

# WGND Meeting

October 26, 2011, Lille



**TB ALLIANCE**

GLOBAL ALLIANCE FOR TB DRUG DEVELOPMENT

# What We're Trying to Accomplish

Efficiently bring to market affordable and easy-to-use regimen(s) that shorten and simplify treatment for DS- and DR-TB in HIV positive and negative subjects

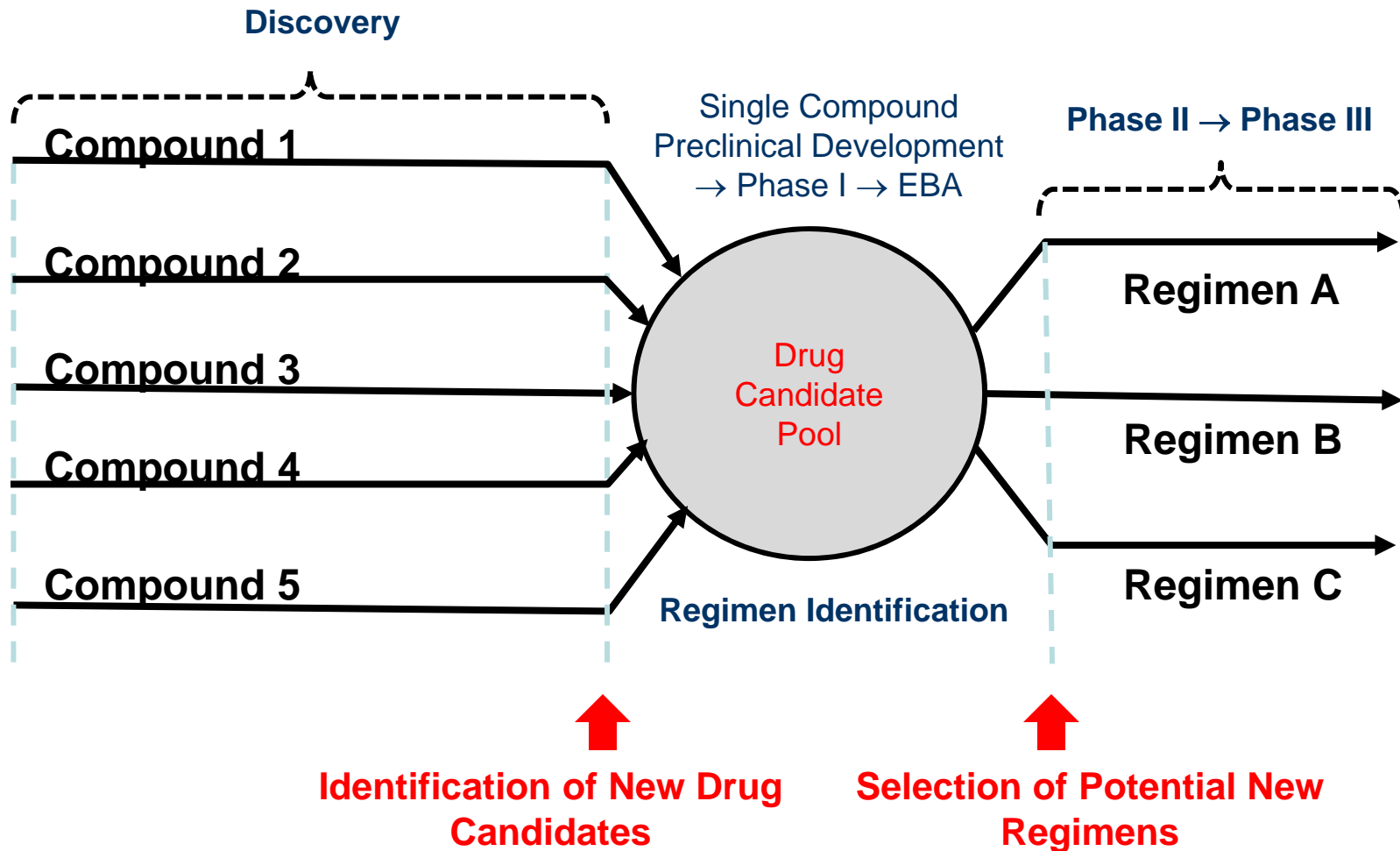
- Ideally, no pre-existing resistance
- Alternatively, delivery paired with appropriate resistance testing



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# TB Drug/Regimen Discovery and Development Process



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Confidential

**NC-001**



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# NC-001: Use of EBA to Test Principles Learned From Animal Models and to Begin Clinical Development of Novel Regimens

NC-001 (first novel combination EBA study)

- J-Z synergy
- Pa-Z additivity
- Pa-J antagonism
- Pa-M-Z an enhanced novel regimen

