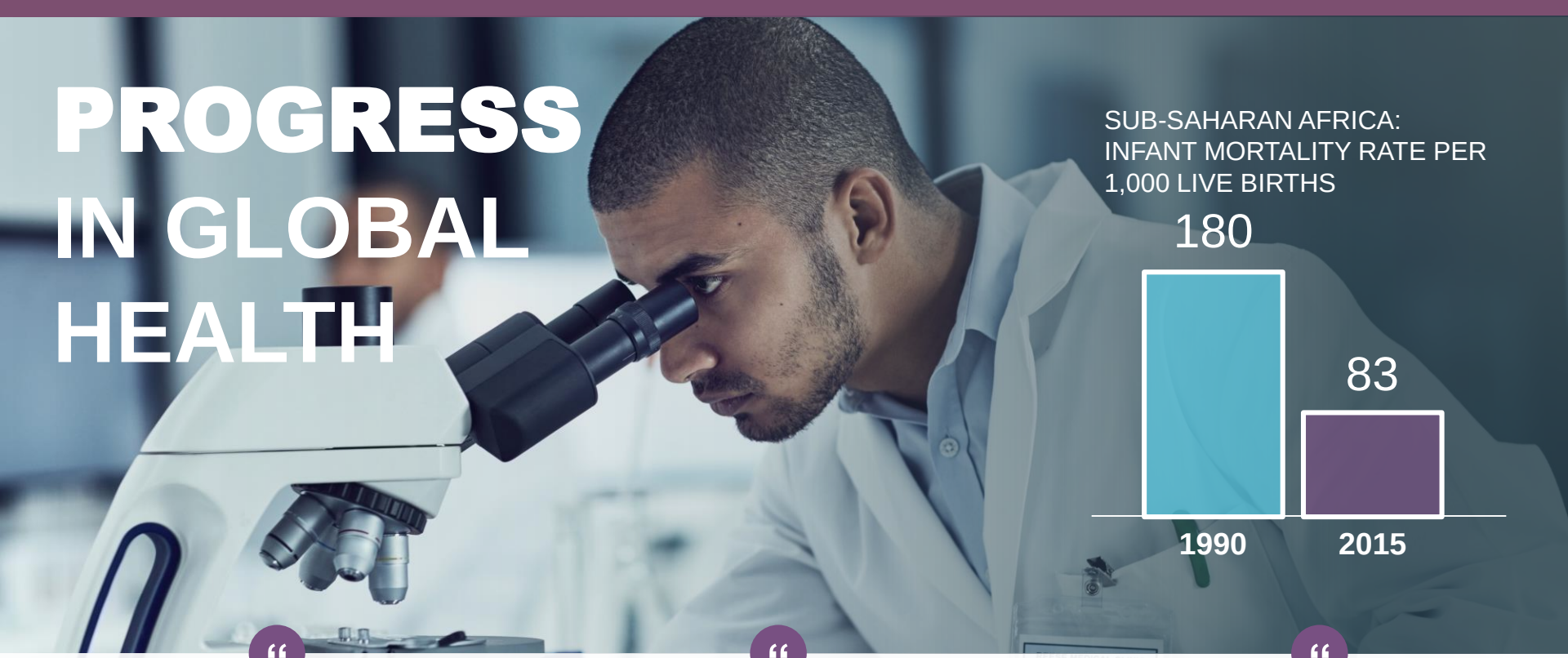

Bill & Melinda Gates
MEDICAL
RESEARCH
INSTITUTE
INTRODUCING THE
GATES MEDICAL
RESEARCH
INSTITUTE

PROGRESS IN GLOBAL HEALTH



SUB-SAHARAN AFRICA:
INFANT MORTALITY RATE PER
1,000 LIVE BIRTHS

“Wiping Out Polio: How The U.S. Snuffed Out A Killer”

NPR, 10/15/12

“Meningitis Vaccine Developed With Gates Foundation Drives Africa Cases to Lowest in Decade”

HuffPost, 6/6/13

“AIDS deaths halve as more get drugs”

