



EIB Advisory Considerations Global TB Vaccine Partnership

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European Investment Bank



- ❖ EIB was created with the Treaty of Rome in 1958
- ❖ EU's policy-driven, long-term lending institution
- ❖ 100% ownership and explicit support by the 28 EU Member States
- ❖ Self-sustaining, non-profit maximizing institution
- ❖ Sizeable callable capital €221bn (95%)
- ❖ Largest Multilateral Development Bank by assets (€508bn in 2012)
- ❖ Largest supranational borrower on the capital markets (€71bn in 2012)
- ❖ Highest credit rating, 0% risk-weighted and the only supranational bank with direct access to a central bank liquidity (ECB)
- ❖ June 29, 2012, the European Council requested the increase of EIB's capital by €10bn, thus all paid-in capital to reach €21.6bn
- ❖ EIB is a majority shareholder in the European Investment Fund (EIF)

EIB Ratings	Long-term	Short-term
Moody's	Aaa	P-1
S&P	AAA	A-1+
Fitch	AAA	F1+

(as of April 2013)

EIB's Advisory Role in the GTBVP



- ❖ As advisor to the Commission, EIB is working with European industrial companies, TBVI, AERAS and the Gates Foundation to examine the possibilities for developing a more effective programme for financing a portfolio of TB vaccines on a risk-sharing basis between public and private sectors through push and pull mechanisms, giving Commission and other donors higher leverage for their contributions
- ❖ Providing an investor/funder perspective in the development of a business case based on updated development cost estimates and market data on TB vaccines from independent consultants
- ❖ Contributing to the development and review the assumptions used in the financial model developed by KPMG to assess the likely costs, time and market potential of TB vaccines.
- ❖ EIB has established, chairs and coordinates the activities of the Working Group with representatives from the European Commission, Gates Foundation, EDCTP, Aeras and TBVI.
- ❖ Substantial progress has been made by the working group on agreeing the overall concept for the GTBVP.

Collaborative Partnership



Working Group Partners:

- ❖ Aeras, TBVI, European Commission (DGRTD) and European Investment Bank (RDI Advisory Services), EDCTP and Gates Foundation

Overview

- ❖ Working group initiated March 2012
- ❖ TBVI/Aeras established a joint portfolio
- ❖ Conducted strategic market analysis
- ❖ Developed the financial model
- ❖ Assessed the commercial viability
- ❖ Established the first draft of the ' Business Case for Investment'

Next Step with Stakeholders

- ❖ Consolidate EU leadership to mobilise public and private resources
- ❖ Engage with wider scientific/academic community
- ❖ Development of a Governance Framework fit for purpose
- ❖ Reach a Heads of Agreement on organisation, business objectives, partnership and budget by March 2014

Reinforce EU Leadership in TB Vaccine Development

- ❖ An estimated two-thirds of all vaccine research is carried out in Europe
- ❖ Europe is the world's biggest manufacturer of vaccines
- ❖ EC, Dutch and British governments represent 3 of the top 5 global donors (5 donors comprise > 80% of funding)
- ❖ EDCTP has invested more than \$42M towards site preparedness, capacity building and clinical trial support in Africa



“Horizon 2020, and particularly EDCTP-2, will be a new journey that will open more avenues for collaboration between Africa, Europe and the rest of the world to address global health challenges such as tuberculosis.”

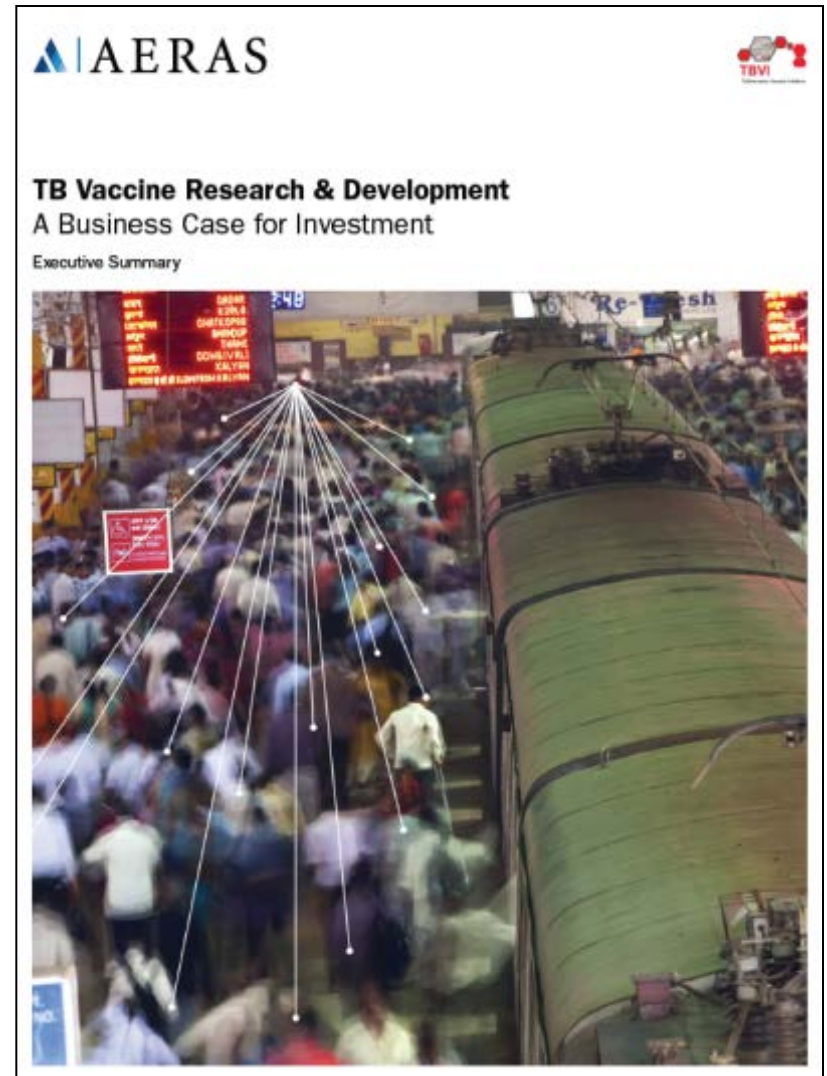
3rd Global Forum on TB Vaccines, March, 2013 (video address)



