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NATIONAL SCHOOL OF TROPICAL MEDICINE

Human Hookworm Vaccine Initiative

A Public Health Value Proposition leading to Societal Impact and Positive Financial Returns

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A Product Development Partnership

Texas Children's Hospital®

Human Hookworm Vaccine (HHV) Initiative

Led by Texas Children's Hospital Center for Vaccine Development

A Product Development Partnership + 18 years track record

Partnering with the academic, public and private sectors to leverage expertise

Advancing R&D and product development that focuses on capacity building, infrastructure development and knowledge-sharing to meet LMIC policies and WHO PQ requirements

Texas Children's Hospital

THE GEORGE WASHINGTON UNIVERSITY
WASHINGTON, DC

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HOOKVAC
THE HUMAN HOOKWORM VACCINE

Hip

SEVENTH FRAMEWORK PROGRAMME

Bringing vaccines to those in need

India - EU Partnership funded by EuropeAID

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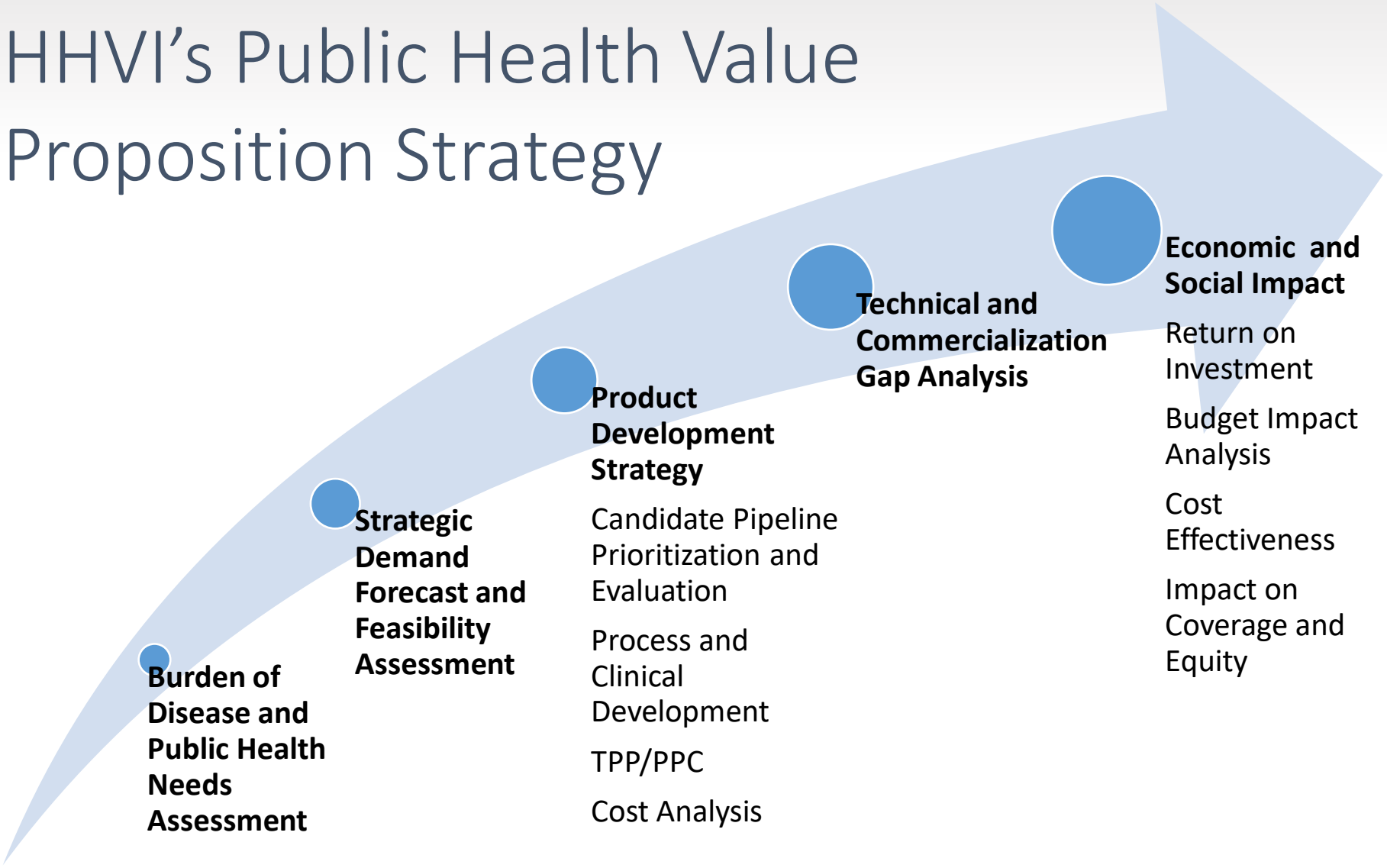
HHVI's Public Health Value Proposition Strategy

