Discovery

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TB ALLIANCE
GLOBAL ALLIANCE FOR TB DRUG DEVELOPMENT

Our Goal and Focus

- Discovery and development of novel drugs that:
  - Significantly shorten therapy (Drug sensitive and resistant disease)
  - Safer than current therapy
  - Address the issue of resistance
  - Convenient: once a day dosing
  - Low cost of goods

- The current portfolio represent a good balance of clinically proven mechanisms/targets as well as novel target, and new chemistries

TB ALLIANCE

GLOBAL ALLIANCE FOR TB DRUG DEVELOPMENT

2014 Q4

Discovery

LEAD IDENTIFICATION

- ATP Synthesis Inhibitors *Calibr*
- Whole-Cell Hit-to-Lead Program *Sanofi*
- Whole-Cell Hit-to-Lead Program *GSK*
- RNA Polymerase Inhibitors *Rutgers University*
- Energy Meta-bolism Inhibitors *AZ/Upenn*
- POA Prodrugs *Yonsei*
- InhA Inhibitors
- Hit ID Program *Takeda*
- Hit ID Program *Daiichi Sankyo*
- Hit ID Program *Shionogi*

LEAD OPTIMIZATION

- Macrolides *Sanofi*
- Ureas *Sanofi*
- Next gen BDQ *Janssen/University of Auckland/UIC*
- Indazoles *GSK*
- Thiophene Carboxamides *Calibr*
- DpRE1 AZ
- Cyclopeptides *Sanofi*
- Mmpl3 Inhibitors
- Next generation Oxazolidinone IMM/BioDuro

Early Development

PRECLINICAL DEVELOPMENT

- TBA-354
- Preclinical TB Regimen Development *JHU*

PHASE 1

- Pharmacokinetics of first-line drugs in children < 5kg *Stellenbsch University*

