Q203 Update
Q203: MOA

- **Bacteria killing by**
  - Inhibition of respiratory chain (cytochrome bc1 complex)

  ![Diagram of the respiratory chain]

- **Host anti-inflammation by**
  - Inhibition of 5 lipoxygenase

References:
- Nature Medicine 2013
- Nature Communications 2016
Q203: Bacteria Killing Activity

- Mouse 4 weeks treatment model shows good efficacy
- Maximum efficacious dose at 10 mg/kg

(Nature Medicine 2013)
Q203: Anti-Inflammation

- Oral administration of Q203 inhibits production of LTB4

- Reduction in numbers of granuloma in mouse TB model

(Unpublished data)

(Nature Medicine 2013)
Q203: Preclinical Studies

- Absorption
  Mouse single dose in fasted condition shows long half life (~90 hour)
  Steady-state after 14 days of dosing
- Distribution
  Mouse mass balance study shows compound distribution to lung
- Metabolism
  Negative DDI sign from in vitro study
  No major metabolite
- Excretion
  Mainly excreted through feces
- Toxicity
  Well established NOAEL up to 28 days
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Q203: Phase 1 SAD

- Dose proportional increase of $C_{\text{max}}$ and AUC$_{\text{last}}$
- No clinically significant changes in safety parameters including ECG
- Food increases absorption around 5 fold
Q203: Phase 1 MAD (on-going)

- Designed to support 14-day EBA study
- Dose escalation up to maximum anticipated efficacious level
Q203: Future Plan

- EBA study planned starting end of 2017
  Standard 14-day EBA with extended combination dosing phase with HRZ or innovative backbone (bedaquiline ?)

- Developing safety and efficacy profile in combination regimen from early stage
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