EBA = early bactericidal activity

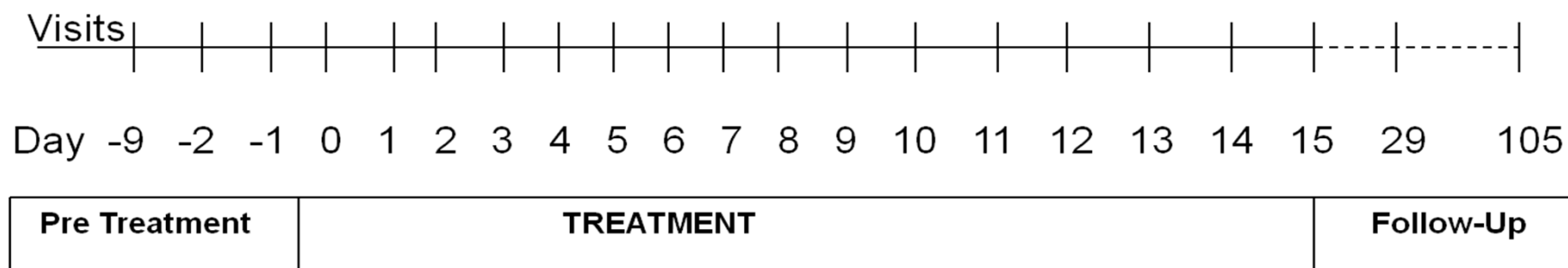
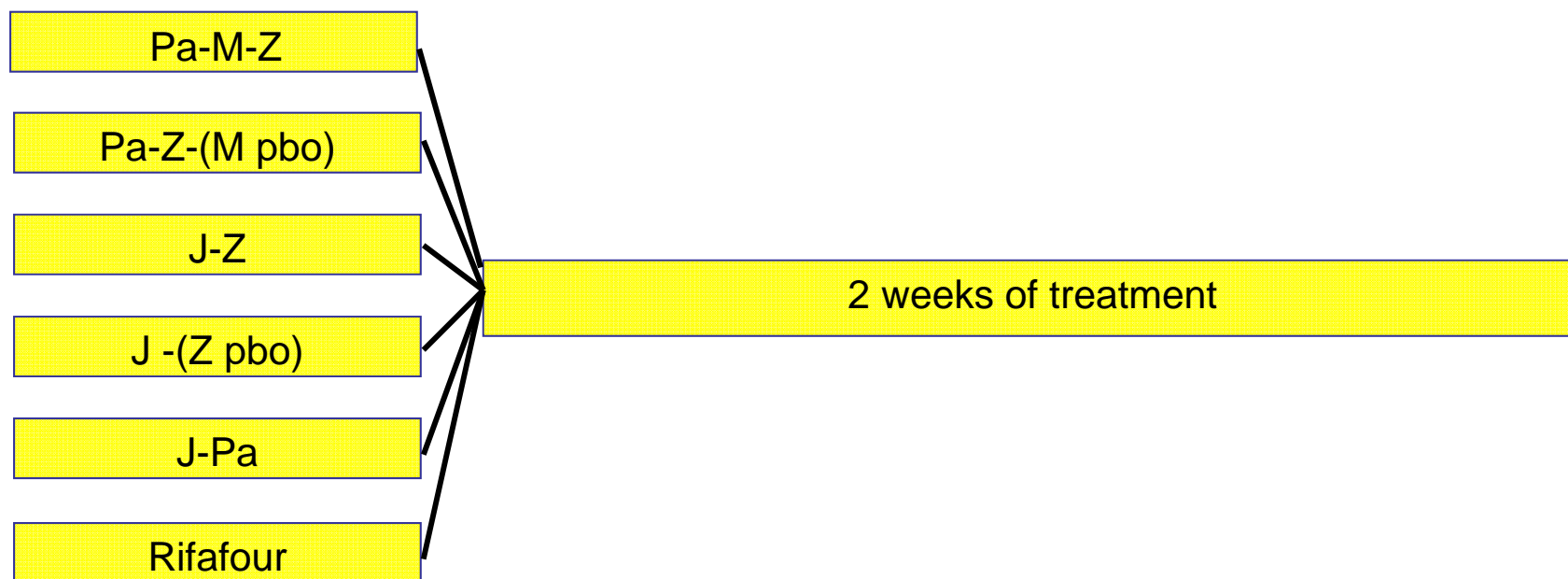
Pa = PA-824; M = moxifloxacin; Z = pyrazinamide; J = TMC207



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# First Novel Combo EBA: NC-001



Pa = PA-824; M = moxifloxacin; Z = pyrazinamide; J = TMC207



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# NC-001 Conclusions

- Validation of mouse data: J-Z synergy, Pa-Z additivity, Pa-J antagonism, Pa-M-Z contributions
- Pa-M-Z an enhanced novel regimen in 2-wk study
  - All three compounds contribute to observed effect
- EBA can distinguish between treatments
  - Just as it has previously distinguished between doses
- CFU and TTP give similar results

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# Post NC-001 Study: Next Steps

- Develop Pa-M-Z for both DS- and DR-TB (in setting of appropriate resistance testing)
  - 2-month “SSCC” study (NC-002)
- Build on J-Z and Pa-Z backbones
- Explore J-Pa building block
- Continue to examine potential regimens in mouse models and bring promising new regimens into clinical development

Pa = PA-824; M = moxifloxacin; Z = pyrazinamide; J = TMC207



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# **NC-002: First Study to Examine DS- and MDR-TB Together Using the Same Treatment for Both**



