

# **The Global TB Drug Pipeline: New Chemical Entities**

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**NIAID, NIH**

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**International Consortium for Trials of  
Chemotherapeutic Agents in Tuberculosis  
(INTERTB)**

**St. George's, University of London**

# 2017 Milestones in TB Drug Research

## Advances in Phase 1 landscape

- **TB Alliance** – IND filed and Phase 1a study of sutezolid completed. [NCT03199313](#)
- **TB Alliance** – IND filed and Phase 1a study of aza-indole TBA-7371 (DprE1 target) begun. [NCT03199339](#)
- **Otsuka** - Phase 1a of OPC-167832 completed. Potential companion drug for delamanid in a pan-TB regimen.
- **Qurient** – Phase 1b trial of Q203 imidazopyridine amide completed in the US (FDA oversight). [NCT02858973](#)
- **GSK** – Phase 1 of oxaborole candidate GSK-070 (GSK3036656) completed. [NCT03075410](#)
- **Institute of Materia Medica, Beijing** – Phase 1 study of TBI-166, an improved analog of clofazimine, planned for October in China.

# 2017 Milestones in TB Drug Research

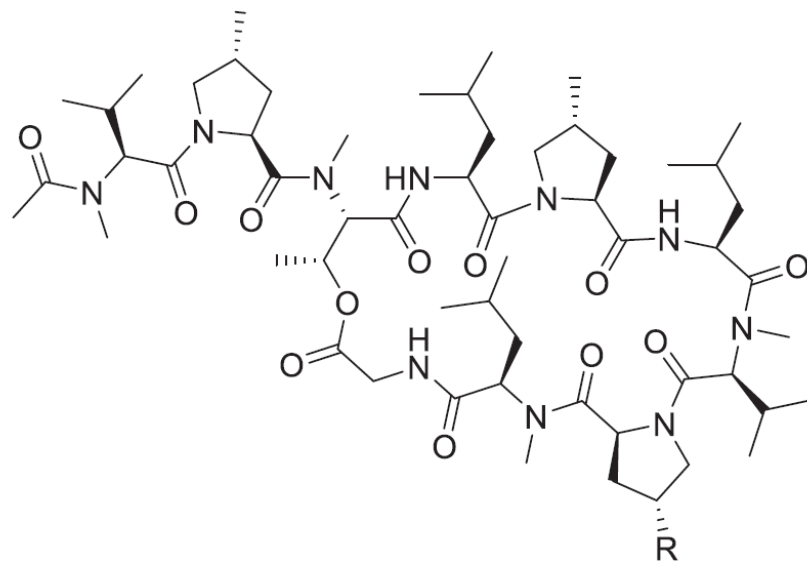
## Significant changes in development landscape

- **iM4TB Foundation (EPFL)** – Receives \$2.4 million grant from BMGF to take PBTZ-169 into clinical trials in Switzerland.
- **University of Munich** – BTZ-043 completing PK/PD evaluations. GMP drug to be available in 2017.
- **Microbiotix** – Compound 1810 selected as lead spectinamide candidate.
- **Lilly Initiative** – Development agreement with Hisun Pharma (China) for production to support inhalation formulation of CPZEN-45.
- **Johnson & Johnson** –Announces partnership with CSIR-IMTECH to Develop Innovative New Tuberculosis Treatments Aug 16, 2017, India
- **GSK** – An inhibitor of Mtb cholesterol metabolism GSK-286 selected as a drug development candidate.
- **UNION** – Announced TheLifePrize (formerly 3P Project) to reward developers/scientists who collaborate and advance TB treatments to clinical phases. [www.thelifeprize.org](http://www.thelifeprize.org)