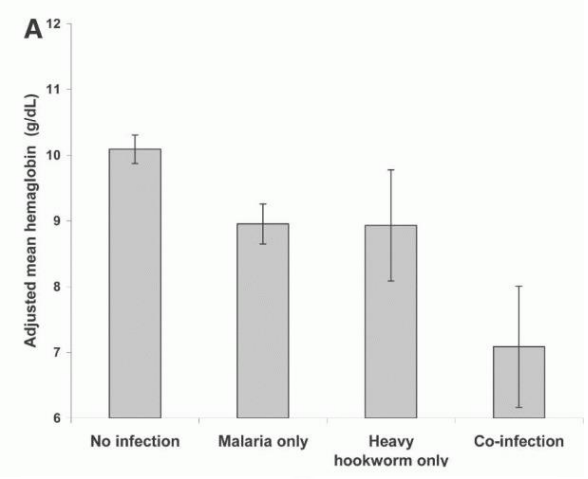


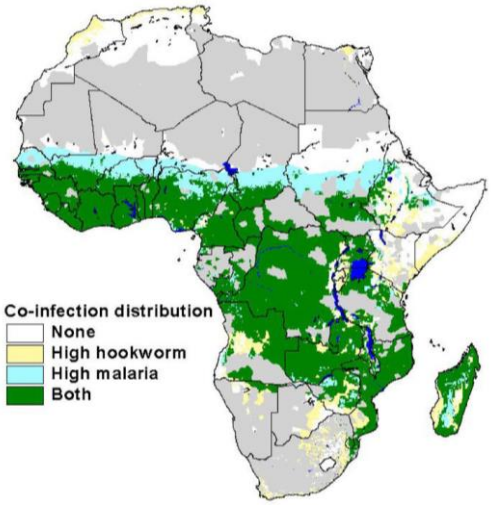
Adapted from Gessner et al., Vaccine 35 (2017) 6255–6263

Human Hookworm

Burden of Disease and Public Health Needs Assessment

- Infects more than **470 million** people
- Ranks **NUMBER ONE** in terms of Years Lost from Disability
- Among the **TOP THREE** in terms of DALYs (4.1 DALYs using 2010 disability weight estimates)
- Prevalent Worldwide – **Overlap with Malaria in Africa**
- Causes **anemia**, malnutrition, physical and developmental delays, hence reductions in future wage earnings





