The Year In Review
An Inflection Point

Mel Spigelman, M.D.
Chief Executive Officer & President

Plotting the Future

Discovery Research	Z. Ma
Clinical Development	A. Ginsberg
Market Access	E. Gardiner
Finances	S. Jasko
Organizational Growth	C. Pero
Resource Mobilization	M. Burke

New TB Drugs:
Discovery, Development and Delivery

TB ALLIANCE
GLOBAL ALLIANCE FOR TB DRUG DEVELOPMENT

Expansion of the Discovery Portfolio

Zhenkun Ma, Ph.D.
Chief Scientific Officer

The Discovery Team

Chris Cooper, Ph.D.

Medicinal chemistry – 20 years at BMS and Pfizer.

Takushi Kaneko, Ph.D.

Medicinal chemistry – 30 years at Pfizer and BMS.

Khisi Mdluli, Ph.D.

Microbiology – 10 years at Cumbre, Chiron/Pathogenesis.

Annette Shadiack, Ph.D.

Preclinical development – 14 years at Palatine, Locus and J&J.

Anna Upton, Ph.D.

TB biology – 6 years at Rockefeller University.

Gerry Waters, Ph.D.

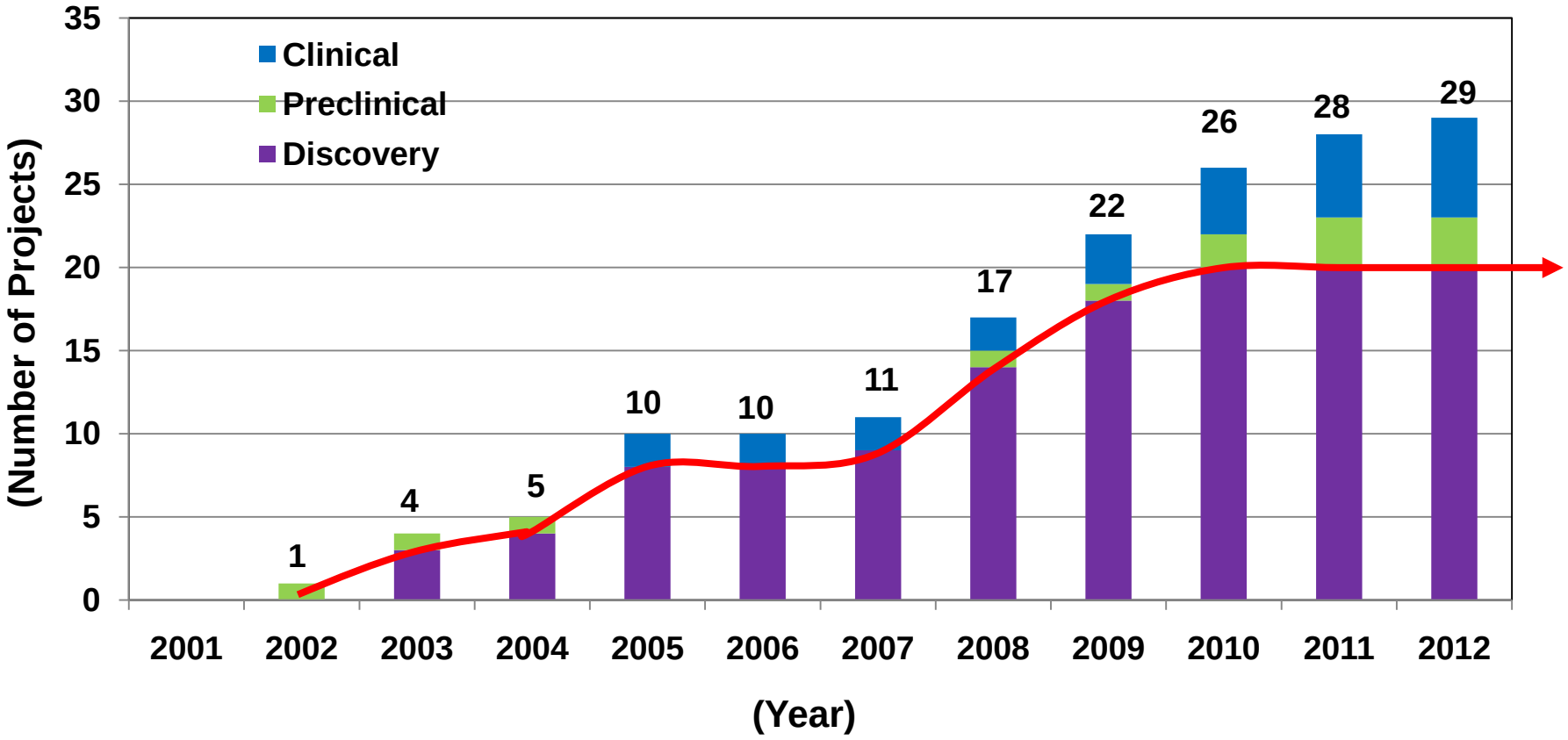
Cell biology – 18 years at Merck and Princeton University.

