Innovation at Janssen across 3Ps

Projects, Programs/Process and People

Uganda, 20th March 2019

Brian Woodfall, M.D.

Overview of the 3Ps

- Projects
  - HIV
  - TB
  - New areas – RSV; HBV; Dengue
- Programs/Process
  - HBV Platform & EU-PEARL consortium on TB Platform study design
  - Technology in Disease Management
  - Ugandan Academy for Health Innovation and Impact
- People
  - R&D Fellowship programs
  - Sikiliza Leo
  - Pepal

J&J Global Public Health

Our Vision

Innovation for all,
everywhere at the same time.

Our Mission

Make relevant innovations
that save lives, cure patients
and prevent disease
available – affordable – accessible
for underserved populations.

Focus on Addressing Serious Unmet Need

Core Focus Areas

R&D, Access, Programs & Operations

Enable a world free from the burden of TB in all its forms

End transmission and help reduce burden of living with HIV

Access, Programs & Operations

Ensure access to quality mental health care and promote wellbeing for those living with mental illness

Systemically eliminate soil transmitted helminths (STH) as a public health problem

Other Areas of Interest & Supporting Platforms

- Vector-borne Diseases (Dengue, Chagas, Malaria)
- Vaccines (Ebola, Zika, platforms)
- Global Health Security

Our HIV Portfolio

Our goal is to reduce HIV-related morbidity and mortality and to help those living with HIV to achieve an undetectable viral-load and improved quality of life.

Through our research and development programs, we drive continuous innovation across the whole continuum of HIV care to:

Simplify and advance therapies including long-acting

Expand access to treatment

Engage and educate communities

Explore prevention tools for women

Work towards a preventive HIV vaccine

Explore potential curative strategies

Darunavir and Rilpivirine: from Single Tablets, to Single Tablet Regimens

Long Acting Therapy for HIV Treatment

- Despite the success of daily oral therapy, considerable interest exists in LA treatment options (simplify adherence, no daily reminder HIV infection, avoid stigma)
- Collaboration Janssen – ViiV for development complete LA regimen
  - Cabotegravir (CAB) is an HIV-1 integrase strand transfer inhibitor
    - Oral 30 mg tablet: $t_{½}$ ~40 hours
    - Long-acting IM injection, 200 mg/mL: $t_{½}$ ~40 days
  - Rilpivirine (RPV) is an HIV-1 non-nucleoside reverse transcriptase inhibitor
    - Oral 25 mg tablet: $t_{½}$ ~50 hours
    - Long-acting IM injection, 300 mg/mL: $t_{½}$ ~90 days

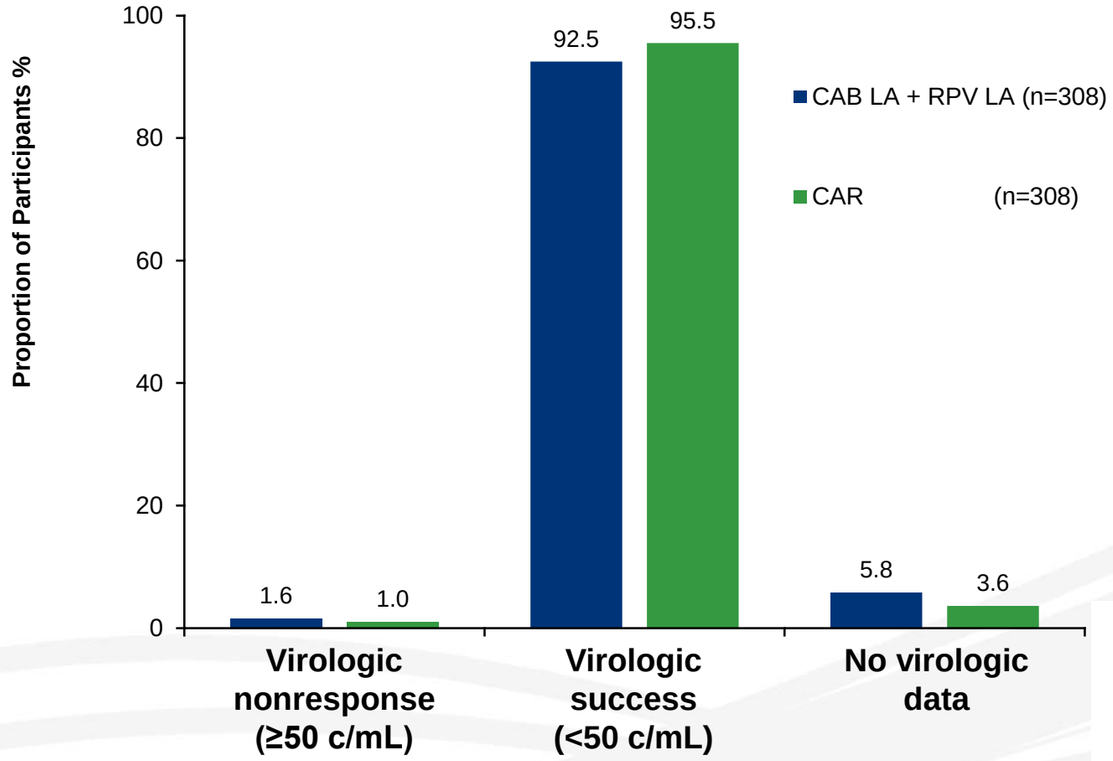
- LATTE-2: CAB LA + RPV LA given every 4 or 8 weeks maintained HIV-1 RNA <50 c/mL for >3 years[1]
- **Two pivotal phase 3 studies (ATLAS[3] and FLAIR[2]) have reached their primary endpoints at 48 weeks**

CAB, cabotegravir; IM, intramuscular; LA, long-acting; RPV, rilpivirine; t½, half-life.

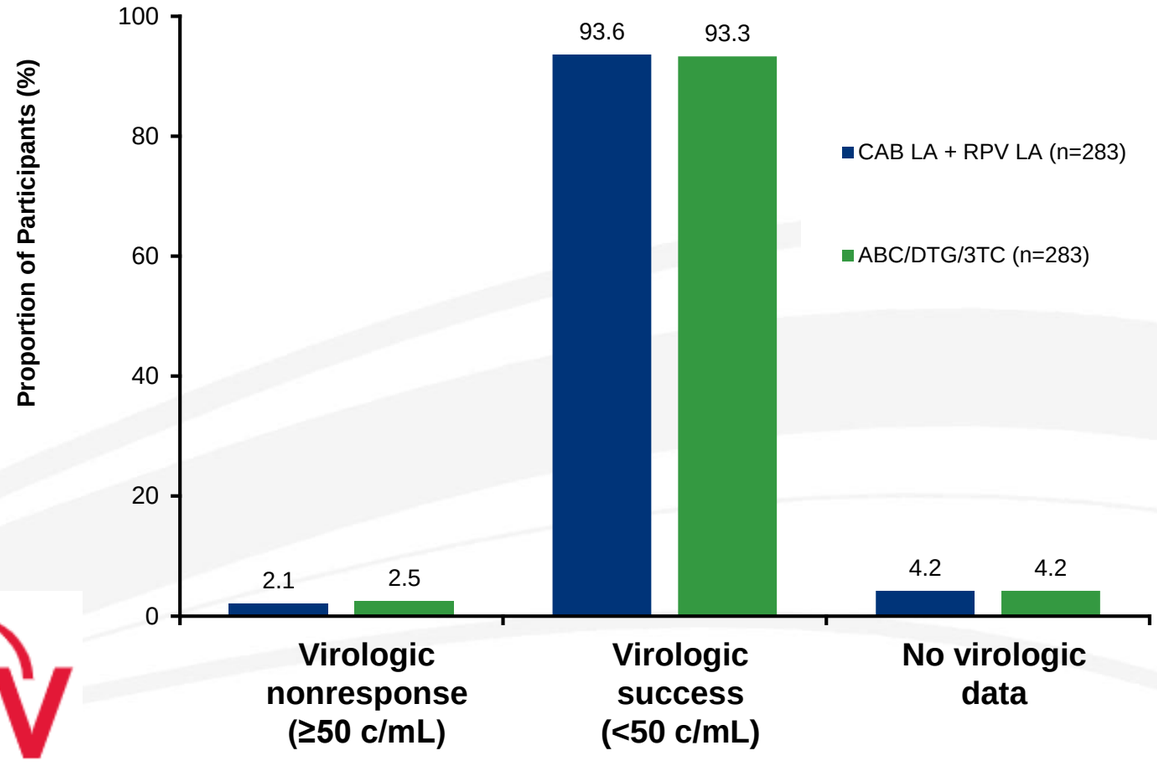
1. Margolis D, et al. HIV Glasgow 2018; UK. Poster 118; 2. Orkin C, et al. CROI 2019; Seattle, WA. Abstract 140; 3. Swindells S, et al. CROI 2019; Seattle, WA. Abstract 139.