Business Case Key Messages



- TB vaccines are our best hope to end the TB epidemic
- Shared public and private sector investment at key stages will offset risk
- Even partially effective TB vaccines for adults and adolescents will have a significant public health impact
- A viable market for TB vaccines exists
- Greater diversification needed in TB vaccine portfolio
- A disciplined portfolio management approach is necessary





Global Portfolio Management Principles



A streamlined decision-making framework in order to advance the global TB vaccine portfolio and realize overall R&D cost efficiencies through effective portfolio management will follow the principles:

- **Optimization:** The framework will utilize existing technical expertise, scientific advisory committees and governance structures of key parties and build new capacity where needed in order to enhance portfolio decision-making and maximize organizational synergies and knowledge sharing.
- **Transparency:** Procedures and decision-making will be clear and objective based on objective gating and priority setting criteria that disclose and avoid any conflict of interest.
- **Sound Financial Management:** Funds will be managed in a rational manner with sufficient control over the use of those resources to ensure that stage gate decision processes are adopted and utilized.
- **Diversification:** The portfolio will be global and diverse to minimize financial risks and create the best opportunity for success; similarly, funding sources should include a broad array of different types of financing to increase the pool of available resources as much as possible.
- **Effectiveness:** The collaboration will offer donors and investors a highly efficient mechanism in order to show value for money, participate in risk-sharing and reduce time to market.
- **Affordability:** Vaccines to be developed will have to be available worldwide at affordable prices.



A dynamic model was developed to address four key objectives:

1. To identify a product development strategy that maximized the public health impact of new TB vaccines;
2. To conduct a strategic market analysis to assess the commercial viability of new TB vaccines;
3. To evaluate portfolio development costs in order to inform on investment strategies by phase of development over time, to support the successful commercialization of at least one new TB vaccine;
4. To demonstrate the cost efficiencies of implementing a portfolio management approach.

Introduction to the Financial Model



- ❖ With the assistance of KPMG, we have developed a unique financial model to help analyze and evaluate the TB vaccine R&D funding gap and to assess the potential use of non-traditional funding sources to advance the portfolio
 - ❖ **The primary purpose of the model** is to put the portfolio management and market assumptions into a robust analytical framework so that we can assess the funding needs and potential financing solutions.
 - ❖ **The model has been designed as a flexible tool** that can be adjusted to run multiple sets of assumptions at every level, using Monte Carlo Simulations.
 - ❖ **There are three key questions** the model seeks to address:
 - ❖ What will it cost to develop the current global TB vaccine portfolio to a point of successful global introduction?
 - ❖ What is the global market potential (from a financial standpoint) of a commercialized TB vaccine?
 - ❖ Does the market potential generate enough financial returns, given the risks, to justify the significant economic investment required to develop the portfolio?



- **Countries in analysis**
 - ❖ 197 countries included in the Applied Strategy Model
 - ❖ 14 countries excluded (no TB and/or birth data 2009)
 - ❖ 183 countries included for analysis

- **183 countries geographic segmentation**
 - ❖ Economies are divided according to 2011 GNI per capita, calculated using the World Bank Atlas method
 - **low income** - \$1,025 or less;
 - **middle income** - \$1,026 - \$12,475
 - lower middle income, \$1,026 - \$4,035;
 - upper middle income, \$4,036 - \$12,475
 - **high income** - \$12,476 or more



