TAG
Treatment Action Group
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WHAT IS NEEDED TO REALIZE UNIVERSAL DST AS A HUMAN RIGHT?

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TREATMENT ACTION GROUP

COLUMBIA SYMPOSIUM ON EMERGING RESISTANCE TO NOVEL TB DRUGS

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THE RIGHT TO SCIENCE

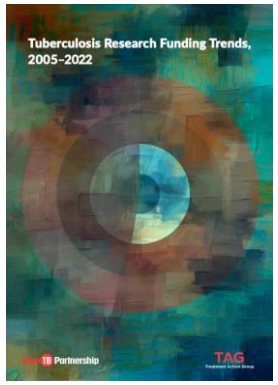
Governments have "**a duty to make available and accessible to all persons, without discrimination, especially to the most vulnerable**, all the best available applications of scientific progress necessary to enjoy the highest attainable standard of heath."

— General Comment 25, Committee on Economic, Social and Cultural Rights

ROLE OF GOVERNMENT:
protect rights (accountability for non-state actors) &
fulfill rights (through funding and supportive regulatory environments)

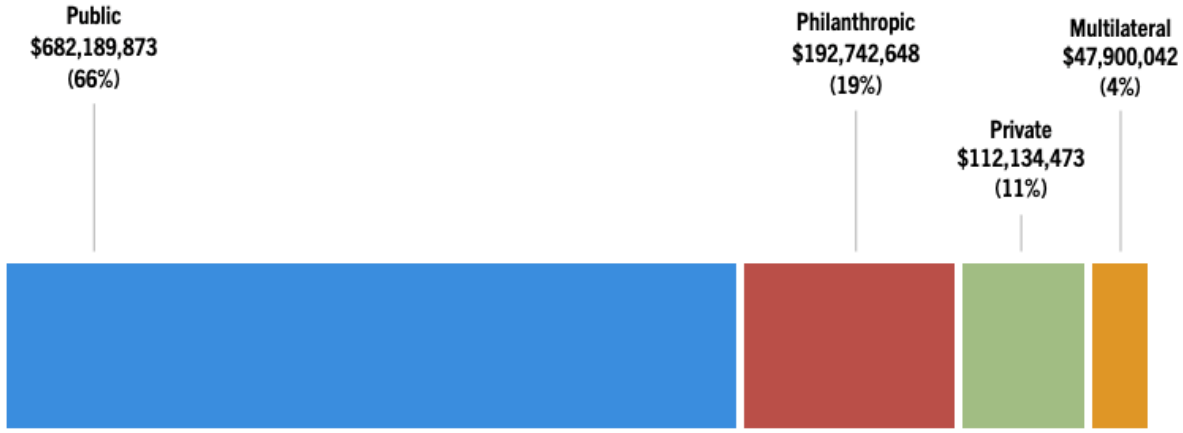
PURPOSIVE INVESTMENT	REGULATORY ENVIRONMENT	ACCOUNTABILITY FOR AFFORDABILITY

PUBLIC INVESTMENT IN TB R&D



Public funders contributed 69% of all TB research financing from 2018 to 2022, giving more money than all other sectors combined. Philanthropies, private-sector companies, and multilateral organizations respectively gave 16%, 10%, and 5% of total funding.

TB R&D Funding by Funder Type, 2022
Total: $1,034,967,036

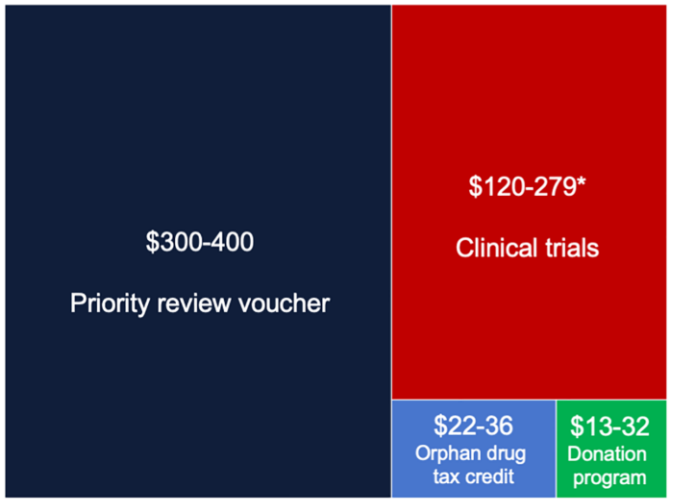


PLOS ONE

Public investments in the clinical development of bedaquiline

Total public investments exceeded J&J's investments by a factor of 1.6–5.1. (Gotham et al., PLOS ONE, 2020)