Objectives of The Discovery Portfolio

To discover a pool of new drug candidates with novel modes of action to enable the rational selection of new regimens:

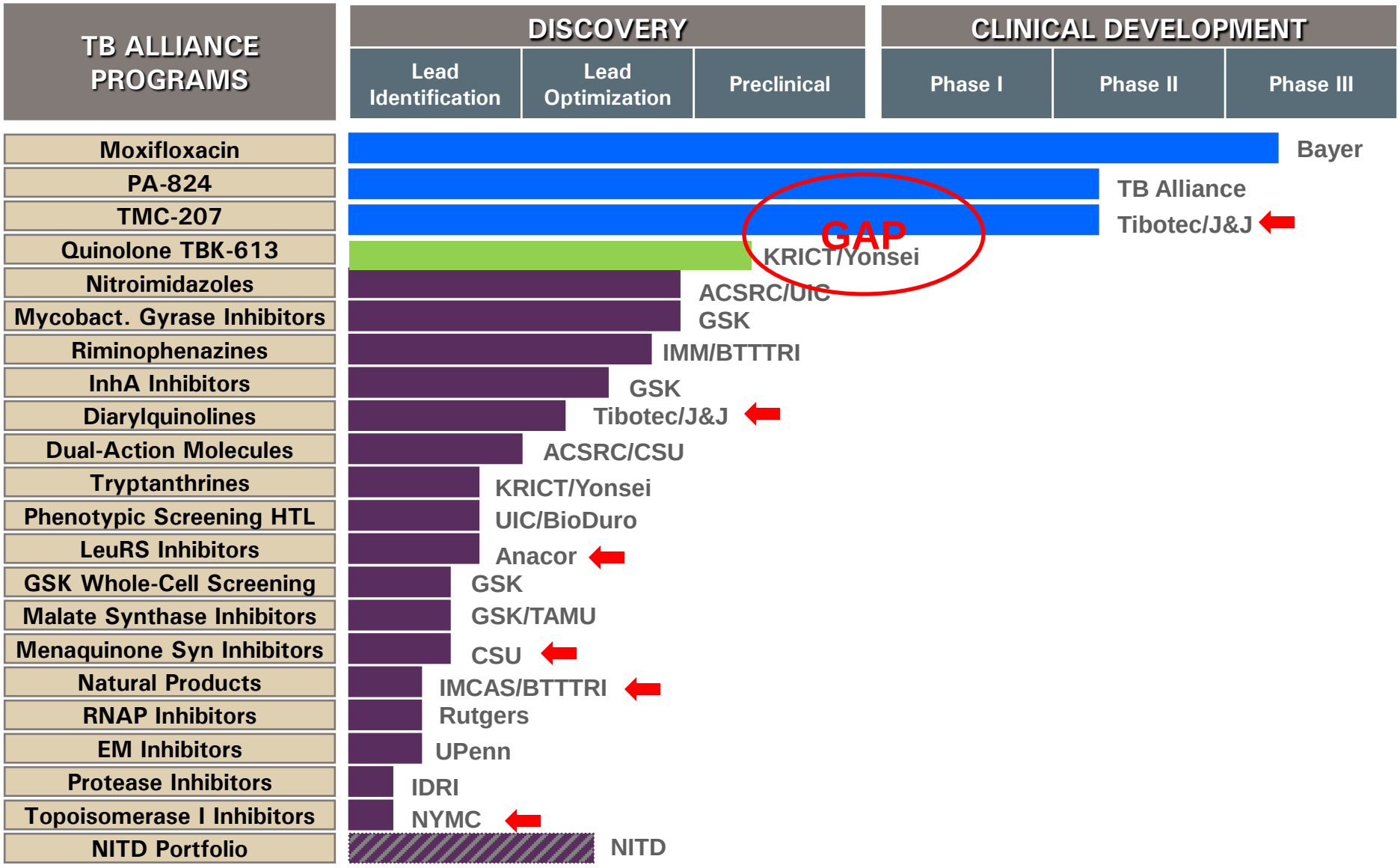
- DS and M(X)DR-TB in < 3 month
- TB/HIV co-infection
- TB in children
- Latent TB infection

Portfolio History and Projection



- Significant portfolio expansion in 2009, with 5 new discovery projects
- Discovery portfolio is approaching steady state in 2010

TB Alliance Portfolio 2009



2009 Highlights

- **Advancement of discovery portfolio to fill the gap in preclinical development :**
  - Nitroimidazoles (preclinical candidate selection)
  - Mycobacterial DNA gyrase inhibitor (preclinical candidate selected)
  - Riminophenazines (preclinical candidate selection)
- **Introduced 5 new discovery projects:**
  - DNA topoisomerase I – Bactericidal inhibitors (New York Medical College)
  - Menaquinone biosynthesis – Ro-series inhibitors (Colorado State Univ.)
  - Natural products – Lead generation (Institute of Microbiology, Chinese Academy of Sciences)
  - Leucyl tRNA synthetase – Oxaborole series (Anacor Pharmaceuticals)
  - ATP synthase – TMC-207 backup (Tibotec/J&J)
- **Terminated 2 existing discovery projects:**
  - Pleuromutilins (lack of efficacy and therapeutic window)
  - TBK-613 (photosensitivity)

Scaling Up Clinical Development

Ann Ginsberg, M.D., Ph.D.
Chief Medical Officer

Growth and Progress

- Expanding the clinical portfolio
- Building the team
- Forging a critical path to novel regimens
- Engaging the community

