

# **Update on Moxifloxacin Development for Tuberculosis**

## **Open Forum II Key Issues in TB Drug Development**

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# TB Alliance-Bayer Agreement

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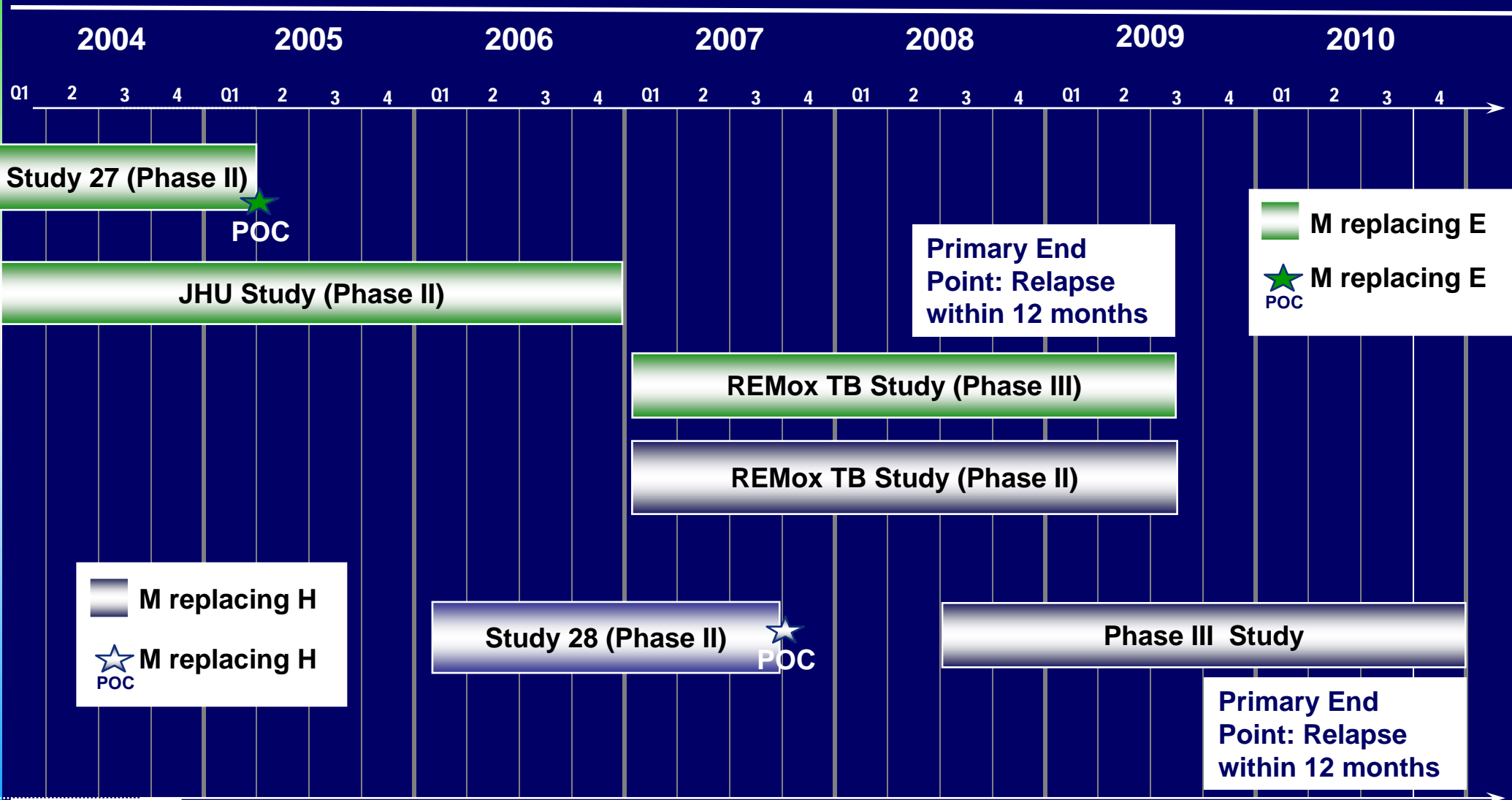
- Goals
  - Coordinate clinical trials to support registration of moxi-based regimen for TB
  - Common GCP/GMP-based clinical trial standards
  - Unified safety data base
  - Unified microbiology database
  - Clinical data-sharing
- Affordability
- By-products of drug development
  - Chart regulatory path
  - Evaluate/validate potential surrogate markers
  - Build clinical trial capacity

# Initial Clinical Development Plan

Trial	Phase	Study Design	Countries	Total N Safety/Micro	Status
TBTC #27	II	Moxifloxacin replaces <b>Ethambutol</b>	USA, Canada, Uganda, South Africa	336 / 321	Results available
JHU	II	Moxifloxacin replaces <b>Ethambutol</b>	Brazil	170 / 163*	Enrollment almost complete
TBTC #28	II	Moxifloxacin replaces <b>Isoniazid</b>	USA, Canada, Uganda, South Africa, Brazil, Spain	410 / 392*	Enrollment almost complete
REMOx TB	II / III	Moxifloxacin replaces <b>Ethambutol</b> Moxifloxacin replaces <b>Isoniazid</b>	Tanzania, South Africa, Zambia	1500 / 1400*	Recruiting to commence in Q1 2007

\*estimated value based on Study 27 data

# Timelines for Moxifloxacin Clinical Development Program for TB



H = Isoniazid (INH); R = Rifampicin; Z = Pyrazinamide; E = Ethambutol; M = Moxifloxacin; POC = Proof of Concept

# Summary of Proposed Clinical Development Plan (CDP)

- Goal: identify moxifloxacin-containing regimen(s) that can shorten treatment duration to 4 months
- Each regimen will have its own CDP
- Each CDP will have at least one Phase III study that is:
  - Adequate and well controlled, double blind, and international in scope
  - Use relapse within 12 months of completing therapy as the primary efficacy endpoint
  - Will enroll subjects broadly representative of the TB patient population
    - With respect to age, gender, HIV status, race, cavitory versus non-cavitory disease etc.

# Charting the Regulatory Path

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- Goals of Regulatory Meetings:
  - Get agency feedback on the pre-clinical, PK and clinical data needed to obtain a formal indication for moxifloxacin
- Meeting with the FDA took place on 23 October 2006
- Meeting with BfArm planned for Q1 2007

# Key Outcomes from the FDA Meeting

- Robust drug-drug interaction data needed with other drugs in the regimen
  - Need to provide evidence that the other drugs used in the standard anti-TB regimen do not significantly alter the PK of moxifloxacin and vice versa
- 2 Phase III studies *required*
  - to be discussed with the agency once data available from 1<sup>st</sup> Phase III study
- Phase III studies:
  - need to enroll broadly representative patient population
  - 12 month follow-up post treatment completion for recurrence/relapse acceptable as the primary endpoint
  - Need to justify choice of delta for non-inferiority Phase III trial design
- Size of the proposed safety database acceptable
  - At least 500 moxi-treated patients in Phase III