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**Question: How To Develop a Novel  
Regimen Most Efficiently in All  
Susceptible Populations?**

**Our Answer: Unified DS and DR  
Development Path**



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# REMox Phase 3 Trial



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# Phase 3 REMoxTB Trial Design

Randomized, Double-blind; Non-inferiority

		Treatment Duration (months)					
		1	2	3	4	5	6
		Intensive			Continuation		
630 participants Standard Regimen	HRZE	HR					
	Placebos						
630 participants Moxifloxacin for Ethambutol	HRZM	HRM					
	Placebos						
630 participants Moxifloxacin for Isoniazid	MRZE	MR					
	Placebos						

 **All participants followed for 12 months post-treatment**

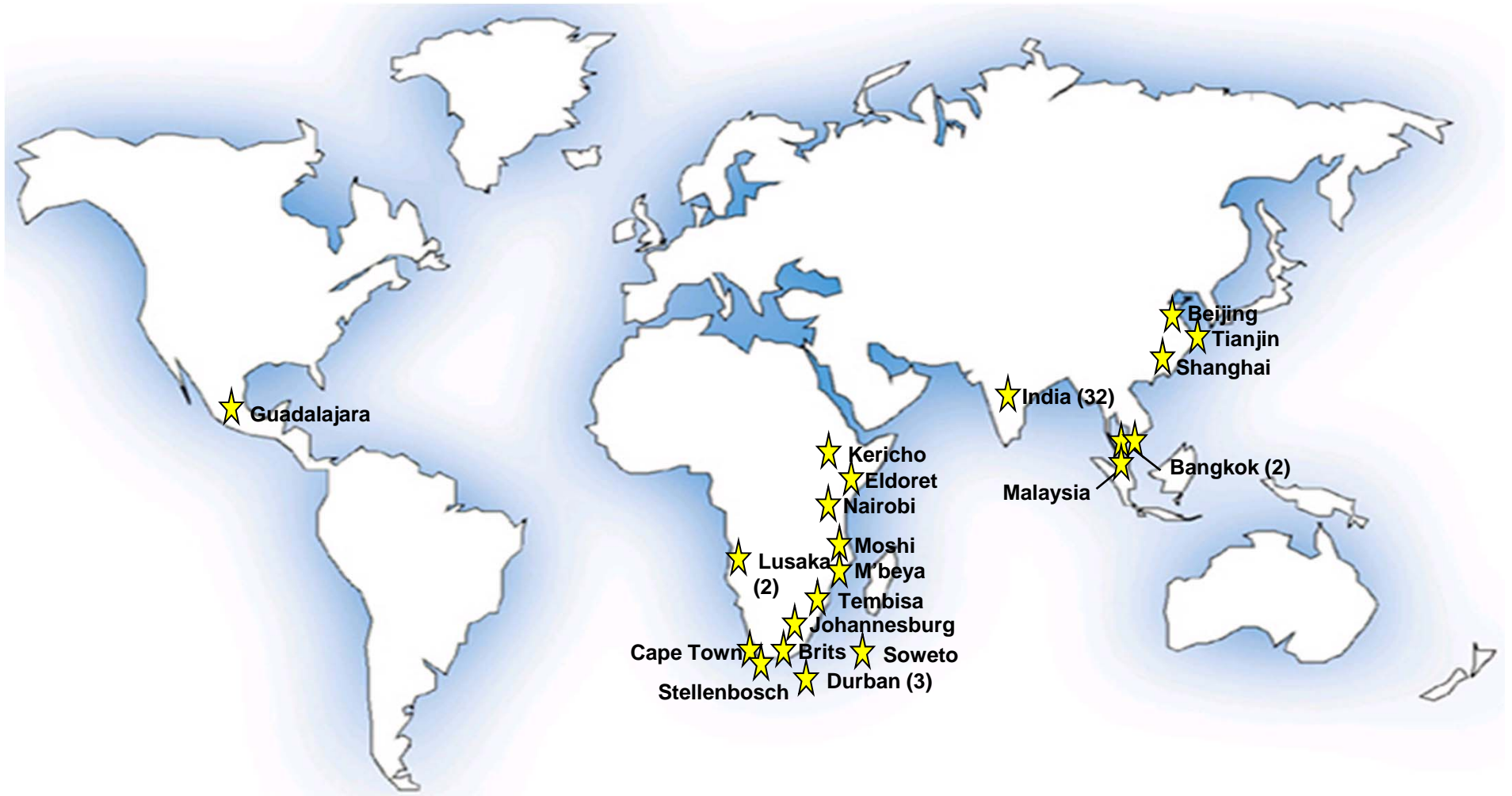
H = isoniazid; M = moxifloxacin; R = rifampin; Z = pyrazinamide; E = ethambutol



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# REMOx Sites



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## *REMOx TB Timeline*

First Patient In:	1Q	2008
Last Patient In:	Dec	2011
Last Patient Out:	Jul	2013
Database Lock:	Dec	2013
Study Report:	April	2014



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***Thank You!***

***And Thank You To Our:***

Funders

Partners

Staff

Stakeholders

Patients



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