where it then facilitates entry of the two additional destructive toxins - Lethal Factor (LF) and Edema Factor (EF) into the cell.

### **Current Standard of Care**

Antibiotics are the first line of defense against anthrax infection. However, early identification and treatment are critical for successful outcome. Even with aggressive antibiotic therapy, five of the eleven victims of the 2001 anthrax postal attacks died, underscoring the need for improved vaccines and anti-toxins for civilian protection. The current FDA licensed anthrax vaccine (BioThrax® Anthrax Vaccine Adsorbed) is approved for the prevention of anthrax infection, but requires five doses over a period of eighteen months to achieve protective immunity. AVA is a first generation anthrax vaccine made from cell free filtrates of whole bacterial cultures of *Bacillus anthracis*. This vaccine was FDA licensed in 1970.

### **SparVax™ Key Characteristics**

SparVax™ is a novel second generation recombinant protective (rPA) anthrax vaccine being developed for administration by intramuscular injection. It contains a single, highly purified protein, Protective Antigen, which is produced using a standard production strain of *E.coli*. SparVax™ has been shown to stimulate protection against anthrax by eliciting a specific immune response to one of the primary proteins excreted by the *Bacillus anthracis* organism. In contrast, the currently available anthrax vaccine, which was developed nearly a half century ago and licensed in 1970, is made from a culture filtrate derived from anthrax bacteria. Consequently, it contains a number of different proteins, some of which are believed to contribute to the adverse events that have been reported in the literature and which prompted agencies like the Institute of Medicine to recommend adoption of newer and safer modern vaccines.

Over the past 50 years, advances in modern vaccine technology have contributed to a vast improvement in public health. Production of new vaccines using modern recombinant protein technology has resulted in highly consistent, pure and well-characterized vaccines that can be made using industrial biotechnology manufacturing capabilities on a large scale to meet flexible needs, such as surge capacity, at a reasonable cost.

Such technologies have been embraced by large pharmaceutical and vaccine manufacturers to produce vaccines with increased consistency and improved purity, such as pneumococcal, meningococcal, staphylococcal, Haemophilus Influenza b, typhoid, and more recently purified vaccines that use proteins produced by recombinant technology, such as Hepatitis B, pertussis and Lyme disease

These modern manufacturing techniques have been adapted for the production of SparVax™ in order that our Nation's military personnel and civilians can benefit from these important advances in modern vaccine technology to the same degree that the civilian population benefits from improvements in commercial vaccine products.

The use of modern vaccine production technologies for the manufacture of SparVax™ has resulted in several advantages:

- First, the use of a conventional manufacturing process provides greater flexibility of manufacturing options and the ability to readily scale up and/or tech transfer the process to meet domestic or international surge capacity demand.
- Second, it has resulted in a high yielding manufacturing process, which enables greater efficiency in the costs of production and therefore a product which is more economical to manufacture.
- Third, the use of new technologies has enabled the development of a highly consistent process, which in turn results in a highly consistent and reproducible product.
- Finally, these advances have resulted in a product with enhanced purity, which will likely contribute to potentially fewer adverse reactions in humans.

### **Development Status**

Phase I and Phase II clinical trials involving 770 healthy human subjects have been completed and showed that SparVax™ appears to be well tolerated and induces an immune response in humans. These studies suggest that three doses of SparVax™, administered over approximately 60 days, should be sufficient to induce protective immunity in humans. In preclinical studies, SparVax™ has also demonstrated the capability to protect rabbits and non-human primates against a lethal aerosol spore challenge of the anthrax Ames strain.

### **Government Funding**

Government funding commitments of up to \$213 million have been awarded to date for the SparVax™ rPA anthrax program, which includes additional funding of up to \$78.4 million under a contract modification for SparVax™ announced on February 23, 2010. SparVax™ had been developed initially by the Defence Science and Technology Laboratory (Dstl) in the United Kingdom. PharmAthene has obtained an exclusive license to the product from Dstl.