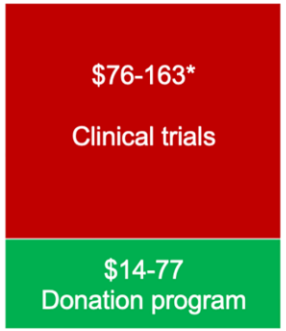
Estimated public sector investments
(USD millions)



*As out-of-pocket expenditures. See analysis for risk-adjusted and capitalized costs

Total: US$455–747 million

Estimated originator company investments
(USD millions)



Total: US$90-240 mil

UNIVERSAL ACCESS TO DST

STEP 3: Being tested

Benchmark

9 All patients with bacteriologically confirmed TB undergo universal drug susceptibility testing*

"Application: Universal DST for this benchmark is defined as testing of all patients with bacteriologically confirmed TB for resistance to RIF, all patients with RR TB for resistance to FQ and all patients with pre-XDR-TB for resistance to bedaquiline and linezolid. These are minimum requirements, and testing for resistance to drugs according to the regimen used is preferred. **Among patients with RIF-susceptible TB, testing for isoniazid and FQ resistance is increasingly important."**

Given available tools and those nearing the end of the pipeline, what is required to realize universal access to DST in practice, as a human right?

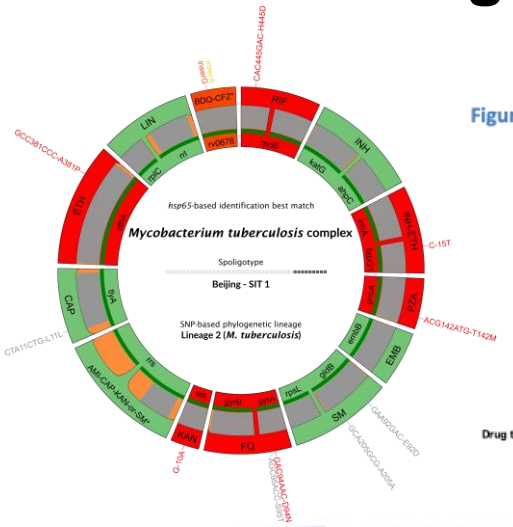
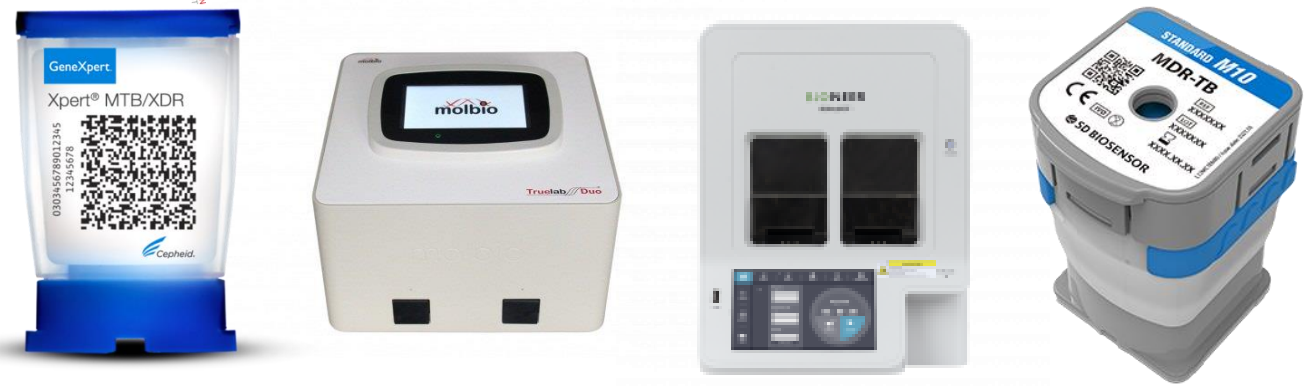
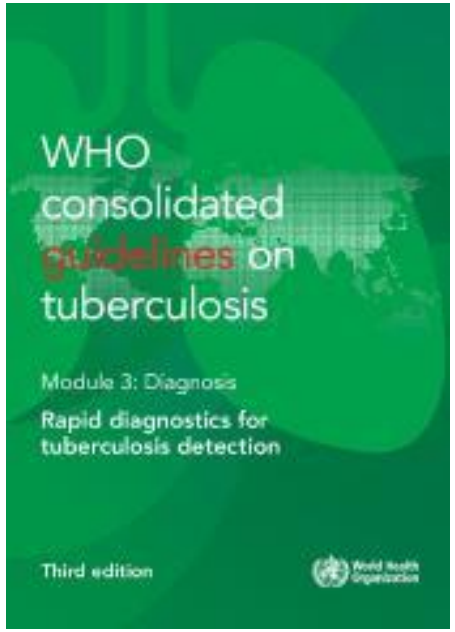


