

Tuberculosis: The Power of Innovation and Partnership

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Global Alliance for TB Drug Development

Washington, DC - March 19, 2012



TB ALLIANCE

GLOBAL ALLIANCE FOR TB DRUG DEVELOPMENT

TB Alliance Vision

Current Treatment



6-30
Months

New Treatments in Development



2-4
Months

Our Vision

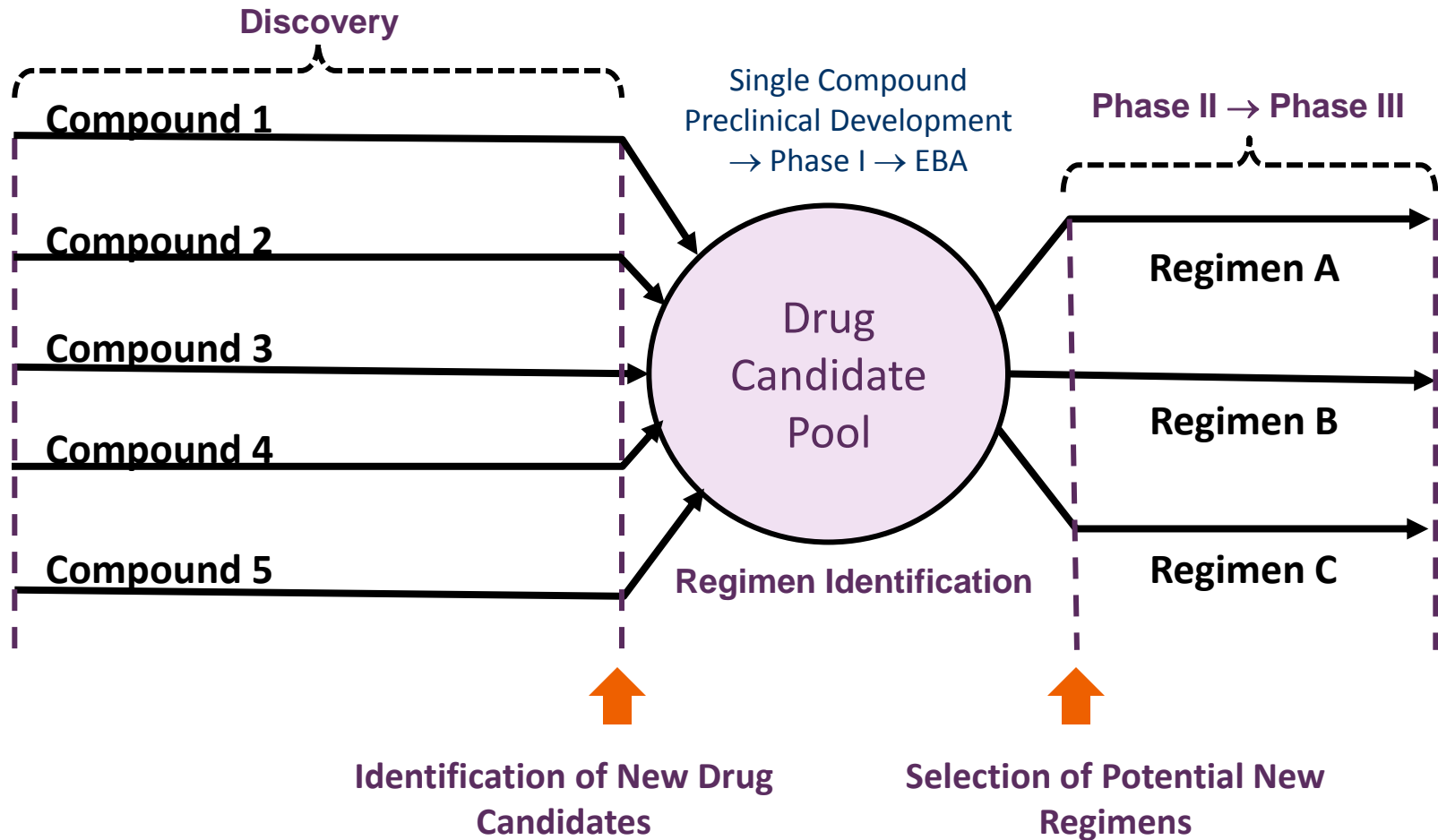


7-10
Days

Success will require novel drug combinations

TB Drug/Regimen

Discovery and Development Process



Launch of the Critical Path to TB Drug Regimens (CPTR)

THE WALL STREET JOURNAL.
AS Thursday, March 18, 2010 THE WALL STREET JOURNAL.

