



PharmAthene

MEDAREX

VALORTIM[®] – PROPHYLACTIC and THERAPEUTIC ANTI-ANTHRAX MONOCLONAL ANTIBODY (MAb)

***Bacillus anthracis* Infection**

Bacillus anthracis is a spore forming, gram positive bacterium that has potential use 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, and then facilitates the entry of the two additional destructive toxins - Lethal Factor (LF) and Edema Factor (EF) into the cells.

Anthrax Monoclonal Antibody: Valortim[®]

Valortim[®] is a fully human monoclonal antibody designed to protect against inhalation anthrax, the most lethal form of illness in humans caused by the *Bacillus anthracis* bacterium. The investigational antibody targets a protein component of lethal toxins produced by the bacterium known as the anthrax protective antigen. The anthrax protective antigen initiates the onset of the illness by attaching to cells in the infected person, and then facilitates the entry of additional destructive toxins into the cells. Valortim[®] is designed to target anthrax protective antigen and protect the cells from damage by the anthrax toxins. In preclinical studies, Valortim[®] both protected against infection, and when administered some time after exposure, it induced recovery and survival in animals exposed to lethal doses of inhalation anthrax spores.

Key Characteristics of Valortim[®]:

- *Fully human monoclonal antibody with affinity for PA.*
- *Prophylaxis setting: Nearly complete protection of animals challenged with more than 100 times the median lethal dose (LD50) of anthrax spores.*
- *Equivalent efficacy at all doses tested; Lowest dose tested = 1mg/kg.*
- *Post exposure setting: Administration at 24-hours post exposure to anthrax spore challenge provided equivalent protection as prophylactic setting.*
- *Therapeutic setting: Significant protection of animals when administered after appearance of disease symptoms.*
- *Antibody binding to a novel site of PA permitting protection after toxins have already attached to the cell.*
- *Superior activity in the toxin neutralization assay (TNA), through a novel mechanism of action.*