Figure 2. Tentative layout of an optimized BMD plate.

	1	2	3	4	5	6	7	8	9	10	11	12
A	Negative GC	1% pos. GC	100% pos. GC	LFX 8	BDQ 1	CFZ 1	RIF 2	INH 2	PMD 2	DLM 0.25	KAN 16	ETO 16
B	EMB 8	DCS 64	LZD 4	LFX 4	BDQ 0.5	CFZ 0.5	RIF 1	INH 1	PMD 1	DLM 0.125	KAN 8	ETO 8
C	EMB 4	DCS 32	LZD 2	LFX 2	BDQ 0.25	CFZ 0.25	RIF 0.5	INH 0.5	PMD 0.5	DLM 0.06	KAN 4	ETO 4
D	EMB 2	DCS 16	LZD 1	LFX 1	BDQ 0.125	CFZ 0.125	RIF 0.25	INH 0.25	PMD 0.25	DLM 0.03	KAN 2	ETO 2
E	EMB 1	DCS 8	LZD 0.5	LFX 0.5	BDQ 0.06	CFZ 0.06	RIF –0.125–	INH 0.125	PMD 0.125	DLM 0.016	KAN *1*	ETO 1
F	EMB –0.5–	DCS 4	LZD 0.25	LFX 0.25	BDQ 0.03	CFZ *0.03*	RIF 0.06	INH 0.06	PMD 0.06	DLM *0.008*	KAN –0.5–	ETO 0.5
G	EMB *0.25*	DCS –2–	LZD 0.125	LFX *0.125*	BDQ 0.016	CFZ 0.016	RIF *0.03*	INH –*0.03*–	PMD 0.03	DLM 0.004	KAN 0.25	ETO –*0.25*–
H	EMB 0.125	DCS 1	LZD *0.06*	LFX 0.06	BDQ *0.008*	CFZ 0.008	RIF 0.016	INH 0.016	PMD 0.016	DLM 0.002	KAN 0.125	ETO 0.125
Drug type	1st line	B	A	A	A	B	1st line	1st line	other	C	C	C



TARGETED NEXT-GEN SEQUENCING



For people with confirmed pulmonary TB and RR-TB, **tNGS: "may be used… rather than culture-based phenotypic drug susceptibility testing"**

Bedaquiline	Phenotypic DST	Se: 67.9 (42.6–93.2)	3 (31)	Low
	Phenotypic DST	Sp: 97.0 (94.3–99.7)	4 (519)	High
Linezolid	Phenotypic DST	Se: 68.9 (38.7–99.1)	4 (31)	Low
	Phenotypic DST	Sp: 99.8 (99.6–100)	6 (1093)	High
Clofazimine	Phenotypic DST	Se: 70.4 (34.6–100)	4 (36)	Low
	Phenotypic DST	Sp: 96.3 (93.2–99.3)	6 (789)	High