BBC, 7/20/17

CHALLENGES REMAIN

525,000
CHILDREN UNDER AGE 5 KILLED BY ENTERIC AND DIARRHEAL DISEASES
each year[1]

430,000
DEATHS DUE TO MALARIA
in 2015[2]

1.7 Million
PEOPLE DIED FROM TUBERCULOSIS
in 2016[3]

1 WHO Diarrhoeal disease fact sheet, updated May 2017
2 WHO Global Malaria Report 2016
3 WHO Global Tuberculosis Report 2016


TOGETHER, THESE TOUGH DISEASES CAUSE OVER
4 DEATHS EVERY MINUTE

ABOUT THE GATES MRI

Location	**Cambridge, MA**
Structure	**Wholly owned subsidiary of the Gates Foundation**
Focus	**Lead Candidate Selection to Phase 2 POC for TB, malaria, enteric diseases and beyond**
Size	**~50 FTEs in Y1, scaling up as portfolio grows**
Compliance and Operations	**Building industry-leading quality systems and clinical operations infrastructure**

DISEASE AREA MODALITIES

SMALL MOLECULE THERAPEUTICS

DIAGNOSTICS / BIOMARKERS[2]

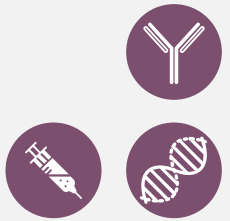
VACCINES

BIOLOGICS[1]

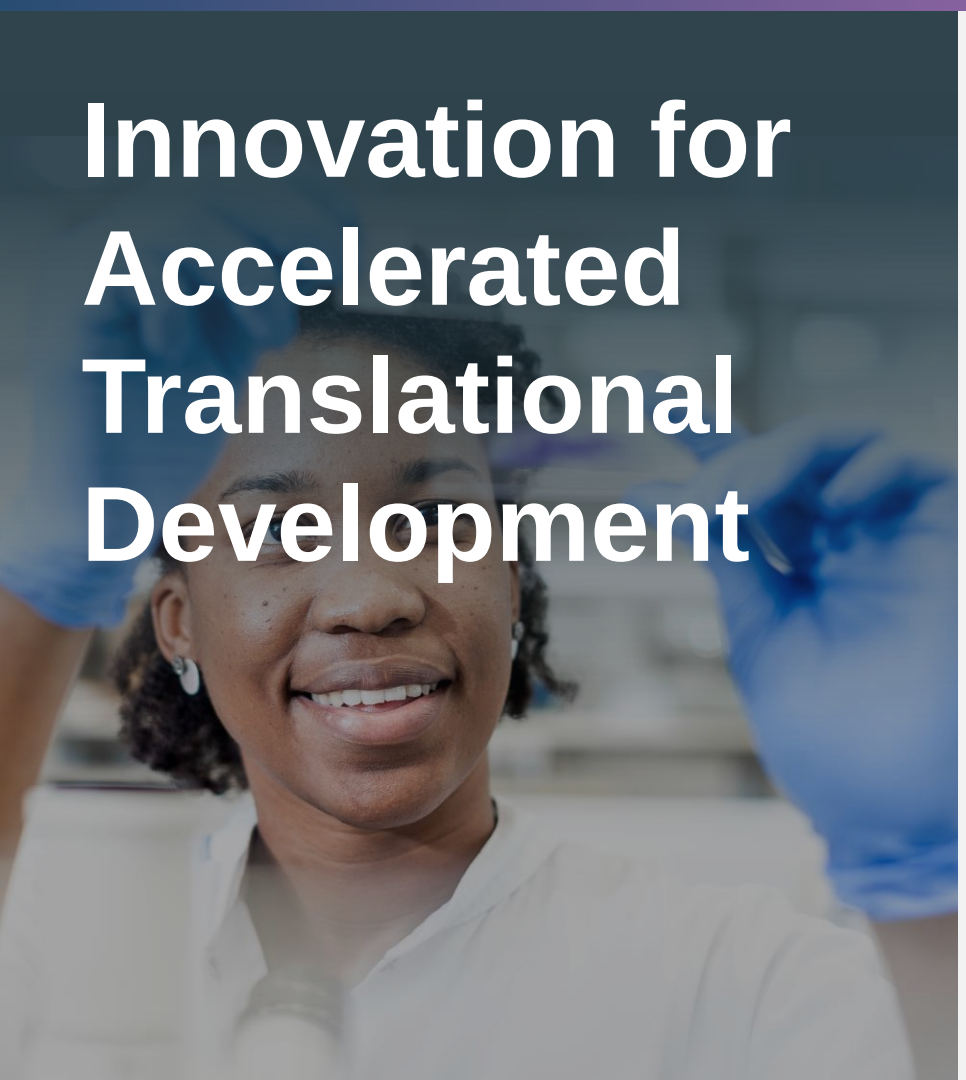
1 Includes mAbs and other non-small-molecule modalities, e.g., RNA, DNA, viral and cell platforms
2 Biomarker optimization for early hand over to diagnostic companies

