

# Setting the Scene on Introduction and Scale-Up of TB Medicines for Children

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High-Level Dialogue on Pediatric HIV and TB in Children Living with HIV

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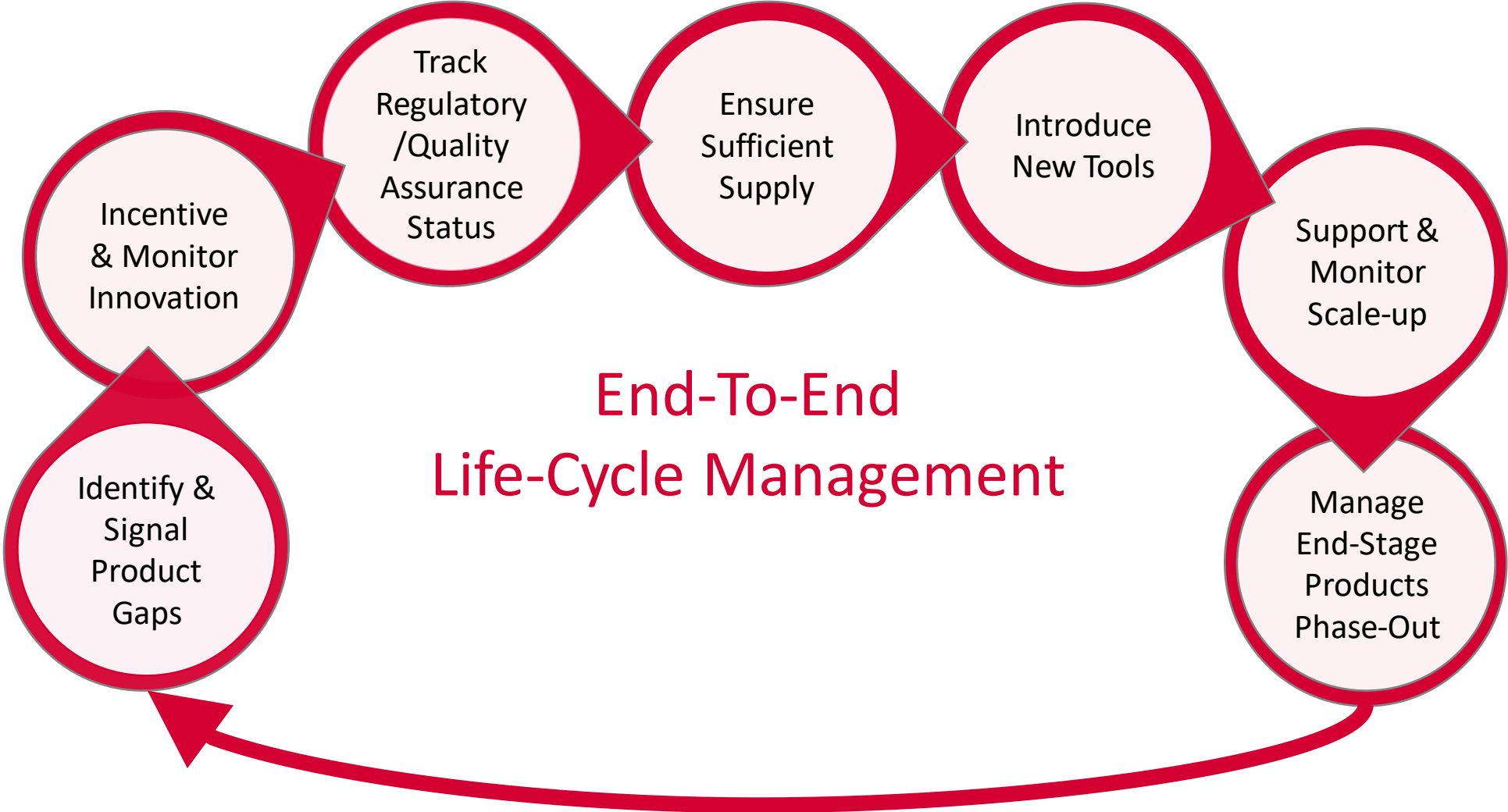
# Session Outline