Expanding the Clinical Portfolio

- 3 active projects:
  - Moxifloxacin (Phase III; REMox TB trial)
    - *Year of building capacity, centrally and in the field*
  - PA-824 (Phase II)
    - *Off clinical hold; completed enrollment for low dose EBA study in S. Africa*
  - TMC207 (Phase II)
    - *First parallel development programs for drug-sensitive and MDR-TB*
      - *14 day, dose-finding EBA protocol under regulatory review*

Expanding the Clinical Portfolio

- Signed agreement with Tibotec (J&J), in June 2009
  - Established the first integrated, parallel development program for drug-sensitive and MDR-TB
  - Developing the next generation of ATP synthase inhibitors

Building the Team

- Expanded the clinical team
  - 1 senior physician (MD-PhD with 8 years at Merck)
  - 1 clinical pharmacologist (PhD with 10 years at Astra Zeneca and 1 year at Pfizer)
  - 2 clinical operations expert (1 MSc with >25 years at Merck; 1 MPH with 7 years at CROs and 8 years at Pfizer)
  - 1 clinical research assistant (MA with 5 years at CROs)
  - 1 safety data manager (Pretoria)
- Pretoria staff now taking the lead on management of EBA studies in S. Africa; REMox site training and initiation, oversight of African and Asian-Pacific sites, and safety data reporting.
- Additional offices being considered in key geographic regions.

Forging a Critical Path to Novel Regimens

- There are now enough new drug classes in late stage development to begin identifying one or more optimized, novel regimens
  - Fluoroquinolones
  - Nitroimidazoles
  - Diarylquinoline
  - Oxazolidinones
  - High-dose rifamycins
  - Ethylene diamine
  - Pyrrole
- *Defining the critical path to development of novel regimens* in an initiative led by the BMGF and in association with the Critical Path Institute and other interested sponsors and stakeholders (regulators, government agencies, foundations, academics)
- Can begin to conceive of one treatment for both drug-sensitive and M(X)DR-TB!

Engaging the Community

- Mechanisms for meaningful communication between the community and researchers to:
  - Ensure research is conducted in an appropriate and respectful way
  - Inform communities about trial status, outcomes and potential risks
  - Obtain community feedback on trial implementation, identify and address community concerns
  - Educate communities about the research process
  - Promote transparency
- Small Grants Program provides small grants to sites participating in late stage trials for site-level community engagement strategies
  - Six REMoxTB sites have Community Advisory Boards (CABs)

Reaching Patients: Building an Access Strategy

Elizabeth Gardiner, M.Sc.

Vice President, Market Access

Market Access

- What are the driving principles?
- What has been achieved so far?
- What is the strategy?
- How are we going to achieve it?
- What can you do to help us?

