

## PARTNERSHIPS TO ACCELERATE TUBERCULOSIS VACCINE DEVELOPMENT

### Expanding the TB vaccine pipeline

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With 14.4 million prevalent cases and 1.7 million annual deaths tuberculosis (TB) remains one of the most serious infectious diseases to date. An estimated 2 billion people are believed to be infected with *Mycobacterium tuberculosis* and at risk of developing disease. HIV-TB co-infection and the appearance of multi- and extensively drug resistant strains challenge current control measures for TB. More effective vaccines are urgently required to control TB more effectively and to reach the eventual target of eliminating TB in 2050. In the recent decade tremendous progress has been made and a rich global TB vaccine pipeline has emerged with 14 new vaccine candidates that have entered clinical development. Eleven of these are currently undergoing clinical testing. An overview of the current TB vaccine pipeline will be presented highlighting some of its promises and challenges. Specific focus will be on the challenge of filling the pipeline with new innovative approaches aiming to prevent disease in target profiles currently not addressed.

### New tuberculosis vaccines in clinical development

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**Background:** The current TB vaccine, bacille Calmette-Guérin (BCG), is largely ineffective in preventing adult pulmonary TB disease, and has had no discernible impact on the growing TB epidemic. Efforts are currently underway to develop new, more effective TB vaccines.

**Methods:** TB vaccines under development could work by preventing infection, primary disease, latent infection or reactivation. Vaccines are also being developed that could shorten the course of chemotherapy. The current TB vaccine development strategy for preventive vaccines includes the development of recombinant BCG (rBCG) or live attenuated vaccines to use as a prime in a heterologous prime-boost strategy, and the development of several novel vaccine candidates that could be used as a booster vaccine in infants, adolescents and adults previously primed with BCG or as a boost to an improved prime vaccine. The goals for new TB vaccines include increased efficacy and increased safety in people latently infected with Mtb and/or infected with HIV as compared to the

Ad35, are in Phase IIb proof-of-concept trials. Three Phase IIb trials of these candidates are currently underway at several trial sites in Africa in two distinct populations—healthy infants and adults with HIV. Combined, the trials are expected to enroll over 8000 volunteers and will provide much needed data on vaccine efficacy in humans.

**Conclusions:** New TB vaccines are essential to reach the global target of eliminating TB. Much progress has been made, but TB vaccine development is a scientifically complex and expensive process. With sufficient resources and positive results from current or near-term clinical candidates, a new TB vaccine could be available by the end of this decade.

### Global partnerships: a key factor in the successful clinical development of vaccine candidate MVA85A

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An effective vaccination strategy is essential to control the TB epidemic. The protection conferred by BCG against pulmonary disease is highly variable, although efficacy against systemic disease in childhood is more consistent. Including BCG in any new vaccination strategy has merit for the non-HIV-infected population. MVA85A is a recombinant poxvirus expressing the immunodominant antigen 85A from *Mycobacterium tuberculosis*. MVA85A was developed by the University of Oxford and since 2002, has been evaluated in a series of Phase I/IIa clinical trials. These trials, which include latently infected subjects and HIV-infected people, have demonstrated MVA85A to be safe and highly immunogenic. The lack of an immunological correlate of protection means the new generation vaccines can only be evaluated in large efficacy trials. Such efficacy trials require the formation of global partnerships for success. Oxford University have formed a Joint Venture with Emergent Biosolutions, called the Oxford Emergent Tuberculosis Consortium (OETC), and OETC have established collaborations with Aeras and with the South African TB Vaccine Initiative, the Clinical Infectious Diseases Research Initiative (South Africa) and Le Dantec (Senegal) in order to test the efficacy of this vaccine. There are now 2 ongoing efficacy trials with MVA85A: one in South African BCG vaccinated infants and the second in HIV-infected adults in South Africa and Senegal.