Late Development

PHASE 2A

- NIX-TB
  - PA-824 / Bedaquiline / Linezolid

PHASE 2B

- NC-005
  - PA-824/ Bedaquiline/ Pyrazinamide

PHASE 3

- STAND
  - PA-824/ Moxifloxacin/ Pyrazinamide

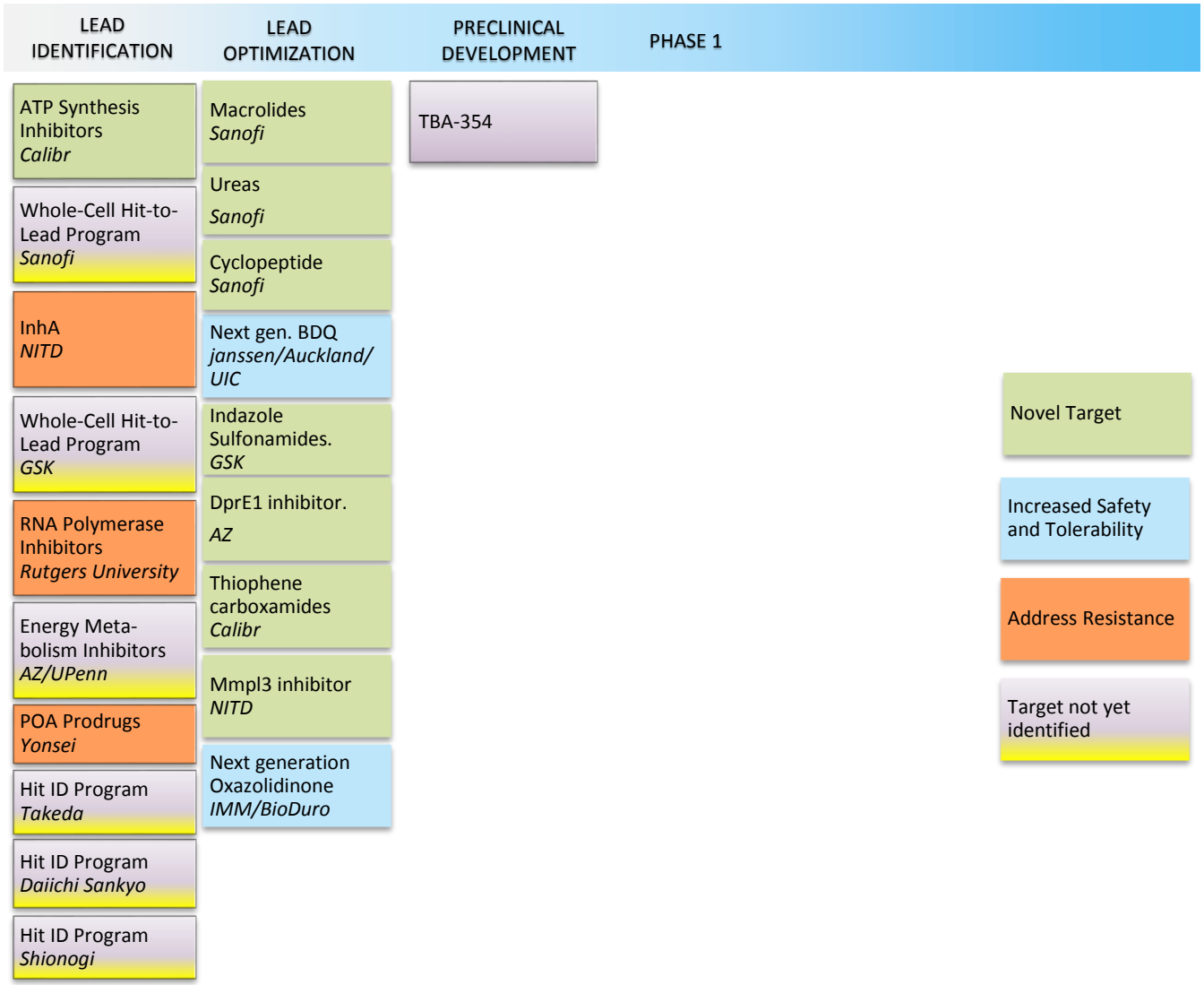
PHASE 4

- Optimized Pediatric Formulations
  - Ethambutol/ Rifampicin/ Pyrazinamide for children > 5kg
  - Isoniazid/ Rifampicin for children > 5kg
  - Ethambutol for children > 5kg
  - Isoniazid for children > 5kg
  - Pyrazinamide for children > 5kg

TB Alliance R&D Partners:

AstraZeneca (AZ)
Bayer Healthcare AG (Bayer)
Beijing Tuberculosis and Thoracic Tumor Research Institute
Calibr
Daiichi Sankyo
GlaxoSmithKline (GSK)
Institute of Materia Medica (IMM)
IMPAACT
Janssen [Johnson & Johnson]
Johns Hopkins University (JHU)
Medical Research Council (MRC)
New York Medical College
Rutgers University
Sanofi
Shionogi
Stellenbosch University
Takeda Pharmaceuticals
University College London (UCL)
University of Auckland
University of Illinois at Chicago (UIC)
University of Pennsylvania School of Medicine
Yonsei University

Balanced Discovery Portfolio



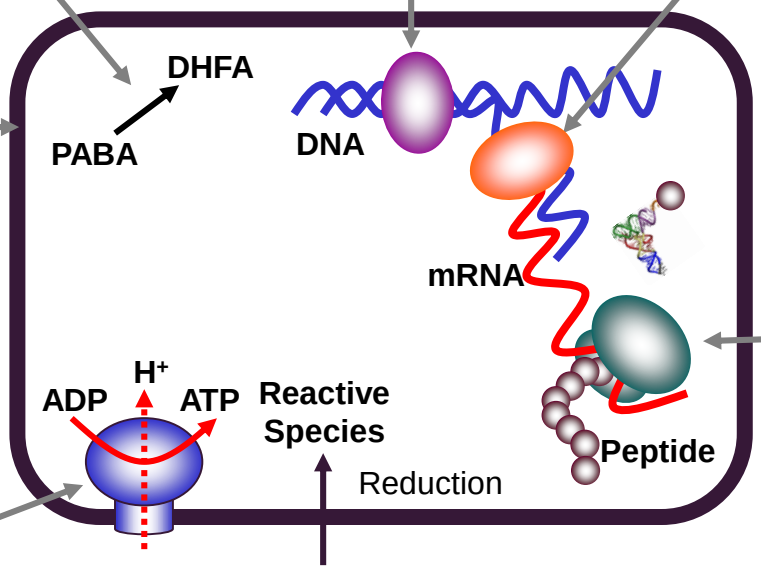
TB Drug Targets/Mechanisms

Folic Acid Metabolism
- *p*-Aminosalicylic acid

DNA Gyrase (GyrA/GyrB)
- Quinolones (Moxi, Gati)

