



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

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

*Bacillus anthracis* is a spore forming, gram positive bacterium that can be – and has been – used as a biological weapon. Following entry into the host, spores germinate and the bacteria replicates, producing the three components of the toxin; Anthrax Protective Antigen (PA), Lethal Factor (LF), and Edema Factor (EF). PA attaches to cell surfaces and forms a pore through which LF and EF gain access to the cytoplasm and cause cell death.

### **Current Standard of Care**

Antibiotics are the first line of defense against anthrax infection; however, rapid 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 treatments, including new vaccines and anti-toxins. 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 first FDA licensed in 1970.

### **SparVax™ Key Characteristics**

SparVax™ is a novel second generation recombinant protective antigen (rPA) anthrax vaccine being developed to protect against inhalation anthrax, the most lethal form of anthrax infection in humans. The active component of the vaccine is highly purified PA which is produced using a standard production strain of *E.coli*. This single protein elicits protective immunity in several models of anthrax infection and is safe, well tolerated, and highly immunogenic in humans. In contrast, AVA 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-defined 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 and meningococcal vaccines and more recently, purified vaccines that use proteins produced by recombinant technology, such as the Hepatitis B vaccine.

These same 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:

- Provides greater flexibility of manufacturing options and the ability to rapidly scale up and/or transfer the process to additional manufacturing sites to meet domestic or international surge capacity demand.
- Results 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.
- Results in a more pure and well defined product that offers the potential for improved safety.

### **Development Status**

One Phase I and two Phase II clinical trials involving more than 700 healthy human subjects have been completed to date. The immune responses in these trials suggest that a level of protective immunity is achievable with three doses of SparVax – two fewer doses than are required with AVA. No vaccine-related serious adverse events were reported in these studies. In preclinical animal studies, SparVax™ has demonstrated the capability to protect rabbits and non-human primates against aerosol spore challenges that greatly exceed the typical lethal dose of anthrax spores.

### **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 in February 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.

### **Third Generation rPA Vaccine Program**

The objective of PharmAthene's third generation program is to develop an rPA anthrax vaccine which can maintain stability for three years at 35°C and induce protective immunity in two or fewer doses. The primary objective of the program is to develop an rPA-based anthrax vaccine that can be stored, transported and used without the need for a conventional cold chain – an important advantage for civilian biodefense deployment within the Strategic National Stockpile.