TB Vaccines Target Product Profiles



	Adolescents & Adults Vaccine
Indication	To prevent active disease
Target Population	≥ 10yo without known active TB
# Doses	2 doses
Vaccination Strategy	Routine vaccination of 10yo, and Mass campaigns in ≥ 11yo, every 10 yrs
Vaccination Coverage Rate Proxy	HPV coverage rate proxy for 10yo
Expected Efficacy	60% improvement in relative efficacy compared to the control arm
Expected Safety	No safety concerns

Infant Vaccine
To prevent active disease
Newborns independent of HIV status
1 dose
Routine vaccination of newborns
BCG
60% improvement in relative efficacy compared to current BCG
As safe as current BCG



Global Discovery/Preclinical TB Vaccine Portfolio

Candidate	Researcher/Sponsor	Geography	Development Stage
oral Ad4	Aeras	USA	Discovery/Pre-Clinical
rBCG	Aeras	USA	
rCMV	OHSU	USA	
att Mtb with altered stress response	Pasteur Institute	France	
Native and recombinant HBHA	Pasteur Institute Lille/Aeras	France/USA	
Inactivated MTBVAC	Zaragoza University	Spain	
MVA	CNBG/Aeras	China	
protein/adjuvant combinations	CNBG/Aeras	China	
LCMV Viral Vector constructs	U Lausanne	Switzerland	
DNA vaccines and EP	U Penn/Aeras	USA	
rBCG Immune Diversion (2 variants)	ETH Zurich	Switzerland	
MVA therapeutic constructs	Transgène	France	
rBCG::Ac2SGL (2 isoforms)	Pasteur Institute Toulouse	France	
ChAd 68 - Ag85A	Oxford	UK	
rec Human PIV2 with TB antigens	NIBIO/JBCGL/Aeras	Japan	

Notes: Discovery and preclinical candidates move in and out of the pipeline based on stage gate criteria on a regular basis. To maintain a robust discovery/preclinical portfolio \$20m is required over the next seven years to facilitate the advancement of 1-2 candidates into the clinic on an annual basis.



Global Clinical TB Vaccine Portfolio



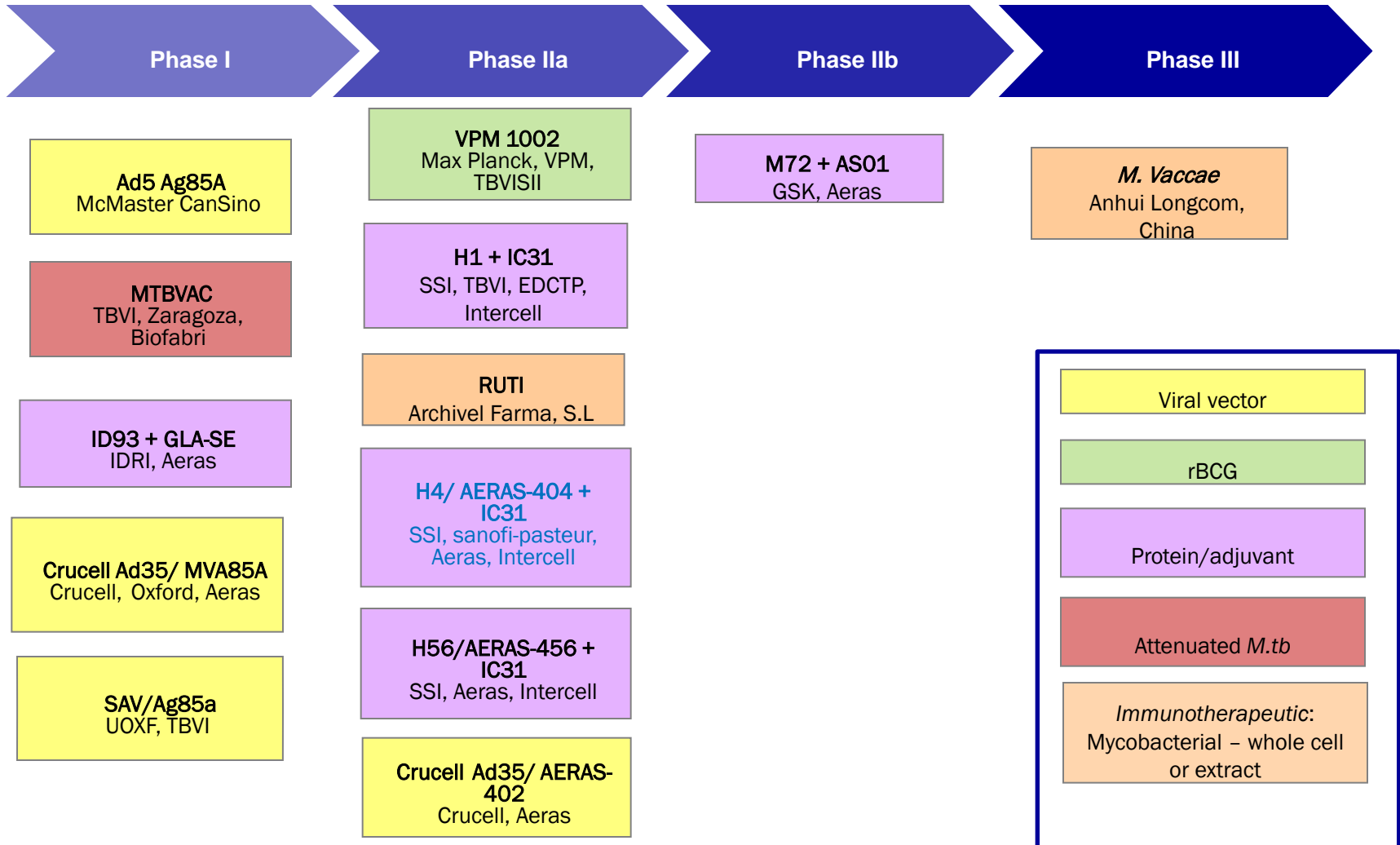
Candidate	Researcher/Sponsor	Geography	Development Stage	Projected Year of Entering Phase 2B/3 Studies
M72/AS01E	GSK Biologicals/Aeras	EU/MNC	Phase 2B	2018**
MVA85A	Oxford/Aeras	UK		down selected
M. Vaccae	Anhui Longcom	China		2013
MTBVAC	Zaragoza University	Spain	Phase 1 / 2A	2017
Aeras 402	Crucell/Aeras	Netherlands		down selected
VPM1002	VPM	Germany		Q4 2014
IM (Inhaled) Ad5 Ag85A	McMaster/CanSino	Canada/China		unknown
RUTI	Pere Joan Cardona	Spain		unknown
H1 IC31/CAF01	SSI	Denmark		unknown
H56 IC31	SSI	Denmark		2017*
ID93/GLA	IDRI	USA		2017*
AERAS402/MVA85A combination	Crucell/Oxford/Aeras	UK/Netherlands		down selected
H4/Aeras-404 + IC31	SSI/Sanofi-Pasteur/Aeras/Intercell	India		2017*
Inhaled MVA85A	Oxford	UK		unknown

