Rising to the Challenge
Making New TB Vaccines a Reality
Message from the Board

Dear TB Vaccine Supporters:

In 2018, Aeras and its partners announced breakthrough data from two Phase 2 clinical efficacy trials providing evidence that TB vaccines can prevent both disease and sustained infection in high-risk endemic region populations. Further studies are needed, but these results have the possibility of changing the trajectory of TB vaccine research. Thanks to the commitment of many partners around the globe, the world now has real hope that new, more effective TB vaccines are possible.

This past year, due to a lack of core funding, Aeras transferred certain resources and expertise to the International AIDS Vaccine Initiative (IAVI) in order to build on the recent findings and accelerate progress towards new more effective vaccines. As such, by the end of 2018 Aeras transferred its preclinical assets and clinical programs, biorepository, clinical staff, funding and other assets to IAVI. There is significant overlap between the TB and HIV/AIDS epidemics, and we hope that all those that have supported and partnered with Aeras over the years will continue to support IAVI as they advance the TB vaccine mission.

In 2019 Aeras will formally cease operations, making this our final report. In the following pages we have highlighted the significant progress made toward new more effective TB vaccines during our twenty-year tenure as the leading tuberculosis-focused Product Development Partnership. We would like to extend a special thanks to our many partners and funders and the many individuals who worked at Aeras throughout the years for their commitment to advancing TB vaccines for the world. We’d also like to thank the many participants in the clinical trials and community members who have been instrumental to our progress.

We have long held — and still believe — that the world will not eliminate TB without a vaccine. With recent progress we have never been closer to a new TB vaccine, but the work must continue.

On behalf of the entire Aeras Board,

Dr. Jacqueline S. Shea, Chairman
Former CEO and Board Member

Lota S. Zoth, Board Chair
Former Senior VP and CFO, MedImmune, Inc.

AERAS 2018
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20+ years of innovation
to stop the world's #1 infectious disease killer

**SINCE 1997, WE’VE WORKED WITH PARTNERS TO:**

- Design and develop CMV-TB, a novel vaccine candidate that demonstrated the highest level of protection seen in a NHP challenge model to date
- Confirm intravenous BCG vaccination can provide near sterilizing immunity in NHPs, providing an opportunity to identify immune mediators of protection
- Build AerasSHARE, the first open access biorepository and provider of custom mycobacterial reagents for the global TB vaccine field
- Develop innovative trial designs that enable human proof of concept efficacy trials to be completed more quickly and cost effectively, conserving scarce resources
- Promote the growth of the global clinical pipeline from 1 to 13+ candidates, and helped develop 9 candidates
- Conduct 35+ clinical trials and develop many of the world’s most experienced TB vaccine clinical trial sites

**2018**

These advances culminated in two major clinical breakthroughs published in the NEJM in 2018 which showed that:

- Revaccination with BCG could prevent approximately half of high-risk African adolescents from developing sustained infection with Mtb
- The GSK protein vaccine candidate M72/AS01e had 54% efficacy in preventing progression to disease in Mtb infected African adults, with nearly 84% efficacy in under 25s.

**Now for the first time in almost 100 years, new TB vaccines are within reach.**
Science

TB kills more people than any other infectious disease, but there is still much to be learned. The partial effectiveness of BCG and the immune system’s natural ability to control TB infections in many people are signals that effective TB vaccines are achievable. But scientists don’t fully understand what type of immune response protects people from TB, or why some people can clear TB infections spontaneously. With very limited financial resources, the TB vaccine field has suffered from constraints that hinder research and progress.

Innovation

Aeras set out to invigorate the R&D pipeline, developing new tools to help evaluate preclinical candidates and move only the most promising clinical candidates forward. Aeras helped create standardized small animal and NHP models of TB disease, standardized immune-assays and reagents and antigen cassettes to enable comparison between candidate antigens and platforms. Formalized stage gates, co-developed by Aeras, allowed the field to move only the most promising candidates forward. And AerasSHARE was established to provide the field with the first open-access biorepository of preclinical and clinical samples and reagents.

Embracing an iterative scientific approach, Aeras helped develop nine different TB vaccine candidates and conducted over 35 Phase 1-2b clinical trials with partners across the globe. Capitalizing on that expertise, Aeras and partners developed the Good Participatory Practice Guidelines for TB vaccine clinical trials, as well as innovative Prevention of Infection and Prevention of Recurrence trial designs that enable human efficacy signals to be detected more efficiently than conventional trials.