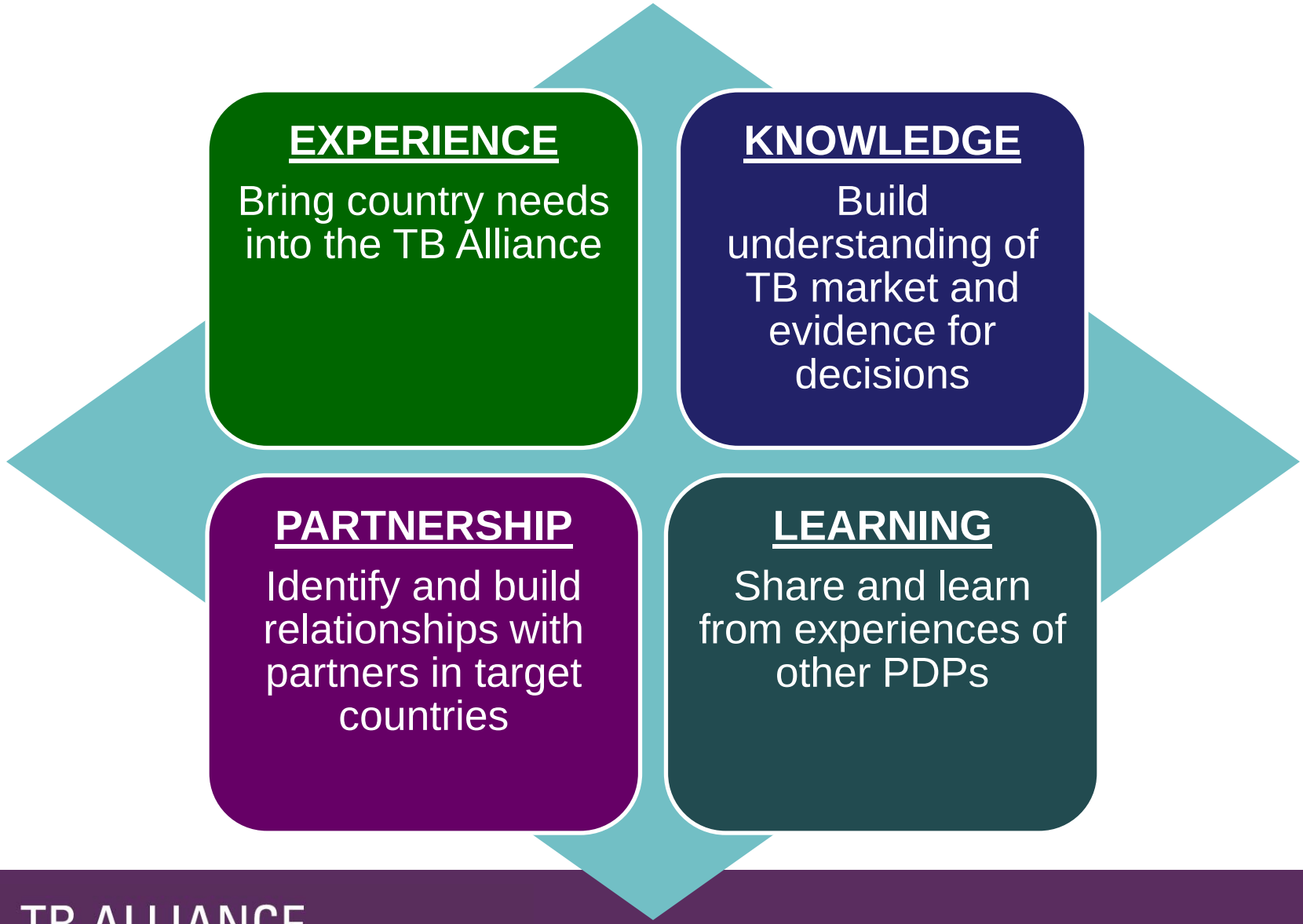
“AAA” Principle

Affordability	• Sufficiently low cost to be procured
Adoption	• Implemented by public programs and private sector
Availability	• Products manufactured and distributed

Achieved to Date

- **Studies**
  - Pathway to Patients (with IMS, 2006)
  - Value Proposition Study (with IMS, 2007)
  - Country Introduction Study (with MSH, 2008/09)
- Demand forecasting (with IMS, 2008 & Applied Strategies, 2009)
- Framework for Adoption (with Retooling Task Force, 2007)
- Access Subcommittee formed with Bayer Schering Pharma
- Market access strategy document drafted

Strategy 2010-2014



Market Access Activities

- Ongoing
  - Consult with R&D team on trial design and other product decisions
  - Participate in WHO/country program reviews, etc.
  - Develop marketing plans for all products in Phase III
  - Track diagnostic development timelines
  - Work via “Introducing New Approaches and New Tools” subgroup of DOTS Expansion Working Group
- 2010
  - Conduct studies of private sector markets & patient perceptions
  - Write moxifloxacin marketing plan
    - *Define “product”*
    - *Specify price and mechanisms to pay for it*
    - *Outline launch plans*
    - *Identify communications needs, including training*
    - *Initiate Phase IV research planning*

