



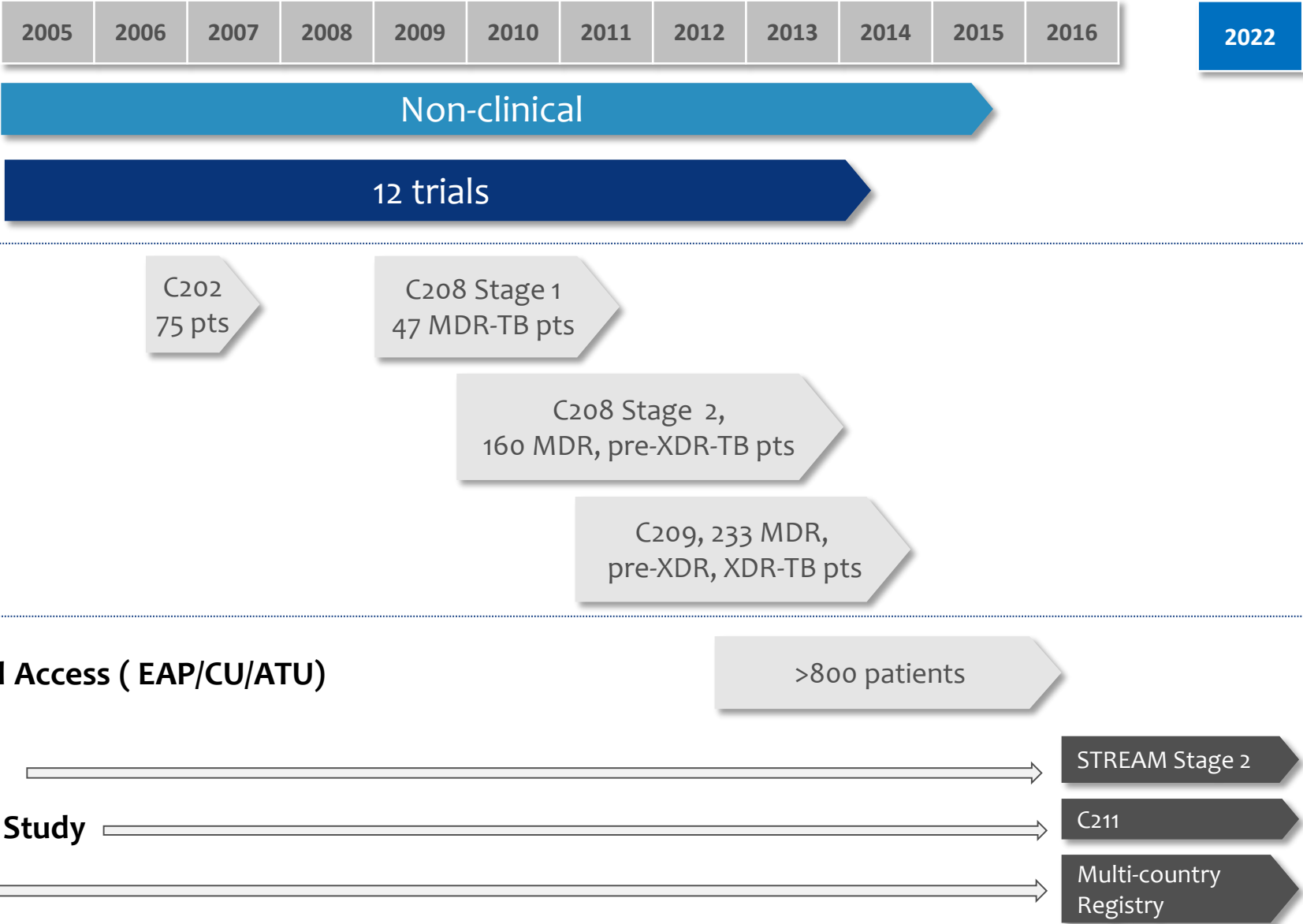
Martin Freeman, Untitled
Diagnosed with AIDS in 1990, Martin lives in
San Francisco where he continues to create new pieces.