ENTERIC AND DIARRHEAL DISEASES

MALARIA



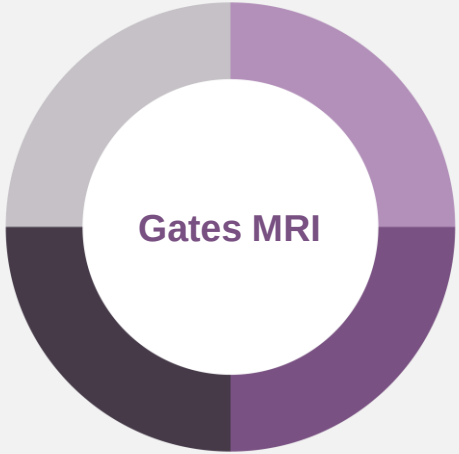
TUBERCULOSIS



Innovation for Accelerated Translational Development

DISCOVERY RESEARCH DECISION SUPPORT AND ACCELERATION

CHEMISTRY, MANUFACTURING AND CONTROLS

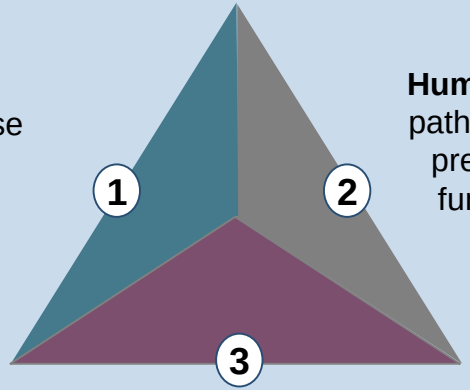


QUANTITATIVE SCIENCE: MODELING, QSP, SYSTEMS BIOLOGY

INNOVATIVE CLINICAL TRIALS (DESIGN AND EXECUTION) AND BIOMARKERS

PROJECT/PORTFOLIO STRATEGY

Product development: Build and optimize the portfolio for each disease area and modality.



Human Disease Biology: Use data on host-pathogen interface in humans to guide better preclinical and clinical development; learn fundamental biology in the context of our studies.

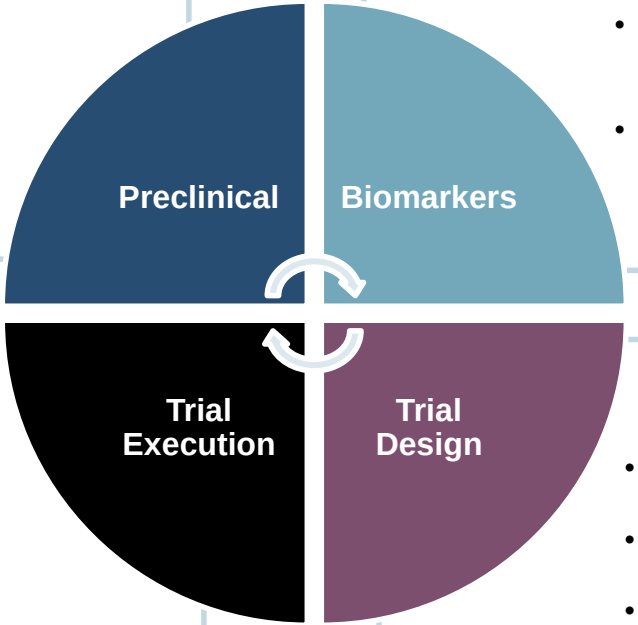
Translational Medicine: Cutting edge and best practices in translational development (**science in the service of strategy**).