# Griselimycin cyclopeptide

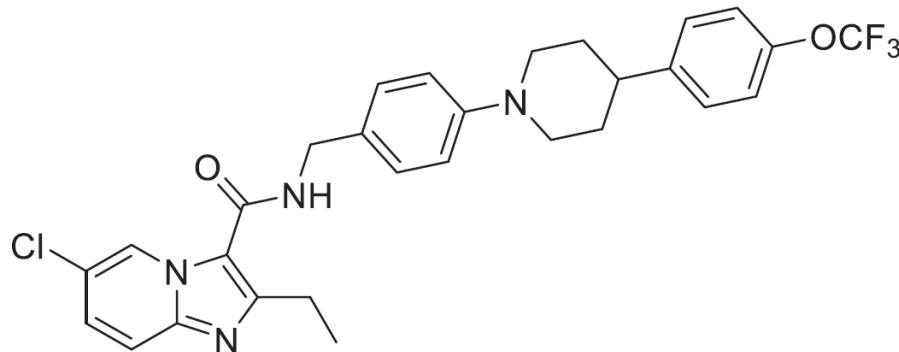
**SATB 082** (Sanofi, TB Alliance)

- Targets DnaN (sliding clamp of DNA polymerase)
- Candidate announced at EMBO Tuberculosis 2016 conference in Paris
- Good efficacy in mice, LORA assay
- Improved safety profile. Some human data from the 1970s.



# Imidazopyridines

## Q203 (Qurient)



- Targets the cytochrome b subunit (QcrB) of the cytochrome bc1 complex - an essential component of the respiratory electron transport chain. Q203 causes depletion of intracellular ATP.
- Q203 has been licensed to Infectex, LLC for Russia and the CIS
- Qurient completed Phase 1b safety studies in the US.

[www.NewTBDrugs.org](http://www.NewTBDrugs.org)