*H56 IC31, ID93/GLA, and H4/Aeras-404 + IC31 are undergoing a head-to-head trial. Only one will advance to Phase 2B/3 trials in 2017. Aeras and TBVI estimate that 4-5 late stage trials will be underway between 2014-2020.

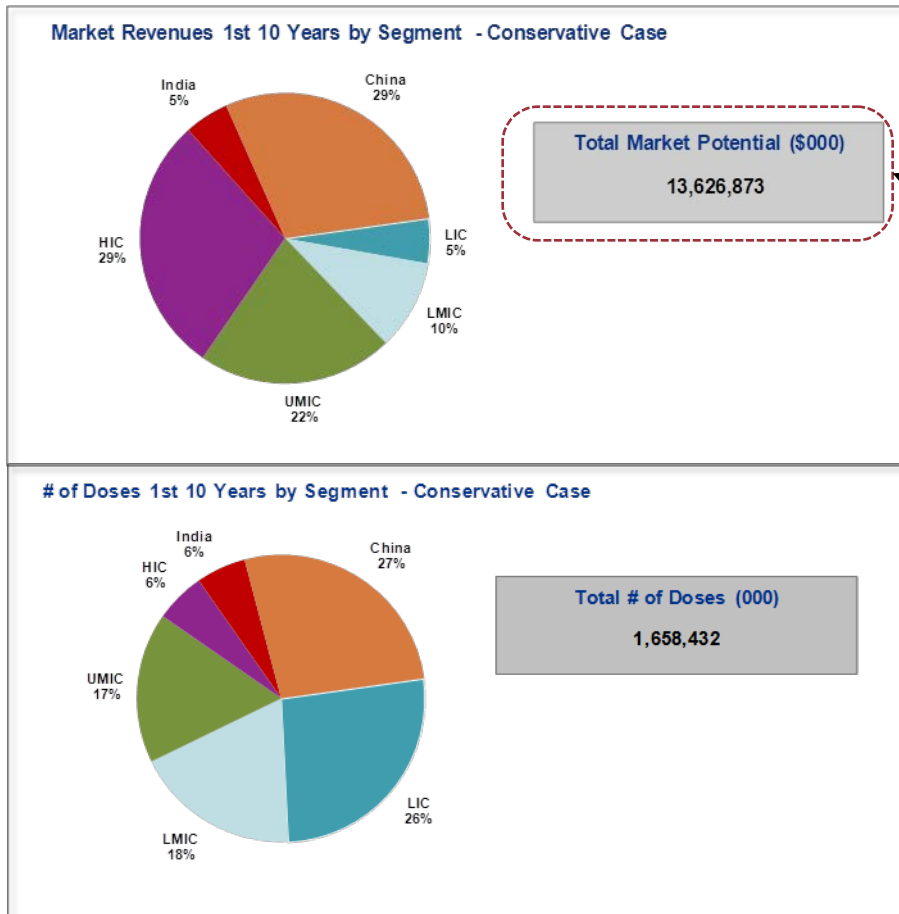
entering into Ph2b in 2013 and expected to enter into Phase 3 in 2018; **Commercialisation earliest would be 2023-24