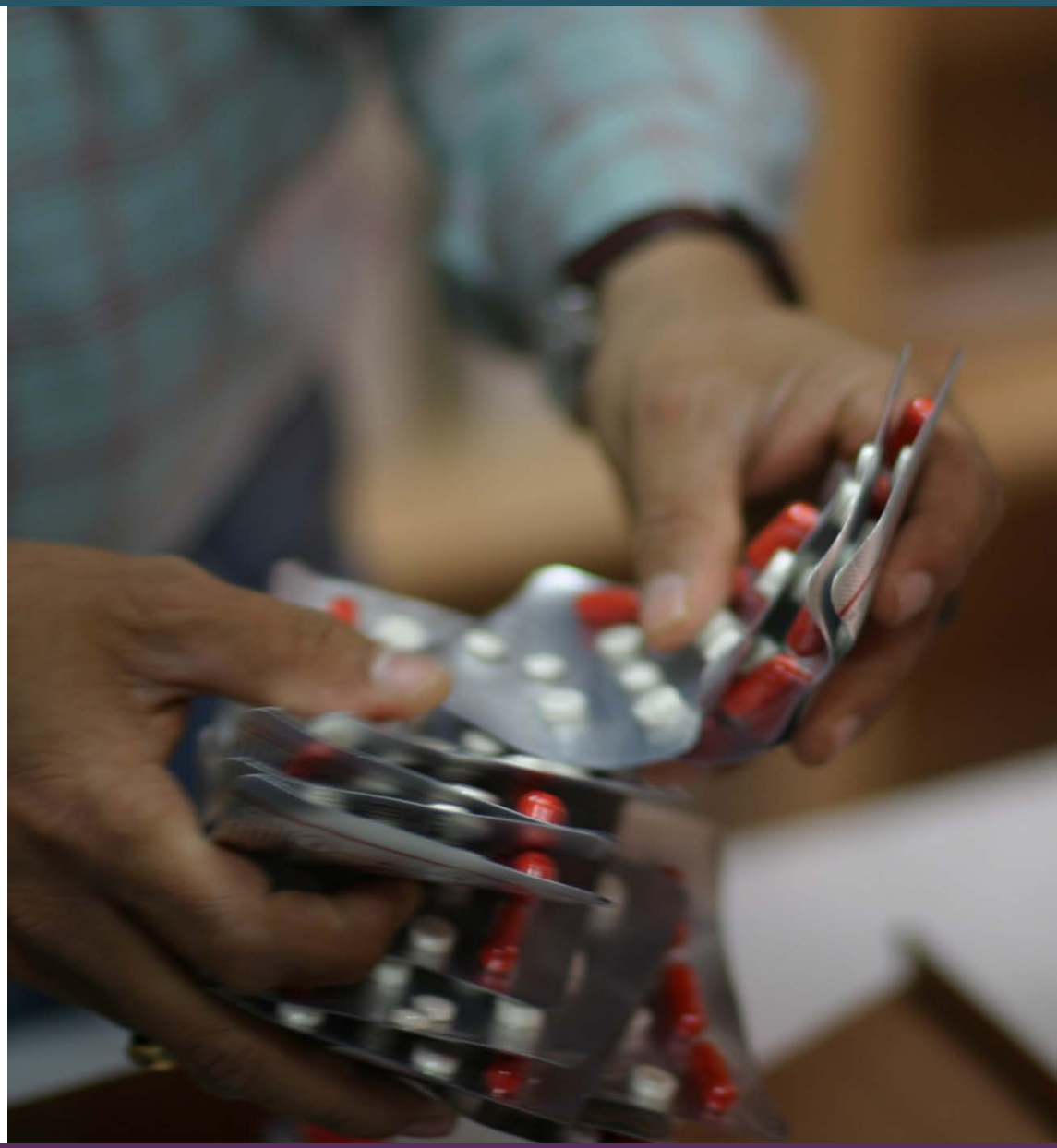
How You Can Help

- Give feedback on this strategy
- Provide ideas about what we need to learn about TB market – and what not to study
- Share real-life TB experiences
- Help collect patient perspectives
- Identify potential partners in specific countries
- Become a partner in one or more countries

Ensuring Institutional Strength

Establishing Financial Sustainability

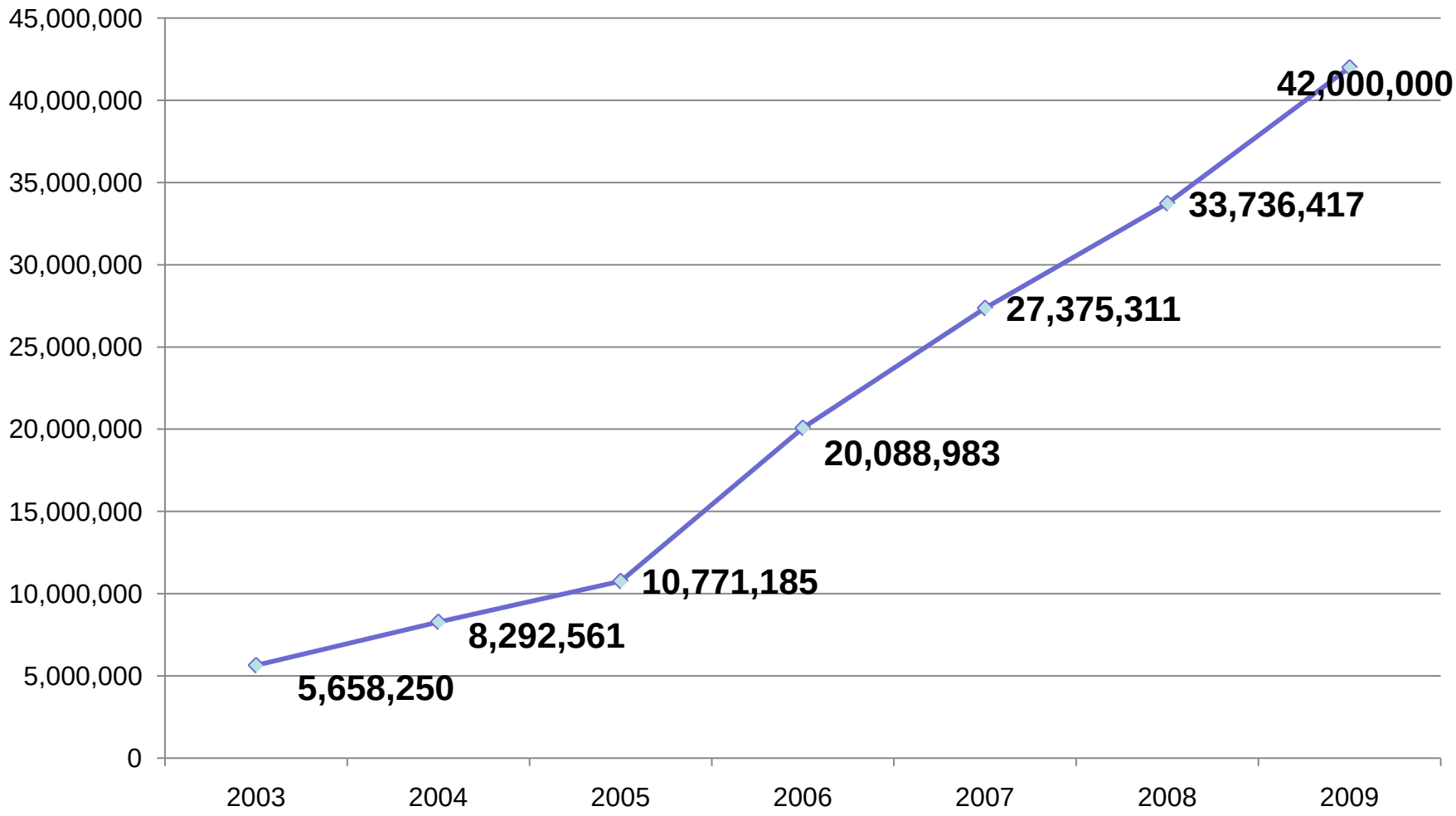
Stephen Jasko, M.B.A.
Chief Financial Officer