RNA Polymerase
- Rifampicin
- Rifapentine
- Rifabutin

Cell wall synthesis
- SQ-109
- Isoniazid
- Ethionamide
- Cycloserine
- Ethambutol
- PA-824
- Delamanid



Protein Degradation

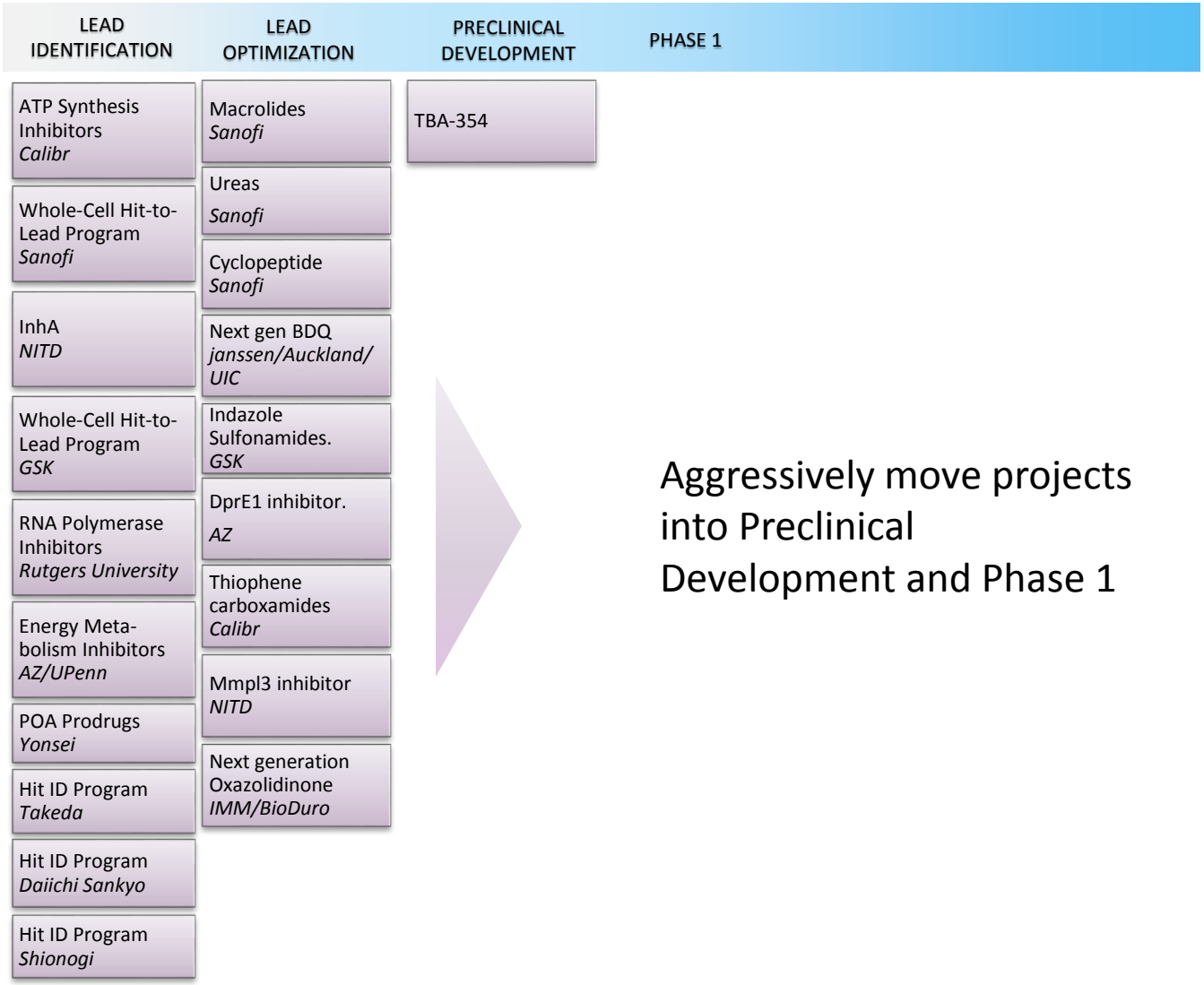
Ribosome (50S)
- Linezolid
- Sutezolid

Energy Metabolism
- PZA
- Bedaquiline

Reactive Species
- PA-824
- Delamanid

Ribosome (30S)
- Aminoglycosides
  - Streptomycin
  - Kanamycin
  - Amikacin
- Capreomycin
- Viomycin