http://www.newtbdrugs.org/

WORKING GROUP ON NEW TB DRUGS Stop TB Partnership

PIPELINE NEWS MEETINGS MEMBERS ABOUT JOIN US

Clinical  
Discovery  
Compounds  
Regimens  
Developers  
Trial Sites  
Trials

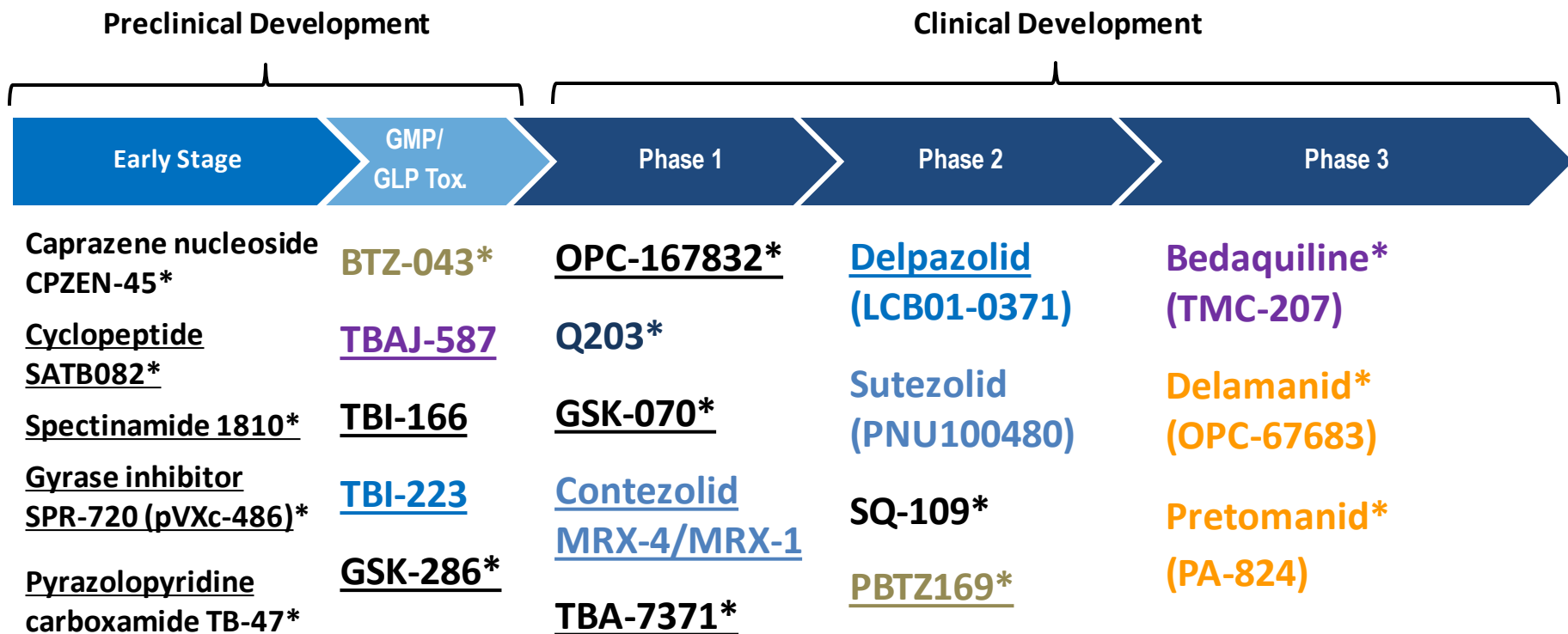
# Accelerating Discovery

New treatments are critical to end the TB pandemic. The Stop TB Partnership's Working Group on New TB Drugs helps coordinate, guide, and accelerate the speed of worldwide development of lifesaving new cures to improve TB therapy. Track the progress of new TB cures with our interactive pipeline.

Track Our Progress

tp://www.newtbdrugs.org/pipeline/clinical

# 2017 Global New TB Drug Pipeline<sup>1</sup>



Fluoroquinolone  
DC-159a

New chemical class\* Known chemical classes for any indication are color coded:

fluoroquinolone, rifamycin, oxazolidinone, nitroimidazole, diarylquinoline, benzothiazinone, imidazopyridine amide.

<sup>1</sup> New Molecular Entities not yet approved, being developed for TB or only conditionally approved for TB. Showing most advanced stage reported for each. Details for projects listed can be found at <http://www.newtbdrugs.org/pipeline/clinical>

Ongoing projects without a lead compound series identified can be viewed at <http://www.newtbdrugs.org/pipeline/discovery>

Underline = new to phase



Updated: October 2017

# Global TB Drug and Regimen Clinical Research<sup>1</sup>

Ongoing Clinical Development Research: Strategy/Optimization/Regimen Development

## Phase 2

**Bedaquiline-Delamanid** (ACTG 5343)

**Bedaquiline - Pretomanid -**  
**Pyrazinamide** (BPaZ) (NC-005)

**Bedaquiline - Pretomanid -**  
**Moxifloxacin** - Pyrazinamide  
(BPaMZ) (NC-005)

**Levofloxacin** with OBR for MDR-TB  
(OPTI-Q)

**Linezolid** Dose-Ranging

Nitazoxanide

Beta-Lactams

**High Dose Rifampicin** (PANACEA)

TB PRACTECAL - regimens with

**Bedaquiline-Pretomanid-Linezolid**

## Phase 3 Regimens

**Bedaquiline-STREAM** MDR-TB  
Trial Stage 2 with oral OBR (9 mo)  
or OBR with injectables (6 mo)

**Bedaquiline-Pretomanid-Linezolid**  
(NiX-TB)

**Delamanid** with OBR for MDR-TB

**High Dose Rifampicin** for DS-TB  
(RIFASHORT)

**Rifapentine - Moxifloxacin** for DS-  
TB (CDC TBTC 31)

**Pretomanid-Moxifloxacin-**  
**Pyrazinamide** (STAND)

## Optimization/Post Market

**Bedaquiline-Linezolid** with  
OBR for MDR-TB (NEXt  
Trial)

endTB 5-Regimen Trial for  
MDR TB

PredictTB – PET/CT,  
biomarkers DS-TB, 4 mo

Clofazimine - formulation  
development

Known chemical classes are color coded: **fluoroquinolone**, **rifamycin**, **oxazolidinone**,  
**nitroimidazole**, **diarylquinoline**, **benzothiazinone**, **imidazopyridine amide**.

