From Supply to Research: *Overcoming Barriers to TB Elimination*

Suraj Madoori

Treatment Action Group

Union NAR

February 23,2017

Acknowledgements

- Mike Frick, Senior TB/HIV Project Officer
- Kenyon Farrow, U.S. and Global Policy Director
- NTCA, ACET
- 3P

Objective(s)

- Describe current issues in access to TB drugs, and medication shortages
- Describe current activities underway and models being considered to address these issues
- Identify at least one advocacy role relevant to TB drug access, and TB R&D funding to ensure a pipeline of new treatments, diagnostics and a vaccine for TB

TAG
Treatment Action Group

Drug Supply and Access Challenges: U.S.

The problem

- U.S. pathway to elimination of TB threatened—flat funding, increased problems accessing drugs and biologics
- Major obstacles to access: shortages, supply interruptions and cost
- Can lead to:
  - treatment interruptions →resistance, longer periods of infectiousness, missed work
  - suboptimal treatment regimens →more toxicity
  - delays in hiring of health care and other professionals
  - loss of precious time and resources from program side

TAG
Treatment Action Group

Table 1: TB Drug and Biologic Shortages in the U.S. 2011-2013

TB Product	Supplier(s)	Reason(s) for Shortage
Isoniazid	Teva West-Ward (VersaPharm) Sandoz	Lack of raw materials; manufacturing discontinuation; other
Ethambutol	Teva West-Ward (VersaPharm) Lupin	Manufacturing discontinuation
Injectable rifampin	Bedford Pfizer West-Ward (VersaPharm)	Increased demand outpacing supply; other
Capreomycin	Akorn	Manufacturing problems; lack of raw materials; sole-source U.S. manufacturer
Amikacin	Teva Bedford (discontinuing production)	Manufacturing problems; lack of raw materials; increased demand outpacing supply
Streptomycin	X-GEN	Increased demand outpacing supply
Kanamycin	APP Pharmaceuticals	No longer produced in the United States
Clofazimine	Novartis	Problem with API
Tubersol	Sanofi Pasteur	Manufacturing problems

2013 Consultation

- **A Silent Crisis: Tuberculosis Drug Shortages in the United States** (January 18, 2013 in Washington DC)
- Cosponsored by TAG, the American Thoracic Society, RESULTS, the Center for Global Health Policy, and PATH
- Meeting participants (>60)
  - TB control program managers, researchers
  - FDA, CDC, GDF
  - Supply-chain managers, pharmaceutical reps /manufacturers
  - Advocates, TB survivors
  - Press

Findings of TAG 2013 consultation

- Too few API suppliers and manufacturers (9 of 15 TB drugs approved in U.S. have single supplier)
- Inadequate interagency communication
- Need for better supply-chain management
- Poor risk-management, both for purchasers (TB programs) through stockpiles and suppliers due to lack of good demand forecasting
- Limited surveillance and tracking around shortages.

http://www.treatmentactiongroup.org/tb/drugs-advocacy/stock-outs/federal-advocacy-meetings/Silent-Crisis

2014 Consultation

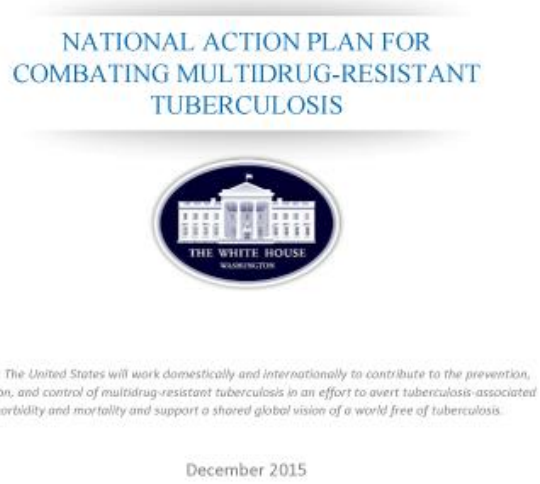
- **Solving the Crisis: Tuberculosis Drug Shortages in the United States** (January 15, 2014 in Washington DC)
- Cosponsored by TAG, National Tuberculosis Controller's Association (NTCA), and PATH
- Meeting participants (24)
  - TB control program managers, researchers
  - FDA, CDC, GDF, HHS
  - Advocates (TAG, ID Society, RESULTS, PATH, ATS, ASTHO)

2014 Findings & Recommendations

- Create a rotating, vendor-managed inventory reserve
- Centralize procurement
- Expand the pool of U.S. suppliers
- Expand markets to maintain existing U.S. suppliers
- Improve communications

White House MDR-TB Plan 2015

- MDR-TB Plan: Drug Shortages
  - CDC to explore national rotating stockpile
  - CDC to work with public/private sector on procurement of drugs and diagnostics
  - Ensure a steady market for off-patent drugs used in TB regimens
- CDC received about $1.7 million in FY 2016 and almost $2 million in FY 2017 to put towards the anti TB drug stockpile (AMR Plan).


NATIONAL ACTION PLAN FOR COMBATING MULTIDRUG-RESISTANT TUBERCULOSIS

THE WHITE HOUSE

Vision: The United States will work domestically and internationally to contribute to the prevention, detection, and control of multidrug-resistant tuberculosis in an effort to avert tuberculosis-associated morbidity and mortality and support a shared global vision of a world free of tuberculosis.