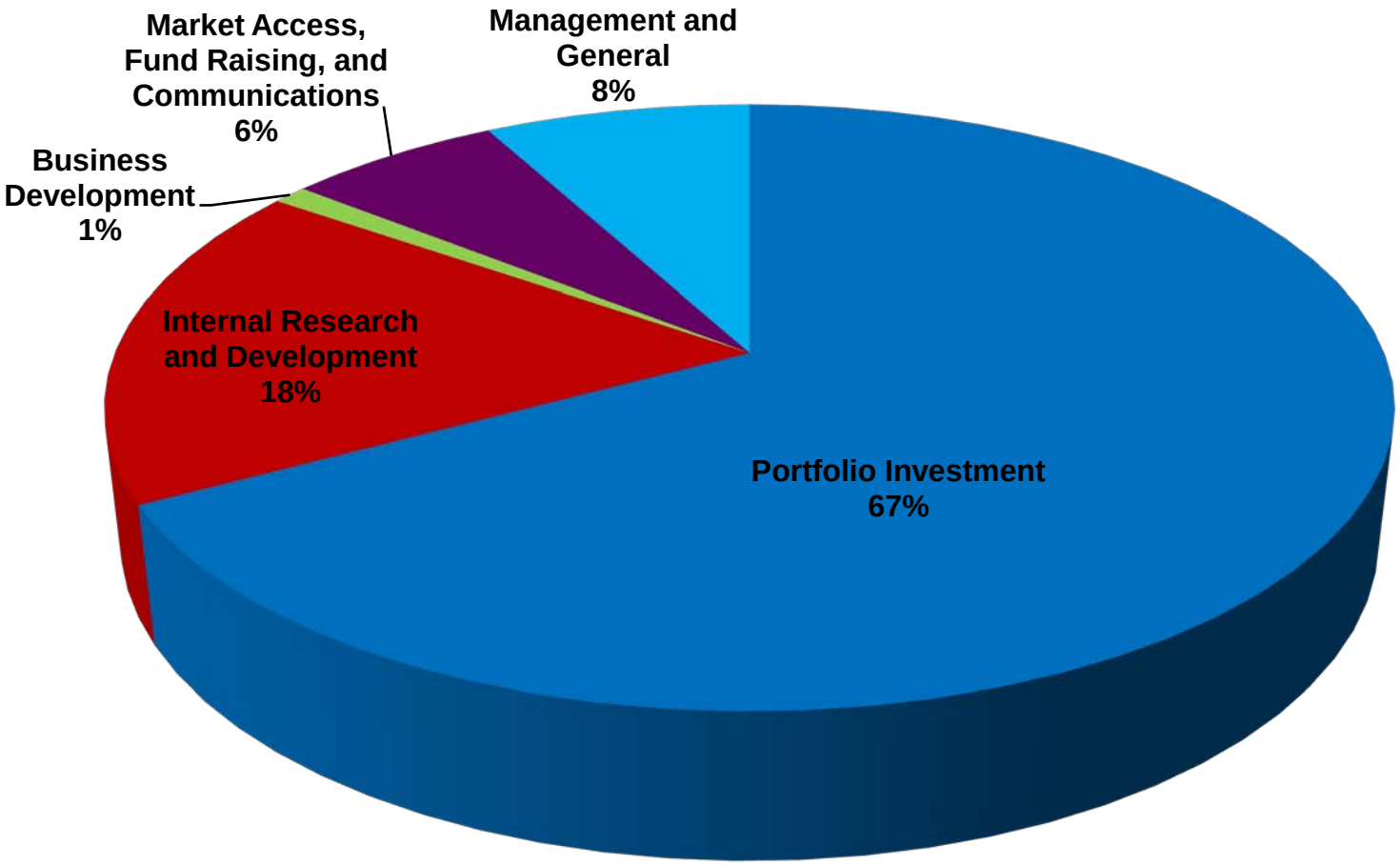
Financial Agenda

- Expenses
  - Trends
  - Composition
- Leveraging Resources
- Clinical Trial Cost Metrics