The Global Clinical Portfolio of TB Vaccine Candidates



Overall Market Revenue Potential



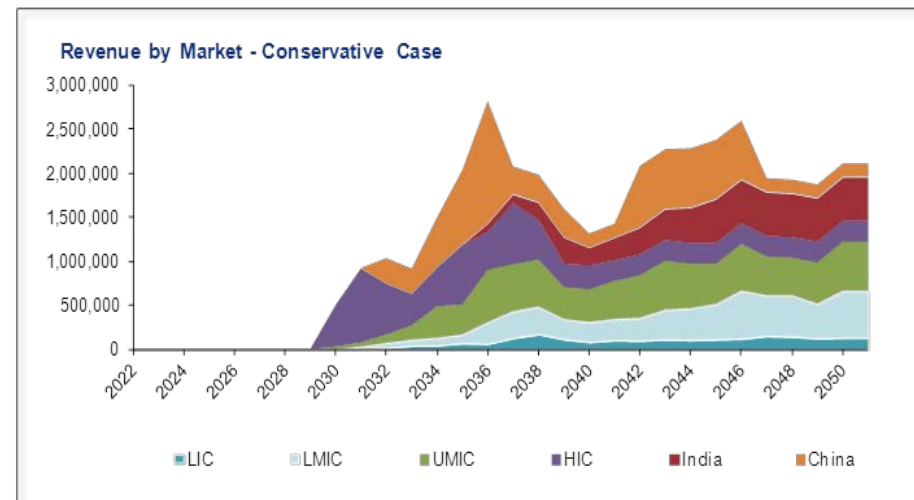
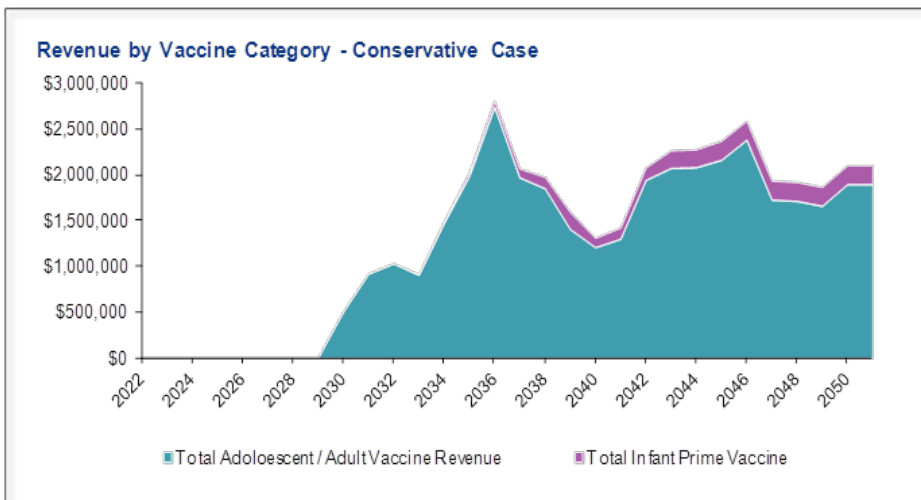
Under the conservative scenario, the estimated market revenue potential is estimated to be in excess of \$13-14 billion in the first 10 years of commercialization

Due to the prices that can be charged, it is estimated that HIC and UMIC would account for about half of the revenue potential, but only 25% of the doses in the first 10 years