- Importance of TB Stakeholder Alignment and Coordination
- TB Medicine Supply Situation
- Introduction of New TB Medicines and Regimens
- Reminder: Treatment Targets versus Treatment Reality
- Lessons Learned and What's Needed Now

# Stakeholder Alignment & Coordination Via TPMAT

TB Procurement and Market-Shaping Action Team (TPMAT)

Comprised of: procurers, donors, implementers, international organizations, NGOs, WHO, civil society, NTPs



# GDF-WHO-GF TB MEDICINES DASHBOARD: Paediatric DR-TB Formulations

## Key Reference Tool

- Organizes, stores, displays info from >15 different sources
- Provides Roadmap for Prioritization, Harmonization, and Improving Access
- Guides NTPs with Selection, Rational Use, Benchmarking

**Pediatric Drug-Resistant TB Medicines Dashboard**

This Dashboard has been developed by **Stop TB Partnership/Global Drug Facility** in collaboration with **USAID**, the **World Health Organization** and **The Global Fund to fight AIDS, TB & Malaria**.  
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**Status**

- Yes (Green)
- No (Red)
- Ineligible for inclusion (Blue)
- N/A (Grey)

Medicines	WHO Guidelines (DR-TB '19)	WHO Guidelines (DR-TB '20)	EMLc submitted	EMLc (2019)	WHO PQ EOI (2020)	WHO PQ submitted	WHO PQ listed	Global Fund List of Pharmaceutical Products	Global Fund ERPEOI (Mar 2020)	Global Fund ERP approved	GDF Catalog
Bedaquiline 20mg tablet	Yes	Yes	N/A	N/A	No	No	No	Yes	No	Ineligible for inclusion	Yes
Clofazimine 50mg tablet/capsule	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes
Delamanid 25mg dispersible tablet	Yes	Yes	N/A	N/A	No	No	No	No	Yes	No	No
Ethambutol 25mg/mL oral liquid	Yes	Yes	Yes	Yes	No	No	No	No	No	Ineligible for inclusion	No
Ethambutol 50mg dispersible tablet	Yes	Yes	No	No	No	Yes	No	No	No	Ineligible for inclusion	Ineligible for inclusion

<http://www.stoptb.org/gdf/medicinesdashboard/>

# Key TB Medicine Harmonization/Prioritization Results Since 2018

## Changes in “Guidance” Docs:

### WHO Model EML and EMLc

- Complete TB overview
- 35 changes

### WHO PQ EOI

- 20 changes

### GF ERP EOIs

- 43 changes over past 5 rounds

### GDF Catalog

- 27 changes
  - 13 additions, 14 deletions

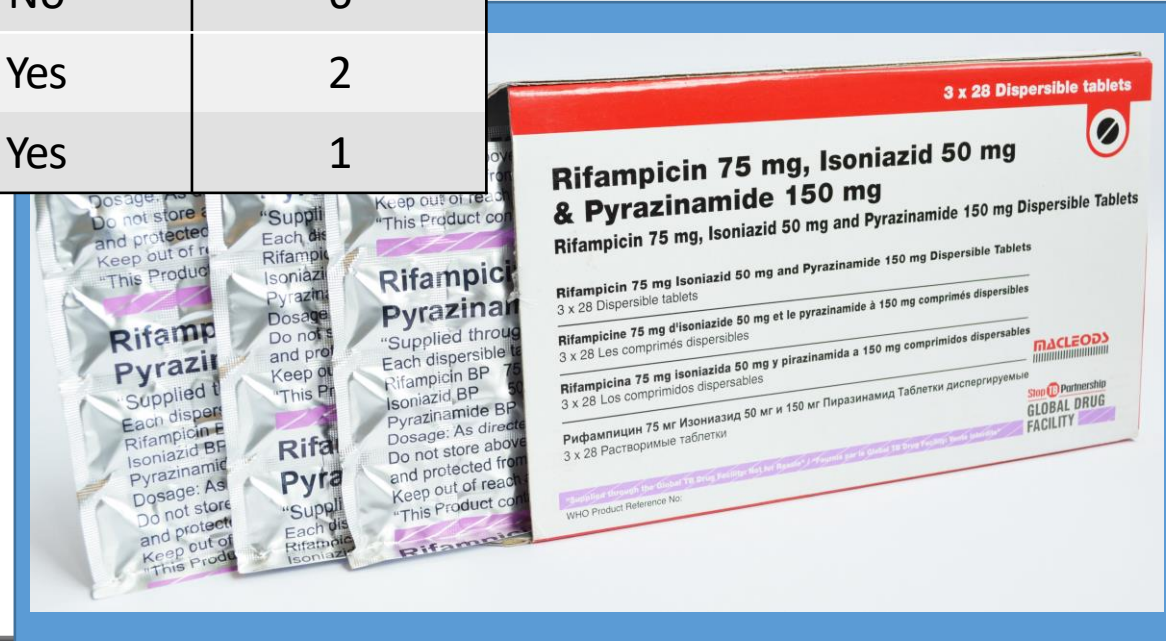
## 5 TB Medicines Prioritized Through GF ERP Ad-Hoc Review Process and Available for Procurement

