Advancing innovations for neglected diseases during and beyond the pandemic

James Duffy, Director Drug Discovery

GHIT-PDP Webinar, Geneva, 3 September 2021 Defeating Malaria Together



Malaria | Human impact

Takes the life of a child every 2 minutes

Can kill within 24 hrs of symptom onset





Threatens **almost half** the world's population

Deprives African countries of **\$12-30 billion** every year



Is associated with drug resistance in Southeast Asia, where an estimated > 20 million cases occur every year



Is both a cause and consequence of poverty and predominantly affects vulnerable populations such as pregnant women and children



A malaria-free world | Future scenarios

"A malaria-free world, which has been WHO's vision since at least 1955, remains the ultimate goal of the global health community," *Dr. Pedro Alonso, director of WHO's Global Malaria Programme*





Strengthen existing malaria controls by improving management and use of available tools

- Stimulating the R&D pipeline for new malaria medicines, vaccines, and mosquito control tools
- Mobilizing new financing from malaria-endemic countries and donors (\$2 billion annually)



PDP model | Transforming drug discovery





MMV | Mission and strategy

MMV was launched in 1999. Our mission is to **discover**, **develop** and **deliver** new, effective and affordable **antimalarial drugs** for vulnerable populations in diseaseendemic countries



While the antimalarial **drug market** is **huge** in terms of those in need, it is **small** in terms of **profit**...

...so MMV shares the costs and risks of drug development with partners and makes antimalarial drug research happen



Antimalarial drug discoveryTarget profileDiscoverDevelopDeliverImage: Discover discoveryImage: Deliver discover d

1. New drugs for treatment or protection Fast acting Long duration

- Kill up to 10¹² parasites in a patient (*c.f.* ACTs clear 4 log₁₀ units in 48 h)
- Typically requires a duration of exposure > efficacious concentration for to 4-6 days (treatment) or 7-28 days (prophylaxis) (*c.f.* Chloroquine T_{1/2} = 20-60 days)
- Oral dose < 100 mg

2. Efficacy against all known field resistance Low propensity for resistance

• New antimalarial drugs must have a low risk of resistance generation (MIR < 7)

3. Developable as a cheap, fixed dose child-friendly combo Patient population

- Cost of treatment/prophylaxis course < \$1 (adult) / < \$0.25 (infants under 2 years)
- No contra-indication for use by children and women of child-bearing potential

Burrows, J. N. et al. Malar. J. 16, 26 (2017)



GHIT | Unlocking Japanese innovation



- Japanese scientists have an unparalleled track record in infectious disease drug discovery
- Japanese organizations have access to novel compound libraries
- Prior to GHIT, MMV had very limited success engaging with Japanese organizations
- Connected MMV to potential partners and helped to build relationship and understanding¹
- Provided clear RFPs, portfolio management, milestone criteria² and governance
- Generous investment (> ¥150,000,000)
- 1. Katsuno, K. Parasitology International, 80, 102232 (2021)
- 2. Katsuno, K., et al. Nature Reviews Drug Discovery, 14, 751–758 (2015)





GHIT-MMV | Malaria drug discovery portfolio



- > 500,000 (novel) Japanese compounds/isolated natural products screened
 - Resulting in 5 Hit to Lead projects and 2 Product development projects
- Novel and 'high value' malaria drug targets investigated: lipid kinases (PI4K), aminoacyl tRNA synthetases (KRS, PRS, etc.), enzymes (DHODH, etc.), etc.
- 4 projects with **potential** to deliver a **drug candidate** in **2022-2023**



A malaria-free world | Impact of COVID-19

- Disruptions in malaria service delivery were projected to lead to a possible • doubling in malaria deaths in 2020 compared to 2018, equating to approximately 800,000 lives lost¹
- Initial data indicates that COVID-19 has had a significant negative impact on • malaria diagnosis and treatment²



- World Malaria Report 2020 (2020) 1.
- 2. The Global Fund: "The Impact of COVID-19 on...Malaria Services and Systems" (2021)



Malaria treatment

PDP model | Beyond the target disease

PDPs are equipped to help prevent and respond to health threats*



- MMV catalyzed the discovery of drugs for COVID-19 with the COVID BOX (a set of 80 drugs with predicted activity against SARS-CoV-2)
- Worked with partners on COVID-19 clinical studies, including ReACT and ANTICOV
- PDPs build local capacity to perform research and strengthen health systems*



- Decades of investment in healthcare infrastructure/personnel enabled swift adaptation of malaria programmes in the light of COVID-19
- State-of-the-art MMV-supported medical
 centers and staff used for COVID-19 testing

*Keeping the Promise Executive Summary: https://www.keepingthepromisereport.org/report-resources

GHIT-MMV | Learnings from the partnership



- Japanese scientists see the value of working on NTD projects and have built productive project teams with strong mutual respect
- GHIT framework has enabled good decision making
- GHIT flexible 'open innovation' culture has allowed different (productive) project team configurations

- Screening Japanese compound libraries has identified novel chemistry and novel targets
- Japanese partners have given expert drug discovery and development input



Final thoughts | Opportunities for partners



- Current focus of MMV discovery
 - Target-based as well as phenotypic projects
 - Series with potential for prophylaxis as well as case-management
 - Neglected patients 'mothers and babies'
 - ...and the challenges
 - Novel mechanism of action
 - Low risk of drug resistance
 - Long duration
 - Pediatric and maternal drug safety
 - ...and the (new) opportunities.
 - Machine learning (AI)
 - Target ID
 - Development of low clearance compounds (and preclinical assays)
 - Development of preclinical assays for reprotoxicity, etc.



Final thoughts | Benefits for partners



Expanded R&D capacity in infectious diseases, strengthened reputation in the global health community

Scientific and access expertise (external and in-house)



GHIT-MMV | Project collaborators



Global Health Innovative Technology Fund





"The GHIT Fund has...a pioneering model of partnership that brings Japanese innovation, investment and leadership to the global fight against infectious disease." Dr. Margret Chan, former Director-General of the WHO



Built on partnerships | Stronger together





Thank you





