endTB clinical trials

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GLOBAL CONSULTATION ON TRANSITION TOWARDS NEW AND BETTER TREATMENTS OF DR-TB AND LTBI

Geneva, 14-16 November 2018


Change
Same

endTB trials summary

endTB*

- Rifampicin-resistant and FQ-susceptible pulmonary TB

endTB-Q**

- Rifampicin- and FQ-resistant pulmonary TB

- Randomized, controlled, open-label, non-inferiority, Phase III trial evaluating the efficacy and safety of shortened treatment regimens containing new and re-purposed drugs for MDR-TB

- Primary endpoint: 73-week favorable outcome

* Evaluating Newly approved Drugs for multidrug-resistant TB

** Evaluating Newly Approved Drugs in Combination Regimens for Multidrug-Resistant TB with Fluoroquinolone Resistance (Q)

endTB

Experimental arms: 39 weeks duration (9 months)

Experimental Regimens	Bedaquiline	Delamanid	Clofazimine	Linezolid	Quinolone	Pyrazinamide
endTB 1	Bdq			Lzd	Mfx	Z
endTB 2	Bdq		Cfz	Lzd	Lfx	Z
endTB 3	Bdq	Dlm		Lzd	Lfx	Z
endTB 4		Dlm	Cfz	Lzd	Lfx	Z
endTB 5		Dlm	Cfz		Mfx	Z
Control	Standard of care control, composed according to WHO Guidelines, including the possible use of DLM or BDQ.					

Sample size: 750
Bayesian adaptive randomization based on efficacy endpoints

endTB-Q

	Bedaquline	Delamanid	Clofazimine	Linezolid	Duration
1	Bdq	Dlm	Cfz	Lzd	**6 mths**
2	Bdq	Dlm	Cfz	Lzd	**9 mths**
C	Standard of care control per WHO Guidelines				20-24 mths

Sample size: 500
Fixed randomisation

Objectives

Primary objective

Assess whether the efficacy of the experimental arms at 73 weeks is non-inferior to that of the control

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Secondary objectives

Efficacy: Compare to control

- Culture conversion in experimental regimens
- Efficacy of experimental regimens at week 39
- Efficacy of experimental regimen at week 24
- Efficacy of experimental regimens at week 104, including failure & relapse

Safety: Compare to control

- Death, grade 3 or higher AEs and SAEs in experimental arms at 73 and 104 weeks

Screening for endTB clinical trial

Pre-screening
RR-TB identified in routine care

Patients are pre-screened and offered simultaneous screening

endTB Screening

- Medical history, concomitant medications, physical examination
- Pregnancy test, complete blood count, ALT/AST, bilirubin, albumin, creatinine, electrolyte testing, HIV and hepatitis serology
- ECG
- Molecular test for RIF
- **Molecular test for FQ**

Enrollment in endTB trial

Enroll in endTB N=750
Meet all eligibility criteria and **FQ-susceptible**

Not eligible
Do not meet ≥1 eligibility criteria

Unified screening for endTB and endTB-Q clinical trials

Pre-screening
RR-TB identified in routine care

Patients are pre-screened and offered simultaneous screening

endTB Screening
(Single process for both studies)

- Medical history, concomitant medications, physical examination
- Pregnancy test, complete blood count, ALT/AST, bilirubin, albumin, creatinine, electrolyte testing, HIV and hepatitis serology
- ECG
- Molecular test for RIF
- **Molecular test for FQ**

