



Open Innovation at GSK Collaboration academy & pharma industry

*Javier Gamo
Director Malaria DPU
Tres Cantos, Spain*

Bangkok Dec 2017

- Introduction to the Diseases of Developing World Center (DDW)
- Three different units with three different business models
- Main pillars of DDW collaborative ways of working
 - Open Innovation and WIPO
 - Open Source
 - Open Lab
- Summary and conclusions

All animal studies were ethically reviewed and carried out in accordance with European Directive 2010/63/EU and the GSK Policy on the Care, Welfare and Treatment of Animals. The human biological samples were sourced ethically and their research use was in accord with the terms of the informed consents

Tres Cantos Medicines Development Campus



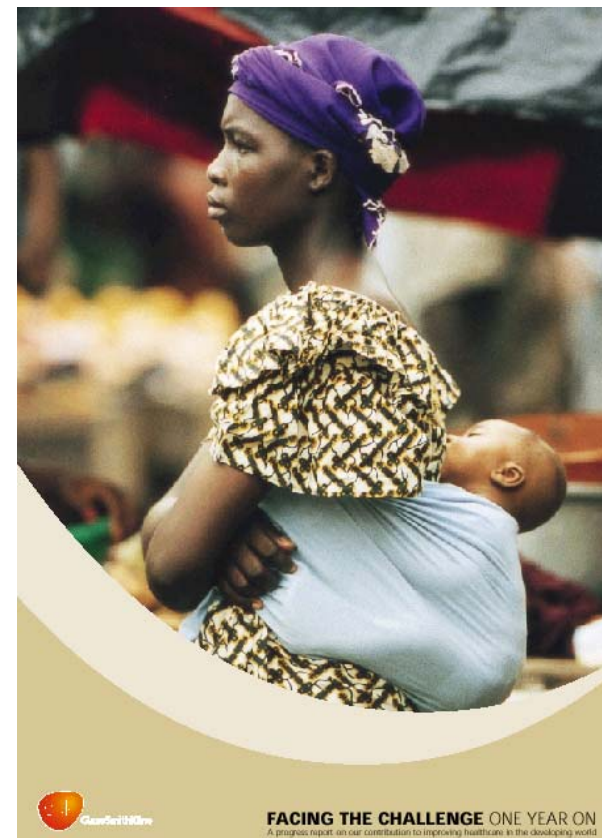
Diseases of the Developing World (DDW)

GSK diseases of the developing world



Tres Cantos Medicines Development Campus

- Focused on R&D in malaria, TB and kinetoplastid diseases
- **Collaborative with key funding partnerships**
- Projects prioritised by unmet medical need - not commercial benefit
- Approx. 120 scientists in Tres Cantos



DDW – Diseases of the Developing World

One site and three DPUs with different business models



Kineto DPU



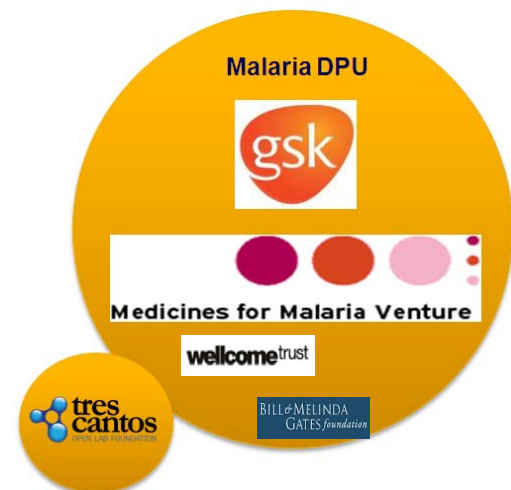
- Virtual unit acting as catalyst
- Untapped area where DDW can add value
- Key partnerships formed

TB DPU



- Partnerships formed place GSK at the cutting edge of TB research
- Pooling of TB expertise through collaborative consortia

Malaria DPU



- GSK has world class malaria research capability
- Scientific advances have provided new opportunities
- Key strategic partnership with MMV, WT & B&MGF

Three pillars of Open Innovation at DDW

Utilize our investment in DDW to act as a catalyst and stimulate research activity outside GSK



Being more flexible with our Intellectual Property

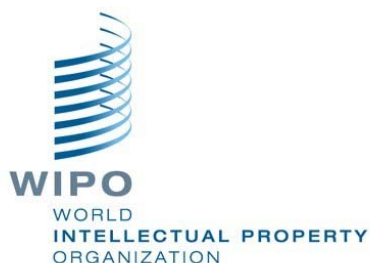
“Patent Pool”

Sharing our data and assets with the worldwide research community

“Open Source”

