



## PIPELINE UPDATE: TB VACCINES REACH PIVOTAL PROOF-OF-CONCEPT PHASE

Three trials will enroll up to 8,200 participants

*Global health efforts will not defeat tuberculosis without a new and more effective TB vaccine. New TB vaccines are urgently needed that elicit more protection than the natural immune response. The original Bacille Calmette-Guérin (BCG) vaccine, the only vaccine currently licensed against TB, has variable efficacy and has not proven adequate to control global TB. Aeras and its partners are employing a prime-boost strategy to improve protection. Aeras is currently sponsoring five booster vaccines and one priming vaccine in differing clinical phases of development.*

The advancement of two TB vaccine candidates to the proof-of-concept stage of clinical development is a significant achievement and demonstrates continued momentum in the TB vaccine field. Three Phase IIb clinical trials of two candidates—MVA85A and AERAS-402/Crucell Ad35—are underway in sub-Saharan Africa, enrolling infants and persons living with HIV.

Phase IIb trials represent a critical checkpoint before progressing to later stages in development. Phase IIb trials take place after a vaccine has been shown to induce a good immune response and have an acceptable safety profile in Phase I and IIa studies. Information gathered in all of these stages will help determine if TB vaccine candidates should be tested in large-scale Phase III licensure trials. At Phase IIb, researchers first evaluate whether the drugs demonstrate the desired clinical effect.

With each advance in clinical trial phase, the size and cost of trials increase. Collaboration among the numerous organizations involved in vaccine development and clinical research remains a critical component of success.



Aeras-sponsored Clinical Trial Locations

### MVA85A

MVA85A is the most clinically advanced TB vaccine candidate. This booster vaccine was designed for infants and adolescents by scientists at Oxford University and uses a recombinant viral vector. Prior to current trials, this vaccine was tested in adults in England, The Gambia, Senegal and South Africa.

### AERAS-402/Crucell Ad35

This booster vaccine was developed by leading European biopharmaceutical company Crucell N.V. and Aeras and uses an adenoviral vector. The vaccine has undergone testing in multiple Phase I and Phase II trials in Kenya, India, South Africa and the United States among healthy adults, adults with previous exposure to TB and adults living with HIV.

### Current Phase IIb Trials

Candidate	Location	Population	# of Participants
MVA85A	South Africa	infants	2,797
MVA85A	Senegal, South Africa	HIV+ adults	1,400*
AERAS-402/Crucell Ad35	Botswana <sup>†</sup> , Kenya, Mozambique, South Africa, Uganda <sup>†</sup>	infants	4,000*

\* expected enrollment; <sup>†</sup> possible future locations

## MVA85A: Phase IIb Infant Trial — South Africa

The Phase IIb trial of MVA85A among infants in South Africa marks the first large-scale clinical trial of a new TB vaccine in infants in over 80 years. The enrollment period of this two-year trial, which is being conducted in the Worcester, Ceres and Robertson areas of South Africa, began in July 2009. Enrollment was completed in April 2011, with 2,797 participants who had already been vaccinated with BCG at birth. MVA85A is administered at approximately 18 weeks of age.

Aeras and the Wellcome Trust are funding this trial of MVA85A, which is being developed by Aeras and the Oxford-Emergent Tuberculosis Consortium (OETC), a joint venture between the University of Oxford and Emergent BioSolutions. Results are expected in 2013. Researchers at the South African Tuberculosis Vaccine Initiative (SATVI), which is part of the University of Cape Town (UTC), are conducting this study.



## MVA85A: Phase IIb Trial among People Living with HIV — Senegal and South Africa

People living with HIV/AIDS are more susceptible to *M. tuberculosis* disease, and 90 percent of untreated individuals die within months of being coinfecting. Therefore, developing a safe and effective vaccine for immunocompromised individuals living with HIV is an important area of focus and has the potential to save millions of lives.

This Phase IIb trial of MVA85A is being conducted in HIV-infected adult populations in Senegal and South Africa. The trial will enroll approximately 1,400 adults ages 18-50 who are infected with HIV. To date, the vaccine has been shown to have an acceptable safety profile and has had no clinically-significant effects on viral load or CD4 count in three studies involving a total of 80 participants living with HIV in Senegal, South Africa and the UK.

The study is being led by the UK Medical Research Council in The Gambia, Aeras, and the University of Oxford. It is being conducted in Khayelitsha, South Africa, by the UCT Institute of Infectious Disease and Molecular Medicine, and in Dakar, Senegal, by the Laboratoire de Bacteriologie-Virologie du Centre Hospitalier Universitaire Aristide Le Dantec. Primary funding support is provided by the European and Developing Countries Clinical Trials Partnership (EDCTP), a European program to accelerate the development of new or improved drugs, vaccines and microbicides against HIV/AIDS, malaria and tuberculosis through partnership with African counterparts. This is the first proof-of-concept efficacy trial in people infected with HIV using MVA85A, which is being developed by OETC and Aeras.



## AERAS-402/Crucell Ad35: Phase IIb Infant Trial — Multiple Sites in Sub-Saharan Africa

This proof-of-concept clinical trial of AERAS-402/Crucell Ad35 is underway in Kenya, Mozambique and South Africa and may expand to additional trial site locations in 2012, ultimately enrolling up to 4,000 participants.

Partners involved in this clinical trial as of January 2011 included Aeras, Crucell, EDCTP, SATVI, the Kenya Medical Research Institute (KEMRI)/US Centers for Disease Control and Prevention (CDC), the Manhica Health Research Centre (CISM) of Mozambique, the National Institute of Allergy and Infectious Diseases (NIAID) of the US National Institutes of Health (NIH) and the Perinatal HIV Research Unit (PHRU) in South Africa.

### Aeras

1405 Research Blvd., Rockville, MD 20850, USA  
Phone: +1 301-547-2900 Fax: +1 301-547-2901  
Follow Aeras on [Facebook](#) & [Twitter](#)

### Aeras Africa Office

Ground Floor, Belmont Square, Belmont Road  
Rondebosch, Cape Town 7700, SOUTH AFRICA  
Phone: +27 21 659 8440 Fax: +27 21 686 6962