<sup>1</sup> Strategy trials, regimen development, open label, repurposed drug studies. Details for  
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<sup>2</sup> OBR = Optimized Background Regimen



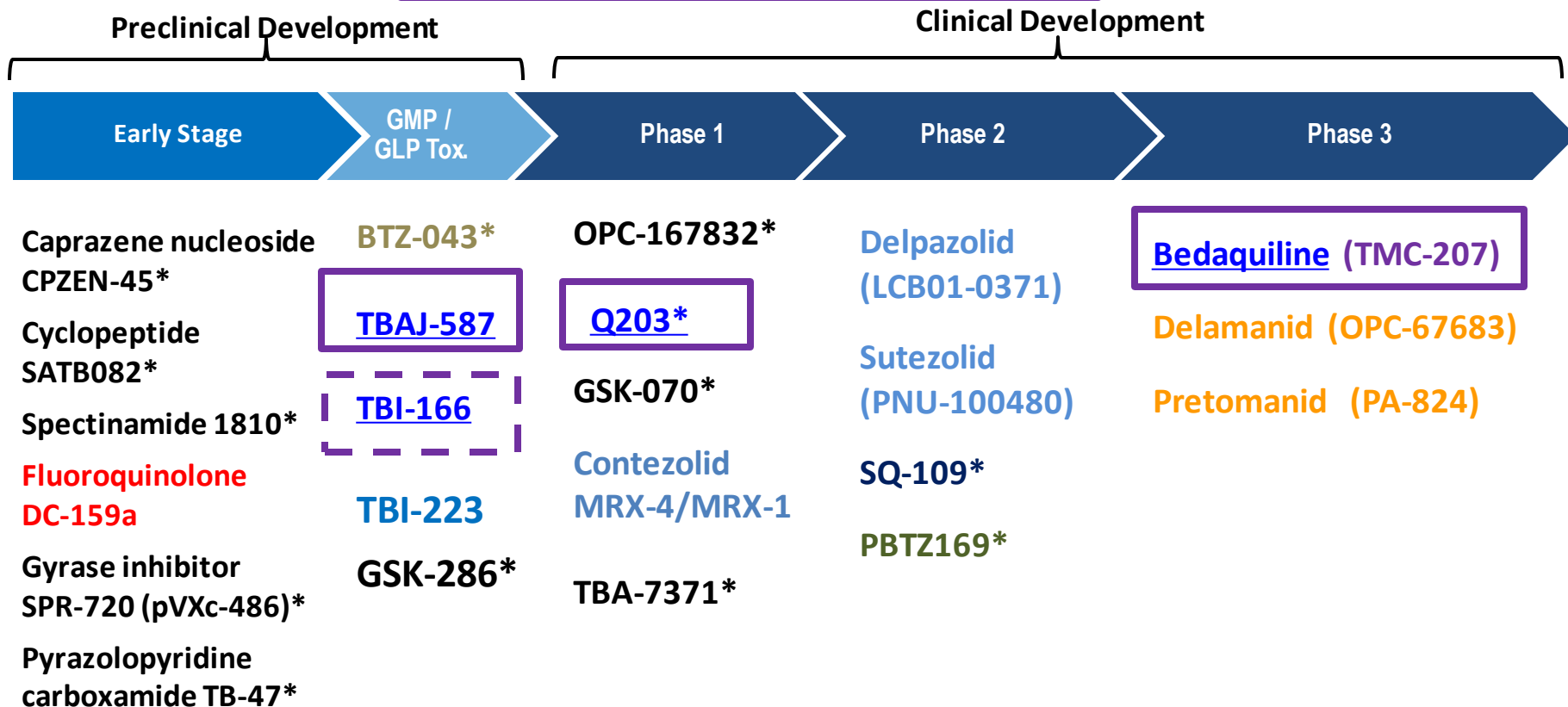
[www.newtbdrugs.org](http://www.newtbdrugs.org)