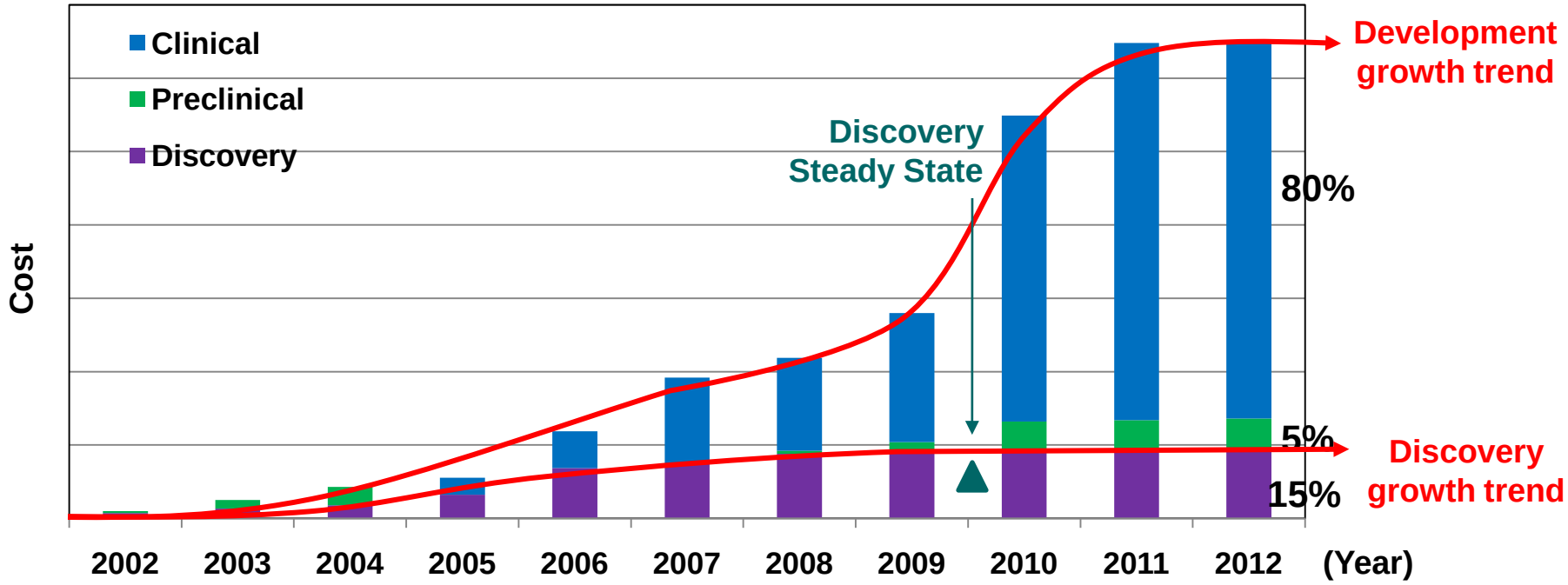
2003 - 2009 Expense Trend



2009 Projected Expenditures ~$42 million



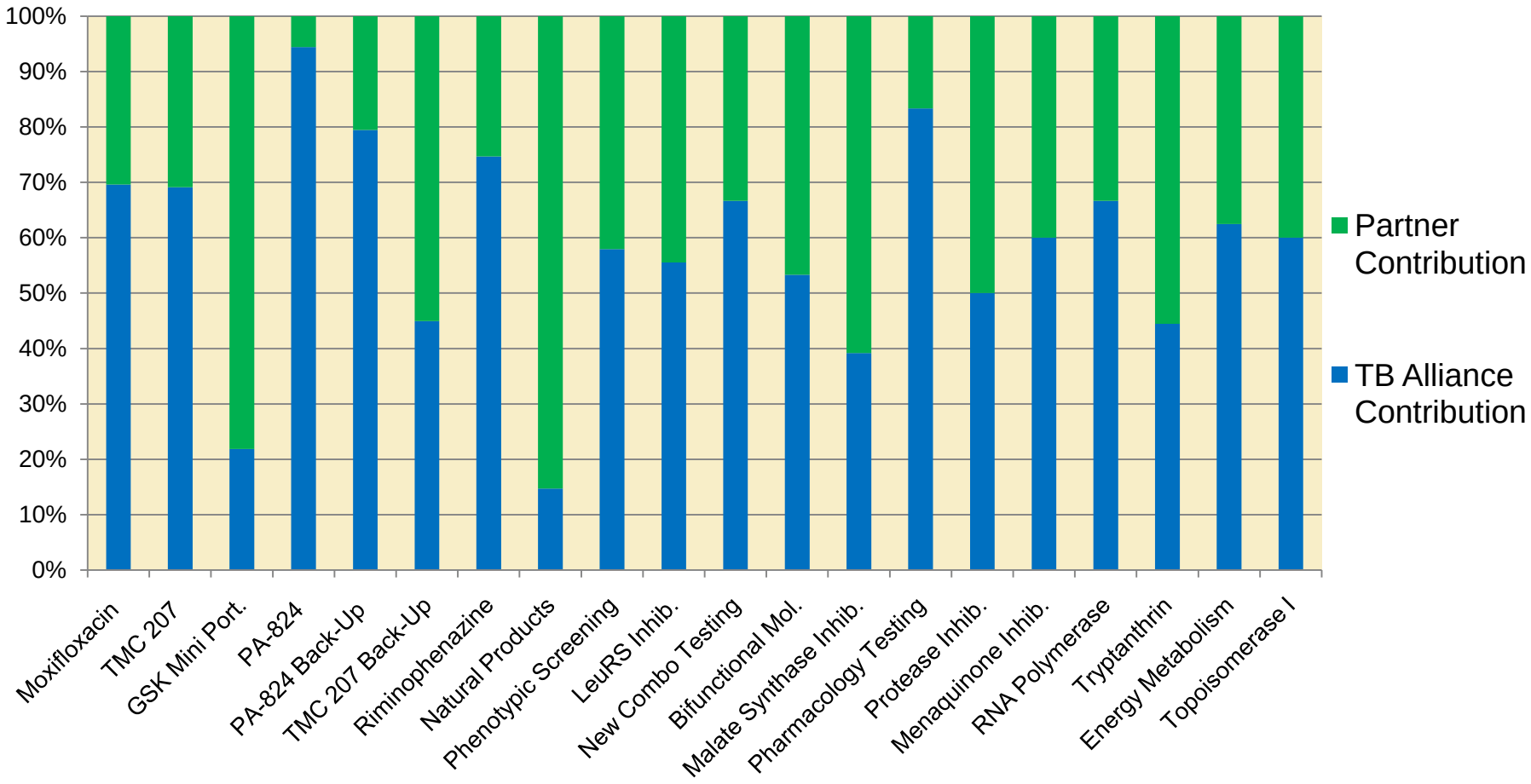
Portfolio Investment – External Expense



- Success drives expense growth
  - Clinical advancement of projects most significant factor
- Continuously optimizing resource usage
  - Identifying more cost effective providers
  - Leveraging partners – every dollar of external spend creates $1.60 of value