Tine De Marez, PhD
Program Management Office Lead for Johnson &
Johnson Global Public Health

21 March, 2017
CPTR



Bedaquiline Clinical Development Program



Registrations

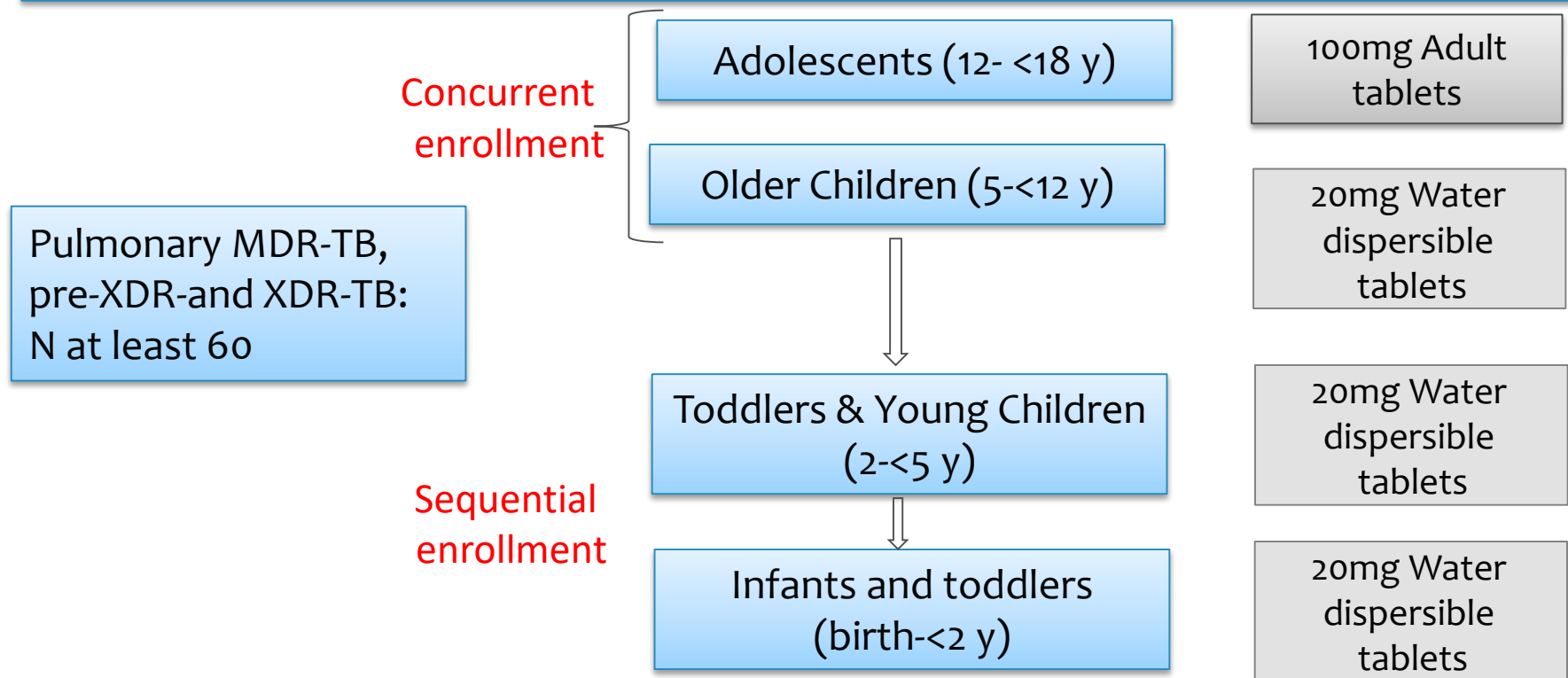


Submitted for Registration

						
Bangladesh	Burundi*	Colombia	Ghana*	Indonesia	Kenya*	Mexico
						
Nigeria*	Rwanda*	Tanzania*	Thailand	Uganda*	Vietnam	Turkey

Pediatrics: C211 Trial Design

Concurrent Age Group Approach in cohorts 1 and 2 & Sequential Enrollment in cohort 3 and cohort 4: PK/Safety