Simultaneously develop product candidates and translational strategy for each disease area, including filling portfolio gaps and building tools for effective translational development

INNOVATION FOR TB DRUGS AND HOST-DIRECTED THERAPIES

- New culture systems for PK/PD assessment
- Acute/chronic animal models that mimic human disease
- Model *ex vivo* and *in vivo* drug synergy

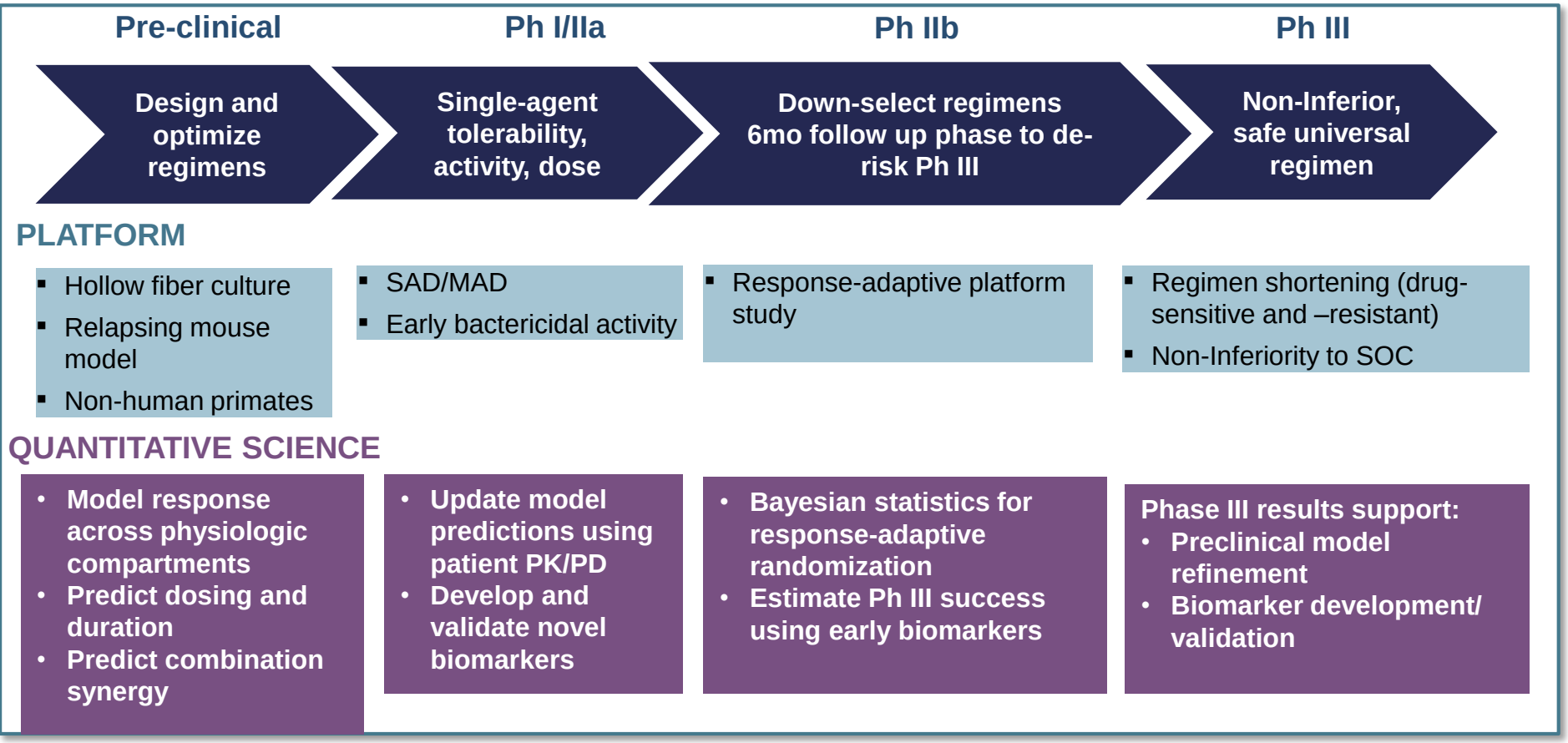
- Quantitative assays for sputum mycobacterial load
- Blood RNA signatures and quantitation of cell-free mycobacterial DNA
- Novel imaging endpoints (FDG-PET; HRCT)