Breakthroughs

Two decades later, the landscape has transformed. In one of the biggest advances in 100 years, candidate M72/AS01E was shown to prevent TB disease in TB infected, HIV-negative adults. The Phase IIb efficacy study conducted by GSK and Aeras showed an overall vaccine efficacy of 54% in the primary analysis, with rates of efficacy up to 84% in younger adults. Final results are expected in 2019.

Preclinical work with OHSU helped identify CMV-TB, a candidate that showed the highest level of protection seen in NHPs to date. Work with the NIH Vaccine Research Center confirmed that intravenous BCG can provide “sterilizing immunity” against TB, providing an opportunity to identify immune mediators of protection.

And Aeras and Sanofi recently showed that revaccination with BCG could significantly help high-risk adolescents clear or control a TB infection. With further study, BCG revaccination could prove to be a useful strategy for preventing TB infection. In the same trial, candidate H4:IC31 provided informative results for future subunit vaccines. The bottom line: we now have promising research paths for both TB infected and uninfected people.
Through the PDP model, Aeras & partners have transformed the landscape of TB vaccine research

**Support**
When faced with the fact that TB killed 1.6 million people in 2017, many people are stunned. TB is a global epidemic that disproportionately affects poor and developing countries and has been long neglected. Even today, there are relatively few advocates for TB vaccine research, lagging interest in the field, and little support for TB vaccine R&D in global TB policy. Because vaccine research takes substantial time and sustained investment, the field has always needed a strong coalition of cross-sector partners and funders sharing knowledge and resources.

**Outreach**
From its outset, Aeras has sought to fill a leadership role in raising awareness about TB. From award-winning videos to international stakeholder meetings, Aeras has worked to grow a network of TB vaccine supporters and build the key partnerships that make progress possible. Aeras also acted as a major scientific convener for the field, serving as the secretariat for the biannual Global Forums and holding multiple specialist meetings with partners to share information, problem solve and drive the science forward.

**Strength in Numbers**
After helping to lead the rallying cry for TB vaccines, the landscape has begun to shift: new, diverse partners have emerged, and support for vaccines has appeared in key global policies. Aeras is no longer one of the few talking about the urgent need for vaccines — global health leaders from NIH, The Union, WHO and beyond have raised their voices to support TB vaccine research.

Over the past two years, Aeras advocated for TB vaccines at the WHO Global Ministerial Conference in Moscow and at the first ever UN High Level Meeting on TB in New York. Cultivating partnerships with vaccine companies, international universities, and other research organizations, Aeras has worked hard to not only expand the network of stakeholders, but to ensure that all stakeholders understand the potential impact of a new vaccine and how we can make it happen. The result: innovation, momentum, and a real belief that new, more effective TB vaccines are both essential and achievable.

**CHALLENGE**

**RESULT**

**ACTION**

Through the PDP model, Aeras & partners have transformed the landscape of TB vaccine research

- 35+ clinical trials conducted
- 9 candidates developed
- 3 efficacy studies published
- 2 major clinical breakthroughs
The single biggest challenge TB vaccines face is lack of investment

Funding

TB is the world’s deadliest infectious disease. But it’s also one of the most severely underfunded global health threats. In fact, the single biggest challenge for TB vaccine research is lack of investment. We will not end TB without new vaccines and vaccination strategies — and new vaccines aren’t possible without sustained global funding and increased financial commitment. The breakthroughs we’ve achieved in the past year would not have been possible without bringing new partners and funders to the table.

Mobilize

Aeras has worked deliberately to gather stakeholders, engage governments across the globe, and move TB vaccine research into the forefront of global health policy and funding discussions. While working to engage and inform new potential partners and expand the network of TB R&D supporters, Aeras also capitalized on the product development partnership (PDP) model, which allowed it to engage in cost effective collaborations with individuals, research organizations, academic institutions, funders, policymakers and others who wanted to advance TB vaccine research.

Opportunity

Through key partnerships and advocacy efforts, Aeras has been able to help open up some new streams of funding and create opportunity for the field. The pipeline now has a more diverse range of candidates and platforms, and the field has researchers from across the globe working on the best TB vaccine research.