Providing access to our know-how and resources

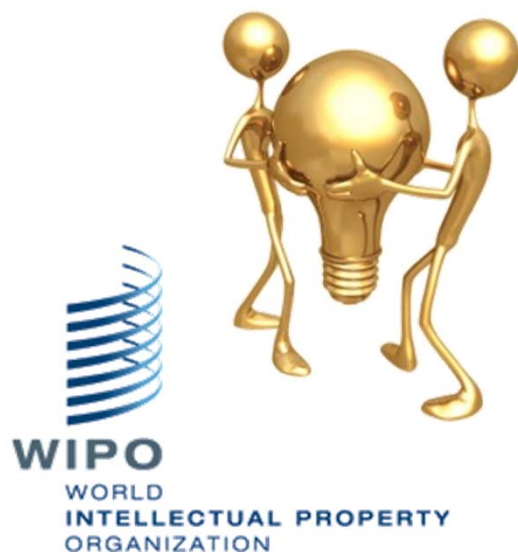
“Open Lab”



Establishment of an independent knowledge pool

2009: creation of POINT (Pool for Open Innovation against Neglected Tropical Diseases)

2010:  as POINT administrator



GSK contribution:

patents

patent applications

further knowledge and expertise

Open source: sharing antimicrobial sets



ACS Medicinal
Chemistry Letters

LETTER

pubs.acs.org/acsmchemlett

An Invitation to Open Innovation in Malaria Drug Discovery:
47 Quality Starting Points from the TCAMS

Félix Calderón,^{*1} David ...
Francisco Javier Gamo,
Araceli Mallo,¹ Pilar Ma...

Thousands of chemical starting points for antimalarial lead identification

Francisco-Javier Gamo¹, Laura M. Sanz¹, Jaime Vidal¹, Cristina de Cozar¹, Emilio Alvarez¹, Jose-Luis Lavandera¹, Dana E. Vanderwall², Darren V. S. Green³, Vinod Kumar⁴, Samiul Hasan⁴, James R. Brown⁴, Catherine E. Peishoff⁵, Lon R. Cardon⁶ & Jose F. Garcia-Bustos¹

Malaria (2010)

Nature 2010 465 (7296) 305

CHEM MED CHEM
FULL PAPERS



DOI: 10.1002/cmdc.201200428

VIP

Fueling Open-Source Drug Discovery: 177 Small-Molecule Leads against Tuberculosis

Lluís Ballell,^{*[a]} Robert H. Bates,^[a] Rob J. Young,^[b] Daniel Alvarez-Gomez,^[a] Emilio Alvarez-Ruiz,^[a] Vanessa Barroso,^[a] Delia Blanco,^[a] Benigno Crespo,^[a] Jaime Escribano,^[a]

Tuberculosis (2013)

ChemMedChem 2013 8 (2)

OPEN

New Compound Sets Identified from High Throughput Phenotypic Screening against Three Kinetoplastid Parasites: An Open Resource

SUBJECT AREAS:
HIGH THROUGHPUT
SCREENING
PARASITOLOGY

Received
3 December 2014

Imanol Peña¹, M. Pilar Manzano², Juan Cantizani², Albane Kessler², Julio Alonso-Padilla², Ana I. Bardera¹, Emilio Alvarez¹, Gonzalo Colmenero¹, Ignacio Cotillo², Irene Roquero², Francisco de Dios-Anton¹,

Leishmania, Chagas & Sleeping sickness (2015)

Sci.Rep 2015 5 8771

Antimicrobial set information is publicly available



www.ebi.ac.uk/chemblntd

BL-NTD Compound Search Results: 174 Hits

Mini Report Cards 2 Please select...

Assay	Min Value	Adjust Range	Max Value
TCMDC: % inhibition of P. falciparum strain 3D7 (at 2uM)	80		100
TCMDC: % inhibition of P. falciparum Dd2 (at 2uM)	50		100
TCMDC: % inhibition of P. falciparum strain 3D7 LDH Reporter Assay (at 2uM)	0		10
TCMDC: pXC50 determination of P. falciparum 3D7 growth	6.9		9
TCMDC: % inhibition of human HepG2 cell line (at 10uM)	0		10
TCMDC: Inhibition Frequency Index (IFI)	0		44

Predicted Target: All
 Available in ChEMBL Database Available Commercially

www.collaborativedrug.com

12869

MW 346.40
 ALogP 3.36
 PSA 49.85
 HBA 5
 HBD 0
 #Ro5 Vio. 0

%iHB 3D7 (2uM) 97
 %iHB Dd2 (2uM) 96
 %iHB 3D7 PFLDH (2uM) 2
 pXC50 3D7 6.90 (125.22nM)
 %iHB HEPG2 (10uM) 0
 IFI 0
 Chemical Cluster NR 830
 Graph Frame Cluster 223

Sources TCMDC-124156, COMMERCIAL
 Synonyms
 Annotations

8312

MW 348.02
 ALogP 3.84
 PSA 51.66
 HBA 5
 HBD 0
 #Ro5 Vio. 0

%iHB 3D7 (2uM) 97
 %iHB Dd2 (2uM) 97
 %iHB 3D7 PFLDH (2uM) 0
 pXC50 3D7 6.96 (105.44nM)
 %iHB HEPG2 (10uM) 0
 IFI 0.75
 Chemical Cluster NR 1070
 Graph Frame Cluster 366