Data Presented at CROI 2019 Show Similar Efficacy of LA Injectable to Daily Oral Therapy

ATLAS: Establish noninferior antiviral activity of monthly LA regiment vs continuing CAR



FLAIR: Establish noninferior antiviral activity of monthly LA regiment vs continuing DTG/ABC/3TC



LA Injectable is a collaboration with ViiV Healthcare

CAB, cabotegravir; CAR, current ART; CI, confidence interval; ITT-E, intention-to-treat exposed; LA, long-acting; NI, noninferiority; RPV, rilpivirine.

Data Science - HIV Drug Resistance Hot Spot Identification

Overall Goal

Identifying HIV resistance hot spots in LMIC's to inform countries and stakeholders on the level, patterns and trends in HIV drug resistance

Scaling Potential

Applicability to other countries, diseases areas

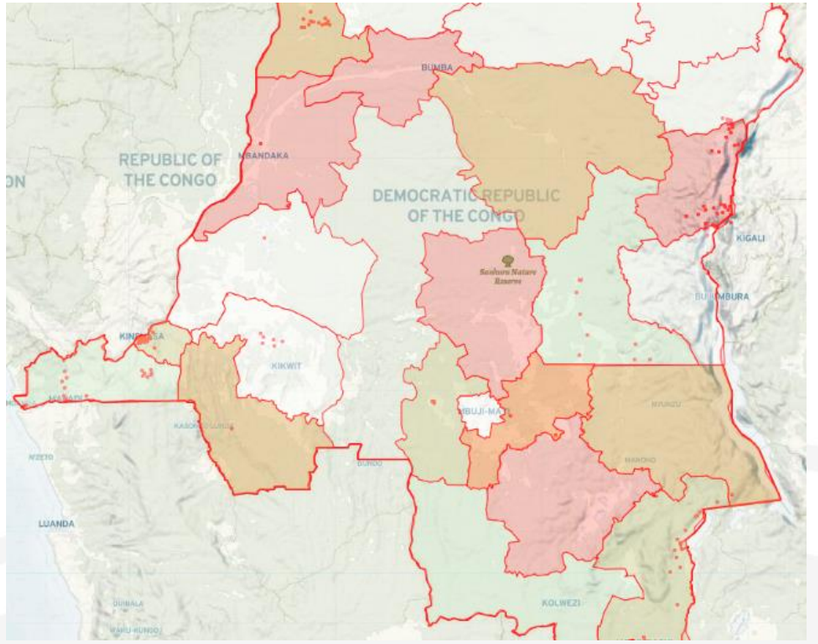
Data & Technologies

Routinely collected data PNLS and Cordaid

Machine Learning, Decision Trees, Random Forest (RF)

BLUESQUARE

Interactive dashboard drug stock risk by DRC province



Global feasibility model implemented

Data engineering

Dashboard

VLS data

Decision Point 1 Model

Decision Point 2 Model

Decision Point 3 Model

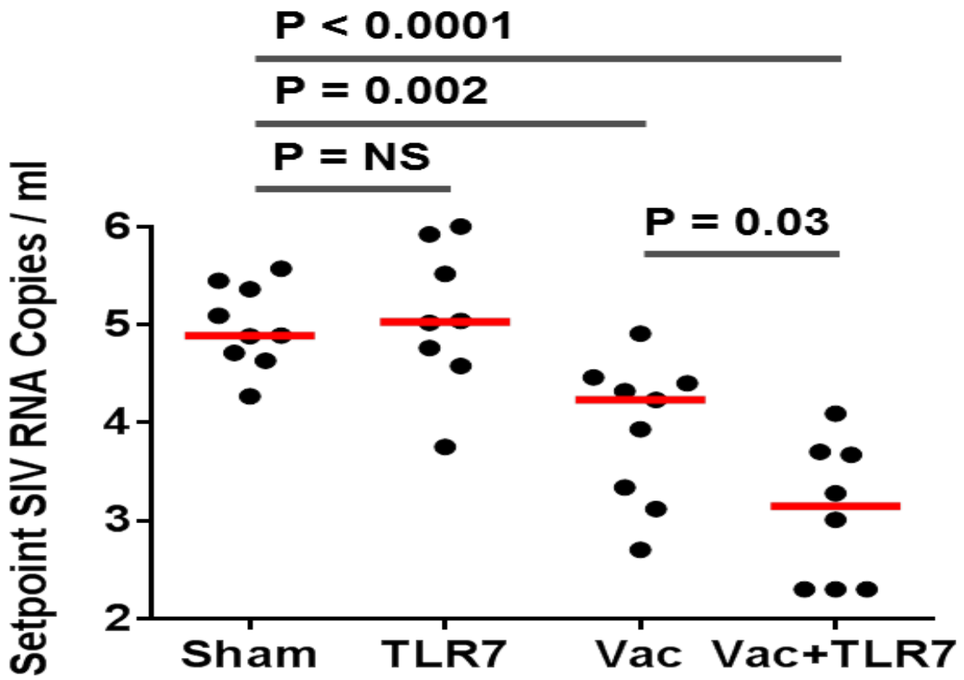
Global Model 2017	DRC kick-off Q1/2018	DRC Dashboard Q2-Q3-Q4/2018	DRC ML Model Q1-Q2/2019	Additional Country/Data Q3-Q4/2019

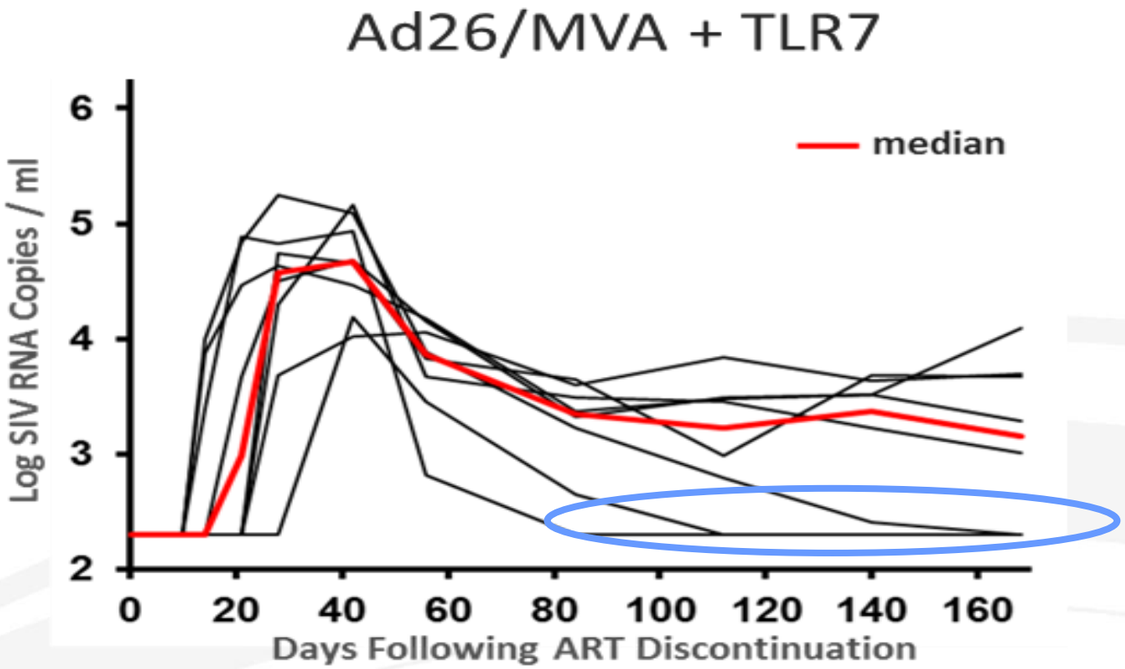
Early Research: HIV Therapeutic Vaccine

Aim: We are collaborating with partners to develop a therapeutic vaccine approach to allow HIV-infected patients to control their HIV infection through robust immunity replacing HAART: treatment-free remission