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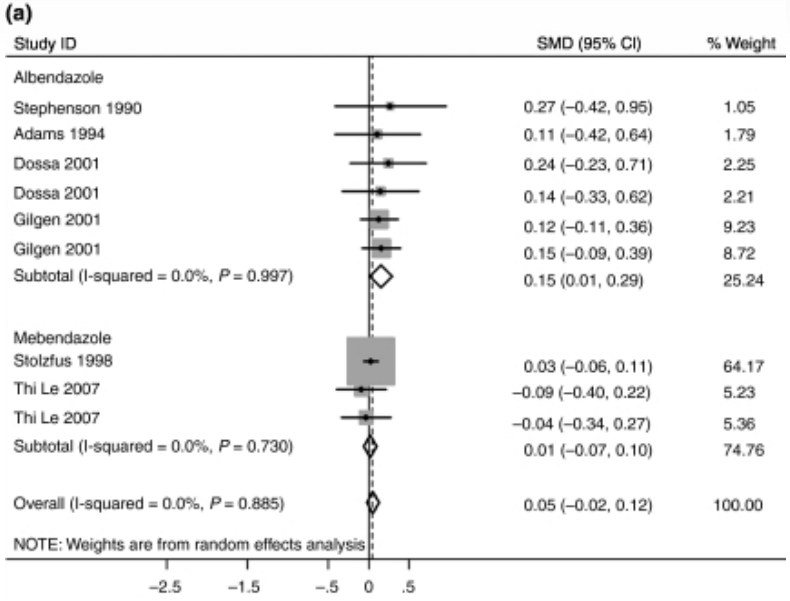
Bartsch et al (2016), Hotez PJ et al. (2010) ; Murray et al, (2012); Smith and Brooker, (2010); Keenan JD et al., (2013) Brooker et al., (2007), Brooker et al., (2006); Smith et al., (2010)

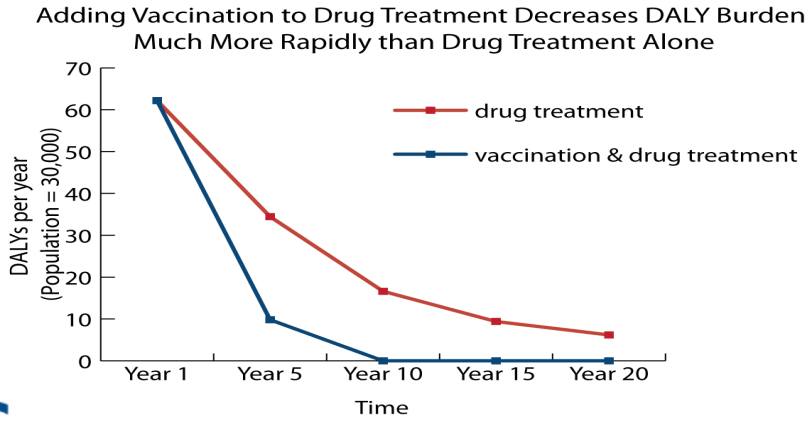
HHV can complement conventional MDA

Current treatment: Small molecule drugs

- Do not prevent re-infection
- Lack of improvement in hookworm anemia
- Low cure rates and variable efficacy, increasing drug failure
- After widespread MDA hookworm infection has remained almost unchanged (13% over the last decade – GBD 2016)
- A survey of NTD experts concluded that prevention will not be feasible using MDA alone – **a vaccine is a strategic necessity**

No overall effect of BMZ
ABZ 1.89 g/l increase in mean Hb
MBZ no apparent impact





Lee et al., (2012); Bartsch et al. (2016) Smith et al., (2010)

Demand Forecast and Feasibility Assessment

Survey of **76** (from 127 invited) **thought leaders** (in research, policy-setting, financing, and/or program implementation) about the **development, value, use, and potential demand** of a human hookworm vaccine and the importance of hookworm as a **disease burden and control priority**

AKESO Associates in 2013

1. Majority agreement - HHV is useful public health tool
2. Vaccine "adds" value to MDA and other control programs (i.e. WASH, Malaria Control and Malaria Vaccine Development)
3. Vaccine has to fit existing health systems
4. Vaccine should be of low cost, produced and used locally
5. Demand determined by:
    1. HHV's performance and safety characteristics
    2. BoD at time of introduction