Leveraging Our Funders' Contributions

TB Alliance Partner Contribution by Project



TB Clinical Trial Cost Metrics

- Total cost for a drug sensitive clinical program > $100 million
- MDR clinical program costs may be higher
  - Fewer patients, but higher per patient costs

Clinical Trial Costs	Per Patient Cost	Total Trial Cost
DS Phase I Single Dose	20,000 to 30,000	0.75mm to 1.25mm
DS Phase I Multiple Dose	25,000 to 35,000	0.75mm to 1.25mm
DS (EBA)	20,000 to 30,000	1.5mm to 2.5mm
DS (Phase 2)	20,000 to 35,000	8mm to 12mm
DS (Phase 3)	20,000 to 35,000	60mm to 80mm
MDR (Phase II/III - 2mth/6mth treatment)	up to 200,000	20mm to 35mm
MDR (open label saftey study)	up to 200,000	20mm to 30mm
MDR (Phase III with long-term followup)	up to 200,000	25mm to 35mm

In USD

Building for Organizational Success

Colleen Pero, M.A.
Chief Administrative Officer

Drivers of Organizational Growth

- Substantial increase in size and complexity of R&D portfolio
- Multiple products in clinical development
- Increased emphasis on Affordability, Adoption, and Availability (AAA)
- Normal organizational maturation

Key Organizational Tenets

Operating Model

- Mission-centered
- Virtual
- Lean
- Highly leveraged & asset-light
- Nimble

Organizational Requirements

- Clear purpose
- Projects externally executed
- Small team, but deep & broad
- External partners share costs & responsibilities
- Ability to execute non-traditional alliances
- Integration of projects at any stage

Individual Requirements

- Passion
- Relationship Management
- Depth & breadth
- Influence vs. control
- Flexibility
- Versatility

Key Competencies

Purpose	Core Expertise	% of Staff
Research & Development	Scientific (biology, chemistry, pre-clinical) Clinical (medical, clinical trial execution, regulatory compliance)	65%
Affordability, Adoption, Availability	Market Research and Launch Planning Policy & Advocacy Community Engagement	10%
Enabling	Resource Mobilization Communications Finance, Admin, Human Resources, IT Business Development	25%

Strategic Growth

	4Q 2008	4Q 2009
New York	18	42
Pretoria	3	5
Brussels	1	0
Total	22	47

Organizational Initiatives (1)

- Increasing communication outreach efforts
  - Visibility in selected geographies (Spain, China)
  - Influence with targeted US and European media
- Upgrading internal operating effectiveness
  - Enhancing business processes
  - Upgrading IT systems

Organizational Initiatives (2)

- Increasing geographic presence
  - Managing clinical trials and community engagement locally
  - Expanding impact of Advocacy, Policy, and Resource Mobilization
- Enhancing efficiency by appropriate internalization of capabilities
  - For example: regulatory expertise, dedicated R&D project management

Challenges & Opportunities in Resource Mobilization

Marshall Burke, Ph.D.
Senior Vice President,
External Affairs

External Affairs
Who We Are

- Resource Mobilization
  - Deepen relationships with current funders
  - Generate new funding; expand and diversify funder base
- Policy and Advocacy
  - Build advocacy partnerships to raise awareness of the need for new TB drugs
  - Secure political commitment to TB drug development among current and prospective multi- and bi-lateral donors
- Community Engagement
  - Foster dialogue between researchers and communities
  - Build understanding of the need for new TB drugs

Our Donors

- Bill & Melinda Gates Foundation
- Irish Aid
- Netherlands Ministry of Foreign Affairs (DGIS)
- U.K. Department for International Development (DFID)
- U.S. Agency for International Development (USAID)

The Global Economic Challenge

As discovery successes bring compounds into clinical trials, costs increase dramatically at a time when:

- Bi-laterals are pulling back, stopping altogether or not fulfilling pledges
- Foundation giving declines as assets erode
- Donor agencies are shifting their focus away from global health towards global warming, etc.
  - Example: excluding BMGF, HIV/AIDS funding declined 3% compared to 2007; 42% of foundations expect their giving to decrease(1)
- Up to 1 billion more people will fall into hunger-based poverty(2) and another 53 million more into absolute poverty in 2009 alone(3), greatly increasing a major risk factor for TB

(1) Funders Concerned About AIDS
(2) Deutsche Welle publication on World Bank/IMF study
(3) UN News Center on World Bank Study

The Opportunity:

1. Diversify our resources
2. Redouble our efforts
3. Get out of the box
4. Maximize our networks

What You Can Do

- If you are from a potential donor country, or have access to a donor organization, **advocate** for greater TB R&D financial support
- If you are from a high-burden country, **advocate** for greater government participation in TB R&D
- No matter who or where you are, ***use your networks*** to raise awareness!

A Call to Action

Together we can deliver hope and health by saving millions of lives within the world's most disenfranchised and forgotten communities.

We are at the cusp of delivering a faster and better cure for this ancient plague – now is not the time to stop. Now is the time to outpace TB.

You are the founding and most loyal supporters of the TB Alliance – we need your ongoing support and help as we continue to advance.