Hypothesis: An immunologic approach inducing potent antiviral cellular and humoral immune responses, in combination with immuno-modulators (and/or latency activators) will control the viral load (and possibly reduce the viral reservoir) in HIV-1-infected patients after discontinuing HAART

Ad26, MVA SIV vaccine + TLR7 regimen in SIV infected ART suppressed NHP provides viral load control in 3 out of 8 animals following ART interruption

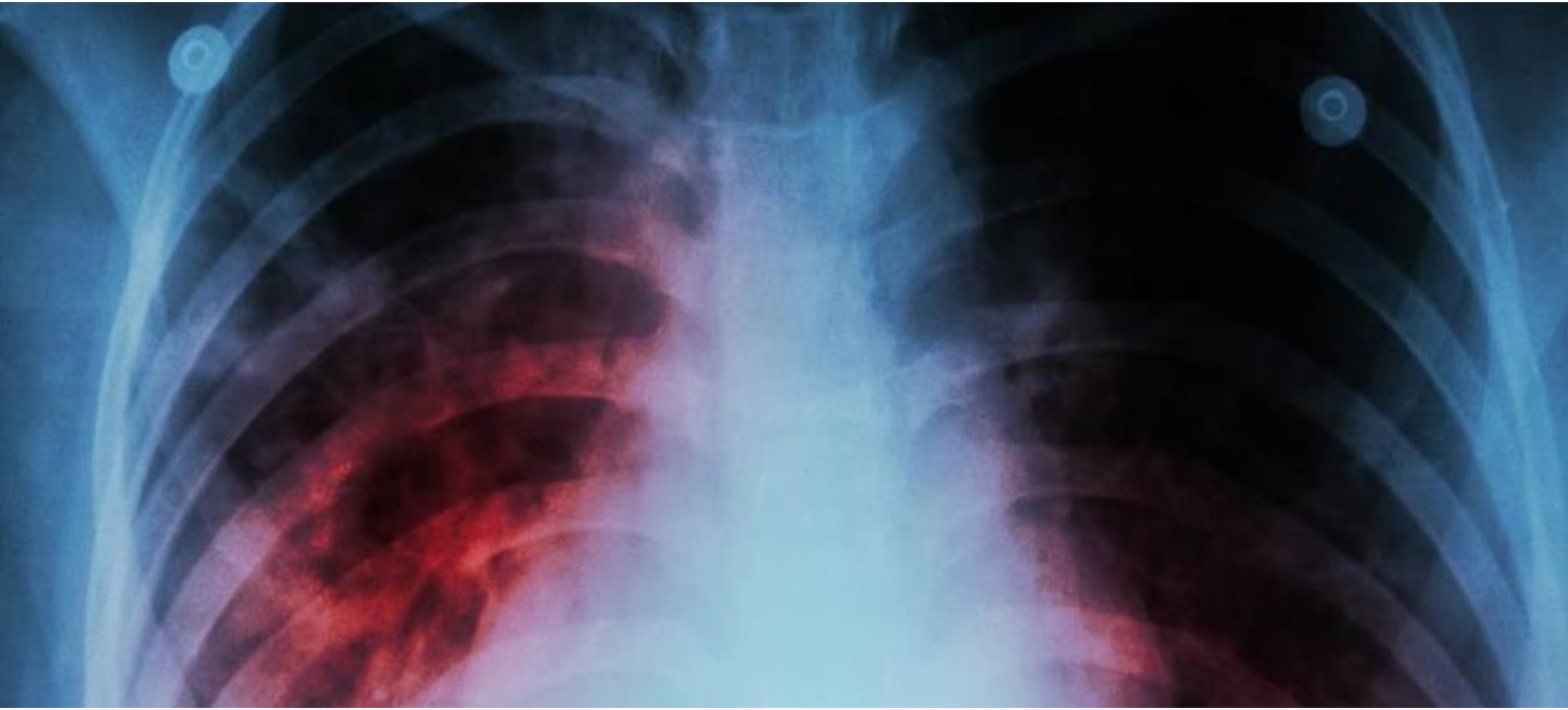




33% (3 of 8) NHPs **virologic control**
to undetectable levels following ATI

Borducchi, Barouch *et al*.
Nature, 2016: 540(7632):284-287

Discovery & Development: Tuberculosis (TB)



Multi Drug-Resistant TB: Huge Unmet Medical Need

TB is the leading cause of death globally from a single infectious agent

Low diagnosis rates

< 23% *of estimated MDR-TB cases detected*

Few treatment options

- **Toxic**
  Severe and difficult to tolerate side effects
- **Lengthy**
  9-24 months
- **Costly**
  $3B annually for just second-line drugs