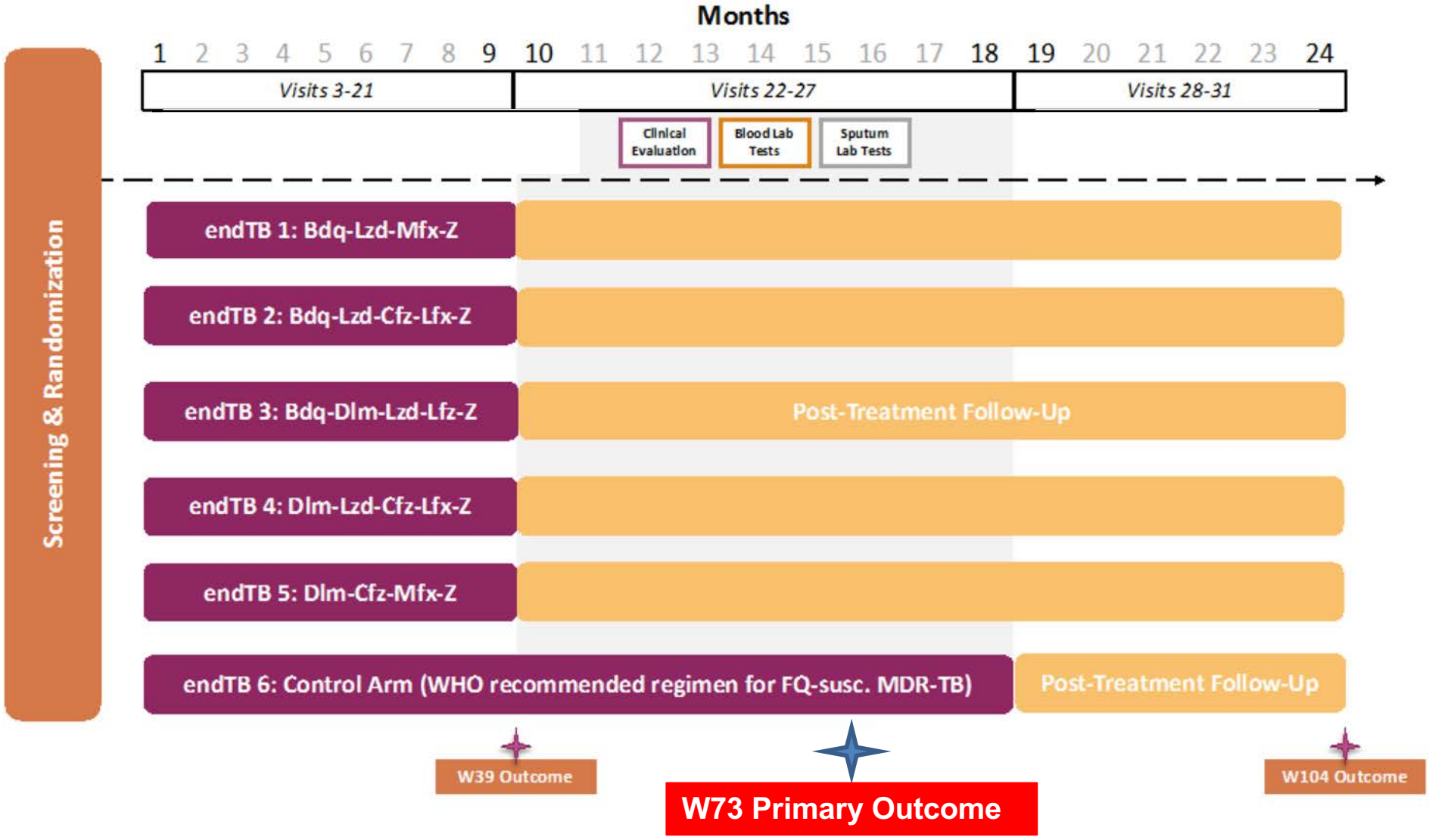
Enrollment in 2 trials N=1250

Enroll in endTB N=750
Meet all eligibility criteria and **FQ-susceptible**

Enroll in endTB-Q N=500
Meet all eligibility criteria and **FQ-resistant**

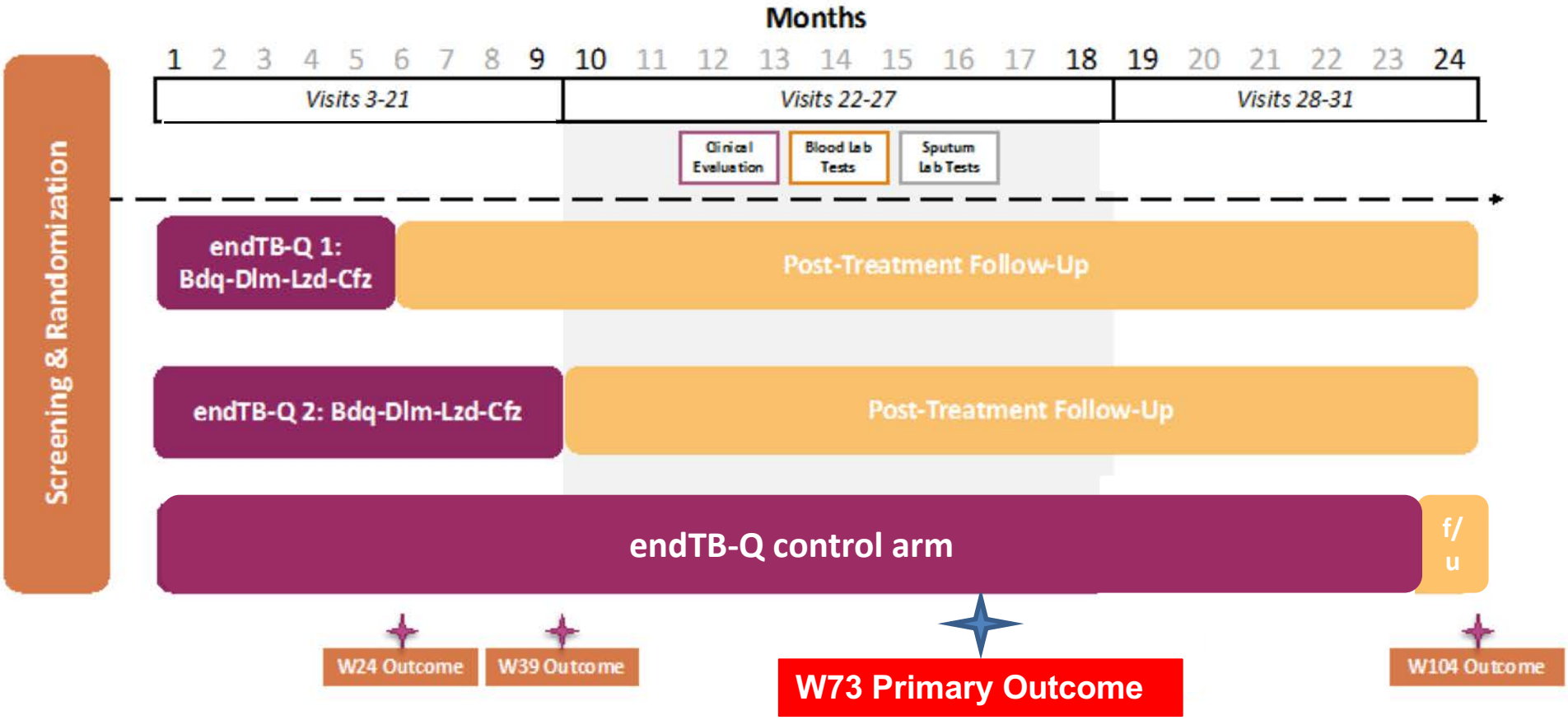
Not eligible
Do not meet ≥1 eligibility criteria

Schematic of the endTB trial



Trial participation in all arms will last at least until Week 73 and up to Week 104. Study follow-up will end after the scheduled Week 73 for the last participant randomized

Schematic of the endTB-Q trial



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Georgia
First patient enrolled
22-Feb-2017

Peru (2→3 sites)
First patient enrolled
18-Jul-2017

Kazakhstan (2 sites)
First patient enrolled
07-Aug-2017

Lesotho
First patient enrolled
10-Jan-2018

South Africa
First patient enrolled
06-Apr-2018

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First patient enrolled
22-Feb-2017