Revenue Market Potential



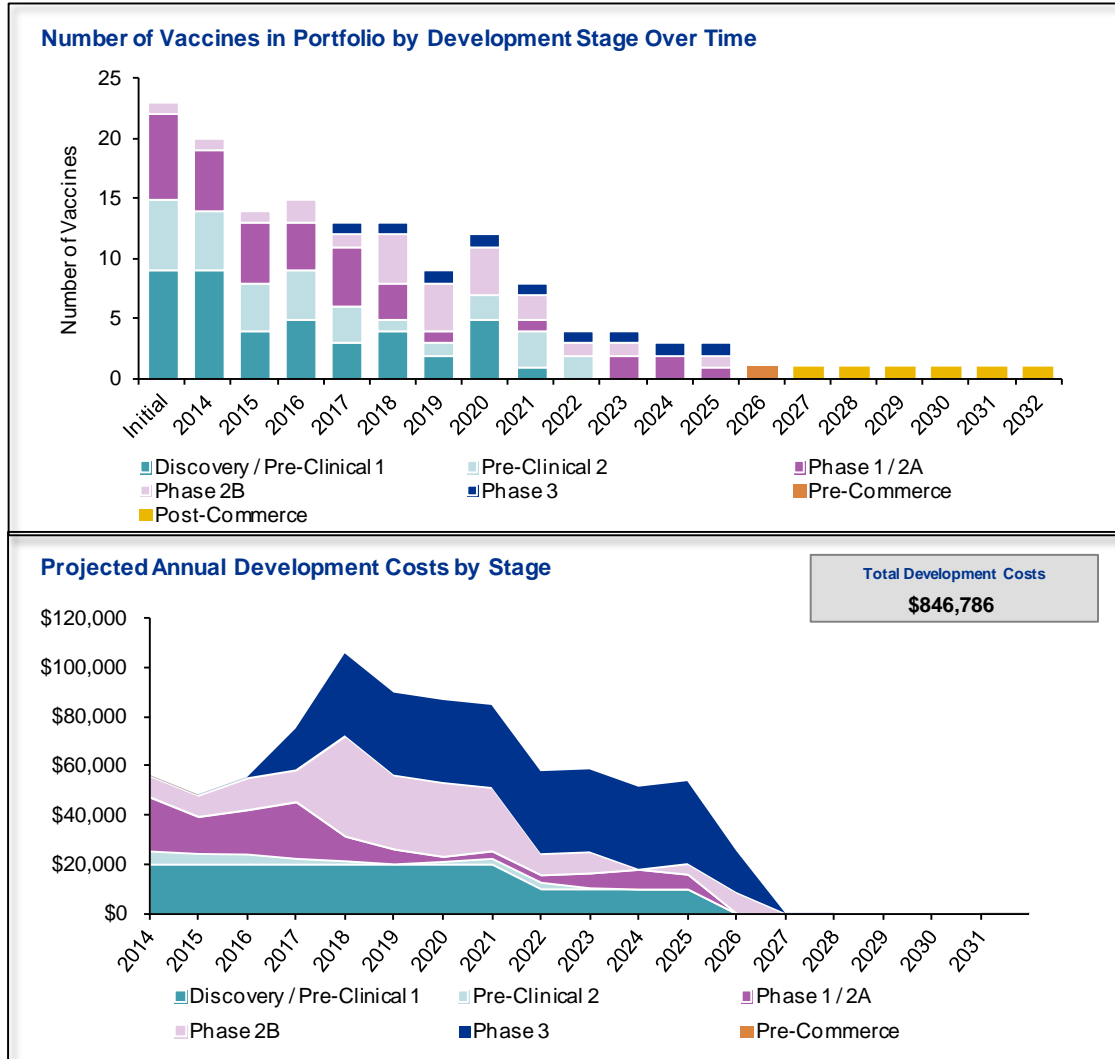
- The following graphs highlight the revenue market potential under the conservative scenario, whereby a vaccine is commercialised in 2030.



The majority of the revenue potential is from High Income Countries, Upper Middle Income Countries and China