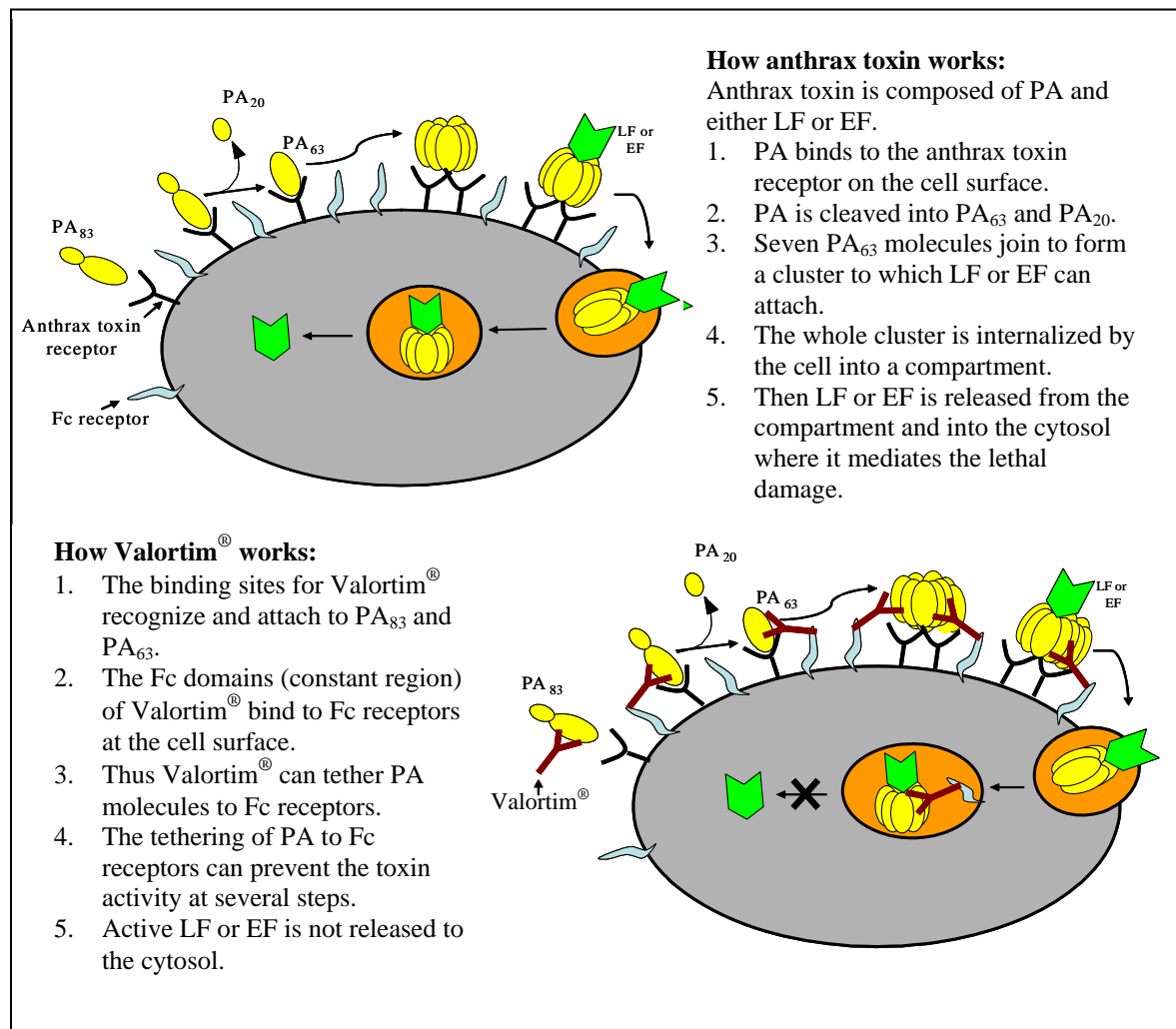
Development Timeline

Preclinical efficacy trials have been completed with Valortim[®] and show evidence of therapeutic activity to symptomatic animals in the rabbit inhalation anthrax model. Studies demonstrate that dose levels as low as 1 mg/kg and serum levels below 20 ug/ml are efficacious in preventing mortality in two animal models (rabbit and monkey) before the clinical course of the disease has initiated. The lowest protective dose has not yet been defined.

A study in non-human primates has demonstrated the potency of Valortim[®] using the potentially most clinically-useful intramuscular route of administration. In this study, the animals were challenged with a target aerosol dose of 200 times the median lethal dose of *B. anthracis* spores; 6 animals received no treatment, 6 animals received 1 mg/kg of Valortim[®] intramuscularly, and 6 animals received 10 mg/kg of Valortim[®] intramuscularly, all at the time of aerosol challenge. None of the animals were given antibiotics or other therapies. All control animals died within one week of the challenge; all treated animals in both dose groups were reported alive 90 days post-challenge.

PharmAthene and Medarex have completed a Phase I open-label, dose-escalation clinical trial to evaluate the safety, tolerability, immunogenicity, and pharmacokinetics of a single dose of Valortim[®] administered intravenously or intramuscularly in 46 healthy volunteers. The Phase I data showed that Valortim[®] was safe and well-tolerated at the doses administered. No drug-related or serious adverse events were reported. In addition, the data suggest that a single dose of Valortim[®] given by the convenient intramuscular route of administration could provide protection against anthrax for up to two months, comparable to what is observed in previously immunized individuals.

Valortim[®] has received Fast Track and Orphan Drug designation from the Food and Drug Administration, indicating that the FDA will facilitate the development and expedite the regulatory review of the product. Total government funding committed to Valortim[®] now exceeds \$24 million.



Medarex and PharmAthene Collaboration

Medarex, Inc. (NASDAQ: MEDX) and PharmAthene entered into a collaborative agreement under which the companies plan to jointly complete clinical development and commercialize Valortim[®]. Valortim[®] was developed by Medarex using its UltiMAB Human Antibody Development System[®] in collaboration with Dartmouth Medical School and United States Army Medical Research Institute for Infectious Diseases (USAMRIID).