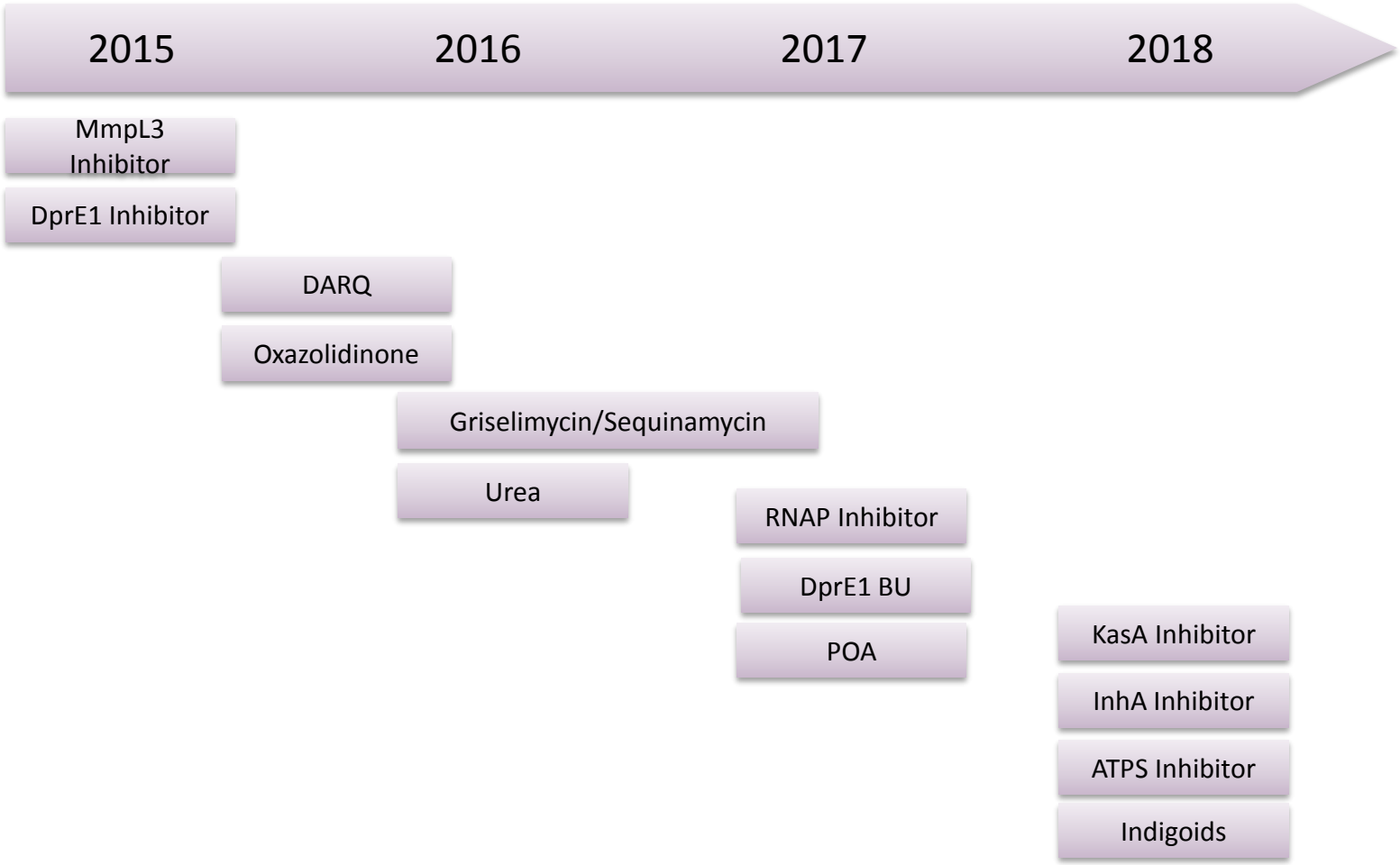
Discovery Portfolio



Discovery Vision – Long Term

- A sustainable Portfolio that delivers an Investigational New Drug (IND) on average each year starting in 2016
  - Delivery of up to 2 Preclinical Development candidates on average each year starting in 2015
- A balanced portfolio of innovative targets and approaches to achieve a significant shortening of the duration of treatment in drug-susceptible and drug-resistant patients

Entry into Phase 0 possibilities and timeline



Potential New projects/Novel Targets