December 2015

Ongoing Challenges

- US domestic challenges connected to global, but resistance and regulatory challenges to harmonization
- No central procurement to negotiate better costs/stabilize supply
- No NTP/patchwork approach by state
- Stockpile ONLY for stockouts, not for other kinds of supply disruptions, including price spikes
- Stockpile is expensive-projected $20mil USD for 6-months rotating supply of first line drugs
- FDA registration too expensive for the low demand
- Price spikes

Sole Manufacturer & Pricing

- In Sept 2015 NTCA was alerted that Chao Center regarding the reported price increase for cycloserine 250 MG CAP 30 UD (*blister pack*) effective 8/21/2015 from **$460 to $10,800USD — a 2000%+ increase over the previous price.**
- Chao Center is the sole manufacturer of cycloserine in the US market
- Not effectively a stockout or drug shortage, but if unaffordable, it may as well be.
- Opportunity with Trump on drug pricing?
- Synergy with HIV drug price escalation

Opportunities: 2016-2017

- ACET – ongoing work with drug supply workgroup
  - Centralized procurement is necessary to control costs and ensure supply
  - GDF manufacturers should be incentivized to register with FDA
    - GDF and pharmaceutical distributors
  - Legislative solution, model ADAP program? Ryan White?
- USG should contract with GDF to monitor in-country supply
- Linking global supply chain issues to US market, and challenges to TB elimination—US TB elimination has to include global elimination