Sources TCMDC-131990
 Synonyms
 Annotations

Thousands of chemical starting points for antimalarial lead identification

Francisco Javier Gamó,¹ Laura M. Smež,¹ Jaime Vidal,¹ Cristina de Cozar,¹ Emilio Alvarez,¹ Jose-Luis Lavandera,¹ Dana E. Vandenberg,¹ Darren V. S. Green,¹ Vinod Kumar,¹ Samiul Hasan,¹ James R. Brown,¹ Catherine E. Peirhoff,¹ Lon R. Cardon¹ & Jose F. Garcia-Bustos¹



An Invitation to Open Innovation in Malaria Drug Discovery: 47 Quality Starting Points from the TCAMS

Félix Calderón,^{1,2} David Barros,¹ José María Bueno,¹ José Miguel Coterón,¹ Esther Fernández,¹ Francisco Javier Gamó,¹ José Luis Lavandera,¹ María Luisa León,¹ Simon J. F. Macdonald,^{1,5} Araceli Mallo,¹ Pilar Manzano,¹ Esther Porras,¹ José María Fandor,^{1,3} and Julia Castro^{1,4}

Malaria (2010)
Nature 2010 465 (7296) 305



Fueling Open-Source Drug Discovery: 177 Small-Molecule Leads against Tuberculosis

Lluís Balcells,^{1,2,4} Robert H. Bates,^{3,6} Rob J. Young,^{3,6} Daniel Alvarez-Gomez,^{1,6} Emilio Alvarez-Ruiz,^{1,6} Vanessa Barroso,^{1,6} Delia Blanco,^{1,6} Benigno Crespo,^{1,6} Jaime Escribano,^{1,6}

Tuberculosis (2013)
ChemMedChem 2013 8 (2)

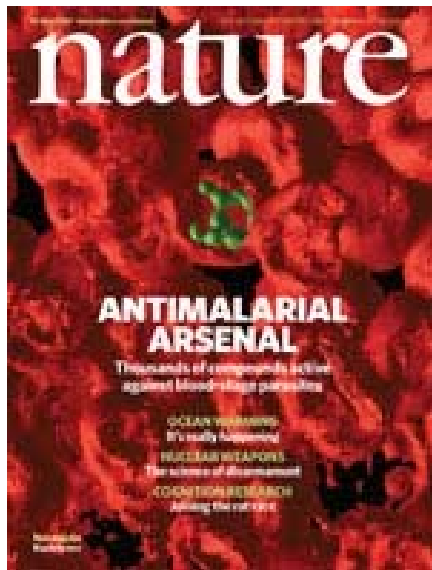
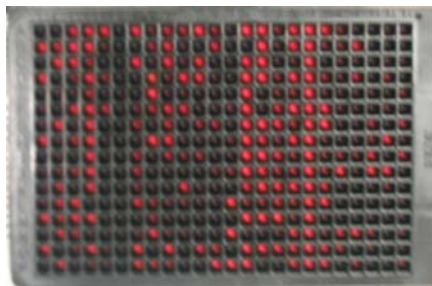
New Compound Sets Identified from High Throughput Phenotypic Screening against Three Kinetoplastid Parasites: An Open Resource

Inmaculada Peña,¹ M. Pilar Manzano,¹ Juan Carrizosa,¹ Alvaro Krasak,¹ Julio Alonso Padilla,¹ Ana L. Bardenes,¹ Emilio Alvarez,¹ Gonzalo Colmenero,¹ Ignacio Collin,¹ Irene Rojano,¹ Francisco de Dios-Antón,¹