*Updated: October 2017*



# Global New TB Drug Pipeline<sup>1</sup>

Targets: Energy / QcrB / ATP Synthase



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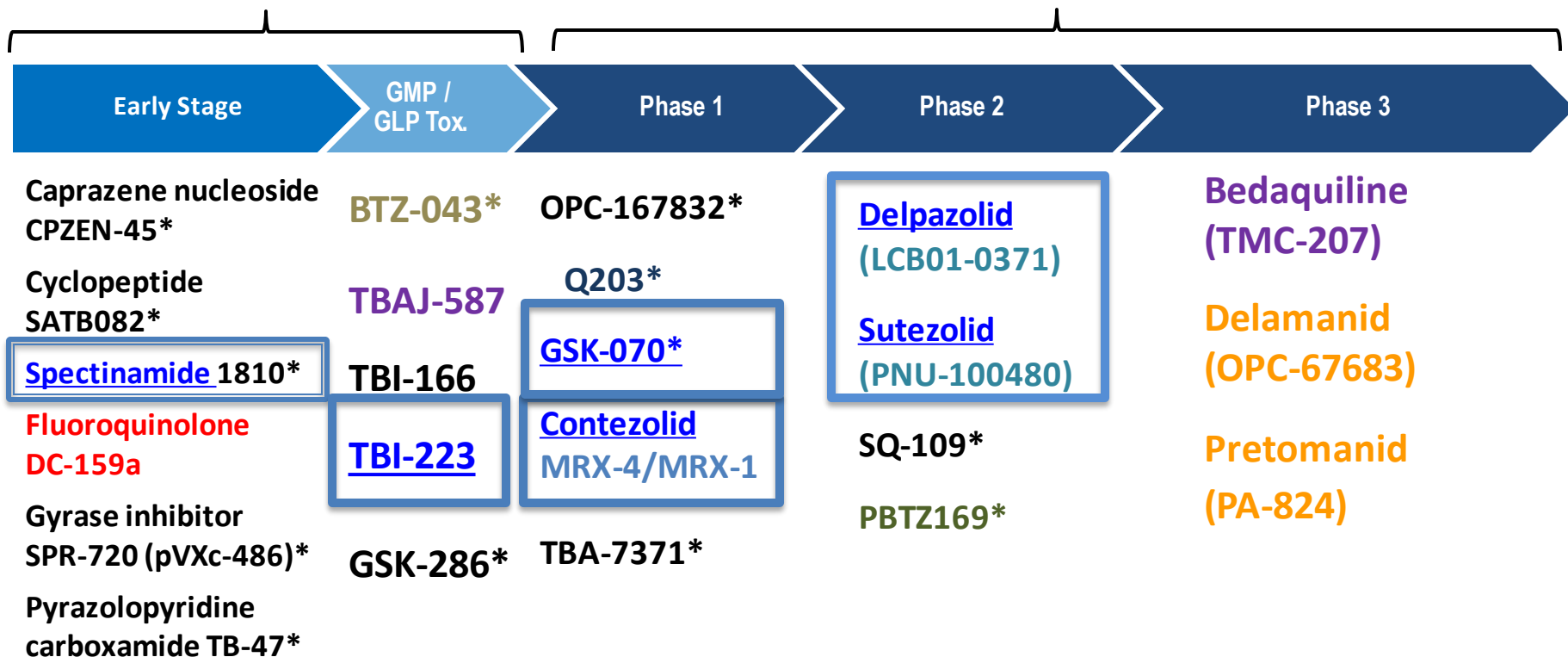
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# Global New TB Drug Pipeline<sup>1</sup>