DO BETTER

TRIPLE TB R&D FUNDING

TB R&D Challenges:
U.S. Role and Opportunities

TAG
Treatment Action Group

Stop TB Partnership

2016 Report on Tuberculosis Research Funding Trends, 2005–2015: No Time to Lose

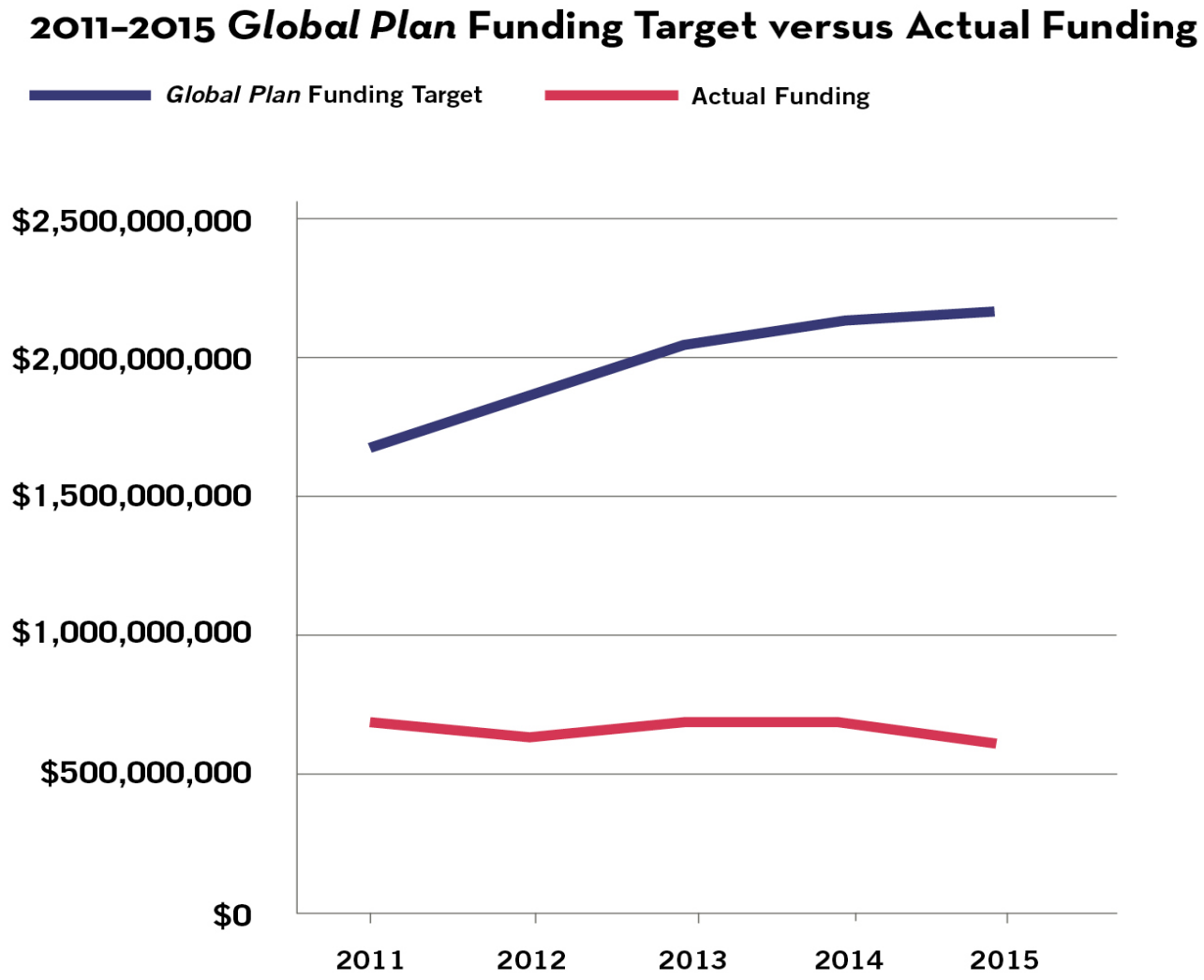
October 2016

Treatment Action Group