Leishmania, Chagas & Sleeping sickness (2015)
Sci.Rep 2015 5 8771

<http://pubchem.ncbi.nlm.nih.gov/>

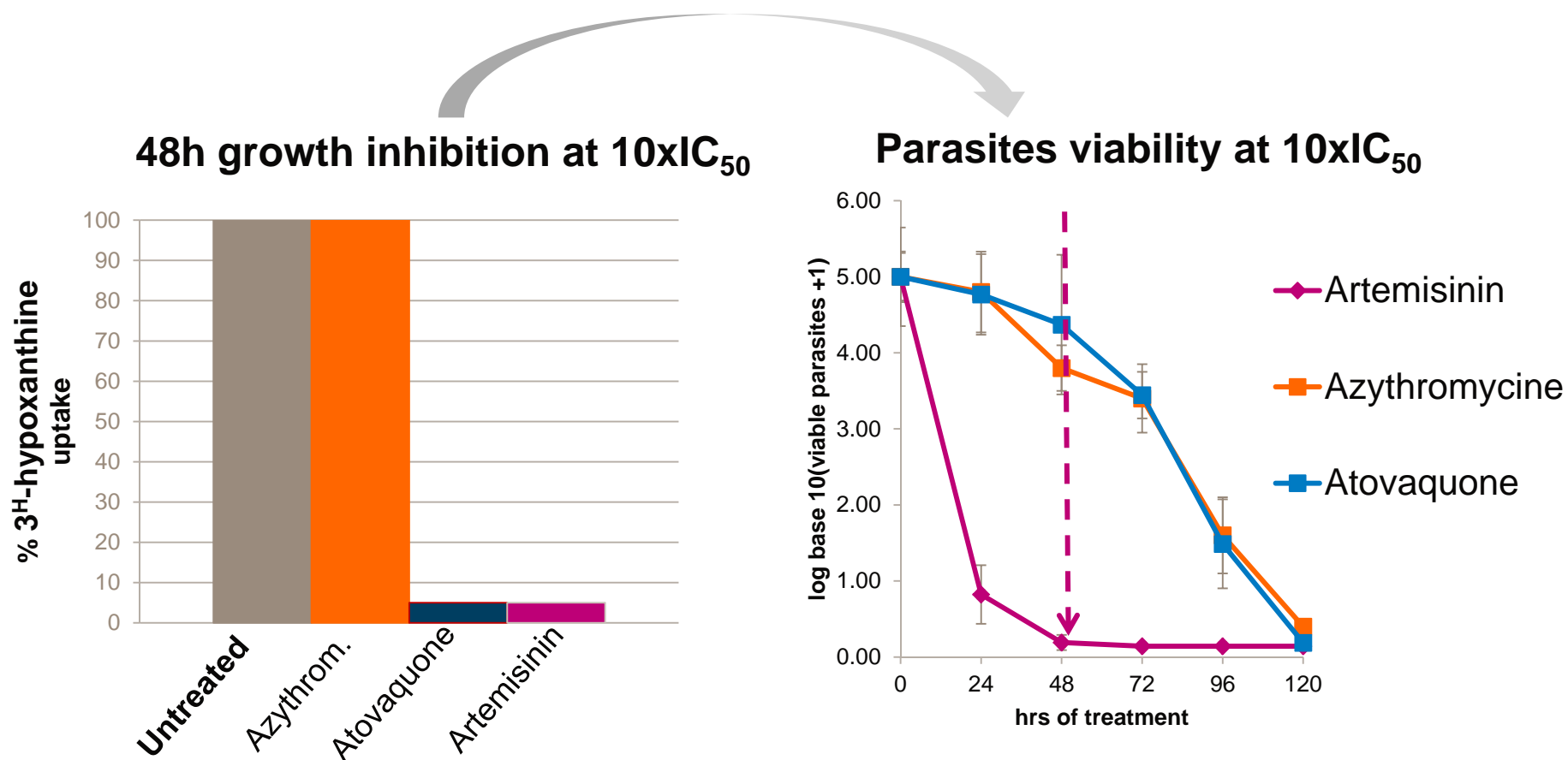
Sharing not only information but samples with the scientific community



Collaborating with scientific community through internal platforms



- Compounds from external partners are profiled using proprietary state-of-the-art assays



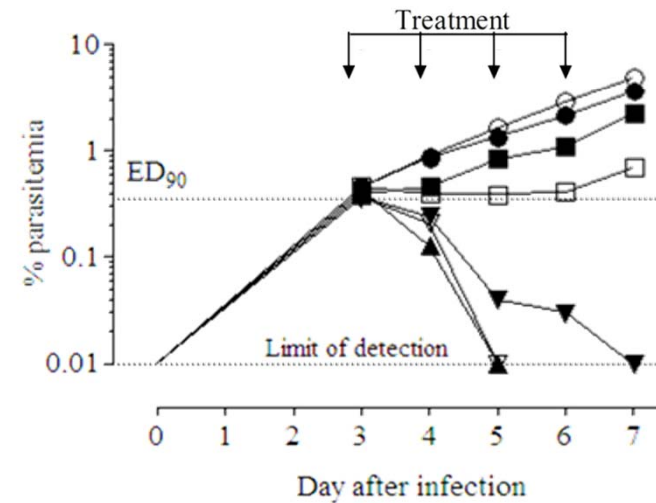
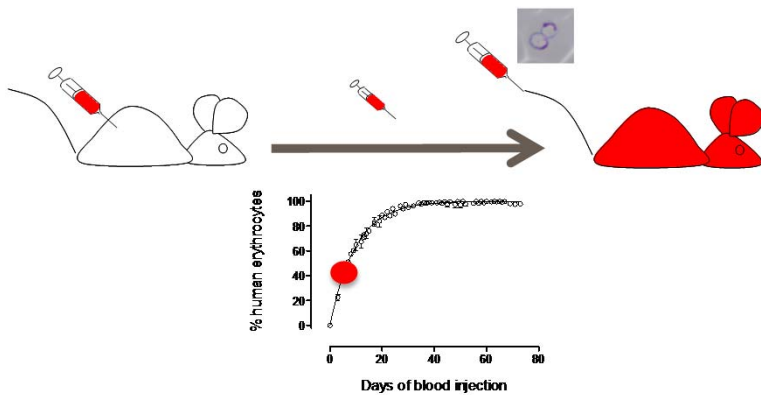
- PRR (**Parasite Rate Reduction**) to determine **killing profile** of antimalarials

