



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

***Bacillus anthracis* Infection**

Bacillus anthracis is a spore forming, gram positive bacterium that has potential use as a weapon of bioterror, which would be particularly devastating if delivered in an aerosolized form. Following germination of the spores, the bacteria replicates and produces two toxins (Lethal Toxin and Edema Toxin) composed of three factors. Anthrax Protective Antigen (PA) initiates the toxin activity by attaching to cells in the infected person, and then facilitates the entry of the two additional destructive factors - Lethal Factor (LF) and Edema Factor (EF) into the cells.

Anthrax Anti-toxin Monoclonal Antibody: Valortim[®]

Valortim is a fully human monoclonal antibody being developed to protect against inhalation anthrax, the most lethal form of illness in humans caused by the *Bacillus anthracis* bacterium. The investigational antibody targets PA, a protein component of the toxins produced by the bacterium. PA initiates the activity of the toxins by attaching to cells in the infected person, and then facilitates the entry of additional destructive factors into the cells. By targeting PA, Valortim is able to protect the cells from damage by the anthrax toxins. In non-clinical studies, Valortim protected animals one hour after spore exposure. When administered at the time animals demonstrated signs of inhalation anthrax, as defined by PA being present in the blood, Valortim induced recovery and survival in animals exposed to lethal doses of inhaled anthrax spores.

Key Characteristics of Valortim:

- *Fully human monoclonal antibody with affinity for PA.*
- *Post-exposure setting*
 - *Nearly complete protection of animals challenged with more than 100 times the median lethal dose (LD50) of anthrax spores.*
 - *Similar efficacy at all doses tested; lowest dose tested = 1mg/kg.*
 - *Administration at 24-hours post-exposure to anthrax spore challenge provided similar protection when compared with administration at one hour after spore exposure.*
- *Therapeutic setting*
 - *Significant protection when Valortim was administered at the time of animals demonstrating signs of inhalation anthrax, as defined by PA being present in the blood*
- *Antibody binds to a novel site of PA permitting protection after factors have already attached to the cell.*
- *Chosen as the lead mAb candidate for development based on its significant activity in the toxin neutralization activity (TNA) assay, demonstrating a mechanism of action that has not been described previously.*

Development Status

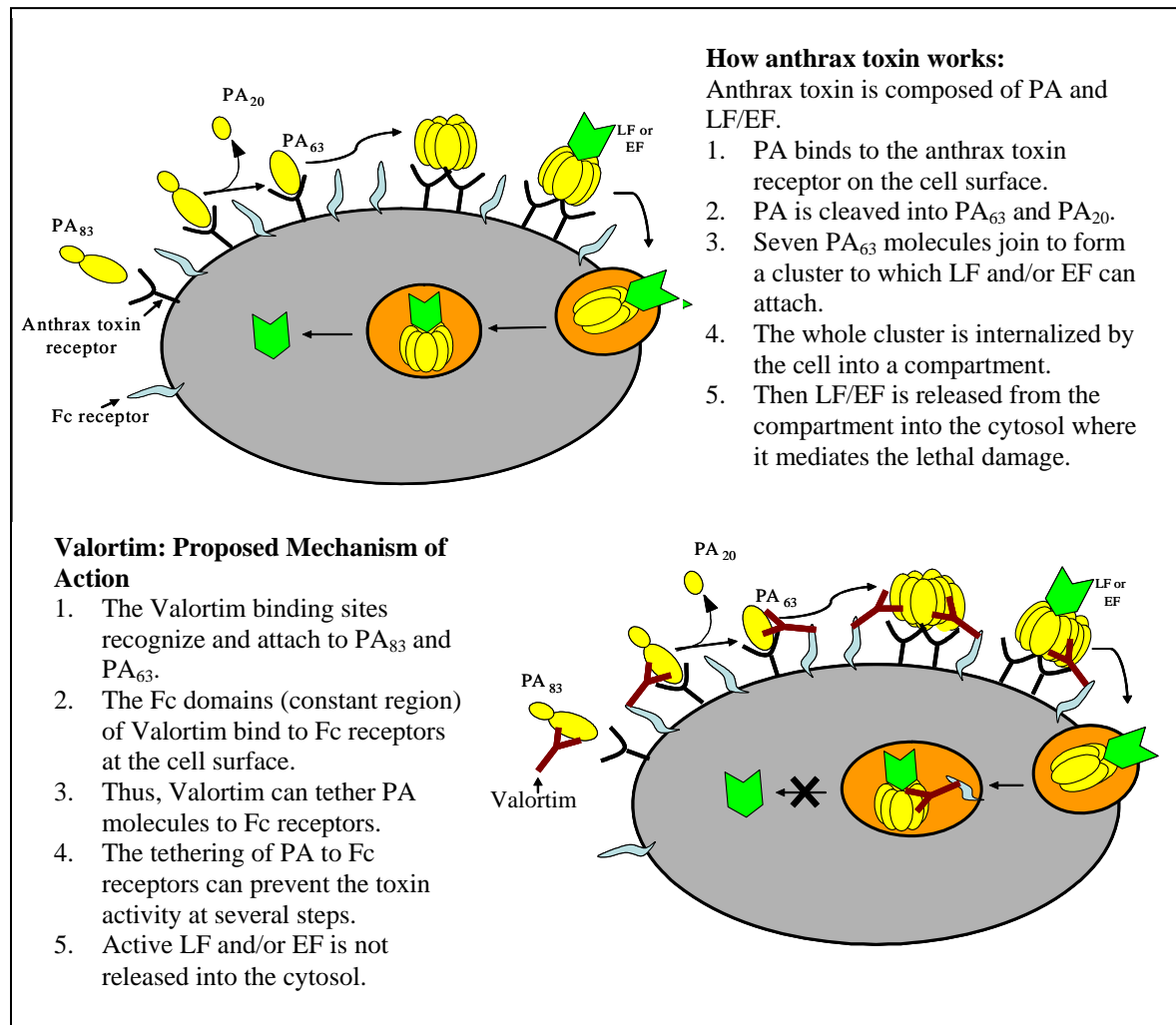
The efficacy of Valortim has been examined in the post-exposure setting (after exposure to anthrax spores but prior to the development of signs of inhalation anthrax) and in the therapeutic setting when animals have demonstrated signs of inhalation anthrax.

In the post-exposure setting, Valortim has demonstrated up to 100% efficacy when dosed as low as 1 mg/kg intramuscularly (IM) one hour after aerosolized spore exposure in non-human primates (NHPs) and up to 90% efficacy when 1 mg/kg was administered intravenously (IV) in rabbits.

In the therapeutic setting, Valortim has demonstrated up to 100% efficacy when administered at the time of PA detection in the blood or upon significant increases in body temperature in rabbits. In NHPs, Valortim has achieved up to 70% efficacy when administered at the time of PA being detected in the blood.

A Phase I, open-label, dose-escalation clinical trial to evaluate the safety, tolerability, immunogenicity, and pharmacokinetics of a single dose of Valortim administered IV or IM in 46 healthy volunteers has been completed.

Valortim has received Fast Track and Orphan Drug designation from the Food and Drug Administration (FDA), indicating that the FDA will facilitate the development and expedite the regulatory review of the product.



Government Funding

Government funding commitments exceeding \$27 million have been awarded to-date for the advanced development of Valortim. Valortim research has been funded, in part, by a NIAID/BARDA contract, NIH VTAD/Challenge grants, DoD appropriations funding, and Maryland Industrial Partnership (MIPs) grants.