By Mike Frick

THE *2011–2015 GLOBAL* PLAN CALLED FOR $9.84 BILLION IN TB R&D FUNDING

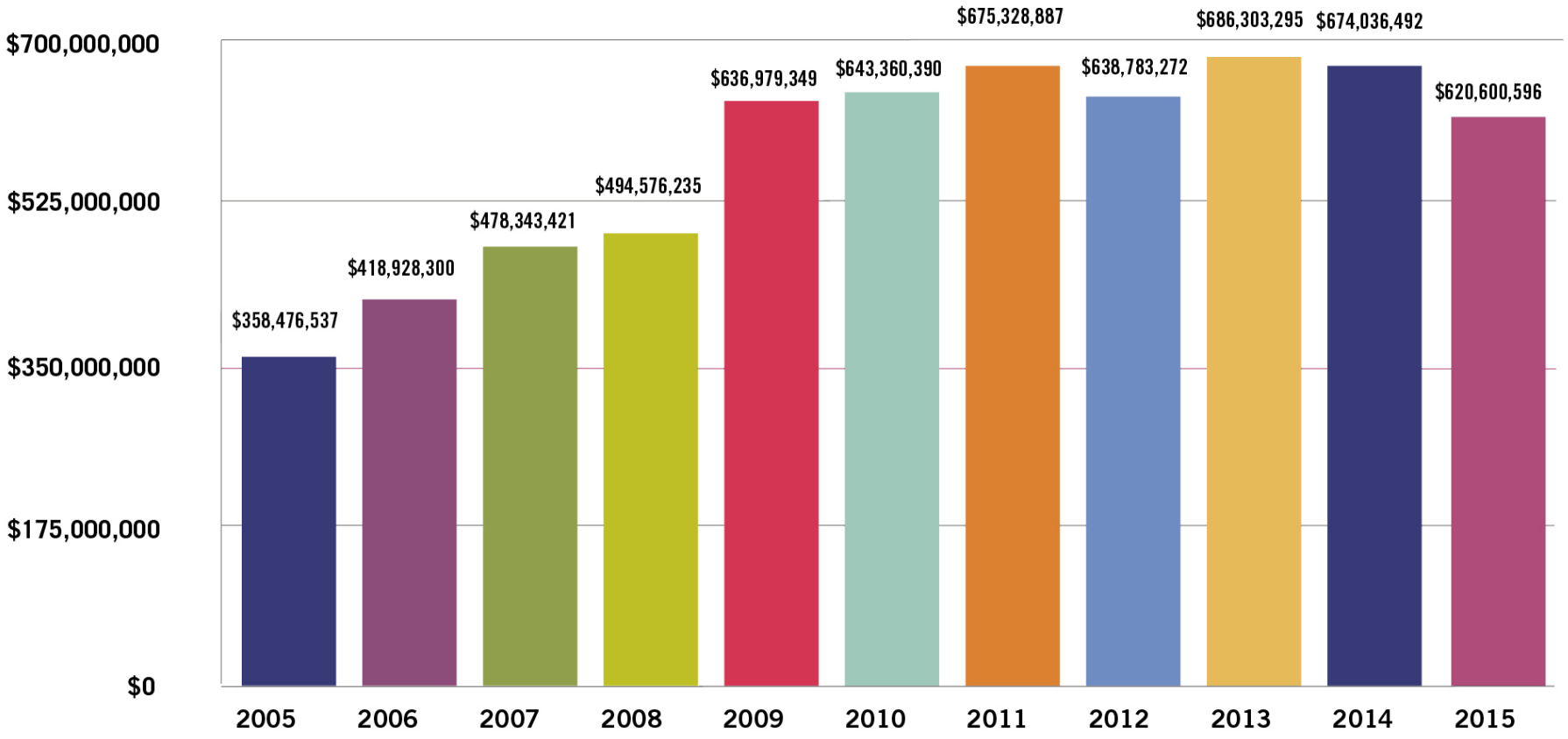
INSTEAD, WE SPENT $3.29 BILLION



IN 2015 TB R&D FUNDING DROPPED BY $53M
FALLING TO ITS LOWEST LEVEL IN 7 YEARS

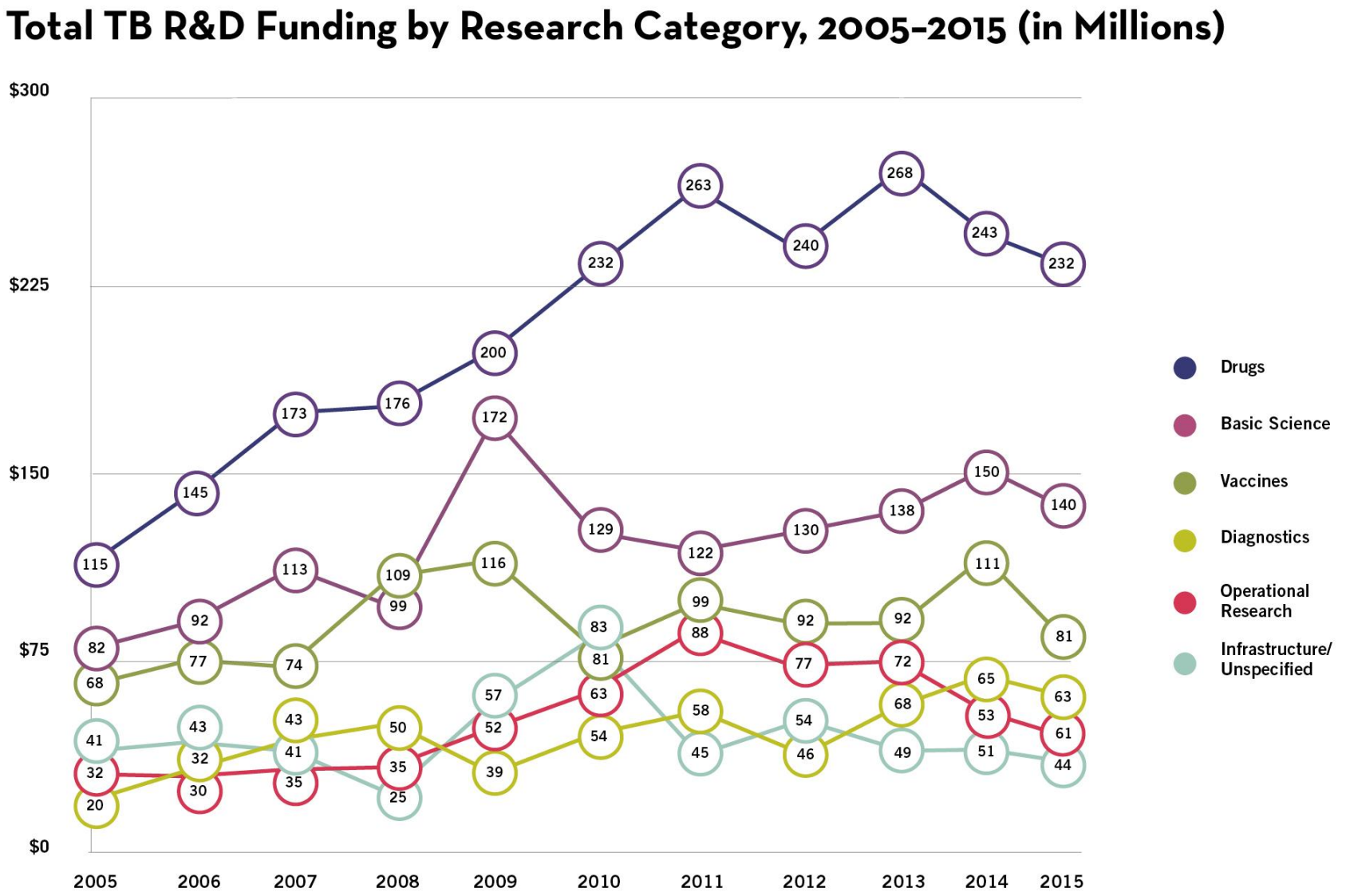
TAG