- 2nd supplier paediatric FDC for DS-T, LTBI
  - increased competition, supply security
- First clofazimine tablets (50mg and 100mg)
  - increased supply security, more suitable for children
- Second supplier clofazimine 100mg capsule
  - increased supply security
- 3HP FDC for TPT
  - new product, improved adherence

# Supply: QA Child-Friendly Formulations for DS-TB and TB Preventive Treatment

Formulation	Dispersible	# QA Suppliers
Ethambutol 100mg	Yes	1*
Ethambutol 100mg	No	3
Isoniazid 100mg	Yes	2
Isoniazid 100mg	No	7
Rifampicin 150mg	No	6
Rifampicin/Isoniazid, 75mg/50 mg	Yes	2
Rifampicin/Isoniazid/Pyrazinamide, 75mg/50 mg/150mg	Yes	1

\*Second formulation in WHO PQ Pipeline



# Supply: 13 Child-Friendly DR-TB Formulations, Despite Tiny Market Size

WHO Classification	Medicine	Formulation	Dispersible	# QA Suppliers
Group A	Levofloxacin or Moxifloxacin	Levofloxacin 100mg	Yes	2
		Moxifloxacin 100mg	Yes	2
	Bedaquiline	Bedaquiline 20mg	Yes**	1
	Linezolid	Linezolid 150mg Under development	Yes	0
Group B	Clofazimine	Clofazimine 50mg	Yes**	1
	Cycloserine or Terizidone	Cycloserine 125mg	No	1
Group C	Ethambutol	Ethambutol 100mg	Yes	1*
	Delamanid	Delamanid 50mg	No	1
		Delamanid 25mg Expected in 2021	Yes	1
	Pyrazinamide	Pyrazinamide 150mg	Yes	2
	Ethionamide or Prothionamide	Ethionamide 125mg	Yes	2

\*Second formulation in WHO PQ Pipeline

\*\*Product label is not dispersible

# Stop TB/GDF Paediatric Drug-Resistant Tuberculosis Initiative

## 3-Pronged Approach to Expedite Product Introduction:

1. Identify early adopters and build demand
  - GDF provided a small contract to Sentinel Project on Paediatric Drug-Resistant TB for clinical support
  - In-kind programmatic support from KNCV, MSF
  - GDF doing quantification, forecasting, phase-in plans, ongoing procurement & supply plans
2. Match supply with demand
  - GDF working with suppliers to decrease batch sizes, lower prices; production planning
  - GDF pooling orders to meet minimum order quantities
3. Procurement support for initial purchases via GDF grants