Candidate Pipeline Prioritization and Evaluation

Prioritized from a pipeline of >12 candidates

Applied a matrix evaluation and scoring system:

- Potential safety risk assessment
- Production and scalability feasibility
- Stability assessment
- Preclinical efficacy
- Known function/structure

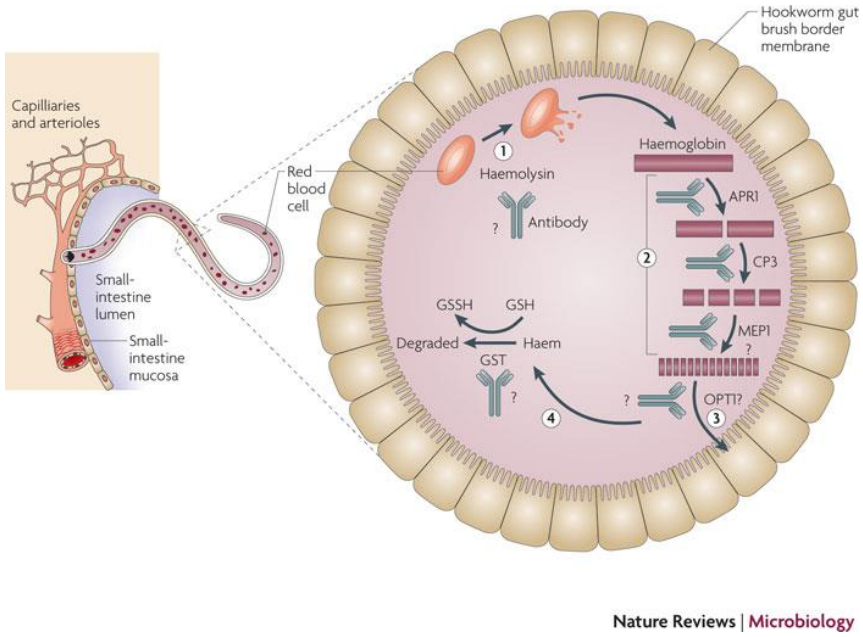
HHV comprised of **TWO** Recombinant Proteins from the adult worm

Na-Glutathione S-transferase-1 (*Na*-GST-1)

Na-Aspartic Protease-1 (*Na*-APR-1)

Vaccine formulation

Recombinant protein adsorbed to Alhydrogel® +/- immuno-stimulants (TLR Agonists – GLA-AF or CpG10104)



Nature Reviews | Microbiology

Hotez PJ, Bethony JM, Diemert DJ, et al. 2011. https://www.ncbi.nlm.nih.gov/books/NBK62497/

Clinical Development

A series of Phase I clinical trials have been conducted in the USA, Brazil, and Gabon

Tested alone and in co-administration

Tested in adult volunteers from non-endemic and endemic areas and in children from an endemic area

- *Na*-GST-1 vaccine tested in 160 volunteers
- *Na*-APR-1 vaccine in 70 volunteers
- Co-administration in 110 adult volunteers
- Co-administration in 48 children volunteers

TARGET PRODUCT PROFILE

Recombinant protein-based vaccine

- **1-2 recombinant antigens + adjuvant**
- **2 or 3 doses**
- **Intramuscular injection**

To prevent moderate and heavy hookworm infections caused by *Necator americanus*

- **Prevention of hookworm-related iron-deficiency anemia & related sequelae**

Pre-school and school-aged children (< 10 years)