Portfolio Evolution 2014-2027 using Monte Carlo Simulations

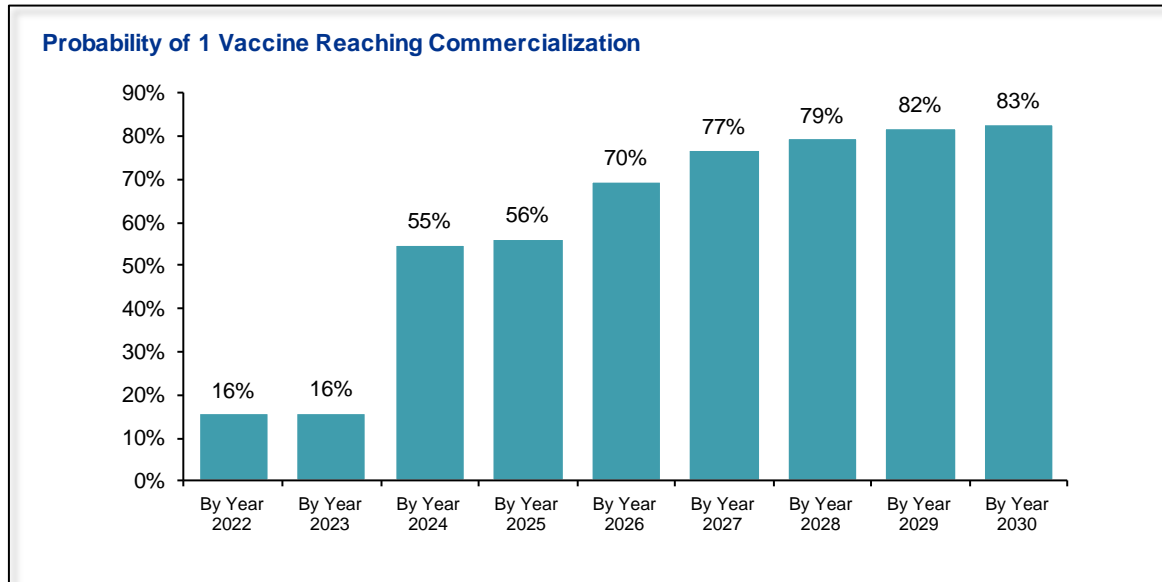




Portfolio Development Probability of Success



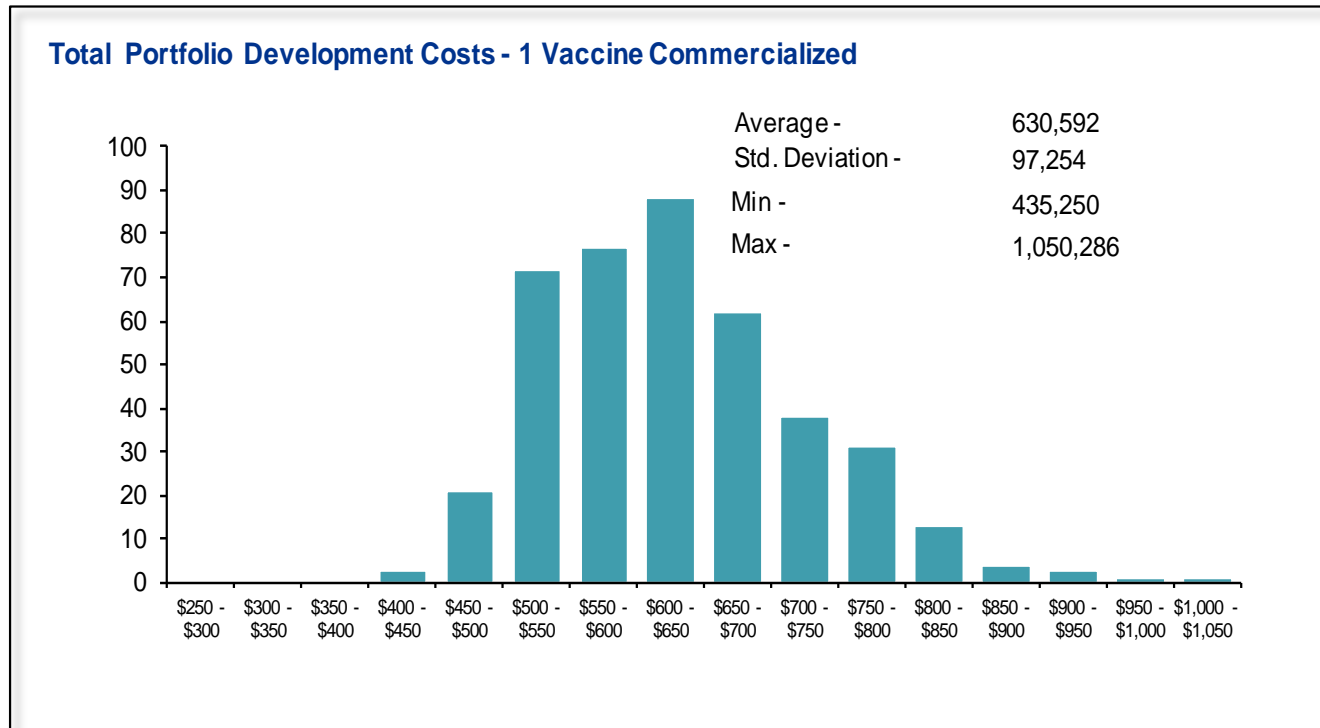
- ❖ The key outputs of the portfolio development analysis are:
 - ❖ Probability of successful commercialization of a vaccine by year
 - ❖ Costs to develop the portfolio to commercialization
- ❖ Given that there are numerous potential outcomes related to the various probabilities of success, the model incorporates Monte Carlo simulation to analyze the various potential outcomes.



Based on the base assumptions and the initial portfolio, there is a 55% probability of having one vaccine commercialized by 2024 and greater than 80% chance of having one vaccine commercialized by 2030