22% *of MDR-TB patients receive treatment* ***= 126K patients***

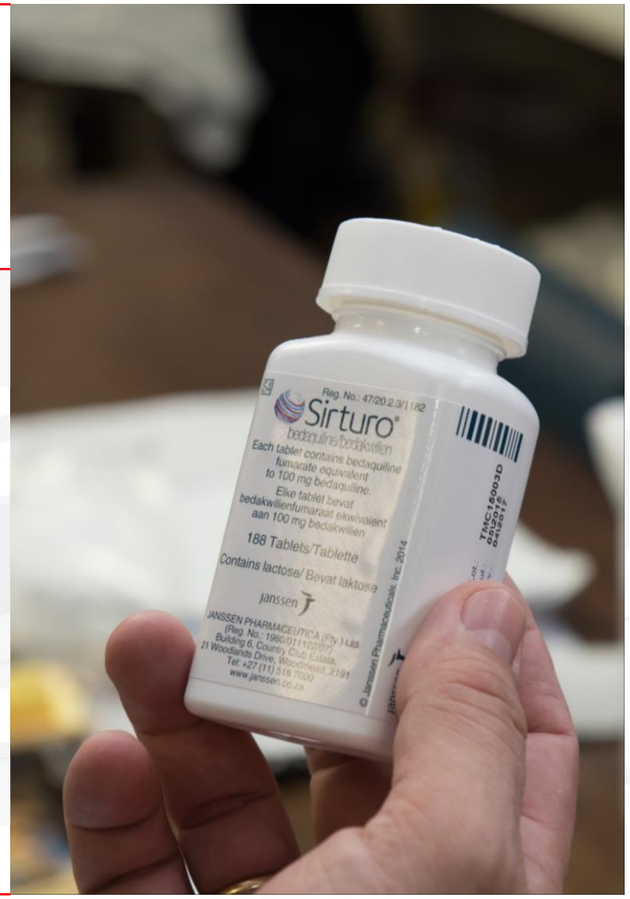
Poor treatment outcomes

Average MDR-TB treatment ***success rate is 50%***

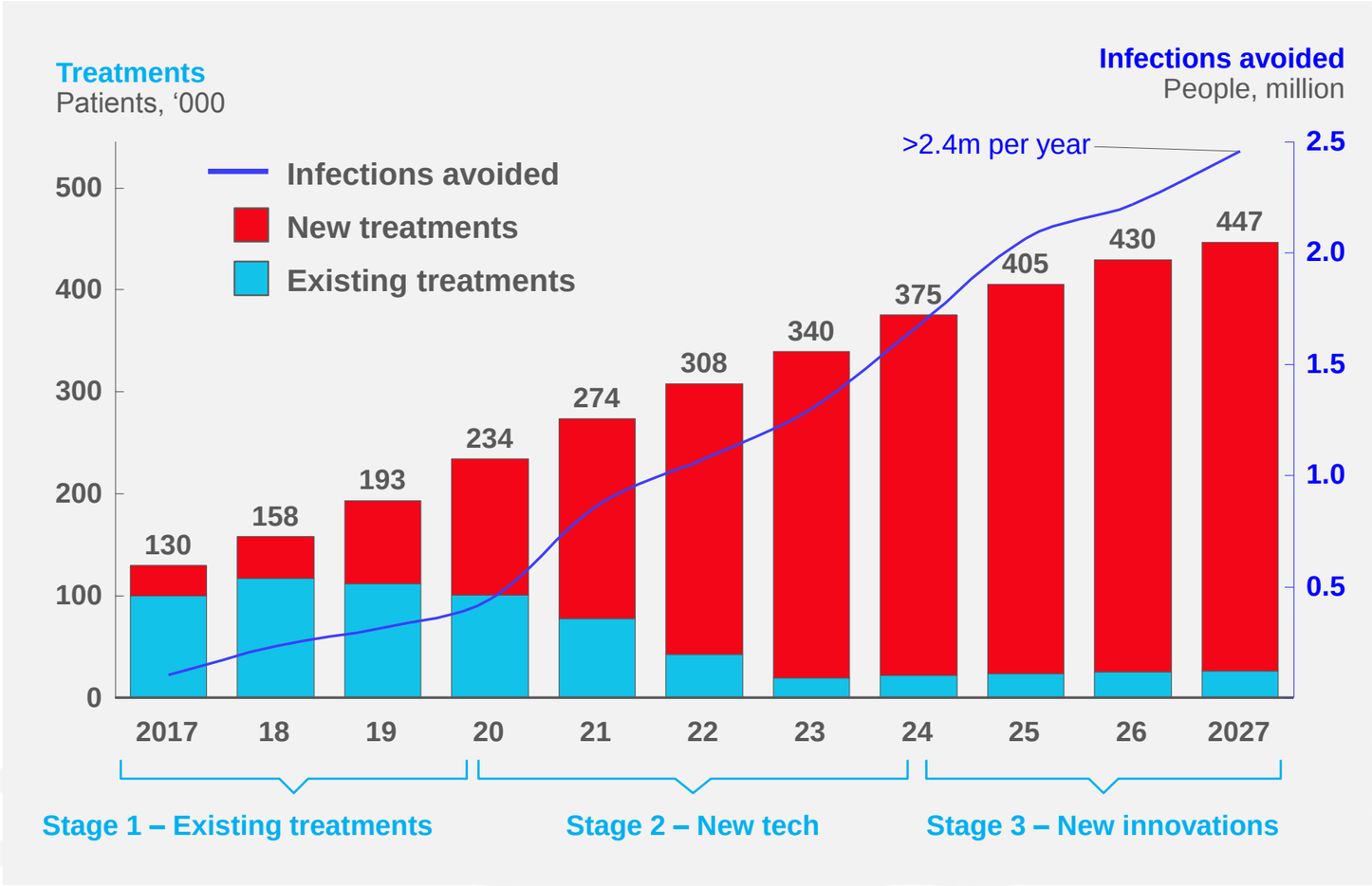
SIRTURO® (bedaquiline)

the first drug with a novel mechanism of action against TB in more than 40 years

Indication	▪ **Combination regimen for MDR-TB in adult patients when an effective treatment regimen cannot otherwise be composed / for reasons of resistance or tolerability.** ▪ **Children and adolescents (<18 years) indication under development.**
Mechanism	▪ ATP synthase inhibitor ▪ First targeted therapy for treatment of TB
Dosing	▪ 400mg QD for initiation period of 2 weeks ▪ 200mg TIW - maintenance period of 22 weeks
Formulation	▪ Oral 100 mg tablet (188-tab bottle and 4x6-tab blister carton) ▪ Water dispersible tablet for <18 years under development
Shelf life	▪ 36 months
Discovered	▪ 1997
Approved	▪ December 31, 2012



TB Innovation isn’t an option, it's a matter of life and death



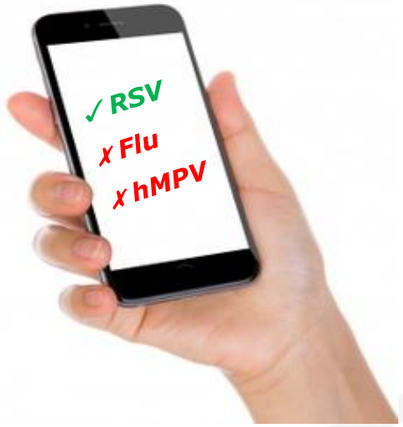
Through innovation, and expansion of WHO guidelines, we project that we can help:

- **Avoid more than 12 million infections** and
- Save 2.4 million lives, *1.8 million using new J&J innovations*

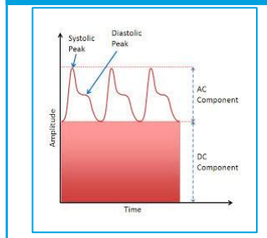
Key Unmet Needs for Respiratory Syncitial Virus

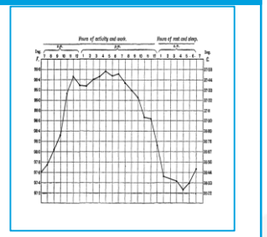
Safe and effective treatment

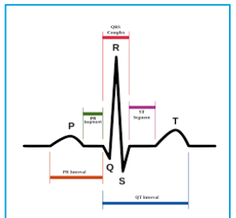
Early diagnosis



Accurate assessment of clinical impact







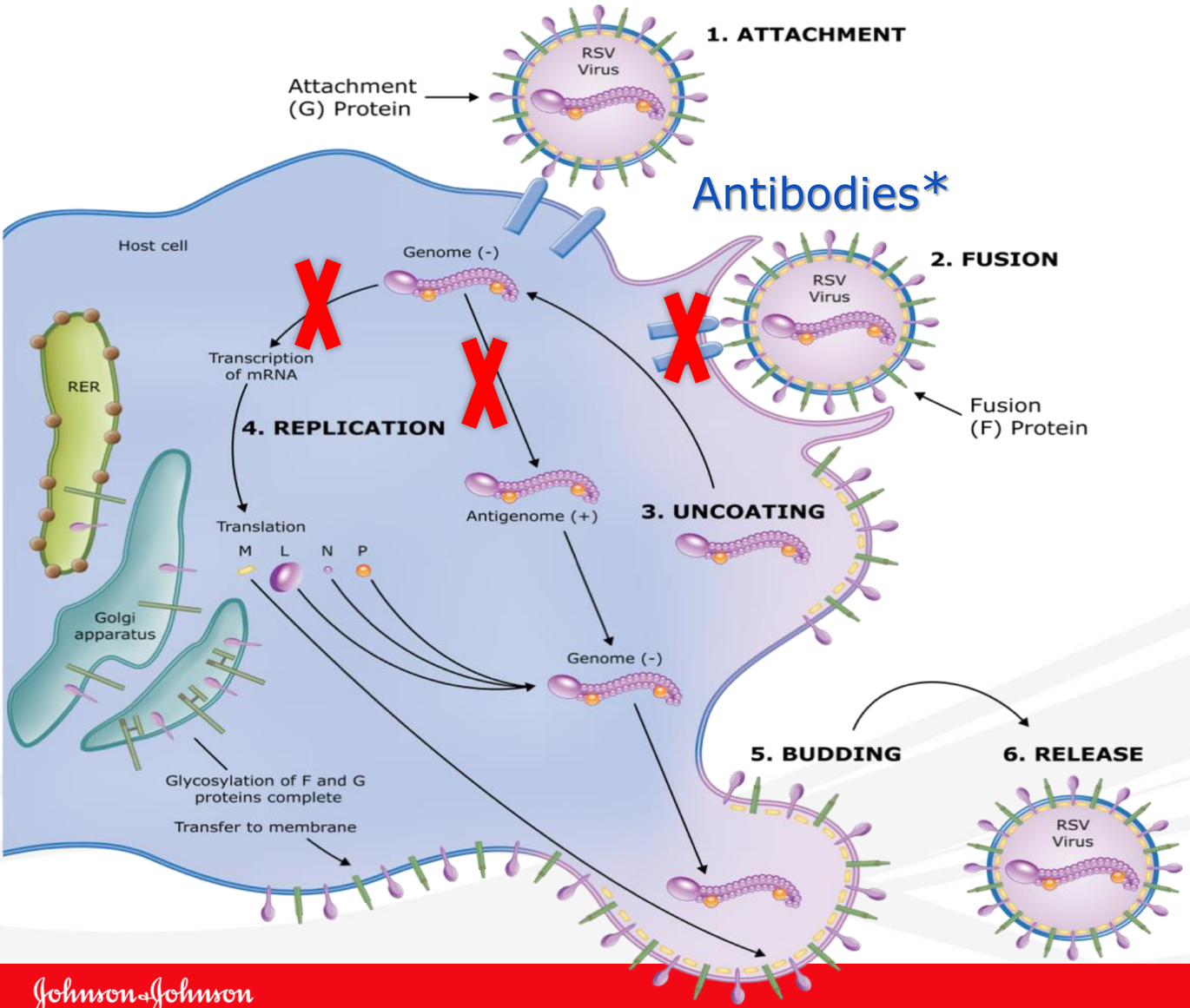
Prevent or lessen severity of complications

- 5MM outpatient visits yearly in G7
- 750k hospitalizations annually in G7
- 3.4 million children worldwide are hospitalized each season
- 200k infant deaths worldwide

https://www.medicalcountermeasures.gov/media/36777/11_willis_immunotherapeutics.pdf.