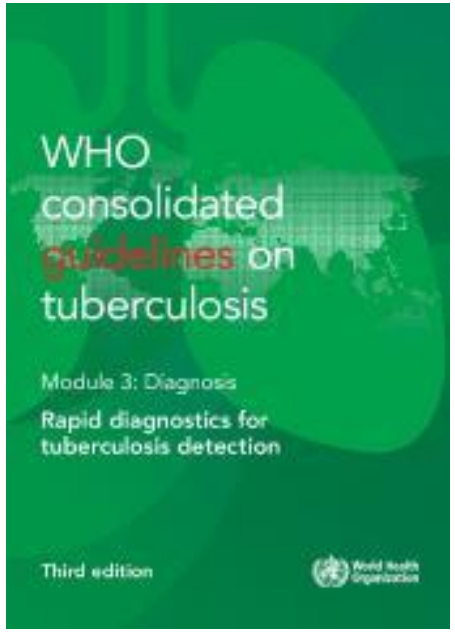
"Centralized versus decentralized placement may have equity implications for access: Given the high-level specialized laboratory infrastructure, specialized human resources and technical complexity needed for targeted NGS, the technology may be suitable for placement only at centralized, reference laboratories. This may have equity access considerations."

"Based on the empirical analysis, the cost of targeted NGS was estimated to be:

- US$ 134 to US$ 257 in South Africa;
- US$ 120 to US$ 198 in Georgia; and
- US$ 121 to US$ 175 in India.

These costs are dependent on patient volume, batching and negotiated cost per targeted NGS kit."

[DISRUPTING] CULTURE



"Since sensitivity for bedaquiline, linezolid and clofazimine resistance is suboptimal [using tNGS]... **Further testing of samples with a susceptible result (using culture-based phenotypic DST) would be warranted,** particularly when the risk of resistance is high… In the case of pretomanid, the basis for resistance has not been fully elucidated; hence, culture-based DST is also required for this drug."

Broth microdilution culture offers more rapid and comprehensive culture-based DST with a time to result of 10-21 days, compared to 2-6 weeks for standard culture.

Figure 2. Tentative layout of an optimized BMD plate.

	1	2	3	4	5	6	7	8	9	10	11	12
A	Negative GC	1% pos. GC	100% pos. GC	LFX 8	BDQ 1	CFZ 1	RIF 2	INH 2	PMD 2	DLM 0.25	KAN 16	ETO 16
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C	EMB 4	DCS 32	LZD 2	LFX 2	BDQ 0.25	CFZ 0.25	RIF 0.5	INH 0.5	PMD 0.5	DLM 0.06	KAN 4	ETO 4
D	EMB 2	DCS 16	LZD 1	LFX 1	BDQ 0.125	CFZ 0.125	RIF 0.25	INH 0.25	PMD 0.25	DLM 0.03	KAN 2	ETO 2
E	EMB 1	DCS 8	LZD 0.5	LFX 0.5	BDQ 0.06	CFZ 0.06	RIF –0.125–	INH 0.125	PMD 0.125	DLM 0.016	KAN *1*	ETO 1
F	EMB –0.5–	DCS 4	LZD 0.25	LFX 0.25	BDQ 0.03	CFZ *0.03*	RIF 0.06	INH 0.06	PMD 0.06	DLM *0.008*	KAN –0.5–	ETO 0.5
G	EMB *0.25*	DCS –2–	LZD 0.125	LFX *0.125*	BDQ 0.016	CFZ 0.016	RIF *0.03*	INH –*0.03*–	PMD 0.03	DLM 0.004	KAN 0.25	ETO –*0.25*–
H	EMB 0.125	DCS 1	LZD *0.06*	LFX 0.06	BDQ *0.008*	CFZ 0.008	RIF 0.016	INH 0.016	PMD 0.016	DLM 0.002	KAN 0.125	ETO 0.125
Drug type	1st line	B	A	A	A	B	1st line	1st line	other	C	C	C

BD's BACTEC MGIT (Mycobacterial Growth Indicator Tubes) system is the main technology used by country TB programs for phenotypic liquid culture-based DST. BD holds a monopoly on the market and hasn't improved or innovated on the technology for 20-30 years!

What must be done to disrupt culture and get BD to improve the technology and reduce time-to-culture-positivity?