Overall Portfolio Development Costs



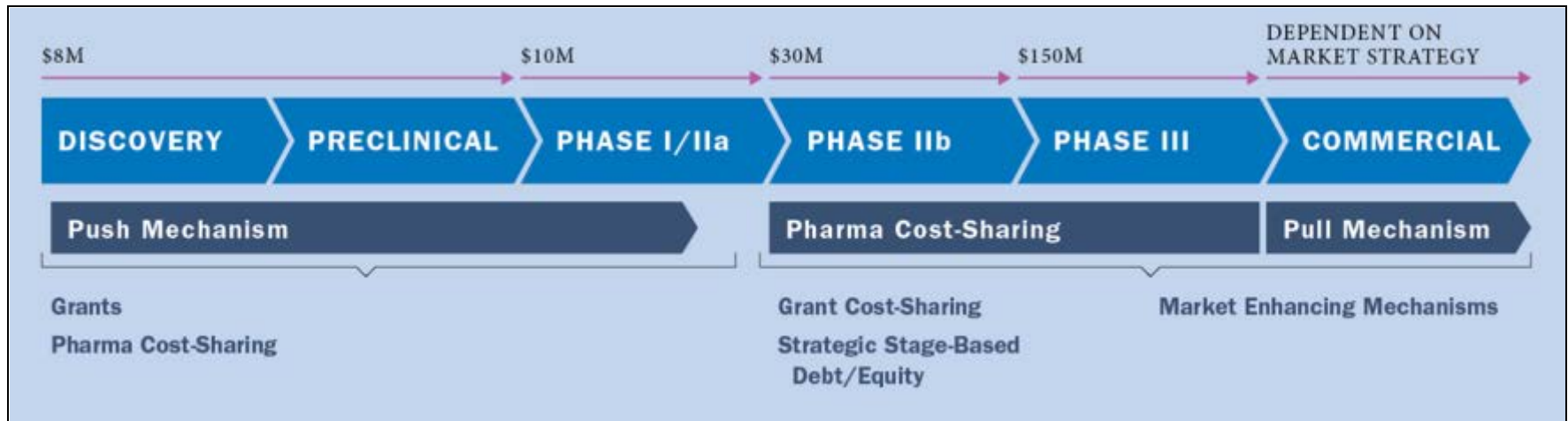
As highlighted in the histogram above (based on Monte Carlo simulation of the various potential outcomes), the estimated cost range for developing one vaccines through commercialization can range from \$435m to \$1,050m, with an average development cost of \$630m.

Public and Private Sector Risk-Sharing



A blended-capital financing structure will enable **appropriate risk-sharing between private and public sectors**:

- With governments' strong economic and public health interest in new TB vaccines, **public funding will be required to support the earlier phases of vaccine development**, where the scientific risk is the greatest
- In return, **industrial partners will be expected to cost-share in the later, more expensive phases of development**





EIB and other Funding Possibilities



Based on our current understanding of the TB Vaccine portfolio's funding requirements until commercialisation, EIB could consider :

- ❖ Direct financing to an IP holder to fund any potential gaps in the product development life cycle (corporate/ structured finance loans, possibly under RSFF)
- ❖ Indirect financing via investment in a mezzanine fund targeting late stage R&D projects in neglected diseases (subject to eligibility checks)
- ❖ Financing of Manufacturing Capacity build-out (subject to eligibility checks)
- ❖ Financing of introductory mass vaccination programmes by MS and selected other governments (subject to eligibility checks)
- ❖ Direct funding of the portfolio of TB vaccines under a full Commission/MS guarantee
- ❖ Necessity to ensure the donors maintain or increase their current commitments, introduction of new donors

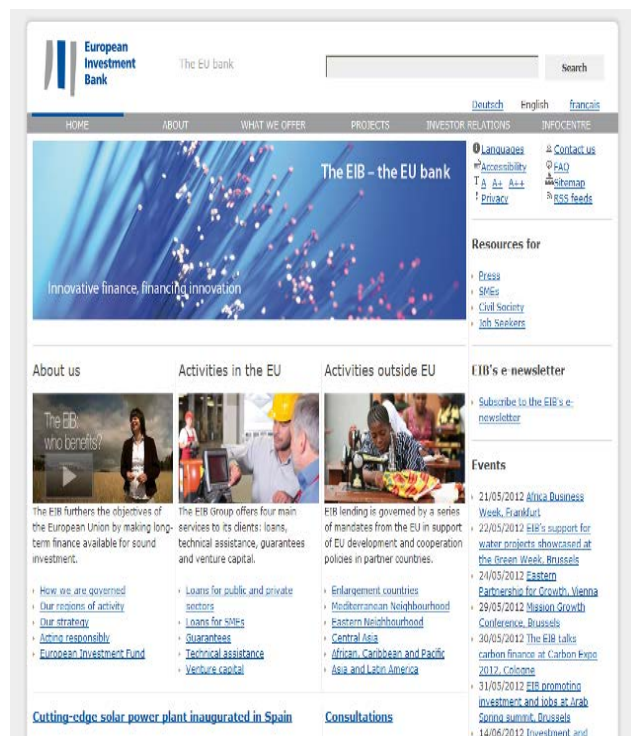
Initial Takeaways from our Analysis To-Date



- ❖ There is a **significant market potential for commercialized TB vaccines**, particularly an **adult/adolescent vaccine**
- ❖ If only an infant vaccine is developed, the overall market potential is more limited and may not support significant investment in the development of the portfolio; however, it is feasible that a vaccine commercialized initially for use in infants, could bridge to an adolescent/adult prime boost approach and thereby increase market share and revenue.
- ❖ The **overall market potential of a successful adult/adolescent vaccine** seems sufficient enough to support meaningful financial returns to industry and potential niche public/private investors in the development of the vaccine portfolio.
- ❖ Having a robust and diverse pipeline of vaccine candidates in early development stages will be critical to attracting investment capital as the portfolio approach increases the likelihood of successful commercialization and thus financial returns.
- ❖ There might be *possible RSFF direct and/or indirect financing* opportunities in late stage R&D phases



Thank you for your attention. Questions?



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