Critical Pathways and Targets: RSV

Prioritization of Biological Pathways and Targets



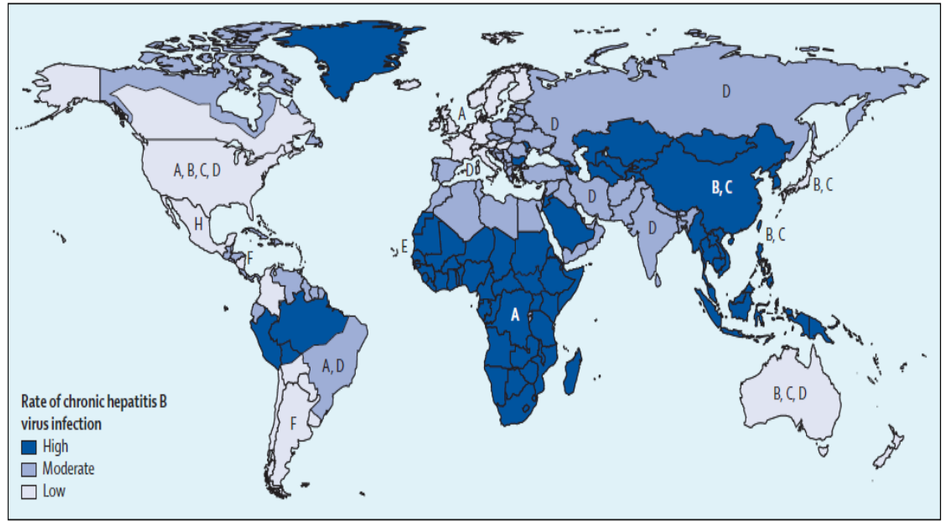
Prioritized Targets:

- **Inhibition of viral replication (polymerase)**
  - Lumicitabine – Nucleoside analog
  - JNJ-7184 - Non-nucleoside inhibitor
- **Inhibition of virus-cell fusion**
  - JNJ-8678 – RSV fusion inhibitor

*Palivizumab approved for prophylaxis

HBV is a significant unmet medical need

- **Most common chronic viral infection in world**
  - **>257 MM chronic carriers**
  - US 930k, EU5 2.2M, Japan 880k, China 87M
- **10th leading cause of death WW**
  - **789K deaths/year**
- **Leading cause of liver cancer**
  - Increased by 62% from 1990-2010
- **Current Treatment options are sub optimal**
- Nucleos(t)ide analogs (NA) for 1 year [or lifetime] → <3% "functional cure"
- Peg-IFN for 48 weeks → only 5-10% "functional cure" and poorly tolerated
- **Functional cure is sustained immune control of infection – will require combinations of drugs including those that lead to HBV-specific T cells**



Janssen Hepatitis B Strategy

Build a Portfolio of Diverse Agents and Advance a Combination Regimen

Intensify Antiviral Treatment

Reduce

cccDNA Formation &

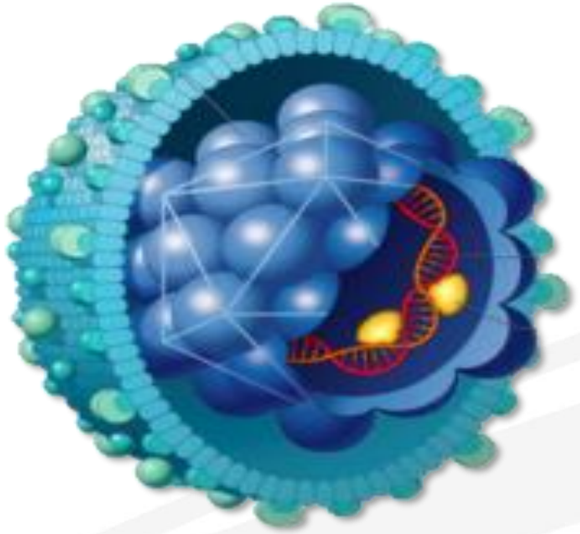
Virus Production

- CAMs
- Nucleos(t)ides

Silence/Eliminate

cccDNA

- cccDNA modulator
- Oligonucleotides
- Gene Editing
- HBx



Boost Immune Response

Boost

Effective HBV Specific T-cell

Responses

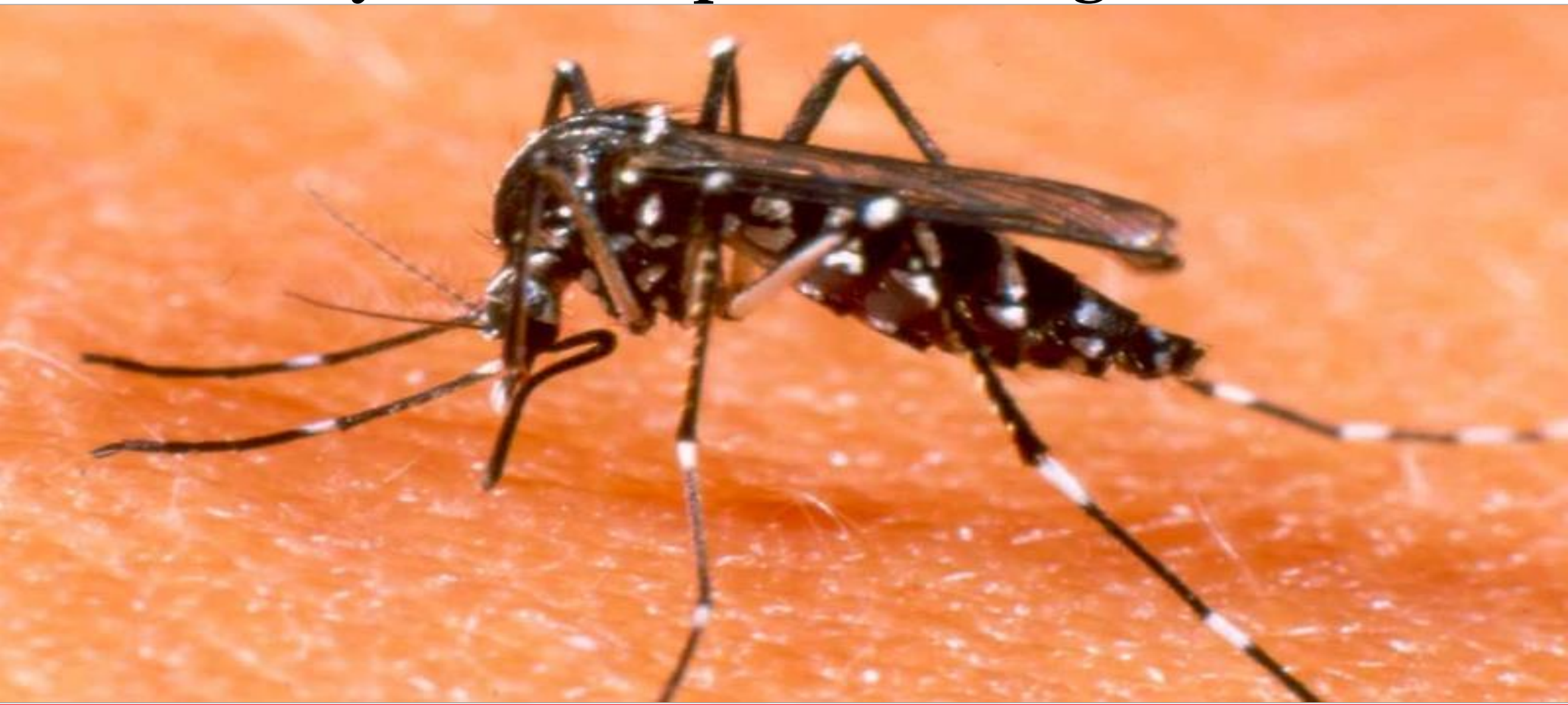
- Therapeutic Vaccine
- Checkpoint Inhibitors

