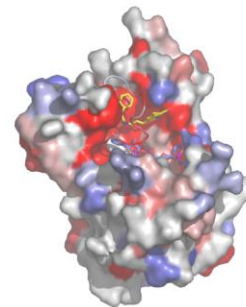


Debio 1453
***N. gonorrhoeae* Fabl**
Program

March 2023

FabI, an innovative target with broad potential

- **Debiopharm has unique expertise in the development of FabI inhibitors:**
 - Proven clinical efficacy of the *Staphylococcus*-selective afabycin in Phase II
 - Debiopharm has a broad IP coverage
 - Debiopharm actively collaborates with the original developers of afabycin
- **FabI inhibitors have potential beyond current front runner:**
 - Exploit structural diversity across species for targeted approaches with various pathogens



● absolutely conserved
○ average conservation
● highly variable

Neisseria gonorrhoeae program overview (1/2)

- **Mission:** To develop a novel oral and/or intramuscular narrow spectrum inhibitor of FabI for drug resistant *N. gonorrhoeae* infections
- **Targeted Indication:** Uncomplicated genital, rectal and pharyngeal *N. gonorrhoeae* infections
- **Development stage:** IND-enabling

Neisseria gonorrhoeae program overview (2/2)

Key attributes:

- New MoA targeting an essential pathway in *N. gonorrhoeae*
- No cross-resistance observed, active on MDR strains
- Pathogen-specific activity: microbiome sparing
- Low potential for emergence of resistance due to interaction with a non-mutable co-factor
- Potential to treat co-infections with *C. trachomatis*

In vitro activity on *N. gonorrhoeae* (Ng) and *C. trachomatis* (Ct) isolates

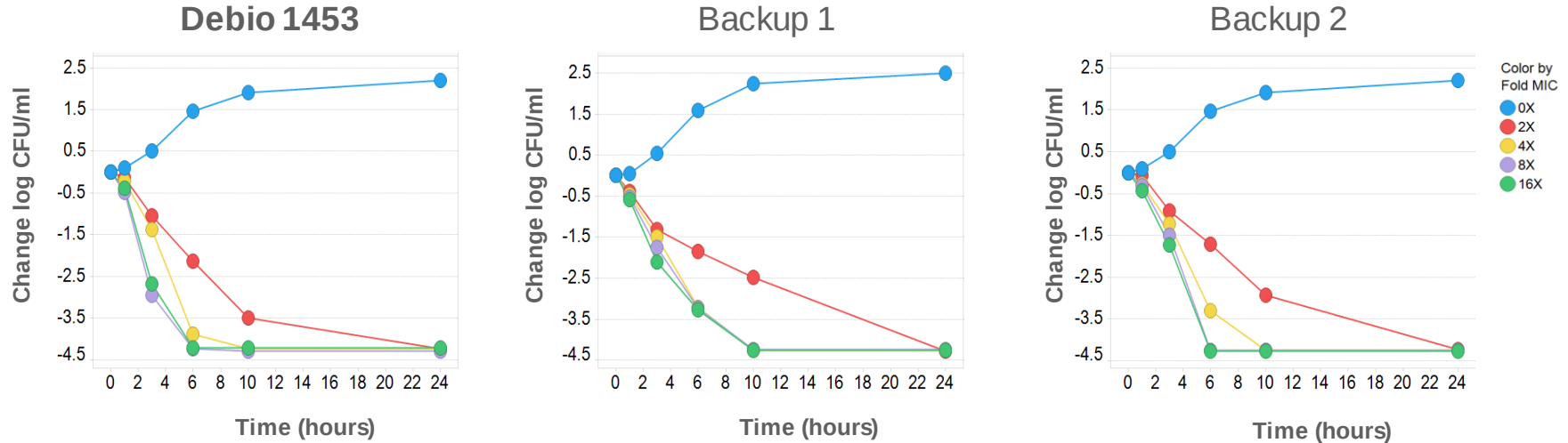
- 74 isolates with a mix of **clinically relevant resistance phenotypes**

Compound	MIC (µg/ml) 74 Ng isolates		
	Range	MIC ₅₀	MIC ₉₀
Debio 1453	0.016 - 0.125	0.06	0.125
Backup 1	0.03 - 0.25	0.125	0.25
Backup 2	0.03 - 0.25	0.125	0.25

- In vitro* potencies of Debio 1453 are **similar against Ng and Ct**

Compound	Ct MIC ₉₀	Ng MIC ₉₀
Debio 1453	0.25	0.125

Bactericidal status achieved at 6-12hrs



- *N. gonorrhoeae* NCTC13822 (CipR, CtrR)
- Similar bactericidal activity demonstrated with several multiresistant strains