Intensive PK weeks 2 and 12; additional PK samples throughout; interim analyses of each cohort and open next cohort after data on 12 subjects

Enrolling in SA, Russia, Philippines
India expected to start enrolling in 2017

Multi-Country MDR TB Registry

A Collaborative Real World Evidence Strategy

Country selection based on:

- **Strength** of treatment **programs**
- **Interest** from the country
- Adoption of the elements described in **WHO Interim Policy Guidance** on bedaquiline
 - **Commitment** to strengthen **pharmacovigilance** if necessary
- A **permissive regulatory environment**

Countries where activities are on-going:

South Africa



South Korea



Bedaquiline DREAM Program Countries

Bedaquiline Resistance Emergence Assessment in MDR-TB (DREAM) is a global drug resistance surveillance study. It aims at monitoring the development of resistance to BDQ and amplification of resistance to fluoroquinolones, 2nd line injectables, and WHO Category 5 drugs over 5 years.

Participating Countries	2015	2016	2017	Total* 2015-2017	2018	2019	TOTAL
S. Africa	280	200	200	680	200	200	1,080
Pakistan	200	200	200	600	200	200	1,000
Turkey	NA	122	~100	~222	~100	~100	300
Lithuania	NA	129	~200	~329	~200	~200	729
Taiwan	481	122	~120	~723	~120	~120	963
Philippines	200	200	200	600	200	200	1,000
Vietnam	NA	200	200	400	200	200	800
Thailand	NA	200	200	200	200	200	800
S. Korea	NA	59	10	69			
India	NA	400	400	800	400	400	1,600
GRAND TOTAL				4,623			8,272

* Total collected

A comparative mortality analysis using retrospective data from the South African Electronic Drug-Resistant Tuberculosis Register (EDRWeb)

Variables	Bedaquiline N=1556 (6.2%)	No bedaquiline 23539 (93.8%)	Total 25095 (100.0)
Age: mean (SD)	37.1 (11.5)	36.3 (12.6)	36.38 (12.58)
Gender: n (%)*			
Male	915 (58.8)	10518 (44.7)	11159 (44.5)
Female	641 (41.2)	13021 (55.3)	13936 (55.5)
History of TB: n (%)*	958 (61.6)	10543 (44.8)	11501 (45.8)
HIV status: n (%)			
Negative	404 (26.0)	6338 (26.9)	6742 (26.9)
Positive	1082 (69.5)	15952 (67.8)	17034 (67.9)
Unknown	70(4.5)	1249 (5.3)	1319 (5.3)
HIV and ART status: n (%)*			
HIV unknown	70 (4.5)	1249(5.3)	1319 (5.3)
HIV negative	404(26.0)	6338 (26.9)	6742 (26.9)
HIV positive	61 (3.9)	2549 (10.8)	2610 (10.4)
HIV positive on ART	1021 (65.6)	13403 (56.9)	14424 (57.5)
Drug resistance pattern: n (%)*			
RR or MDR-TB	919 (59.1)	21955 (93.3)	22874 (91.1)
Pre-XDR	253 (16.3)	776 (3.3)	1029 (4.1)
XDR-TB	384 (24.7)	808 (3.4)	1192 (4.7)
Deaths*	119 (7.6)	4288 (18.2)	4407 (17.6)
Duration on treatment (months): mean (SD)	7.2 (4.4)	9.7 (7.4)	9.6 (7.3)
Year of initiation of treatment: n (%)*			
2014	153 (9.8)	11717 (49.8)	11870 (47.3)
2015	1307 (84.0)	10956 (46.5)	12263 (48.9)
2016	96 (6.2)	866 (3.7)	962 (3.8)

¹Missing data: Bedaquiline=159; No bedaquiline=2236; SD=standard deviation; TB=tuberculosis; HIV=human immunodeficiency virus; ART=antiretroviral therapy; MDR=multidrug resistant; XDR=extensively drug resistant; * P<0.05 (Chi-squared test);

A comparative mortality analysis using retrospective data from the South African Electronic Drug-Resistant Tuberculosis Register (EDRWeb)