# Paediatric DR-TB and the Role of Pooled Procurement

## On the Supply Side:

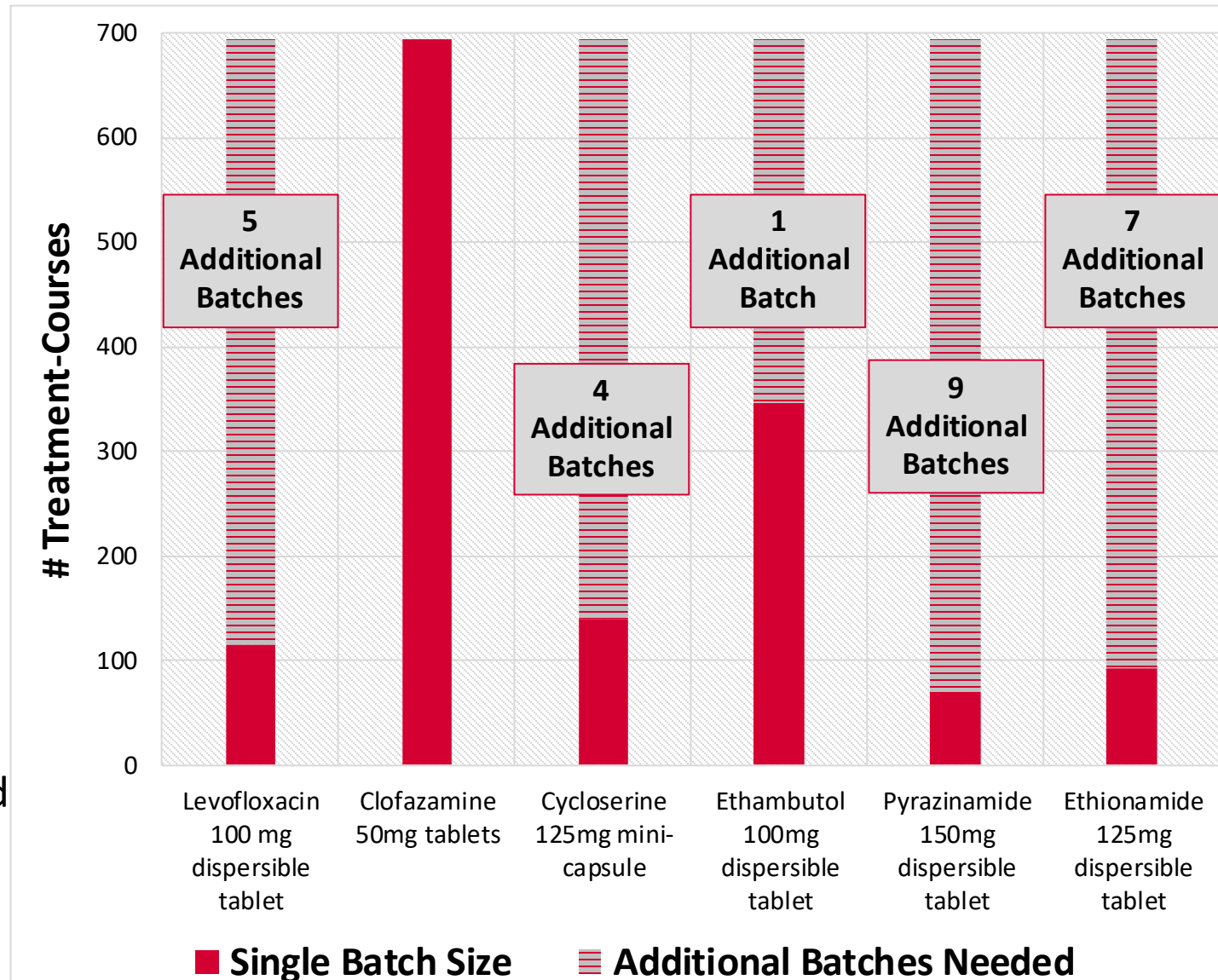
- Need 5 medicines to treat DR-TB
- Batch sizes vary for each medicine
  - 10-fold variation: 70-700 treatment courses
- Suppliers want to sell a full batch; otherwise,
  - Price and/or lead time will increase
  - remaining shelf life will be low

## On the Demand Side:

- >60% countries treat < 20 kids per year
- A high-volume country treats ~100 kids
- No single country has sufficient demand to achieve optimal price and supply terms

## GDF Pooled Procurement:

- Aligns supply (batch sizes) with global demand
  - Derisks suppliers
  - Ensures reliable, optimal, timely products and prices for NTPs