- Assay qualification/validation
- Real-time monitoring

- Model-informed dose/regimen selection
- Response-adaptive randomization
- Umbrella study for multiple regimens

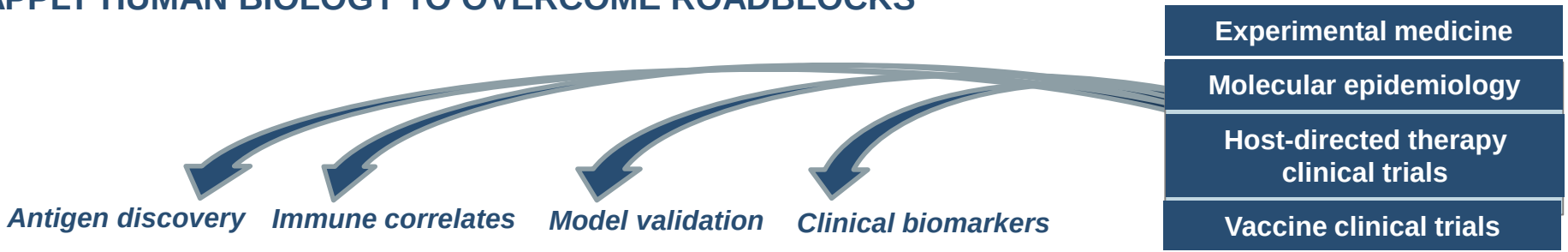
INNOVATION FOR TB DRUGS AND HDT



Adapted from David Hermann, BMGF

INNOVATION FOR TB VACCINES

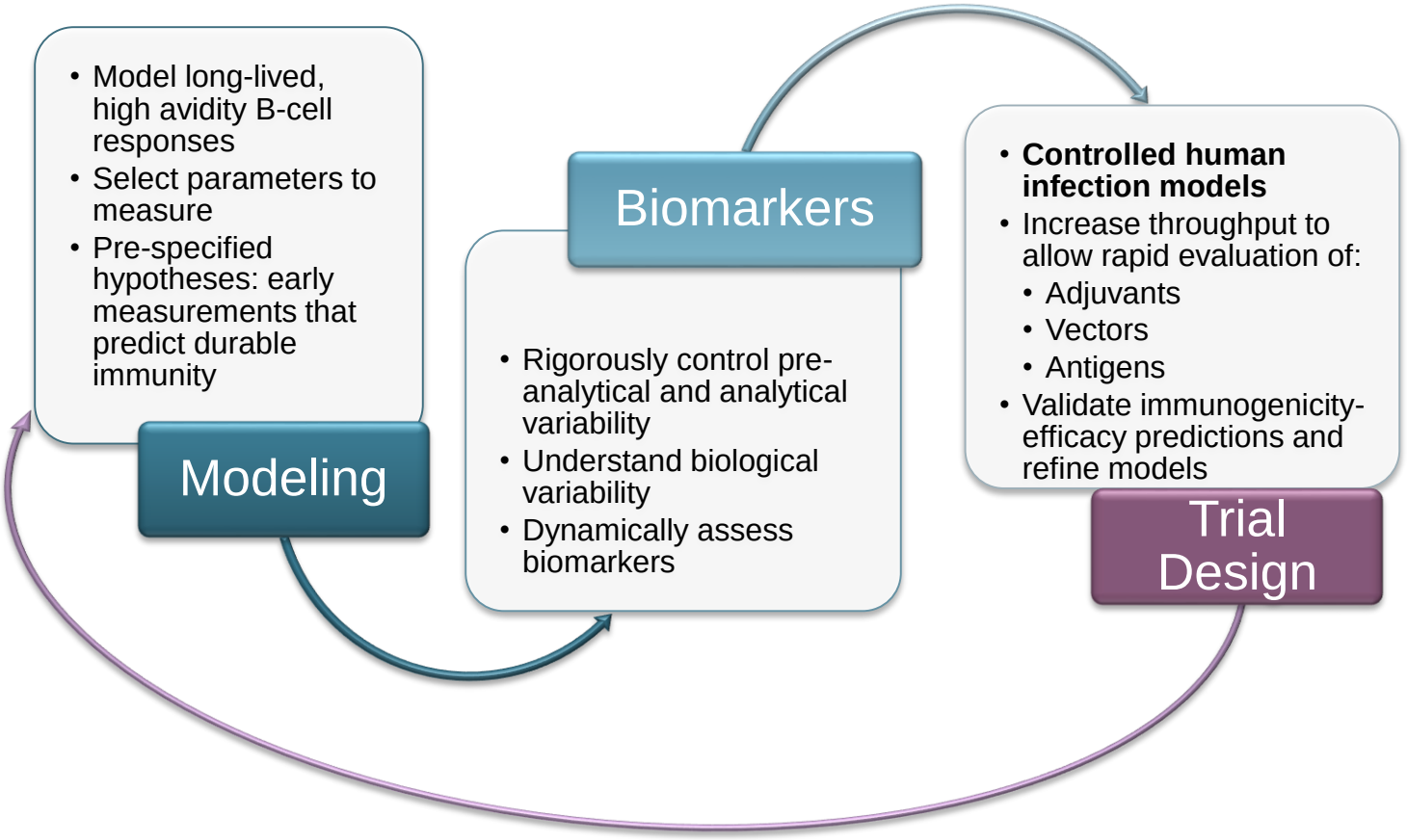
APPLY HUMAN BIOLOGY TO OVERCOME ROADBLOCKS



ROADBLOCKS

• Antigenic determinants of protection unknown • Key immune cell subsets not well correlated with protection	• Small animal models not always predictive of clinical outcome • Non-human primate models need optimization	• No human challenge model • Lack of standardization for immune correlates	• Lack of good surrogate endpoints for prevention of infection	• 10K+ subjects needed for prevention of disease studies