Treatment Action Group

Total TB R&D Funding, 2005-2015

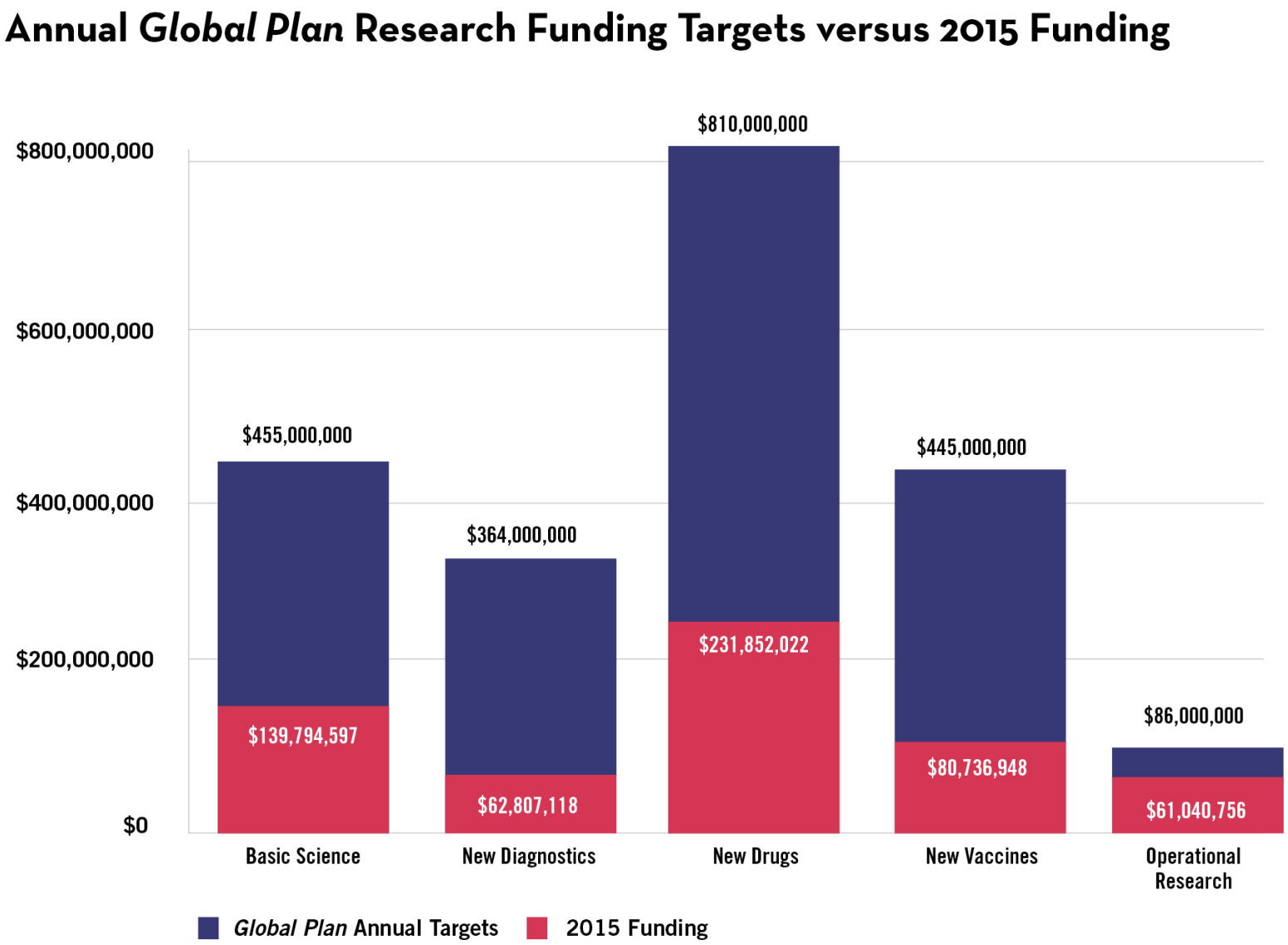


IN 2015 FUNDING DROPPED IN ALMOST EVERY CATEGORY OF TB RESEARCH

TAG
Treatment Action Group



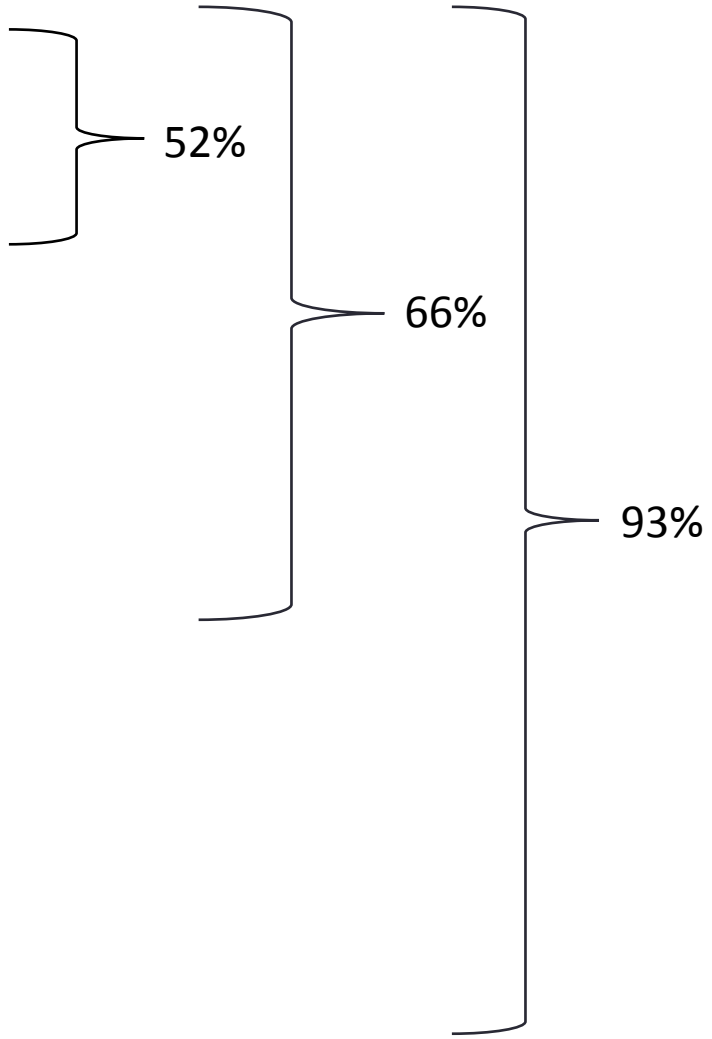
Funding fell short of ambition in every category of TB R&D