RAPID MOLECULAR DST

WHO Target Product Profile for rapid DST in peripheral centers

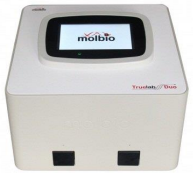
Minimal drug resistance targets:
RIF + INH + FQ + BDQ

Optimal pricing:
RIF + INH + FQ: max US$5

"The price of a test affects access and requires due consideration**… Ideally, the price of tests should be based on evidence of the actual cost of goods and estimated volumes, and a reasonable profit margin**… Ensuring access to tests while maintaining business interests can be achieved through fair pricing"

Urgent need to scale up access to rapid decentralized DST for RIF, INH, and FQ

Cepheid's Xpert MTB/XDR:
- INH, FQ
- WHO recommended in 2021

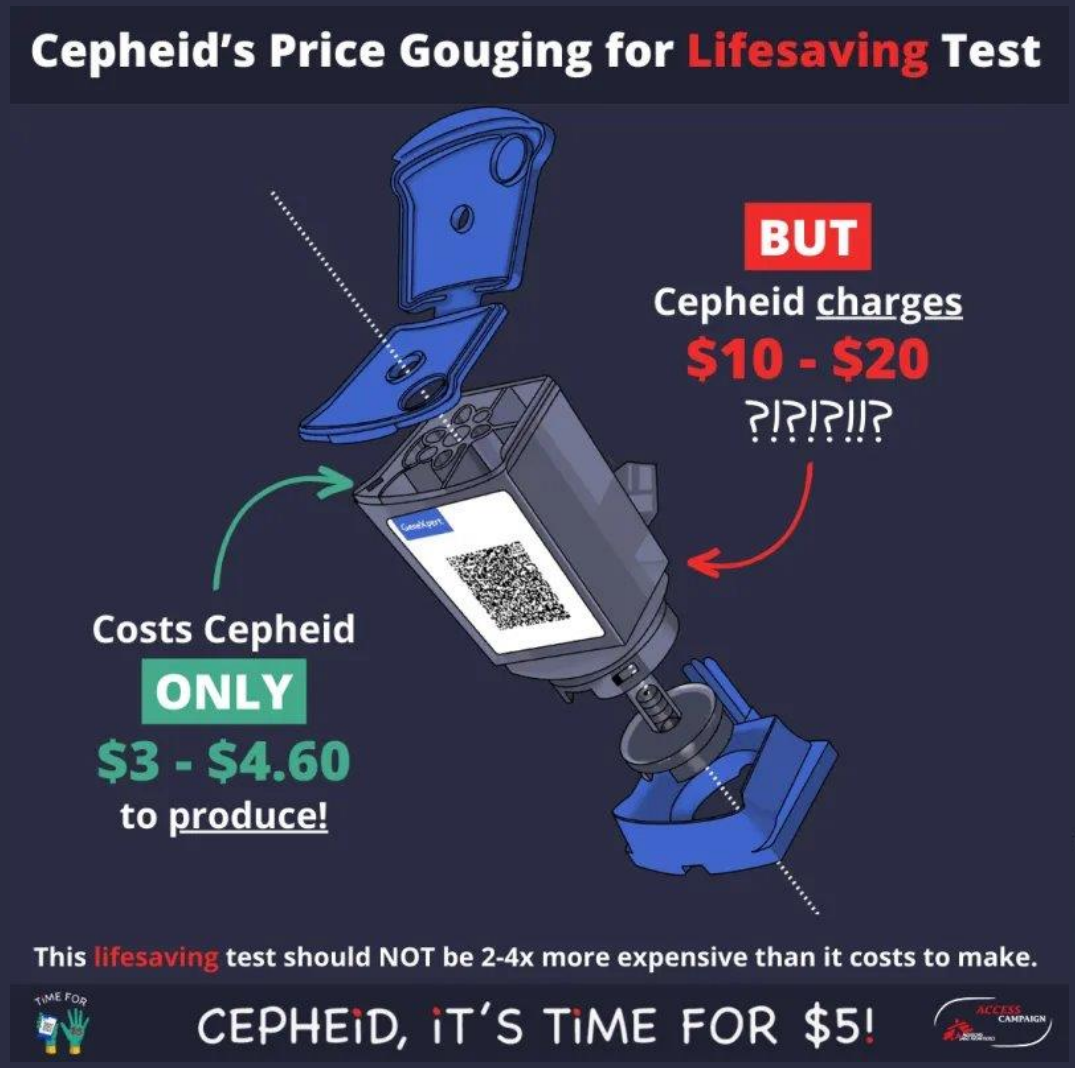


Molbio's Truenat:
- INH, FQ (separate chips)
- WHO review in 2024

Bioneer's IRON-qPCR RFIA Kit:
- RIF, INH, FQ
- WHO review in 2024

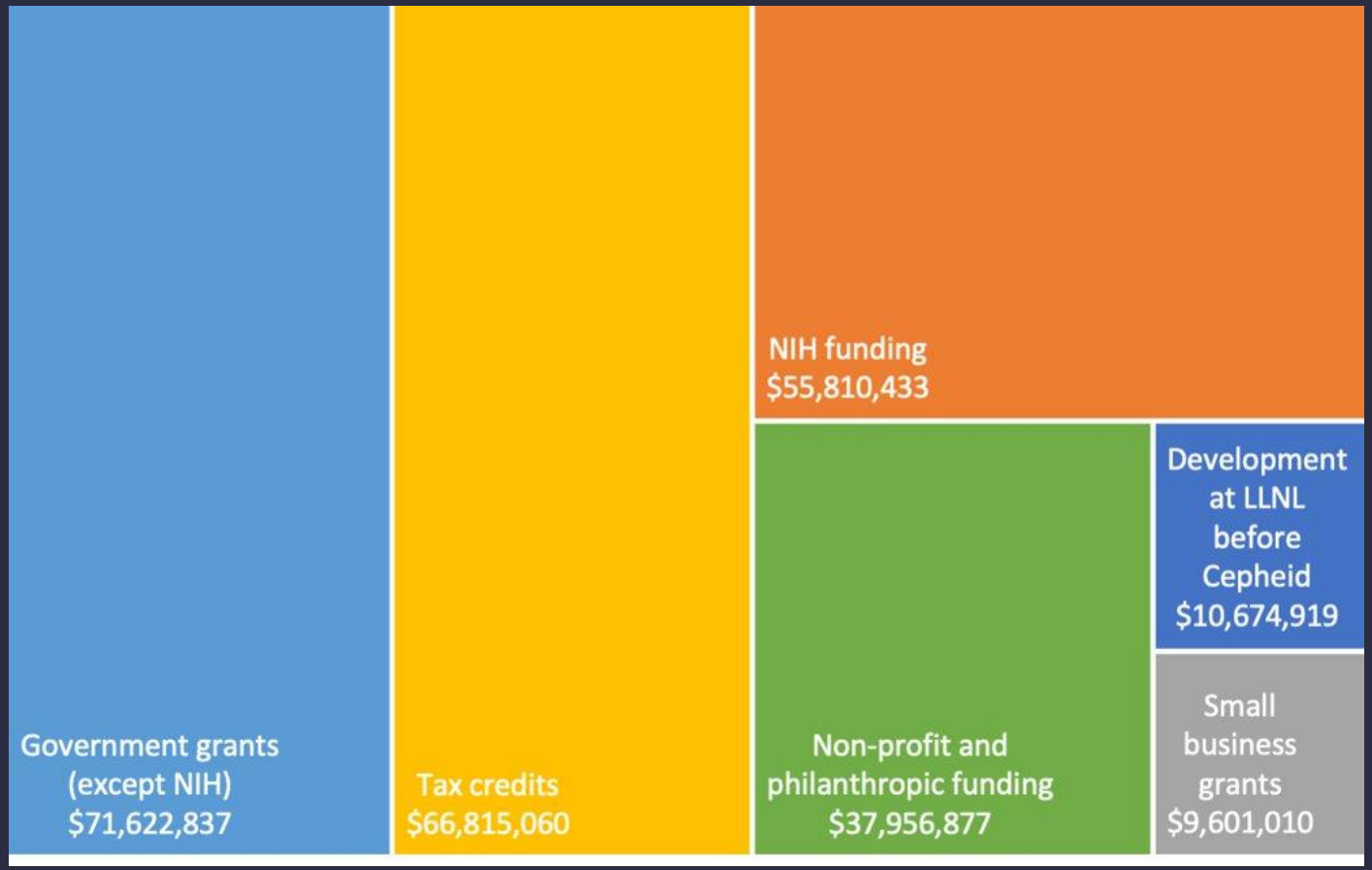
SD Biosensor's STANDARD M10 MDR-TB:
- RIF, INH
- WHO review in 2024

Why do we ask for $5 ?