Targets: Protein Synthesis

Preclinical Development

Clinical Development



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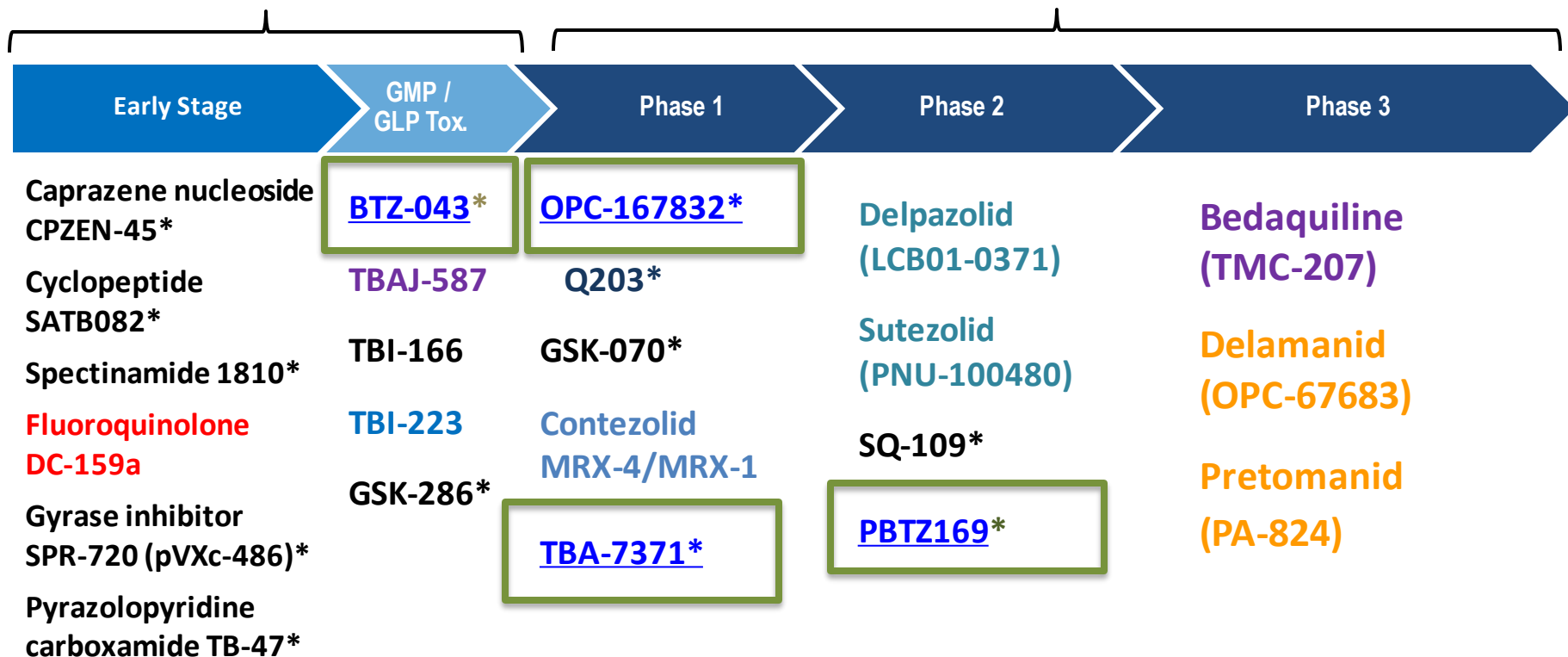
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# Global New TB Drug Pipeline<sup>1</sup>