INNOVATION FOR MALARIA AND SHIGELLA VACCINES



PROGRESS THROUGH **PARTNERSHIP**

1

DISCOVERY/ RESEARCH

EARLY RESEARCH PARTNERS

Academic centers/Institutes
Pharma industry
Product development partnerships

2

TRANSLATIONAL DEVELOPMENT

TRANSLATIONAL DEVELOPMENT PARTNERS

Academic, clinical, industry, and community partners

3

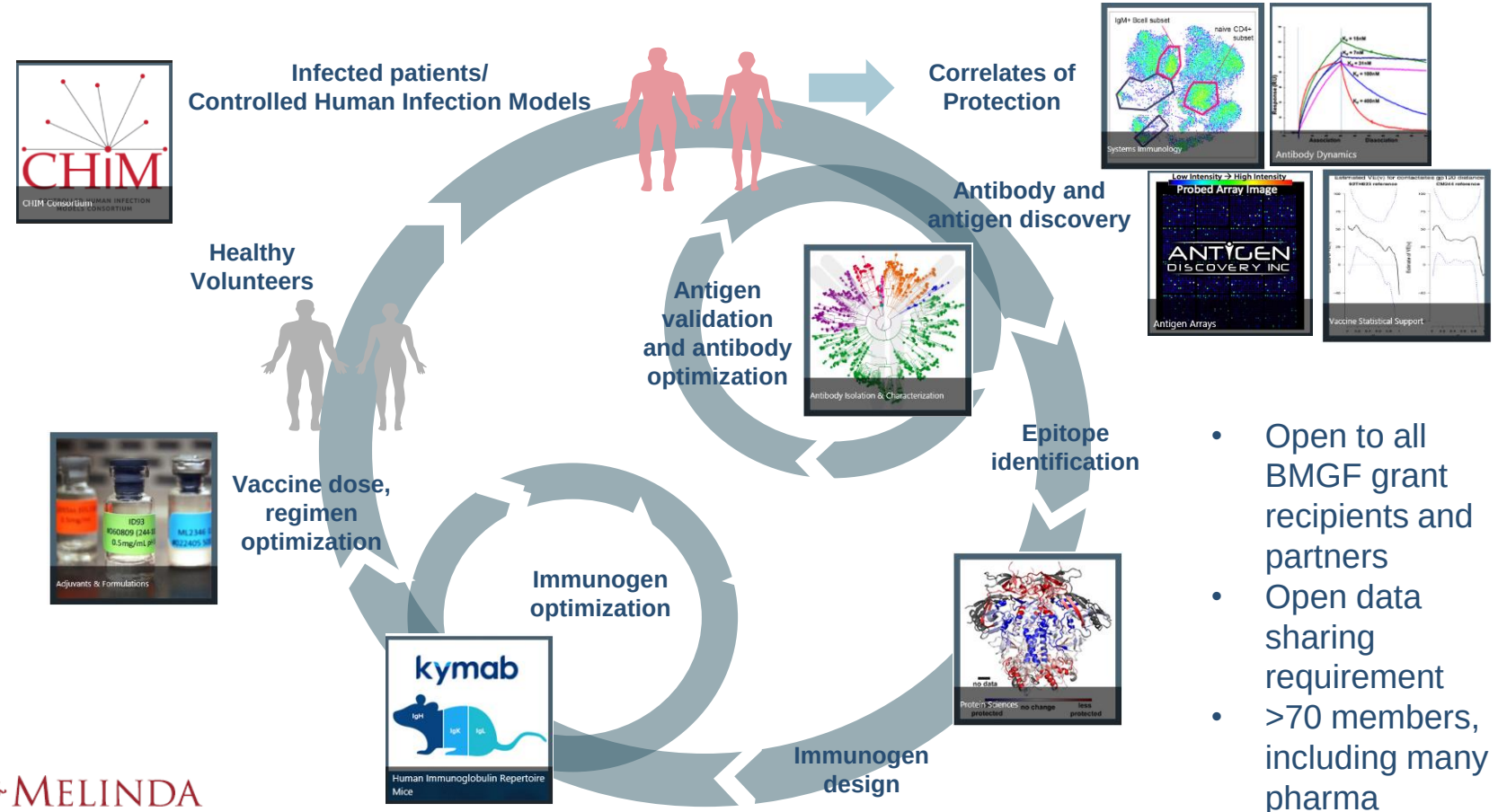
LATE PHASE DEVELOPMENT

LATE DEVELOPMENT PARTNERS

Pharma industry
Product development partnerships

Benefits applied across the whole of the global health ecosystem

GLOBAL HEALTH VACCINE ACCELRATOR PLATOFRM



- Open to all BMGF grant recipients and partners
- Open data sharing requirement
- >70 members, including many pharma

BILL & MELINDA GATES foundation

Shared Challenges in Immuno-Oncology and Tuberculosis

	Immuno-Oncology	TB Vaccines/HDT
Antigenic Determinants	Germline vs. neoantigens vs. viral	Dominant Th1 epitopes vs. subdominant
Optimal phenotype of responding T-cells	Phenotype and epigenetic state of 'exhausted' T-cells	• Th1 vs. CTL, vs. innate lymphoid cells • Tissue resident vs. circulating T-cells
Good vs. bad inflammation	• Chronic IFN signaling • Co-opted wound healing • Good and bad myeloid phenotypes	Type I IFN vs. IL-1
Inter/intra-lesional heterogeneity	• Heterogeneous lesion responses • Tumor and T-cell clonal heterogeneity • Intralesional distribution of immune cells	Heterogeneous lesion responses
Host immune competence	• Cancer-induced immunosuppression • Microbiome	• Co-infection, malnutrition, • Microbiome

Multiple opportunities for cross-disciplinary collaboration


OUR ONLY BOTTOM LINE IS THE
NUMBER OF LIVES SAVED