# 62 Countries Procuring Child-Friendly DR-TB Formulations via GDF's Paediatric DR-TB Initiative



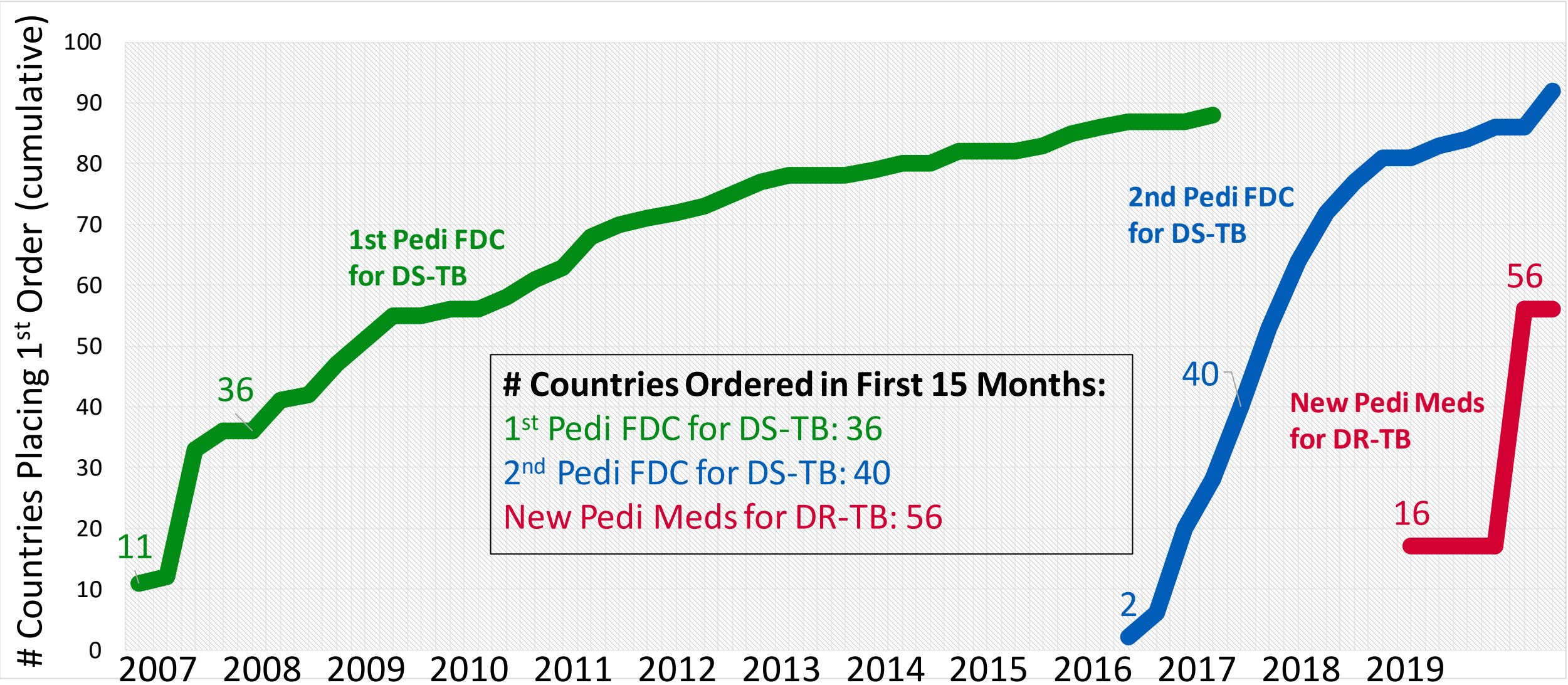
**New country in 2020**

**Funding:** Government of Japan and USAID

**GDF Implementing Partners:** Sentinel Project, KNCV, and MSF

- |                           |                        |                        |
|---------------------------|------------------------|------------------------|
| 7. Botswana               | 27. Kenya              | 47. Republic Moldova   |
| 8. Burkina Faso           | 28. Kyrgyzstan         | 48. Rwanda             |
| 9. Cameroon               | 29. Lesotho            | 49. Senegal            |
| 10. Chad                  | 30. Liberia            | 50. Sierra Leone       |
| 11. Côte d'Ivoire         | <b>31. Madagascar</b>  | 51. Somalia            |
| 12. DRC                   | 32. Malawi             | 52. South Africa       |
| <b>13. Djibouti</b>       | <b>33. Maldives</b>    | <b>53. South Sudan</b> |
| <b>14. Dominican Rep.</b> | <b>34. Mali</b>        | 54. Tajikistan         |
| <b>15. Eq. Guinea</b>     | 35. Mongolia           | 55. Tanzania           |
| <b>16. Eritrea</b>        | 36. Morocco            | 56. Thailand           |
| 17. Eswatini              | 37. Mozambique         | 57. Turkmenistan       |
| 18. Ethiopia              | 38. Myanmar            | 58. Uganda             |
| <b>19. Gabon</b>          | 39. Namibia            | 59. Uzbekistan         |
| 20. Georgia               | <b>40. Nepal</b>       | 60. Viet Nam           |
| 21. Ghana                 | 41. Niger              | 61. Zambia             |
| 22. Guinea                | 42. Nigeria            | 62. Zimbabwe           |
| 23. Haiti                 | 43. Pakistan           |                        |
| 24. India                 | 44. Papua New Guinea   |                        |
| 25. Indonesia             | <b>45. Paraguay</b>    |                        |
| 26. Kazakhstan            | <b>46. Philippines</b> |                        |

# Uptake Comparison of New Pediatric TB Formulations



## Paediatric TB – Treatment Targets vs Treatment Reality

2022 Targets 2018 UN High-Level Meeting on TB	2019 Treatment Estimates from 2020 WHO Global TB Report	2019 Disease Burden Estimates from 2020 WHO Global TB Report
Treat <b>3.5 million</b> children with TB	<b>500,000</b> children treated	1.2 million new pedi TB cases