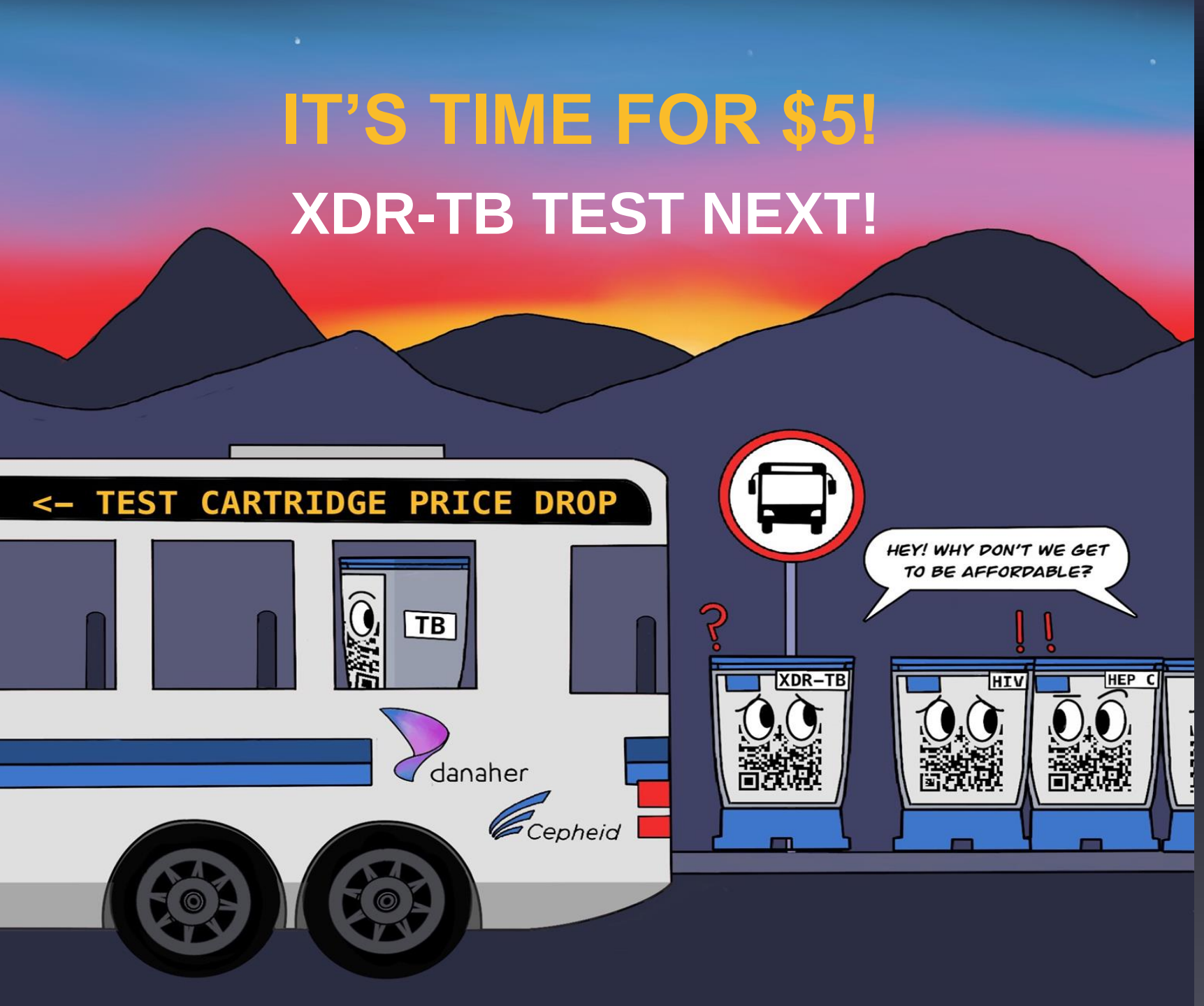
Public investments in GeneXpert technology

At minimum: 252 million U.S. dollars



BILL & MELINDA GATES foundation

FIND Diagnosis for all



A price drop to $7.97 for only the Xpert MTB/RIF test is not enough.

We need Danaher & Cepheid to also drop the price of the Xpert MTB/XDR test which is still priced at $14.90!