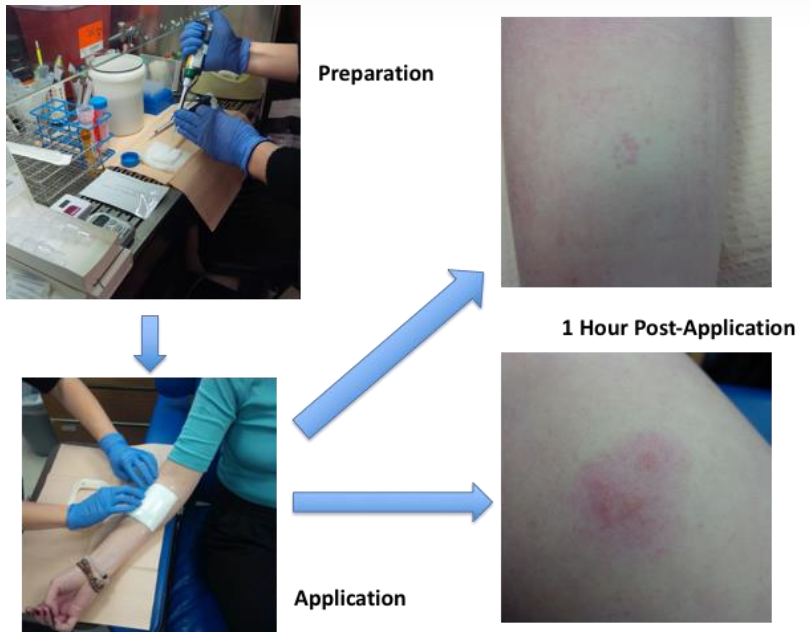
Vaccinations incorporated into existing mass drug administration programs

In these studies, the vaccine was consistently found to be safe, well tolerated and induced anti-*Na*-GST-1 & anti-*Na*-APR-1 IgG antibodies

Ongoing Clinical Activities

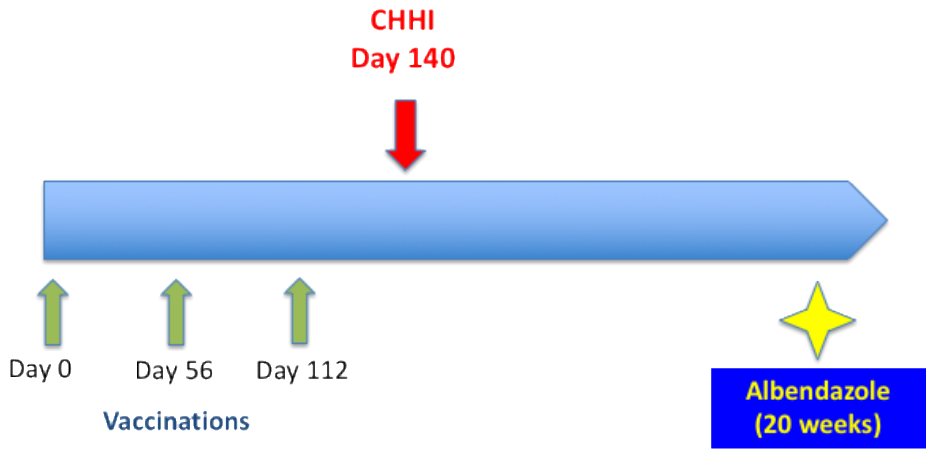
Controlled Human Hookworm Infection (CHHI) model

- Developed in US under US FDA IND
- Established the *Na*L3PU at GWU: *Necator americanus* infectious Larvae 3 Production Unit
- US hookworm-naïve adults N = up to 30
- Single application of 25, 50, or 75 L3 larvae
- Tolerable and quantifiable infection status & intensity



Phase 2: Vaccination + CHHI Study

- Randomized, placebo-controlled trial
- 48 Healthy, hookworm-naïve adults in US
  - *Na*-GST-1/Alhydrogel®
  - *Na*-GST-1/Alhydrogel® + GLA-AF
  - *Na*-GST-1/Alhydrogel® + CpG 10104
  - Infectivity controls (injected with placebo)
  - Challenge with 50 Larvae



Technical and Commercialization Gap Analysis

- Analysis focused on balancing scientific and financial requirements to optimize the result and impact of the HHV
- Risk & mitigation measures tuned to optimize the process, balancing anticipated costs and timing of each phase and to speed up implementation
- Defined the potential for the initial target markets (Brazil, India, Indonesia)
- Anticipated impact on socio-economic benefits
- Identified the potential for implementation