funding is highly concentrated

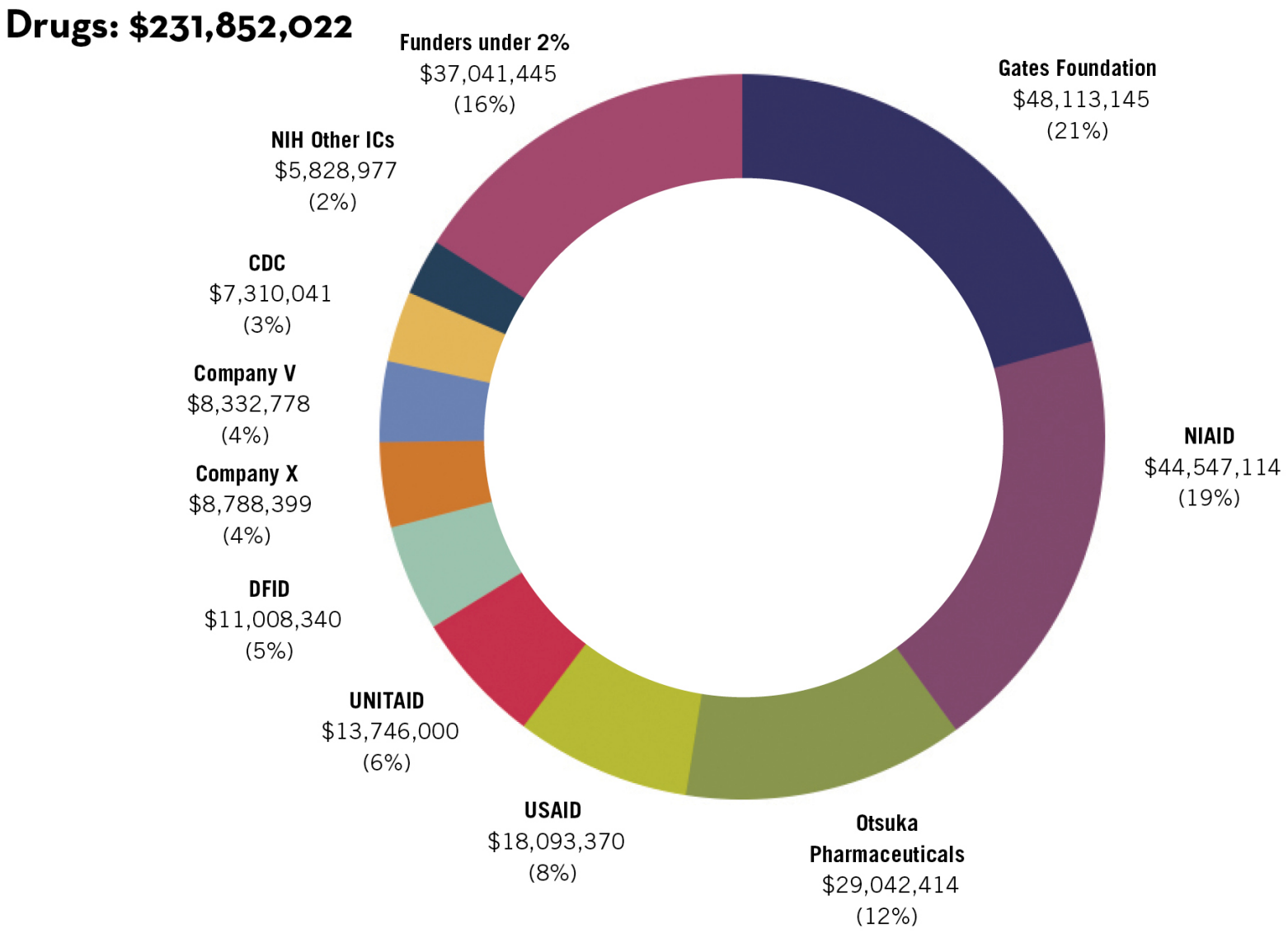
"We are sitting with the U.S. taxpayer." —Valerie Mizrahi

1. US National Institutes of Health	$213,606,591
2. Bill & Melinda Gates Foundation	$110,985,743
3. U.S. Agency for International Development	$34,053,650
4. Otsuka Pharmaceuticals	$29,042,414
5. U.K. Department for International Development	$23,034,975
…	
30. French National Agency for Research	$2,362,871



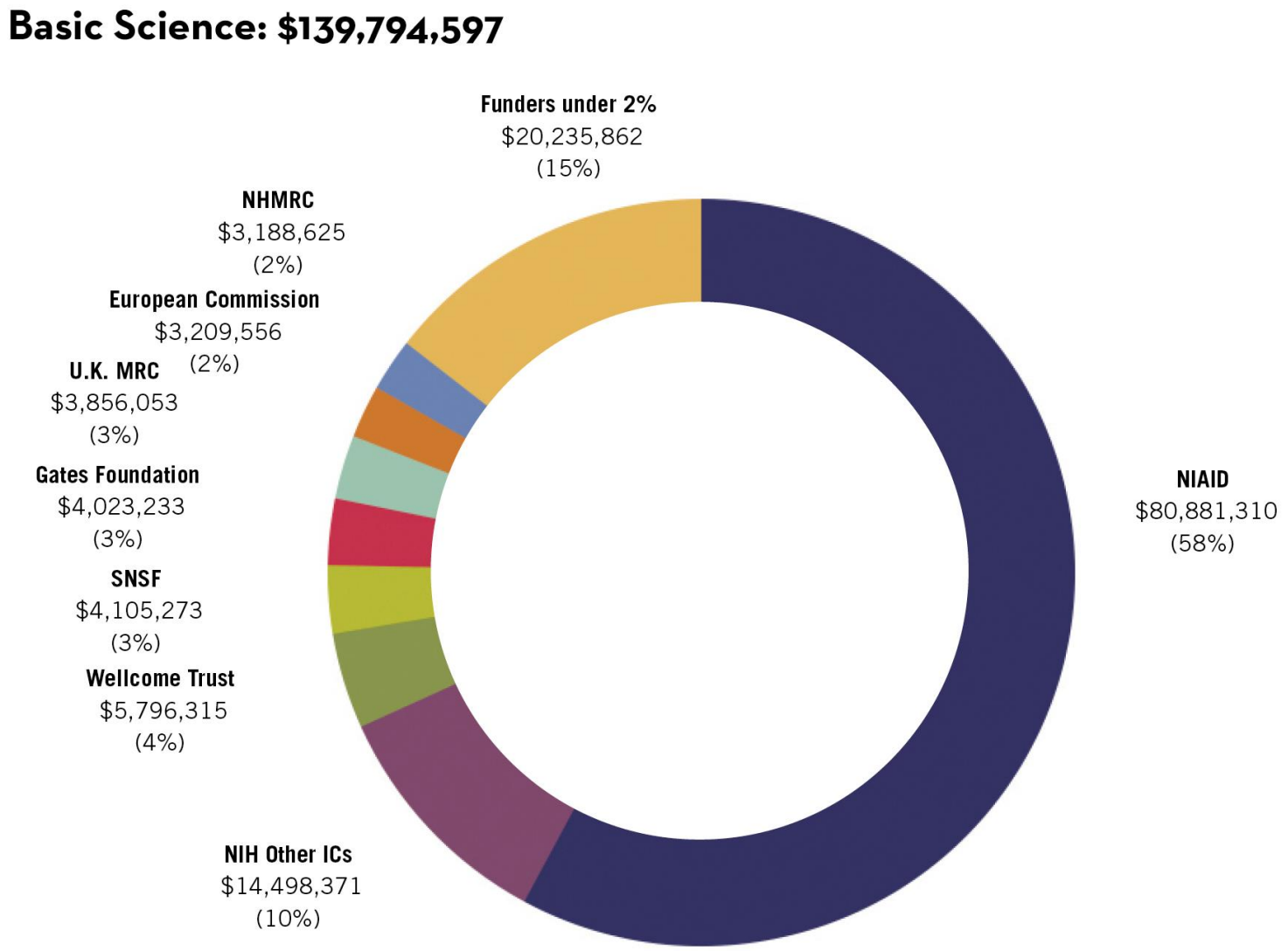
This degree of concentration also applies within specific categories of TB research