Low frequencies of resistance in single step resistance assays

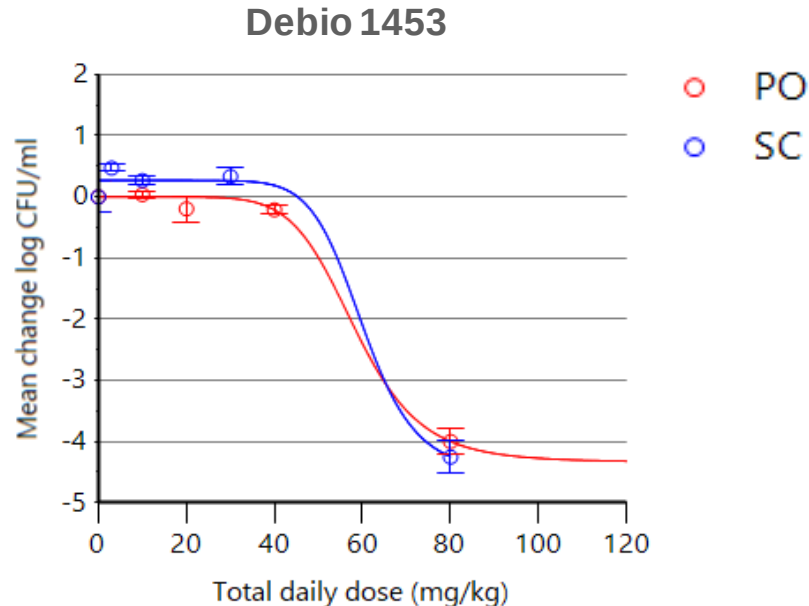
Compound	<i>N. gonorrhoeae</i> 6926		<i>N. gonorrhoeae</i> 6804		<i>N. gonorrhoeae</i> 13822	
	Fold MIC	FOR	Fold MIC	FOR	Fold MIC	FOR
Debio 1453	4		4	1.06E-09	4	$\leq 2.81\text{E-}10$
	8	$\leq 3.85\text{E-}10$	8	$\leq 5.27\text{E-}10$	8	$\leq 2.81\text{E-}10$
	16		16	$\leq 5.27\text{E-}10$	16	$\leq 2.81\text{E-}10$
Backup 1	4		4		4	2.81E-10
	8	$\leq 3.85\text{E-}10$	8	$\leq 5.27\text{E-}10$	8	$\leq 2.81\text{E-}10$
	16		16		16	$\leq 2.81\text{E-}10$
Backup 2	4		4		4	
	8	$\leq 3.75\text{E-}10$	8	$\leq 6.90\text{E-}10$	8	$\leq 2.65\text{E-}10$
	16		16		16	

Strain phenotypes: 6926 - susceptible, 6804 - cipR, t_eR, NCTC13822 -t_eR, cipR, azmR, croR

- **Maximum 4-fold MIC increase** for Debio 1453 in multistep selection assays (30 passages)

Efficacy via SC and PO routes in mouse NG model for Debio 1453

- Efficacy and PK/PD package on a standard female **mouse vaginal gonorrhea model***
- **Consistent and quantitative dose-response obtained** via both oral and SC route
 - ED₅₀: 40-58 mg/kg
- **Excellent efficacy** demonstrated after one day of treatment (4 log kill)



*Song et al, Local and humoral immune responses against primary and repeat *Neisseria gonorrhoeae* genital tract infections of 17 β -estradiol-treated mice. Vaccine 2008 p. 5741–5751.

Debio 1453 key ADMET properties

- Advanced compounds show **excellent *in vitro and in vivo* safety**
- **Medium-high oral bioavailability** in rats and dogs
- Low hepatic extraction
- **PO and IM efficacy POCs** to cover worldwide market
- PK/PD index ($fAUC/MIC$) identified
- Human PK predictions **compatible with single daily administration from one to three days**

Debio 1453 Drug Candidate Opportunity

- **First-in-class || New MoA || Microbiome sparing || Low Emergence of Resistance**
- **Program endorsed by CARB-X potentially up to IND enabling studies completion**
- **IND ready: H2 2024**
- **Expected patent protection: YEAR 2039 + 5 (2044)**
- **Business proposition:**
 - **Licensing-out**
 - **Co-development with option for Partner to fully license at IND or Phase I**



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