U.S. NEWS

FDA Is Easing Way for Drug Cocktails

Agency Draws Up Guidelines for Approving Two or More New Drugs Together to Fight Deadly Diseases Such as TB, AIDS

By MARK SCHWARTZ

The Food and Drug Administration is devising guidelines that could accelerate testing and approval of multiple regimens for some of the world's most deadly diseases.

At least two pharmaceutical companies are poised to take advantage of the forthcoming policy: a group of 10 drug companies and several nonprofit organizations sponsored by the Bill and Melinda Gates Foundation to develop medicines to fight tuberculosis, and pharmaceutical giant Merck & Co. and AstraZeneca PLC, which are jointly testing two anticancer agents.

Many diseases, such as AIDS, tuberculosis and cancer, require multiple-drug regimens. Each drug cocktail can prevent the development of drug resistance, because the microbes or cancer cells need to undergo more mutations to escape several drugs than to escape one. By streamlining the process in different ways, drug combinations

In the Pipeline | Tuberculosis compounds currently in development

Developer	Experimental drug	Class	How it kills the TB bacteria
Tubotec Johnson & Johnson subsidiary; Global Alliance for TB Drug Development	TMC-207	Diairylpiperazine	Disrupts cellular energy production
Otsuka Pharmaceutical	CPC-47683	Nitroimidazole	Disrupts synthesis of lipids and proteins
Global Alliance for TB Drug Development	PA-824	Nitroimidazole	
Legion	LL-3958	Pyrimidine derivative	Not well understood
Sequella	SO-109	Ethylendiamines	Affects cell wall, may have other mechanisms

Sources: Global Alliance for TB Drug Development; Stop TB Partnership Working Group on New TB Drugs; WHO monitoring, Shenzhen Hu and Christian Lindbergh, article in *Current Medicine*.

what research would be required in the test tube, animals and humans to determine side effects, proper dosage and each drug's contribution to any cause certain side effects. "Society wouldn't tolerate this degree of uncertainty," except for drugs to treat rare diseases, she said.

Multidrug-resistant cases—exceeding half a million annually—take two years to treat with drugs that often cause severe side effects but only

Development of TB drugs and cocktails

- 1952: First combination therapy using three drugs
- 1966: One drug in cocktail replaced
- 1970s: Fourth drug added to cocktail
- 1980s: One drug in combination replaced

executives of 18 drug companies. A representative of Novartis, a Swiss pharmaceutical company, participated in the current tuberculosis collaboration. On Thursday in Washington, D.C., the foundation is expected to unveil the collaboration, in which all partners agree to share data and test new drugs in combination treatments early in the development process.

For companies, sharing the cost of clinical trials and bringing proven combinations to market more quickly might save money. But if a regimen fails, it could give every drug in it a bad reputation, which could be costly to overcome, even for drugs that ultimately prove safe and effective. And there are thorny questions on how competing companies should share data, decide which drugs to combine into regimens, and market their drugs.

The Gates collaboration, known as the Critical Path to TB Regimens, includes drug giant Pfizer Inc.



BILL & MELINDA GATES foundation

Pfizer

ANACOR PHARMACEUTICALS

Celgene GLOBAL HEALTH

CRITICAL PATH INSTITUTE
collaborate · innovate · accelerate

SEQUELLA Incorporated

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SANOFI

AstraZeneca

NOVARTIS

BAYER

Johnson & Johnson

REAGAN - UDALL FOUNDATION FOR THE Food and Drug Administration

Cepheid. A better way.