Boost Innate

Immunity

- TLR Agonists
- RIG-I Agonists

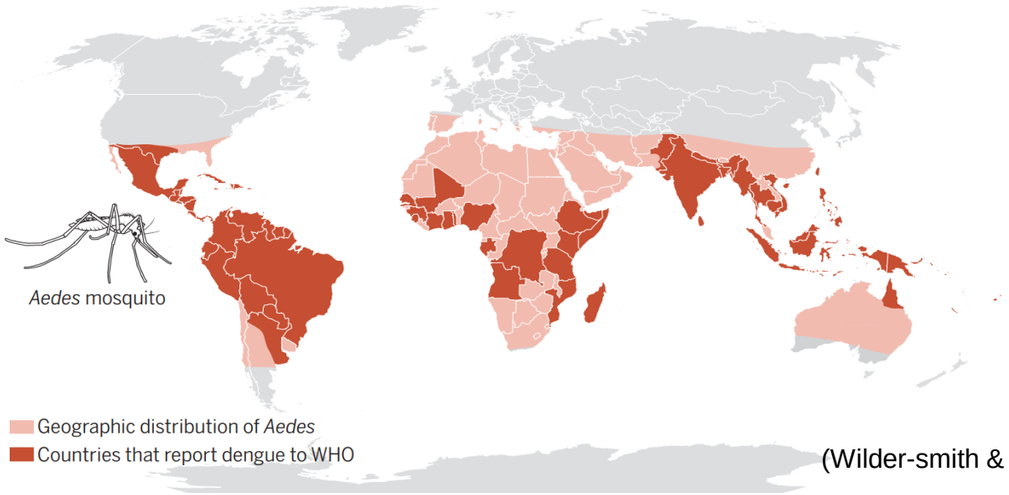
Discovery & Development: Dengue



Dengue: A Major Unmet Medical Need

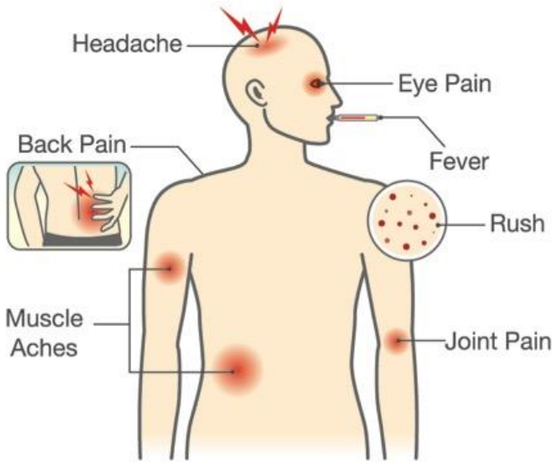
Epidemiology and Global Health concern

- Flavivirus – 4 serotypes
- Most important mosquito-borne viral disease (WHO, 2009)
- 4 billion people at risk, 390 million infections, yearly
- 100 million symptomatic infections
- Estimated global cost: $3.7 - 19.7 billion USD (2013)



(Wilder-smith & Gubler, 2015)

Pathogenesis



Dengue haemorhagic fever / dengue shock syndrome

Treatment

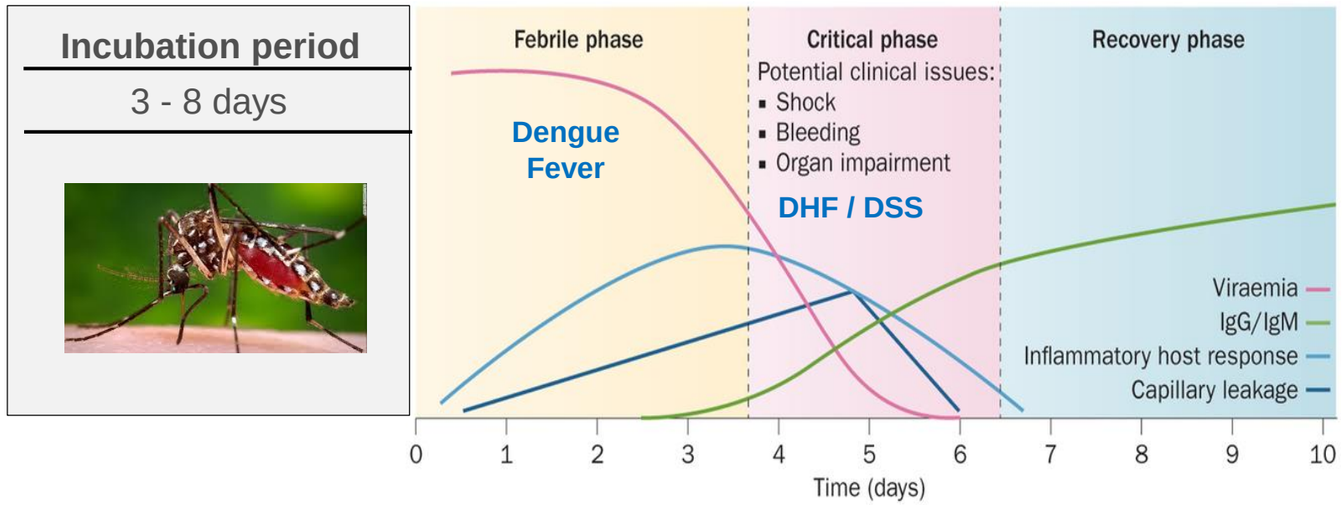
- **No dengue-specific antiviral treatment available**
- WHO adapted recommendation for Dengvaxia®
- Vaccine only used in dengue seropositive individuals, based on point-of-care Dx (not yet available)

Immediate widespread vaccine use is not foreseen

Implementing a Dengue Prophylactic Approach

Disease course

Yacoub, *et al.* 2014.*Nature Reviews Cardiology*.



Therapeutic intervention:

- What drives the pathogenesis of Dengue?
- Limited therapeutic window?

→ **Implement a prophylactic intervention strategy**

- *PrEP in Traveler setting:* 1 month intervention (cfr. Malaria prophylactic approach).

Start medication prior to travel → **Enter endemic area** → **Back to home**

Preparative medication | *Taking medication in endemic area* | *Follow up medication*

- First-in-class antiviral small molecule for the treatment and/or prevention of dengue, both for travelers to and vulnerable populations living in dengue-endemic areas

Data Science - Dengue Hot Spot Identification

Overall Goal

Identify Dengue Hot Spots in support of executing the Dengue clinical trial(s) at the right time in the right locations

Scaling Potential

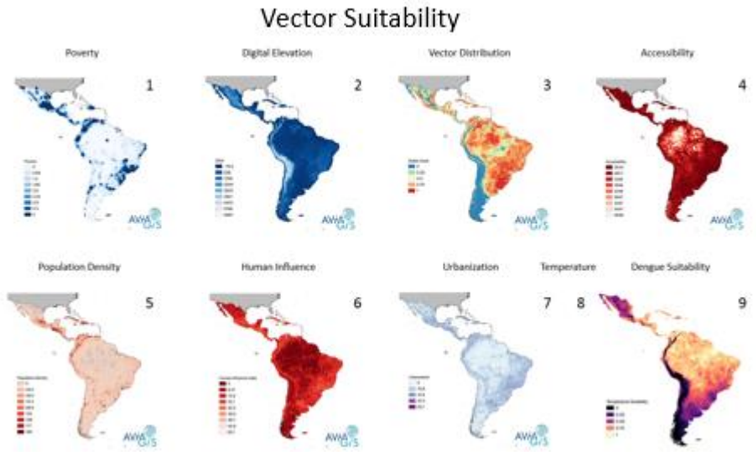
Applicability beyond Dengue clinical trials, community notification, prevention.