Treat <b>115,000</b> children with DR-TB, Including <b>~47,000</b> children < 5 yo	<b>~9,000</b> children treated for DR-TB, Including <b>~500*</b> children <5 yo	30,000 new pedi DR-TB cases, Including <b>~12,000*</b> in <5 yo
Provide preventive treatment for TB to <b>4 million</b> children < 5 yo by 2022	<b>~433,000</b> children <5 yo treated	

\*Estimate; data for children <5 yo not provided in Global TB Report

Biggest gap of missing people with TB is in kids under 5 yo,  
where 65% of kids are missing

## Lessons Learned

- A tiny market size doesn't need to be a barrier to development of child-friendly formulations
- But pooled procurement a MUST for such low-volume medicines
- Market stewardship with end-to-end visibility and organization harmonization are critical - especially when phasing-out old formulation(s) and phasing-in a new formulation(s)
- Very few missing formulations, but
  - Taste-masking inconsistent or absent across formulations; acceptability is unknown
  - New research findings may result in need for new formulations, pending WHO review
  - Strategic market planning and coordination will be needed to choose optimal formulations and engage suppliers to maintain and not reverse current market evolution
- TB Community – especially paediatric community– already well coordinated and well positioned to expedite and expand access to TB treatment

## What's Needed Now

- Broad-based commitment to prioritize children – address stigma & discrimination; build treatment literacy, advocacy, awareness
- Set and meet realistic but ambitious targets
- **Investments to increase case-finding and enrollment of children**
  - Better diagnostics
  - Household post-exposure management of children to identify kids who need treatment and prevention using family-friendly models
  - Donor recognition that innovation isn't just about developing new tools
- Improved reporting and recording to support finding missing kids; disaggregation of disease burden and treatment data for kids < 5 yo; data on TB/HIV coinfection
- Research to fill treatment and dosing data gaps in children
- Acceptability research to guide paediatric TB target product profiles, ensure product consistency in development
- Derisk and incentivize suppliers in a manner that doesn't distort the market; ensures fair competition
- Dedicated funding to catalyze and expedite uptake of new formulations
- New approach for registration (or waivers) for such low-volume products

# Thank you

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## Acknowledgements

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