TAG
Treatment Action Group



The most concentrated side of the TB R&D Pipeline is its beginning: basic discovery

TAG
Treatment Action Group

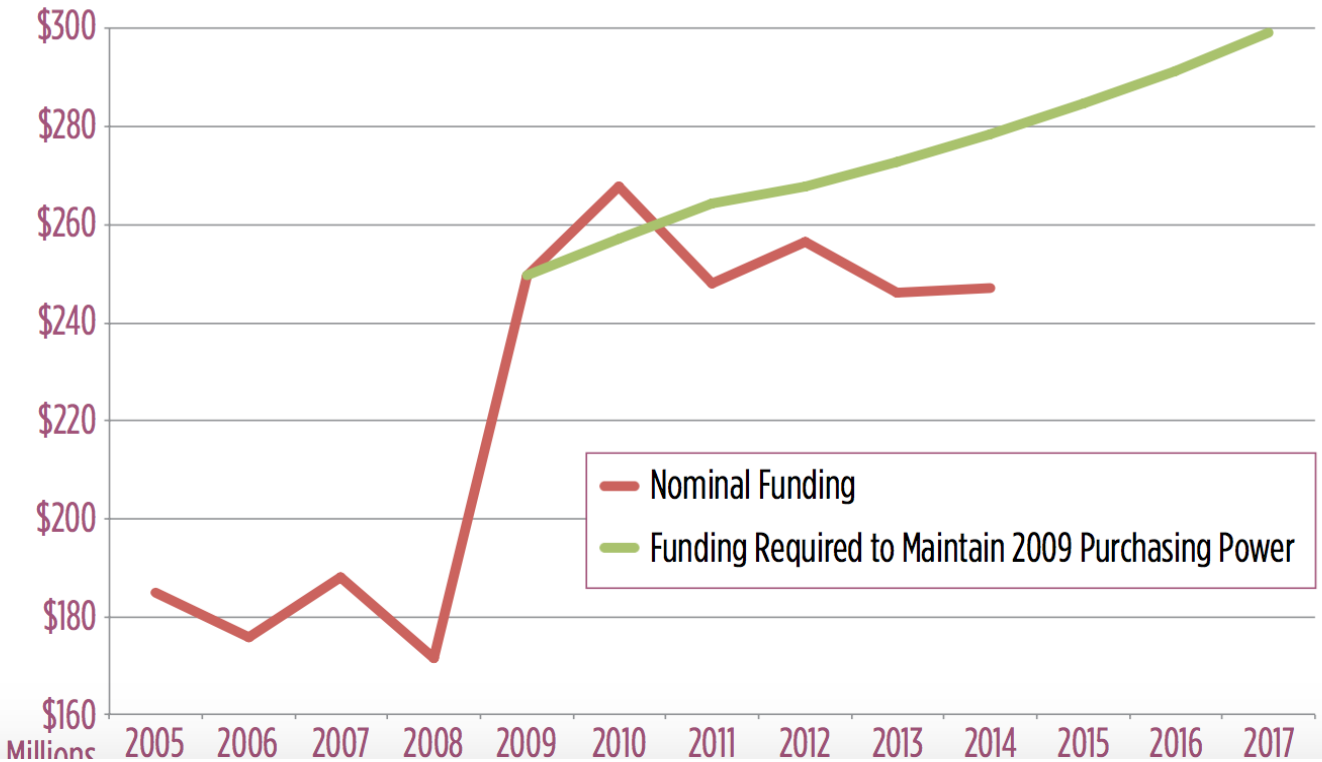


Taking a closer look:

Flatlined Since 2009: U.S. Science Purchasing Power and Parity in TB R&D

The U.S. government leads the world in committing resources to TB research, contributing 37% of the $674.0 million in global funding in 2014. However, its allocation for TB has stagnated since 2009 and has fallen in terms of purchasing power as inflation erodes the value of flatlined investments.* To maintain previous levels of research support in real terms, nominal funding must increase (Figure 1).[4]

Figure 1. Nominal versus Adjusted U.S. Government Funding for TB R&D



How do we turn this around?