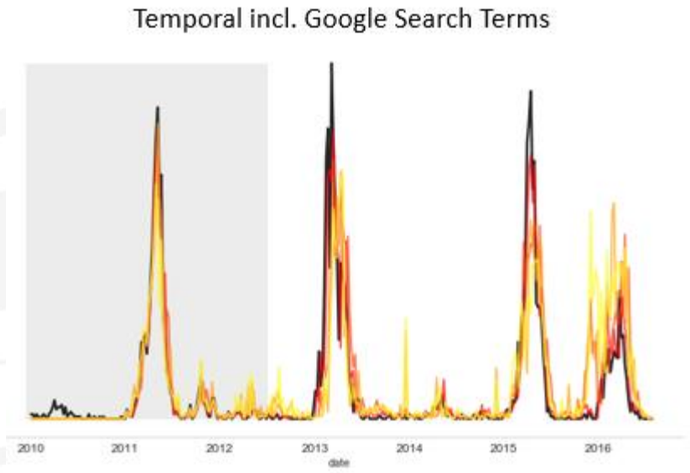
Data & Technologies

Global Gridded Geographically Based Economic Data v4…

Machine Learning – Random Forest (RF)

Google Search Terms





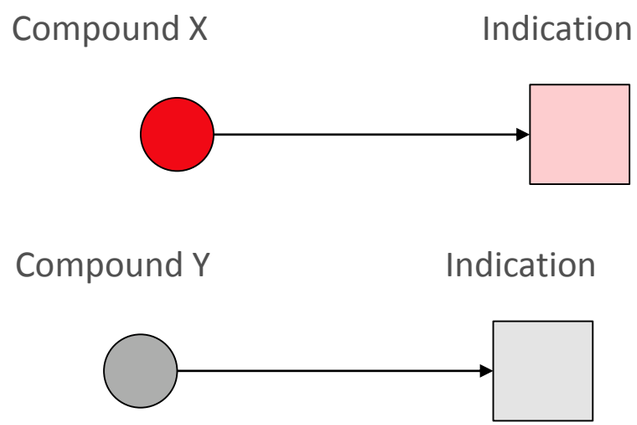
Crude Spatial	Crude Spatial-Temporal	Detailed Spatial-Temporal	Ensemble
Q1/2019	Q2/ 2019	Q1/2020	Q2/2020

Programs/Process @ Janssen

Platform trials in Hepatitis B

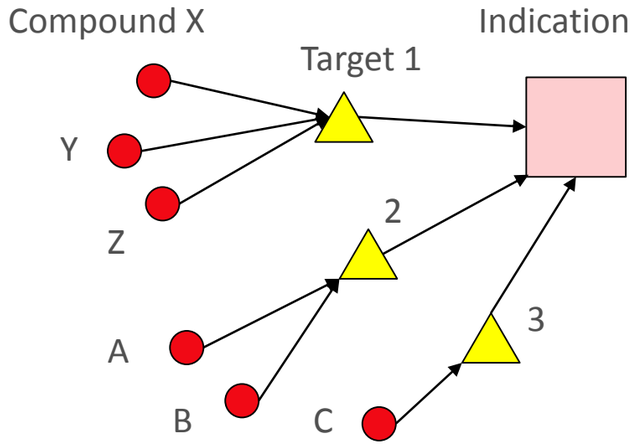
Separate studies versus platform studies

Base Case



Traditional clinical trial:
Study *one compound* against *one indication* at a time

More Efficiency



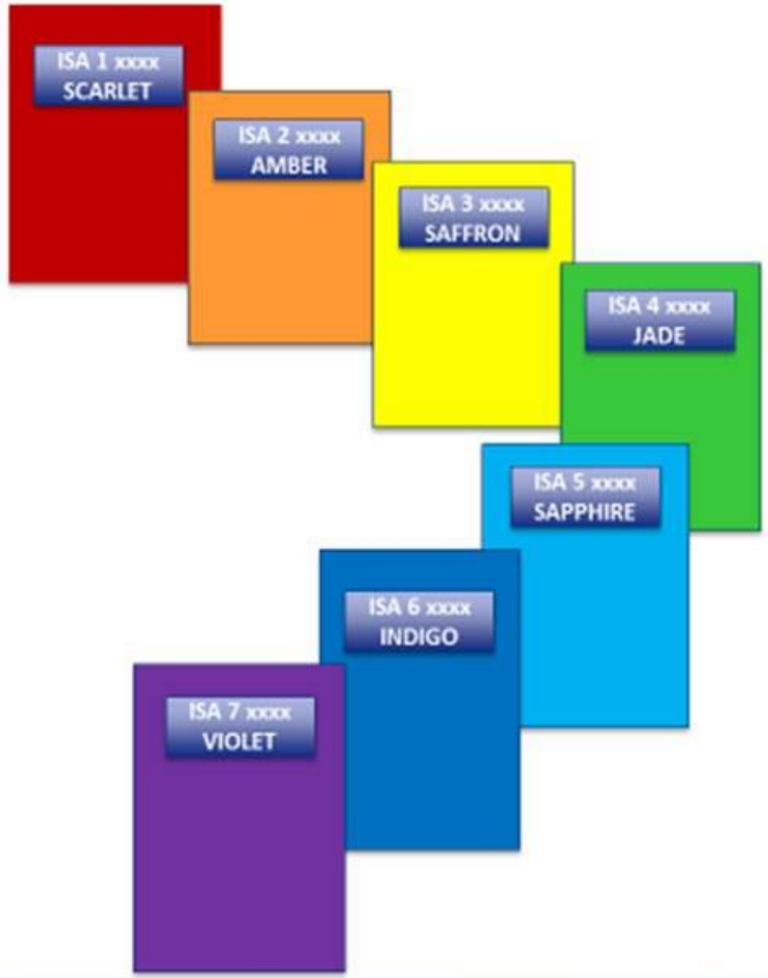
Platform trials:
Efficiently study multiple compounds, potentially multiple targets in one operational set-up

Master protocols to study multiple interventions

In a platform trial, a **Master Protocol governs the entire study**, which includes the key study design elements

Drug specific data are provided in **Intervention-specific Appendices (ISAs)** which are added as new interventions/compounds enter the trial

Janssen platform study in HBV



Towards Platform studies
for new Mycobacterium tuberculosis (TB) regimens

- **EU-PEARL: “EU Patient-cEntric clinicAl tRial pLatforms”**
  - a Consortium of European Academic and Industry Partners to develop the Operational and Regulatory Development framework for platform studies sponsored by the EU Commission and the Industry Partners

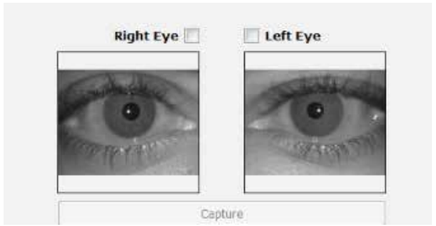
- Work Package # 5 is focused on anti TB drugs/compounds
  - develop **“selection criteria”** for drugs/combinations into the Platform Trial
  - develop master platform trial protocols (phase 2a, 2b/c and pivotal phase 3)
  - Include **new biomarkers** into trials and drug development decisions
  - Trial implementation strategy, tailored to TB-endemic developing countries
  - Develop TB lab assessment and standardisation framework
  - **assess feasibility** of integrating public health system data and networks to facilitate patient enrolment
  - develop a **sustainability** plan for full implementation

Technology: Disease Management

Leveraging Technology to Ensure Innovation is Well Accepted & Successfully Deployed

Disease Management Strategies with mHealth (Ebola, HIV, TB, Mental Health)

Community engagement strategies



Develop & install identification tools

Implement mobile technology

Capacity building

- Technical training & expertise in biometric identification and mobile technology
- Community engagement training

Ugandan Academy for Health Innovation and Impact

Ugandan Academy for Health Innovation and Impact

Johnson & Johnson CORPORATE CITIZENSHIP TRUST

Vision
Sustainable health care accessible to all in Uganda

Mission
To improve health outcomes through innovations in clinical care, capacity building, systems strengthening and research, which inform policy and practice, with a strong emphasis on HIV and TB

Budget & Sustainability
5-Year grant from J&J CCT & Janssen GPH (2015) with incremental external partnership funding models

Pillar 1: Clinical Management

- Support guideline and policy development
- Strengthen use of HIV VLM and DRT in clinical routine
- m-health interventions in clinical routine supporting healthy behaviors and adherence to treatment

Pillar 2: Capacity Building

- Post-Doc, PhD & Masters Program
- Open access peer-reviewed online training platform (**4,740 accounts**)
- Janssen Fellowship Program

Pillar 3: Local Science

- Connect for Life™ m-health in urban and rural sites (**2,393 patients**)
- Long Term Cohort (LTC) at IDI (**1.000 HIV patients** on ART >10y)
- Sub-granting via open RFA´s supporting future demonstration projects (**12 sub-grantees**)

Highlighted as Best Practice example for ‘Capacity Building’ in ATMI 2018 REPORT

22,354 beneficiaries supported in 2017-2018

The Fellowship Program

The Global Public Health Research & Development Fellowship Program

Why?