Bedaquiline N = 1556 (6.2%)	No Bedaquiline N = 23,539 (93.8%)	Total N = 25,095 (100%)
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Type of analysis and population	ES (95% CI)
1. Cox regression*	
a. Includes BCAP patients	0.50 (0.41, 0.61)
b. Excluding BCAP patients	0.48 (0.39, 0.59)
c. No history of TB treatment	0.48 (0.34, 0.68)
d. History of TB treatment	0.46 (0.36, 0.61)
e. MDR patients	0.51 (0.39, 0.67)
f. Pre-XDR patients	0.35 (0.20, 0.61)
g. XDR patients	0.21 (0.14, 0.32)
h. HIV negative patients	0.83 (0.56, 1.22)
i. HIV positive not on ART	0.24 (0.06, 0.96)
j. HIV positive on ART	0.86 (0.75, 0.97)
2. Logistic regression**	
a. Excluding BCAP patients	0.39 (0.31, 0.51)
b. No history of TB treatment	0.42 (0.28, 0.62)
c. History of TB treatment	0.38 (0.28, 0.53)
d. MDR patients	0.51 (0.37, 0.68)
e. Pre-XDR patients	0.49 (0.25, 0.97)
f. XDR patients	0.34 (0.19, 0.58)
g. HIV negative patients	0.67 (0.43, 1.06)
h. HIV positive not on ART	0.11 (0.02, 0.48)
i. HIV positive on ART	0.35 (0.26, 0.47)

Overview of bedaquiline containing regimens being studied by various groups

- STREAM stage 2: 6 vs 9m **Bedaquiline** containing regimen vs WHO and Bangladesh regimen (STREAM stage 2)
- **Bedaquiline**/Delamanid + WHO SOC for MDR (END-TB programmatic use PIH/MSF)
- Delamanid+**Bedaquiline**+LZD+CFZ+other: MDR 9m FQ S+ (END-TB PIH/MSF)
- Delamanid+**Bedaquiline**+LZD+CFZ: MDR 9&6m FQ R+ (END-TB-Q PIH/MSF)
- Pretomanid+**Bedaquiline**+LZD+other: MDR 6m (Practecal MSF)
- Pretomanid+**Bedaquiline**+LZD for XDR 6 or 9m (NiXTB TB Alliance)
- **Bedaquiline**+Delamanid: PK, safety, tolerability for Pre-XDR/MDR (NIH)
- **Bedaquiline**+LZD+PZA+LEV+ETOH+INH for 6-9 m v- SOC w/injectable for 24 m (NExT Trial in SA)
- 3-4 drug regimen including **Bedaquiline** and Delamanid in SA (USAID)

Our Response: Working Together



BEDAQUILINE DONATION PROGRAM

-  Four-year program
-  Up to 30,000 treatments
-  Over 100 eligible countries
-  Global Fund aligned
-  Appropriate use in accordance with WHO Guidelines
-  Programmatic experience



Four-year program



**Up to 30,000
treatments for eligible
patients**



**Over 100 low and
middle income
countries**



**Global Fund
eligibility criteria**



**Use in accordance with
WHO Guidelines**



**Insights into
programmatic use**

- | | | |
|------------------------|---------------------------|-----------------------|
| • Armenia | • Kenya | • Tajikistan |
| • Bangladesh | • Kyrgyzstan | • Thailand |
| • Belarus | • Lesotho | • Turkmenistan |
| • Benin | • Liberia | • Uganda |
| • Cameroon | • Moldova | • Tanzania |
| • Cote d'Ivoire | • Myanmar | • Uzbekistan |
| • Djibouti | • Namibia | • Vietnam |
| • DR Congo | • Niger | • Zimbabwe |
| • Ethiopia | • Nigeria | |
| • Georgia | • Pakistan | |
| • Guinea | • Papua New Guinea | |
| • Haiti | • Peru | |
| • Indonesia | • Philippines | |
| • India | • DPR Korea | |
| • Jordan | • Sudan | |
| • Kazakhstan | • Swaziland | |

***Impact to
date:***

5,200 orders placed

**2,796
shipments to
40
countries**



**BEDAQUILINE
DONATION
PROGRAM**



USAID
FROM THE AMERICAN PEOPLE