Collaborating with scientific community through internal platforms

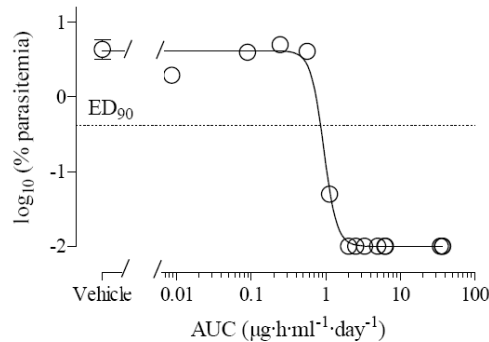


- Compounds from external partners are profiled using proprietary state-of-the-art assays

Mice engrafted with human RBC



4-day test
ED₉₀



- ***P. falciparum* humanized mouse** model to assess efficacy against real pathogen

Joining forces: the Open Lab



ABOUT THE OPEN LAB

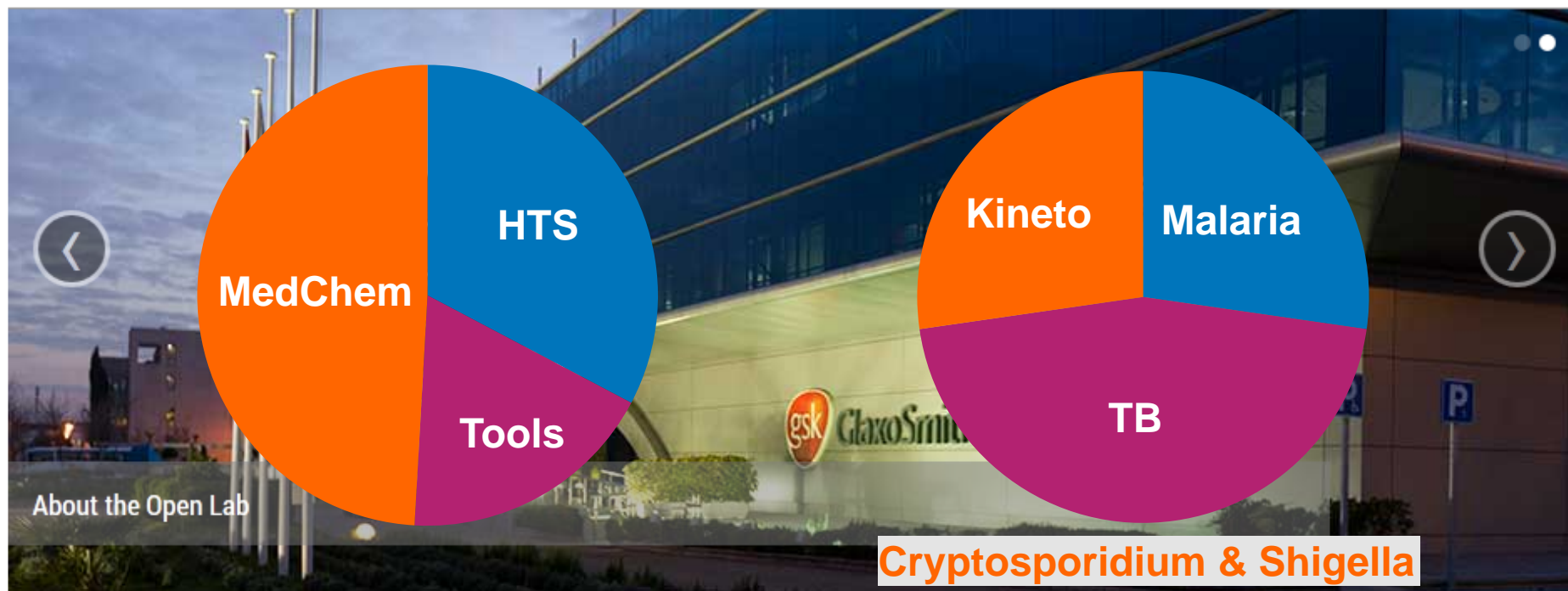


OUR APPROACH

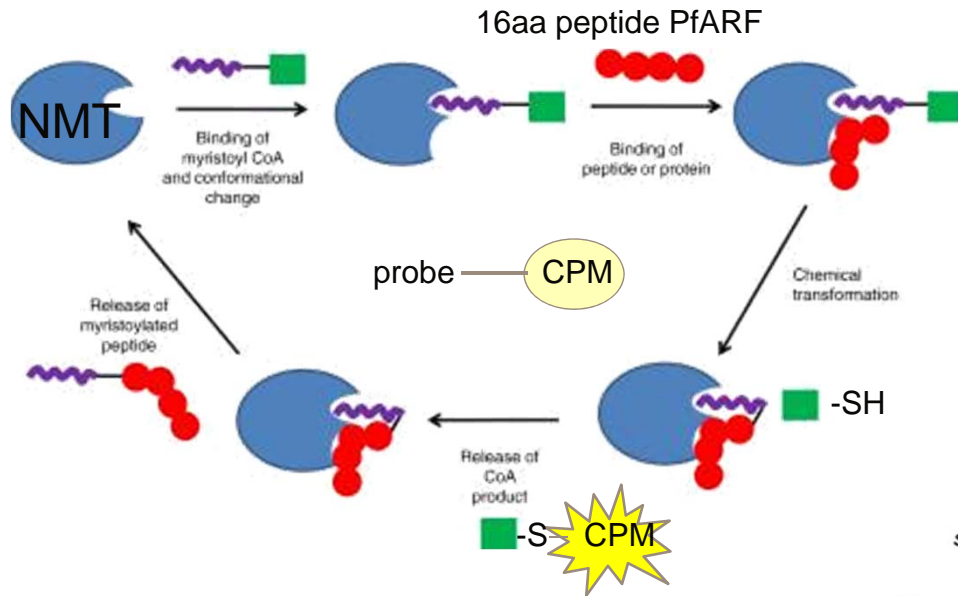