But TB vaccine R&D is still severely underfunded. We’ve made immense progress this past year with only a fraction of the funding that will be needed to reach success. Investments in TB vaccine R&D averaged $95 million per year over 2011-2016, less than half of the $250 million per year experts believe is needed to fully develop a successful new TB vaccine. Too few funders are still bearing the large burden of research costs, and without an influx of investment, the world is in danger of losing the momentum gained over the past decade. Now is the time for TB vaccines — we simply cannot afford not to invest in future TB vaccine research.

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The single biggest challenge TB vaccines face is lack of investment.

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<tr>
<th>Number of Deaths in 2017</th>
<th>Amount of Research &amp; Development Investment</th>
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<tr>
<td>TB 1.6 million</td>
<td>$100.3 million</td>
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<tr>
<td>HIV 940,000</td>
<td>$845 million</td>
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<td>Ebola 11,310 (2014-2016 outbreak)</td>
<td>$244 million</td>
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The employees, associates and Board members of Aeras have dedicated nearly two decades of service in the fight to end TB. We are gratified that our work — supported by a large number of funders and partners — has produced a legacy of real hope for the future of TB vaccines.

To ensure this hard-won momentum is maintained, Aeras has completed the transfer of preclinical assets, key clinical assets and staff to the International AIDS Vaccine Initiative (IAVI) — a trusted and motivated partner who will now work to fight the world’s two most deadly infectious diseases. This transfer will enable the continuity of Aeras’ core TB vaccine clinical programs, expand IAVI’s clinical development capabilities, and ultimately accelerate progress towards new, more effective vaccines for both the TB and HIV communities.

This is a pivotal moment: the opportunity to make a game-changing impact on the TB crisis has never been closer. But ultimate success will not be achieved without strong partnerships, diversity of scientific thought, and global commitment to TB vaccine research and development. The field desperately needs investment and vocal advocates. Now, more than ever, the world needs all of us to step up and fight for TB vaccines.

We offer heartfelt thanks for your support these many years and your commitment to the Aeras mission: bringing new, effective, affordable, accessible TB vaccines to all who need them.

- Demand necessary investment
- Include TB vaccine R&D in global TB policy
- Support innovation with diverse partnerships and approaches
A sincere thanks

To our many partners and funders, including:

- Albert Einstein College of Medicine
- Australian AID
- Bill and Melinda Gates Foundation
- BioFabri
- Biomedical Primate Research Centre
- CanSino
- China National Biotec Group
- Chinese Center for Disease Control and Prevention
- Colorado State University
- Dartmouth Geisel School of Medicine
- European & Developing Countries Clinical Trials Partnership (EDCTP)
- Emergent Biosolutions
- US Food and Drug Administration
- GHIT Fund
- GSK
- Harvard
- Infectious Disease Research Institute
- Institute Pasteur de Lille
- Johnson & Johnson
- National Institute of Allergy and Infectious Diseases
- Oregon Health & Science University (OHSU)
- Okairos
- Public Health England
- Sanofi Pasteur
- Statens Serum Institut
- Stop TB Partnership
- Temple University
- The Government of the Netherlands
- Transgene
- Trudeau Institute
- TuBerculosis Vaccine Initiative
- The Research Council of Norway
- Tuberculosis Vaccine Initiative
- UK AID – Department for International Development
- University of Alberta
- University of Massachusetts
- University of Oxford
- University of Pittsburgh
- US Centers for Disease Control and Prevention
- US Department of Defense
- Wellcome Trust
- Wuhan University

To our clinical site partners, including:

- The Aurum Institute
- BE PART
- Wellcome Centre for Infectious Diseases Research in Africa (CIDRI-Africa)
- Centre for Infectious Disease Research in Zambia (CIDRZ)
- Desmond Tutu HIV Centre – University of Cape Town
- Ekhaya Vac
- HIV Vaccine Trials Network
- IMPAACT
- Kenya Medical Research Institute
- Kid Cru
- National Institute for Medical Research, Tanzania
- Perinatal HIV Research Unit (PHRU)
- Setshaba Research Centre
- South African TB Vaccine Initiative
- TASK Applied Science
- University of Cape Town Lung Institute
- University of St Louis
- Wits Reproductive Health and HIV Institute - Wits University
- Zambart
TB vaccines are achievable, make them a reality.