TAG
Treatment Action Group

Activism, community and political will




“There can be no end to TB without an end to political indifference in this R&D agenda.”

~ Lynette Mabote, ARASA

National

- No more unfunded national action plans!
- No more national action plans in which TB is an afterthought!

TAG
Treatment Action Group

National Action Plan for Combatting Multidrug-resistant Tuberculosis

- Released with no funding and followed by a Presidential budget that proposed cutting USAID's spending on TB by $45 million.
- Developed as a standalone plan after the National Action Plan for Combating Antibiotic-Resistant Bacteria was released with *only 4 mentions of TB.*
  - CARB-X—a new public-private partnership to spur antimicrobial development—grew out of a recommendation of the National AMR Plan.
- Opportunity: Developing a TB R&D coalition in D.C.
- Opportunity: Building-in TB R&D in funding requests: FY 2018

REGIONAL

A view from the Southern African Development Community (SADC) from activist Lynette Mabote

- “Support for TB R&D within SADC has been insignificant and largely viewed as insignificant in SADC’s development agenda.”
- “Only two countries in the SADC region (Malawi and South Africa) spend above one percent of their GDP on R&D, a target endorsed by the African Union in 2006.”
- “The SADC regional development plan does not have clear R&D or TB R&D indicators.”
- “R&D is not thought of as a matter of national policy. [There is a need to] devise actionable strategies which support R&D resource mobilization.”

TRIPLE TB R&D FUNDING

Dorothy Namutamba, a TB activist with ICW-Eastern Africa and co-chair of the TBTC Community Research Advisors Group, shared a similar analysis about the lack of regional cooperation on TB R&D in Eastern Africa.

GLOBAL

Turn toward multilateral, multi-sectoral mechanisms
for funding R&D

- 3P
- CARB-X
- Longitude Prize
- GHIT Fund
- GAMRIF

- UNITAID

- Unresolved issues:
- New money? Or old money channeled in different ways?
- Nature of private sector involvement varies.
- Which countries will lead public-sector investments?
- Need to develop governance ‘best practices’ related to accountability and transparency.
- Are we moving toward a legally-binding Global R&D Treaty? How will it be situated in relation to existing mechanisms?

Political Declaration of the High-Level Meeting of the General Assembly on Antimicrobial Resistance

- "Recognize that the keys to tackling AMR are…sustained research and development for new antimicrobials and alternative medicines, rapid diagnostic tests, vaccines and other important technologies, interventions and therapies; promoting affordability and accessibility; and resolving the lack of investment in R&D."

But! No targets, timelines, or concrete plans.

UNITED NATIONS SECRETARY-GENERAL'S
HIGH-LEVEL PANEL ON ACCESS TO MEDICINES

Recommendations touch on 3 themes:

1. Intellectual property laws and access to health technologies
2. New incentives for research and development

> "It is imperative that **governments increase their current levels of investment** in health technology innovation to address unmet needs."
>
> "Stakeholders…should **test and implement new and additional models of financing** and rewarding public health research and development, such as the transaction taxes and other innovative financing mechanisms."
>
> "The UN Secretary-General should initiate a process for governments to negotiate global agreements on the coordinating, financing, and development of health technologies, **including negotiations for a binding R&D Convention that delinks the costs of research and development from end prices** to promote access to good health for all."

3. Governance, accountability, and transparency

Sources

- Shah N, Barry P, True L, et al. Drug interruptions: a new challenge for treating multidrug-resistant tuberculosis in the United States. Poster session presented at: American Thoracic Society International Conference; 2012 May 18–23; San Francisco, CA.
- Food and Drug Administration (U.S.). Drug Shortages [Internet]. 2013 May 14 (cited 2013 May 14) Available from:http://www.fda.gov/Drugs/DrugSafety/DrugShortages/ucm314742.htm
- LoBue, Philip (U.S. Centers for Disease Control and Prevention, Division of Tuberculosis Elimination, Atlanta, GA). E-mail communication. 2013 November 14.
- Frick, Mike. 2016 Report on Tuberculosis Research Funding Trends: 2015-2015 No Time to Lose. Treatment Action Group. 2016 November 30.
- Madoori, Suraj. Breathing Life into Flatlined U.S. Government Funding for Tuberculosis Research: FY 2017–2020 Allocations and Recommendations . Treatment Action Group. 2016 May 30.

Thank you!

- Suraj Madoori, Senior Health Policy Officer
  - Email: suraj.madoori@treatmentactiongroup.org
  - Twitter: @srj_madoori

- Mike Frick, Senior TB/HIV Project Officer
  - Email: mike.frick@treatmentactiongroup.org
  - Twitter: @mwfrick

- Kenyon Farrow, U.S. and Global Policy Director
  - Email: kenyon.farrow@treatmentactiongroup.org
  - Twitter: @kenyonfarrow