www.openlabfoundation.org

RESEARCH PROJECTS

COLLABORATE WITH US

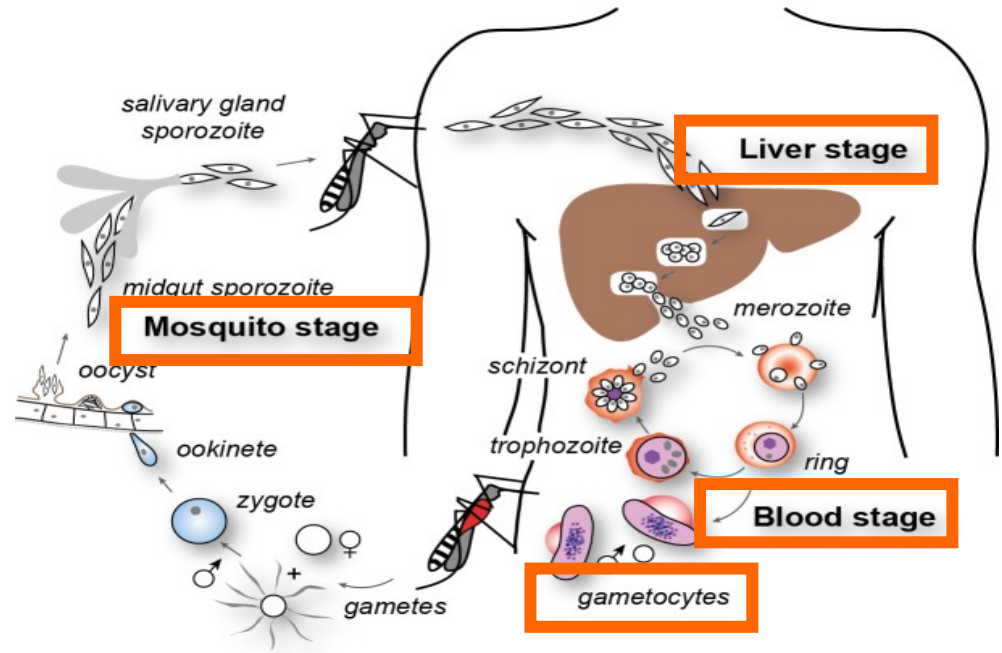


Open Lab project: antimalarial NMT inhibitors



Center for Infectious Disease Research

Prof. Alexis Kaushansky
Dr. Anke Jarupa



Adapted from Cowman et al. 2012

High Throughput Screening for NMT inhibitors



GSK screening collection + TCAMS (1.7 M compounds)

Primary HTS (PvNMT@ 10 uM)

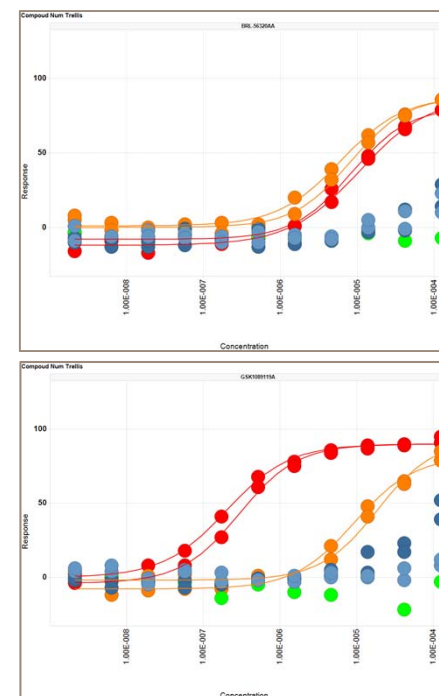
Confirmation
(PvNMT@10uM, n=2)