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First patient enrolled
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endTB Clinical Trials

endTB update:
7 opened sites in 5 countries

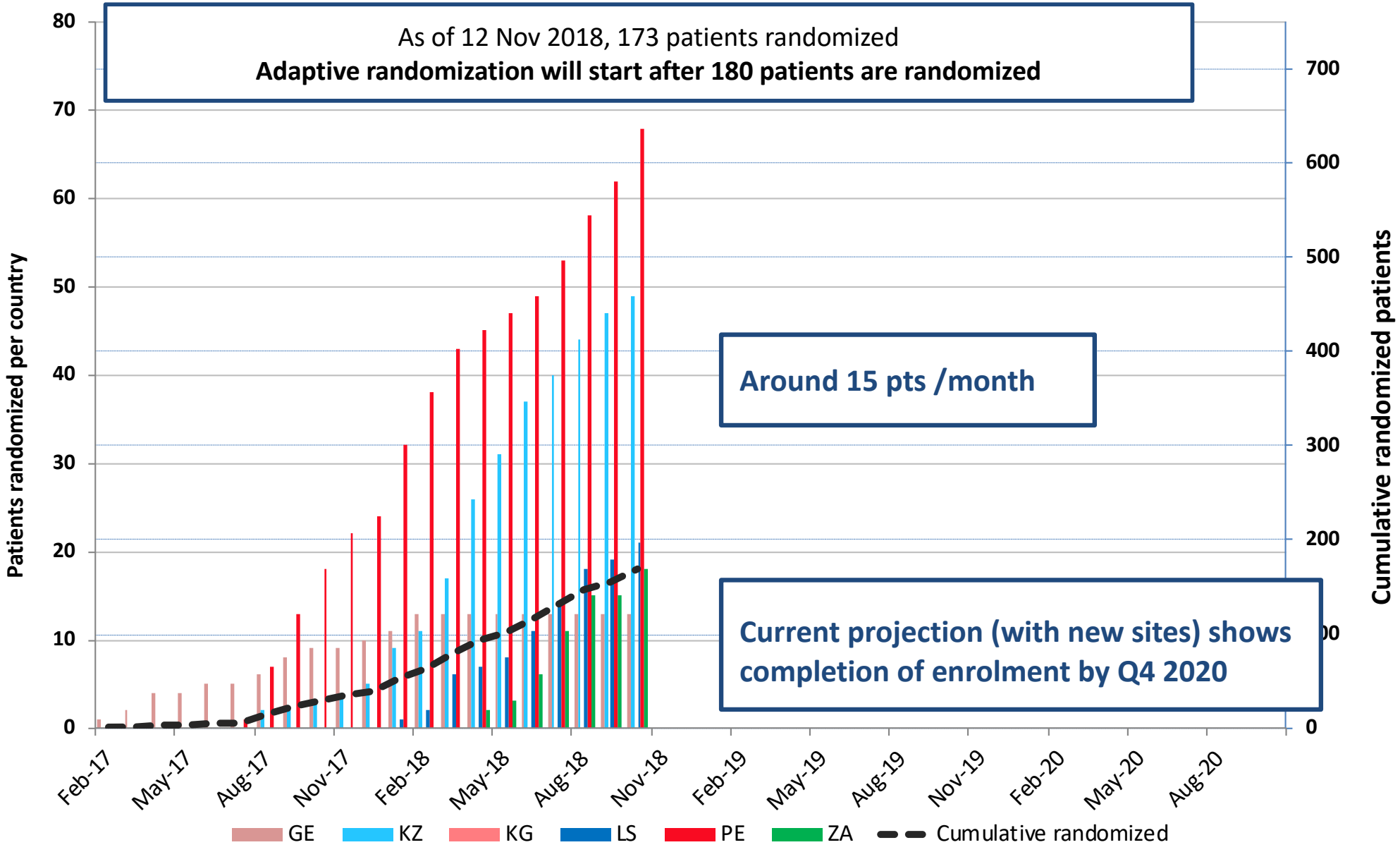
Objective:
12 sites in 6 countries

Pakistan
Under preparation – target Feb 2019

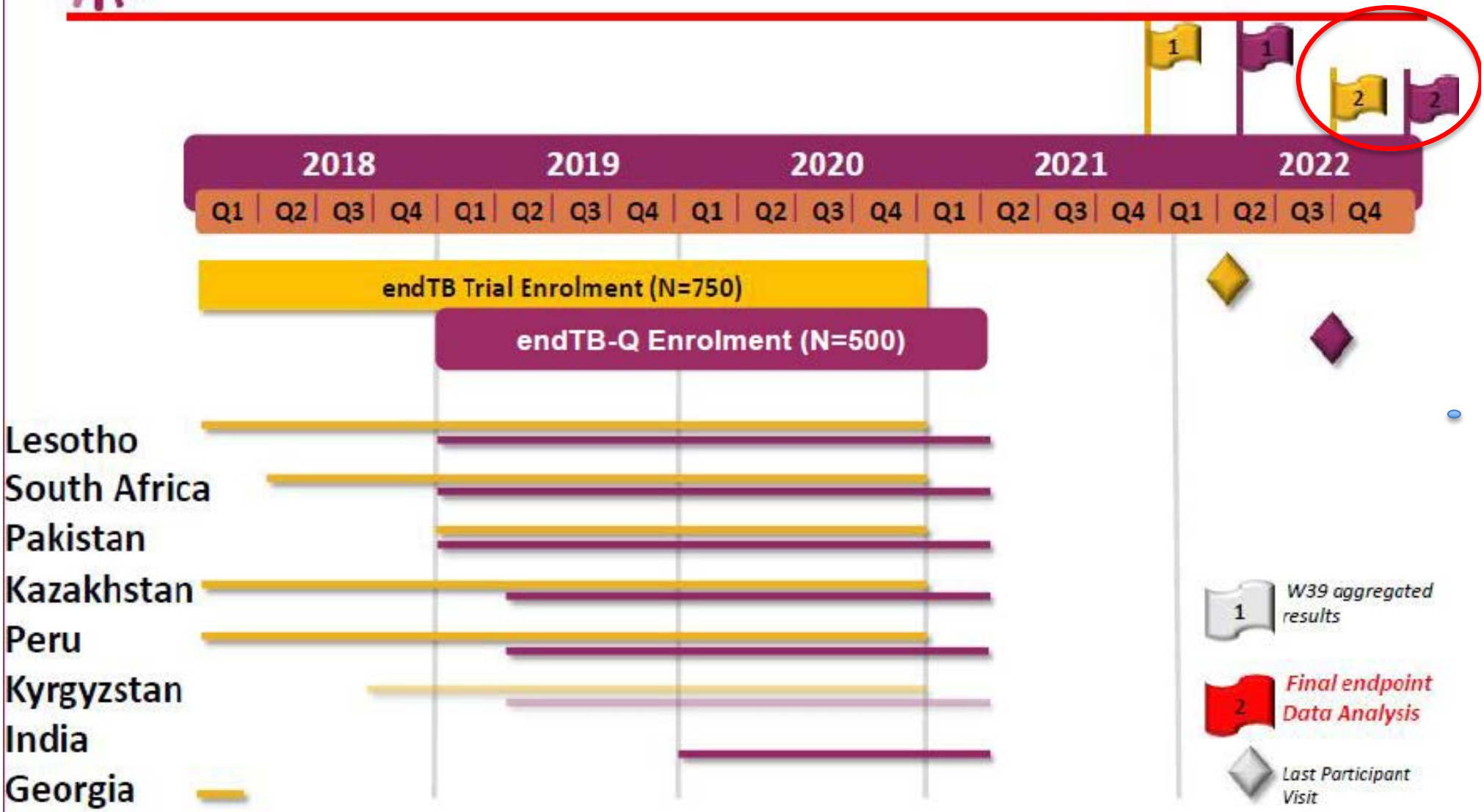
Potential new sites
KZ (Astana and Karaganda under assessment)

India
Potential sites
To be assessed

Recruitment Update



Timeline of endTB and endTB-Q



Acknowledgements

MEDECINS SANS FRONTIERES

Partners In Health

IRD Interactive Research & Development

Harvard Medical School

epicentre ÉPIDÉMIOLOGIE • EPIDEMIOLOGY

Institute of Tropical Medicine Antwerp

Unitaid Innovation in Global Health

Sites and central teams

Ministries of Health and NTPs:
Georgia, Kazakhstan, Lesotho, Peru, South Africa

Thank you