- Address high medical needs locally
- Close the R&D knowledge & experience gap
- Build local drug development capacity & networks

What?

- 2-years on the job training in Janssen
- Core Drug Development Activities
- Quality, Ethics, Leadership
- Epidemiology & Public Health (ITM Antwerp)

Profile & Practicalities?

- TB, HIV, NTD, Public health
- Mid-career, Leader, Team-player
- Paid leave of absence & Janssen compensates all local costs
- Return to home country – no brain drain

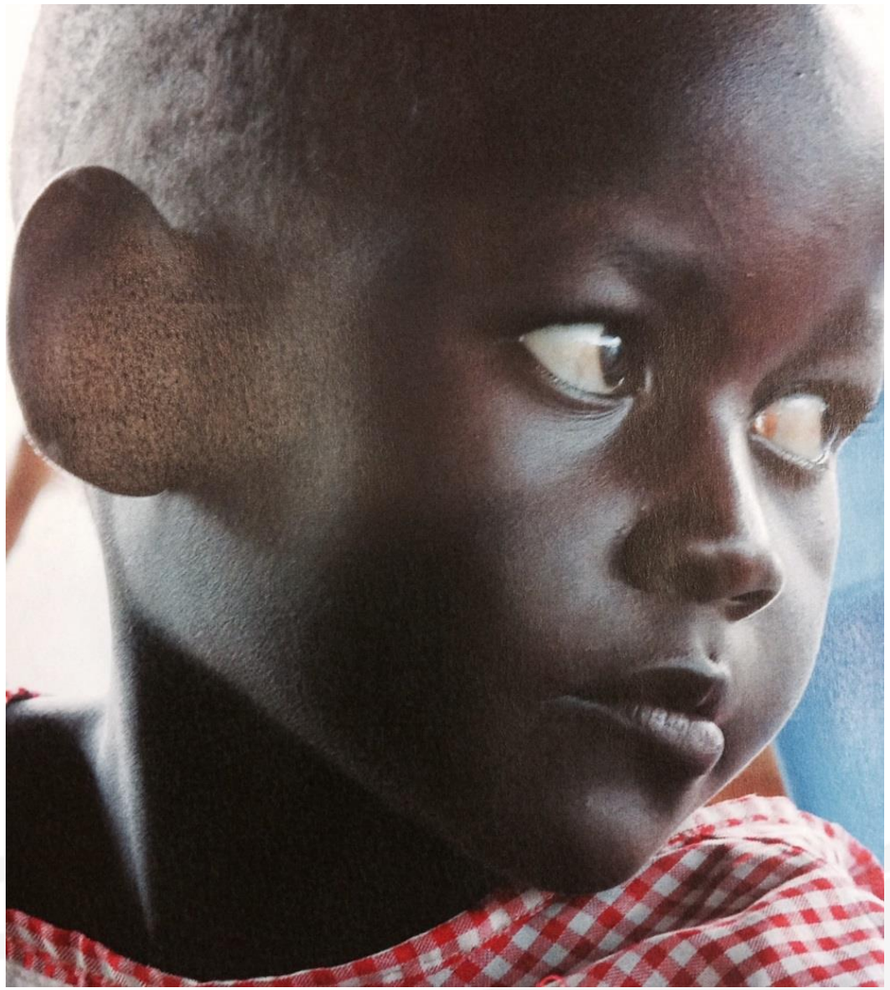
Outcome?

- Academic- teaching, capacity building
- Initiate local clinical research & participate in international development programs
- Review CTA & NDA for Health Authorities
- Work in generic/pharmaceutical companies

SIKILIZA LEO

“Sikiliza Leo” is a ki-swahili proverb

it means **“listen today”**… to find solutions for tomorrow



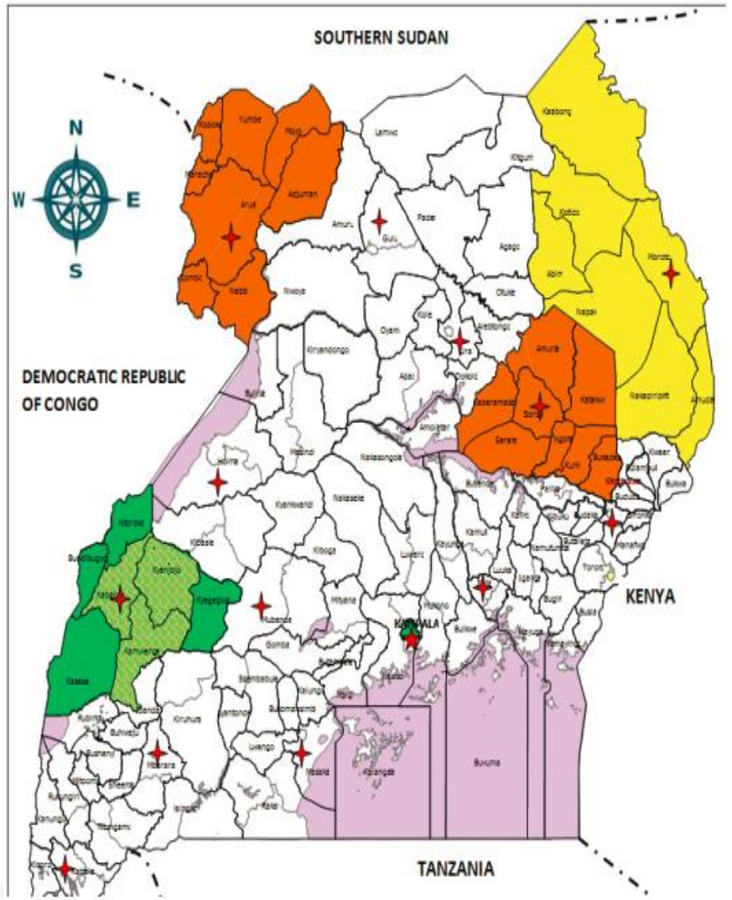
Founded in 2002 by a group of people in Tororo district in Uganda, inspired by Dr. Jens Van Roey and Dr. Dorothy Ochola, whose younger brother Peter Ochola died of AIDS that year

Supported by the Sikiliza Leo working group at Janssen Global Public Health

Our goal

- Sustainable support of development of the local communities with attention to the most vulnerable

Pepal Uganda Caring Together



Health facility performance and leadership reviewed, supported, and encouraged by district health team leaders and political representatives

1. Train health facility staff and VHTs in teamwork, time management, and communication

2. Lead health facility staff and VHTs to develop action plans

Data brought to life at facilities during monthly staff meetings to review team performance

3. Quarterly follow up visits to review action plans completed and identify additional operational gaps

District Mentors
Provided leadership training and mentorship skills in supporting health facilities reducing operational gaps and improving performance management

District Leaders
Training to strengthen leadership and governance of health facilities

Health Facility Staff and VHTs
Receive leadership training and identify operational gaps and implement cost effective action plans to address them and review team performance

Conclusion: 3Ps @ Janssen, J&J

- Our Infectious Disease & Vaccines organization works closely with Global Public Health as **every patient deserves accessible, affordable, appropriate & acceptable** innovative medicines and solutions

- Our innovation begins with the **discovery and development pipeline**, supported by programs & technologies focused on accelerating progress

- We focus on **long term sustainability** and place **people and partnerships** at the core


Janssen
Infectious Diseases
& Vaccines
PHARMACEUTICAL COMPANIES OF
Johnson & Johnson