Dose Responses
(PvNMT, PfNMT, hNMT1,
hNMT2, Cs)

Compound
selection

Commit to Start of chemistry

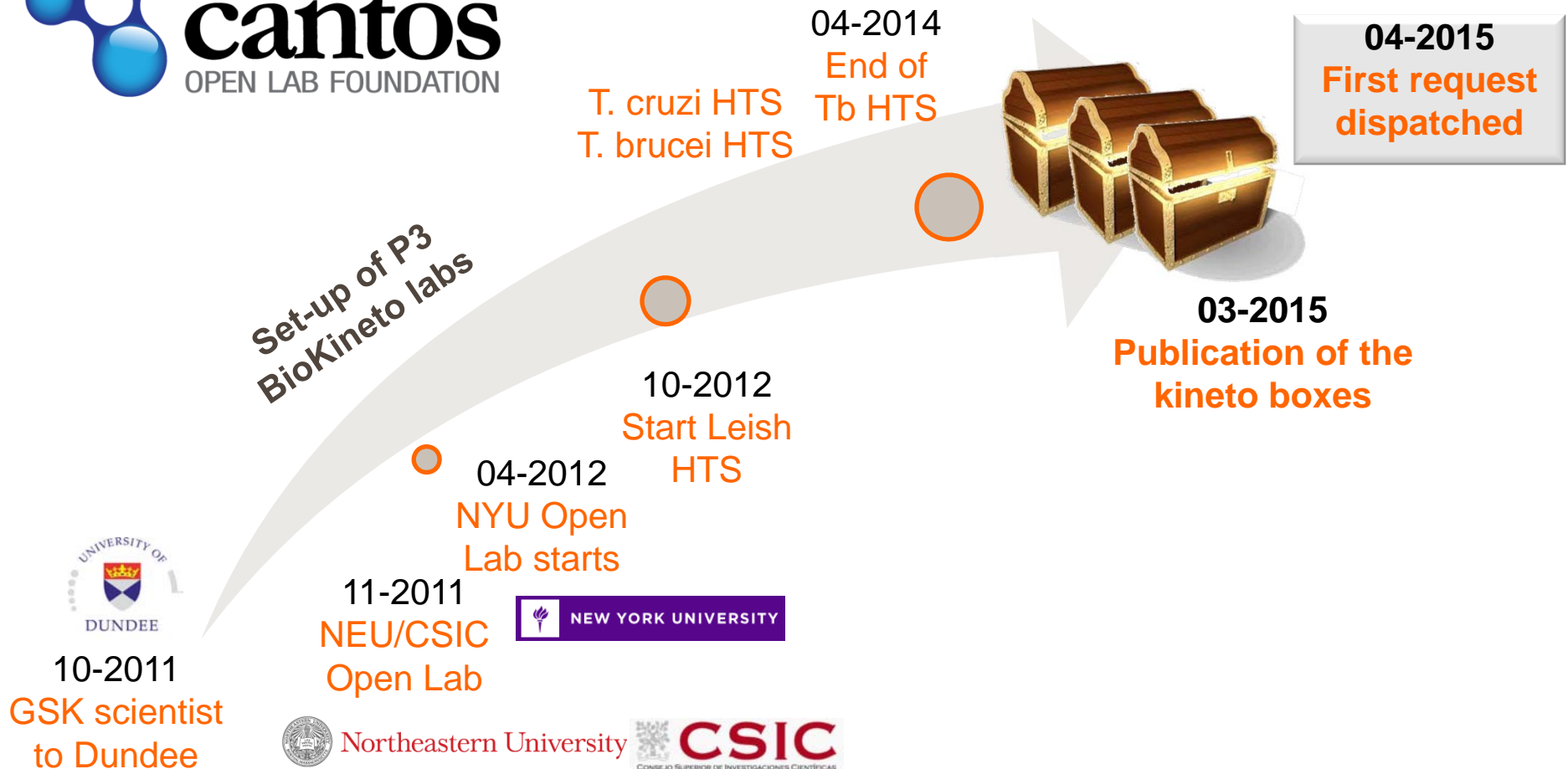
1536 well plate format
3 weeks for the primary
screening



PfNMT
PvNMT
hNMT1
hNMT2
Cs



Open Lab collaboration to build kineto boxes



Kineto Boxes



Each box contains ~200 high-value compounds:

- **in vitro efficacy**
 - pIC₅₀>5 versus relevant phenotypic assays
 - 13 readouts per compound
- **Safety**
 - Selective over cytotoxicity assays
 - No overt *in silico* alerts
- **Physicochemical properties**
 - Chemically tractable hits
 - MW <500, cLogP <5, PFI <6-7, *in silico* CNS permeability (*T. brucei*)
- **Exemplars of novel chemical space**



Open Lab Portfolio: December 2016



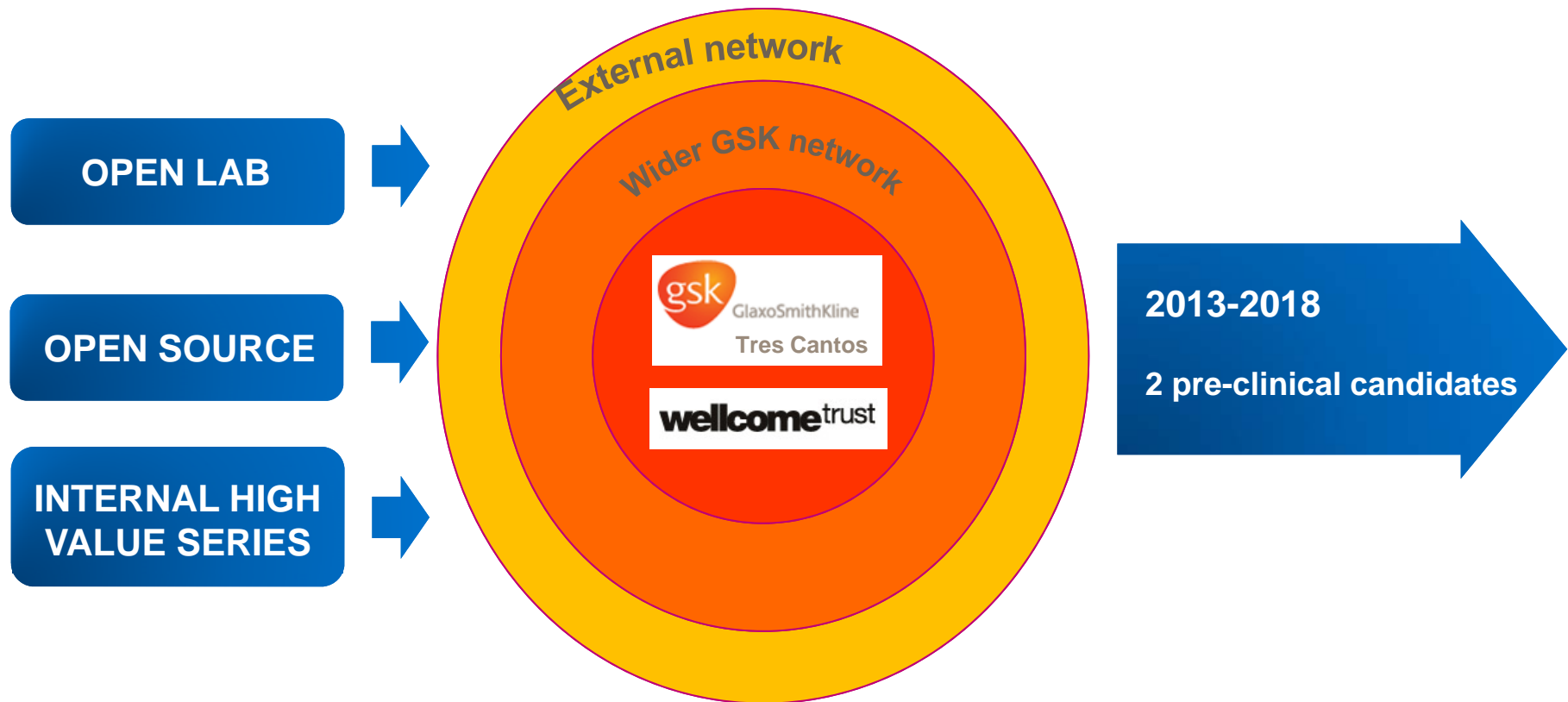
3 APPROVED*

25 ACTIVE

32 COMPLETED

2 Open Lab projects have currently entered pre-candidate selection phase
US\$60M funding obtained from follow-up grants

The WT/GSK DDW Drug Discovery Engine



12 hit to lead projects worked out to date
4 projects in lead optimization (3 preCandidates)
First Candidate expected by 4Q2017

**PRESS
RELEASE**



Issued: Friday 3rd May 2013, London UK

**Funding boost for GSK's open innovation research
into diseases affecting the developing world**

In summary



- Partnerships between academy and industry is a real possibility
- Through three main pillars GSK is pioneering productive collaborations
 - Open Patent and WIPO
 - Open source
 - Open Lab

Collaboration is key to accelerate drug discovery in diseases of the developing world

**Thank you to all our partners and
those at GSK**

**We are always open to ideas for projects,
collaborations, visits...**