gsk GlaxoSmithKline

VERTEX

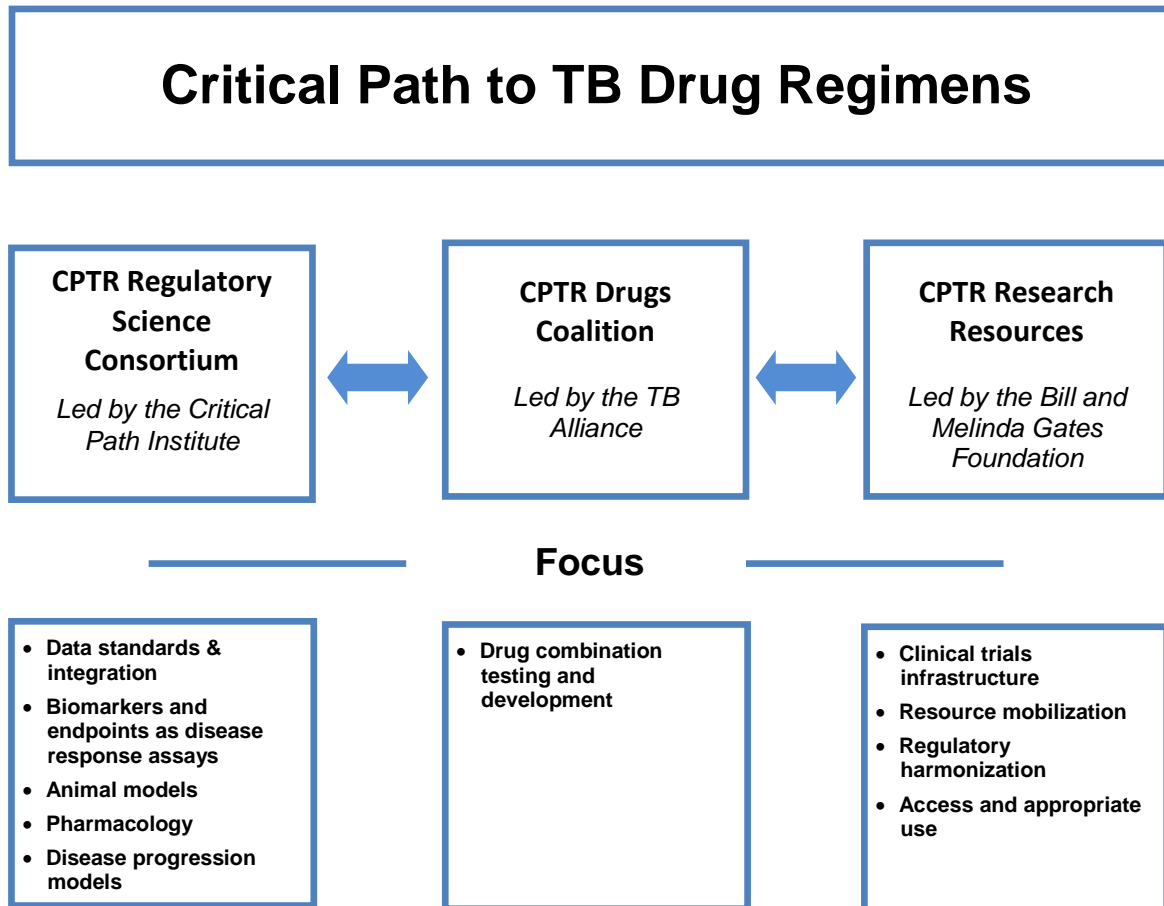
TAG Treatment Action Group

Otsuka

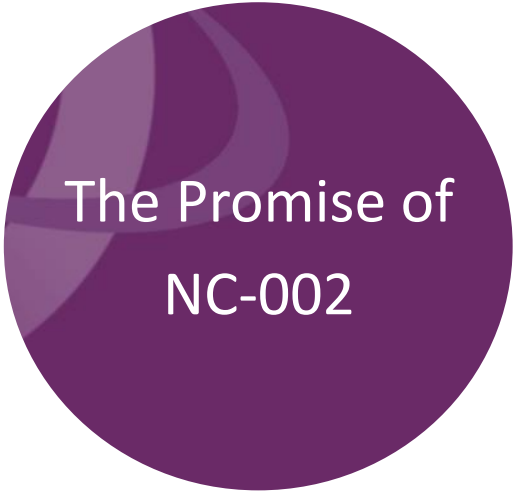
EDCTP

CPTR Initiative

Tackling Challenges to TB Drug Development



NC-002 – A New Pathway to Treating TB



The Promise of NC-002

- Oral, once daily regimen consisting of PA-824 + moxifloxacin + pyrazinamide (PaMZ)
- 8-week trial at 8 sites
- Promising attributes of NC-002
 - First-ever testing of a regimen in both DS- and MDR-TB patients at the same time
 - Potential for major impact
 - shorten MDR-TB therapy by 80%
 - decrease cost of treating MDR-TB by 90%
 - compatible with simultaneous use of anti-retrovirals (ARVs)
 - dramatically ease delivery and distribution logistics
- Pace and scope of new TB regimen trials to accelerate in 2012-13

A world
without TB...



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