India
Children at risk: 220.6 million

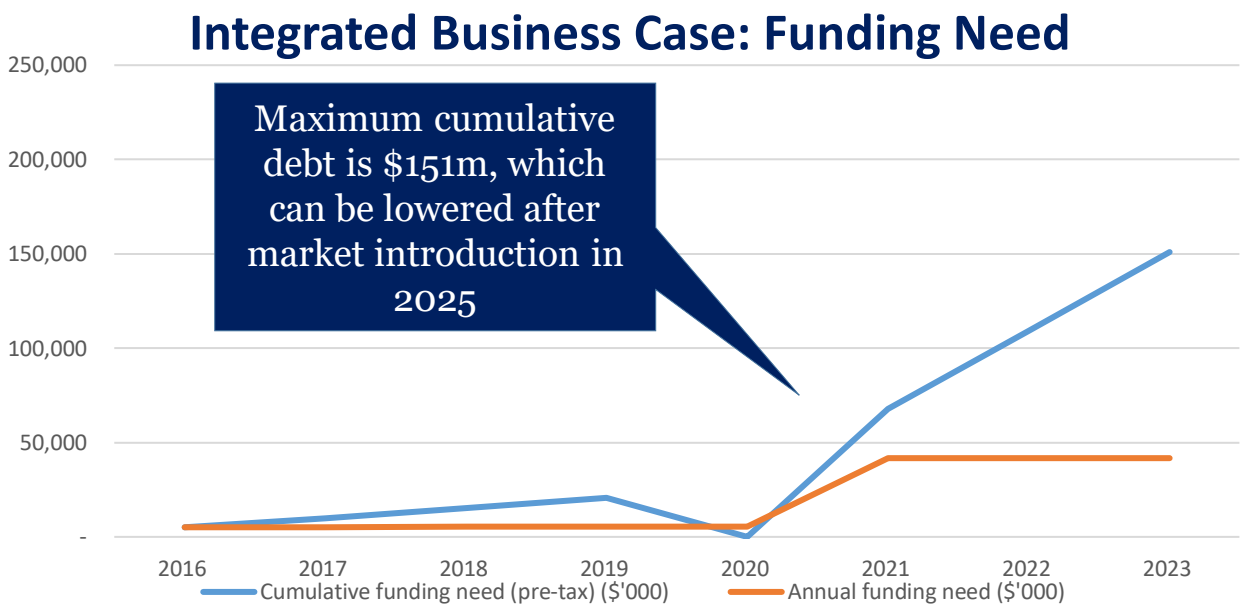
Brazil
Children at risk: 11.8 million

Indonesia
Children at risk: 67.7 million

Financial modelling of HHV development costs

- Time per development phase
- Patient sample size per clinical trial phase
- Development cost per phase
- Probability for moving from one phase to another
- Financial limitations
- Risk & mitigation measures
- Comparable cases of infectious and neglected disease vaccine
- Expert opinions

The funding need accumulates to $151 million in 2023*



The probability unadjusted cumulative return on sold vaccine equals the full investment requirement ($151 million)