**Targets: Cell Wall DprE1**

Preclinical Development

Clinical Development



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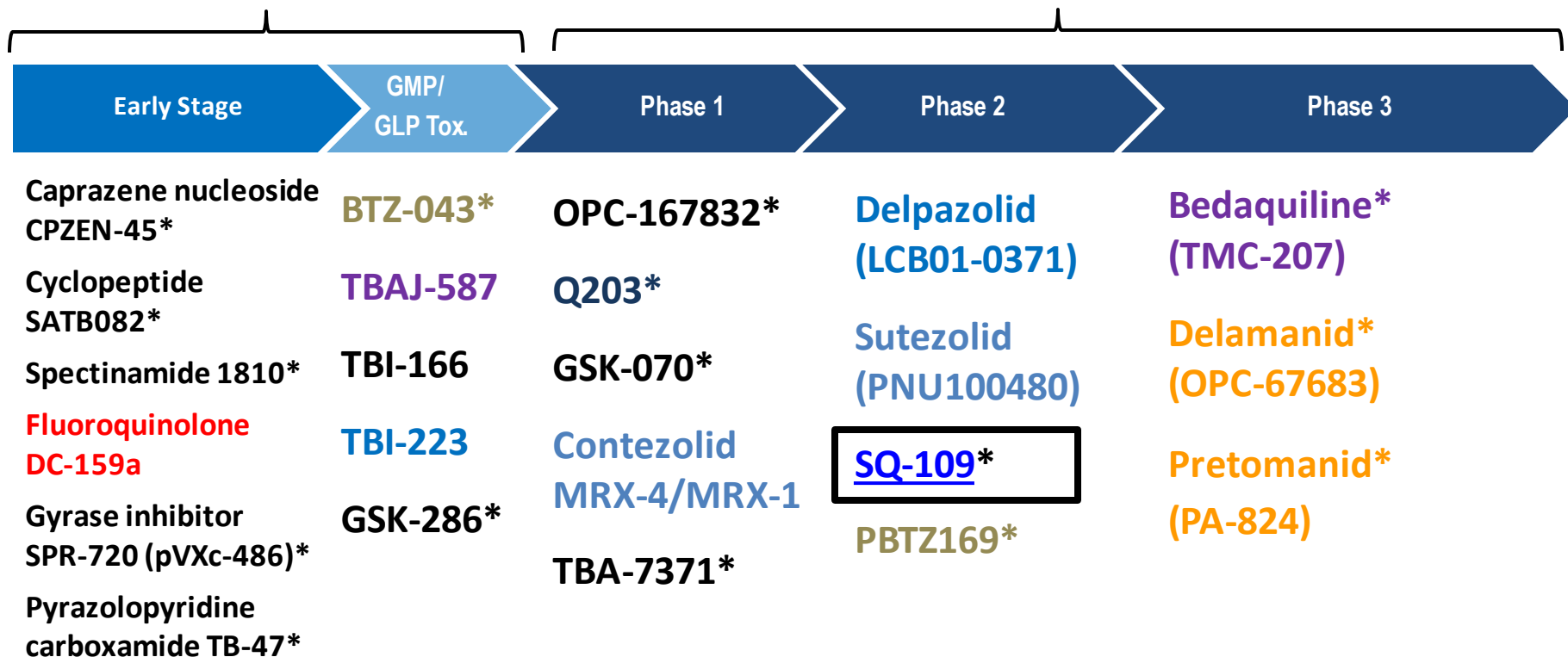
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# Global New TB Drug Pipeline<sup>1</sup>