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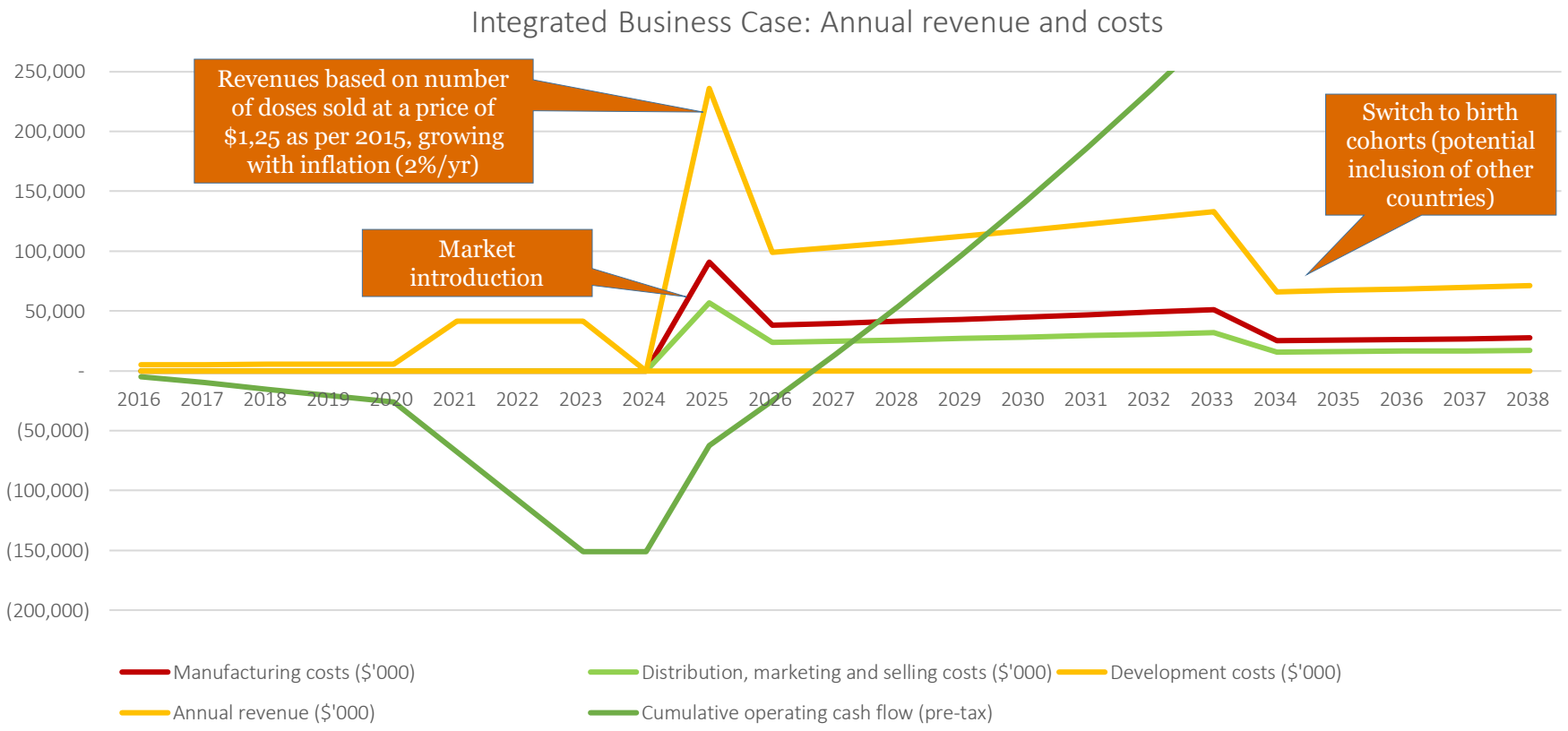
Financial modelling of HHV costs and benefits

HHV generates **an internal rate of return of 11.7%** probability adjusted
With a **discount rate of 15% the probability unadjusted net present value is $11.6 million**



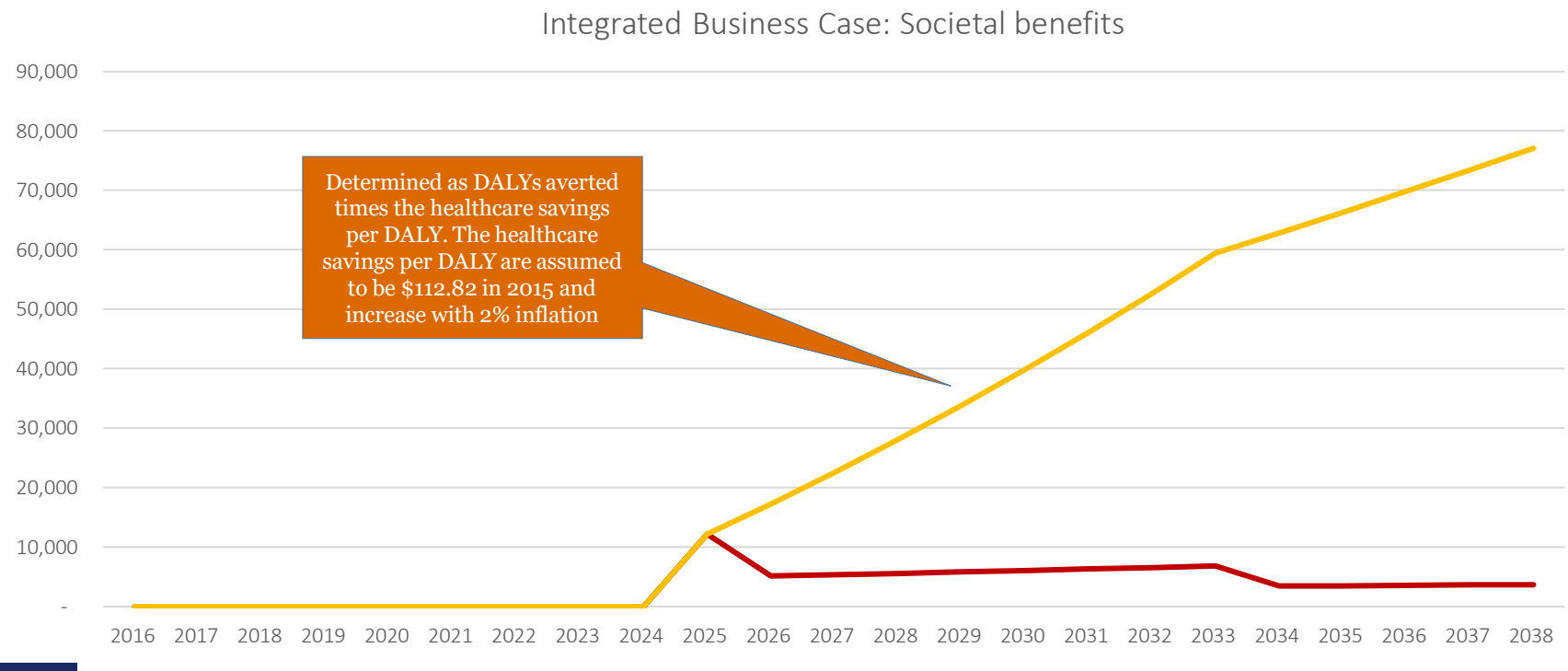
Cumulative cash flow will turn positive in 2027
Net present value will turn positive in 2032

Modelling impact of vaccination on healthcare savings

Vaccination results in $77 million in healthcare savings by 2038 in the target countries

>500.000 total DALYs averted through vaccination by 2038 in the target countries

The average healthcare savings per DALY in dollars in the target countries ($112.82 weighted average in target countries), multiplied with the total annual DALYs averted by vaccination in the target countries, results in the total societal benefits expressed in US dollars per year.

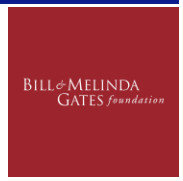


Thank You

WE ARE COMMITTED TO:

- Achieving improved health outcomes in the most cost-effective manner possible
- Early inclusion and understanding of LMICs needs and preferences
- Incentivizing disease-endemic country ownership
- Building self-reliance and sustainability

Ministry of Foreign Affairs



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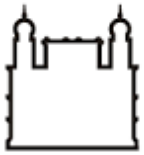

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