Targets: MmpL3

Preclinical Development

Clinical Development



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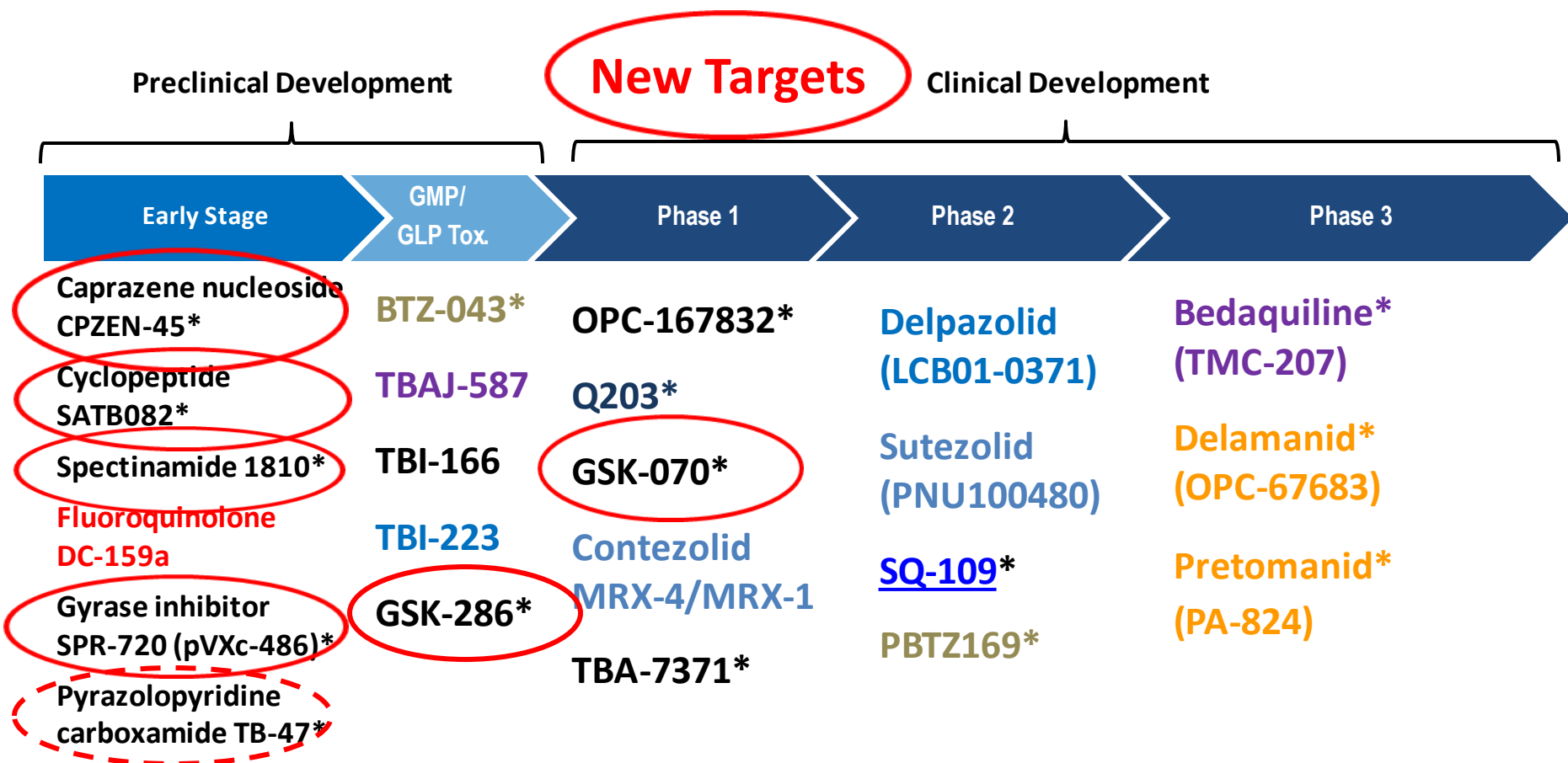
# The TB Drug Accelerator

The TBDA is a groundbreaking collaboration between eight pharmaceutical companies, eight research institutions, and a product development partnership to facilitate early TB drug discovery.

How it works...



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# Current Status of the 2017 TB Drug Pipeline

- Candidates with **novel mechanisms** of action are progressing into Phase 1 studies. Many more will be needed to overcome historical attrition rates and emergence of resistance.
- Open innovation, **collaboration**, and sharing of data are moving discovery and lead optimization forward at a faster rate.
- Translational research groups with **pharmaceutical company** participants are working to create a more robust pipeline.