

# State of the Network

Sharon Nachman, MD  
IMPAACT Network Chair  
28 June 2022



**ANNUAL MEETING**  
2022

# State of the Network: A Snapshot



- ▶ Research agenda
- ▶ Network activities and achievements
- ▶ Study updates and achievements
- ▶ Upcoming studies and protocols in development
- ▶ Continued and new partnerships



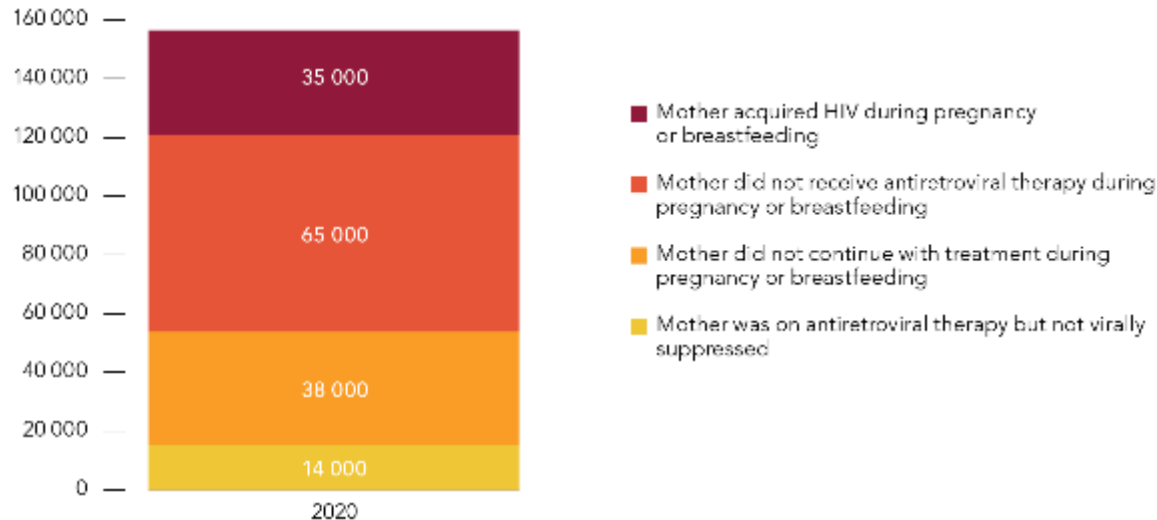
# IMPAACT's Goal

To improve health outcomes for infants, children, adolescents, and pregnant and postpartum people who are impacted by or living with HIV by evaluating novel treatments and interventions for HIV and its complications and for tuberculosis and other HIV-related conditions

# Why Do We Need Research in Infants, Children, Adolescents and Pregnant Women?

In 2019 there were 150,000 new pediatric HIV infections.  
This estimated remained the same in 2020.

**New vertical HIV infections by cause  
of transmission, global, 2020**

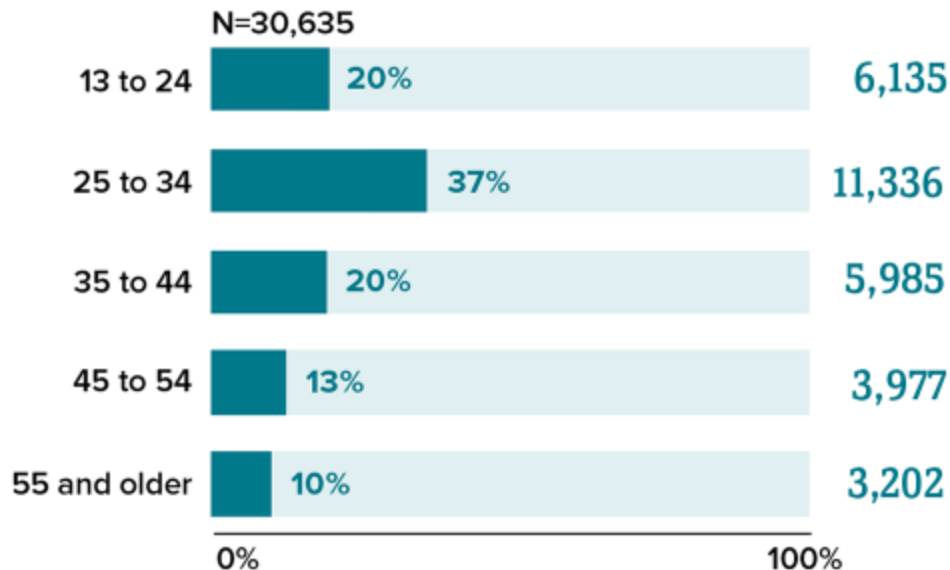


Source: UNAIDS epidemiological estimates, 2021 (<https://aidsinfo.unaids.org>)



# New diagnoses disproportionately affect adolescents and young adults

People aged 13 to 34 accounted for more than half (57%) of new HIV diagnoses in 2020.



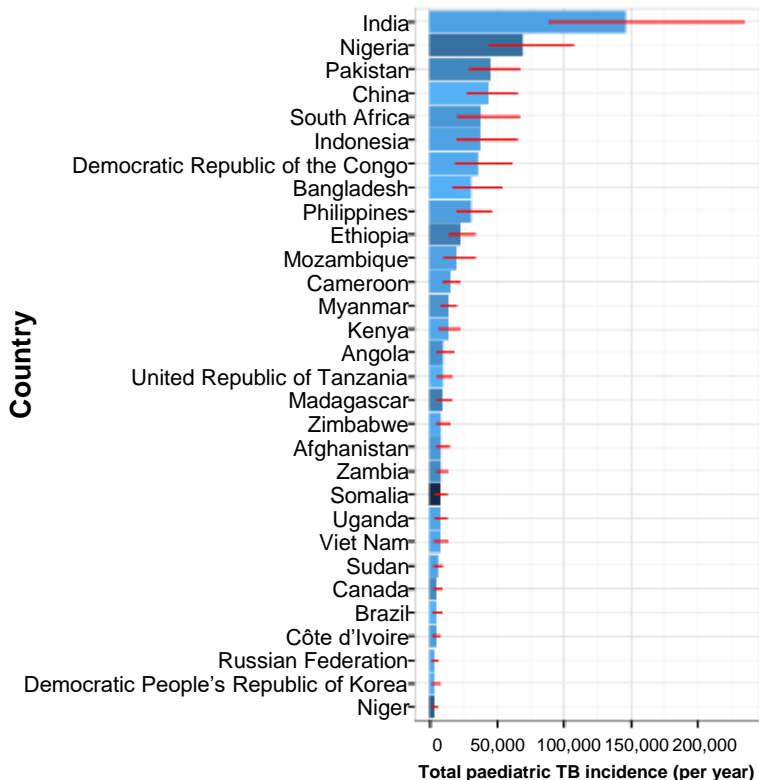
Source: Centers for Disease Control and Prevention. HIV Surveillance Report, 2020; vol. 33. <https://www.cdc.gov/hiv/library/reports/hiv-surveillance.html>. Published May 2022. Accessed 08 June 2022.

# However, important progress has been made in optimizing treatment regimens for children

- ▶ In particular, there has been a dramatic decline in the procurement of inferior nevirapine-based regimens for children in recent years, accompanied by progressive uptake of newer solid formulations of more potent regimens, including lopinavir/ritonavir and dolutegravir

Source: Start Free, Stay Free, AIDS Free: Final report on 2020 targets. UNAIDS. Published July 2021. <https://www.childrenandaids.org/>. Accessed 08 June 2022.

# Global burden of TB in children (< 15 years)

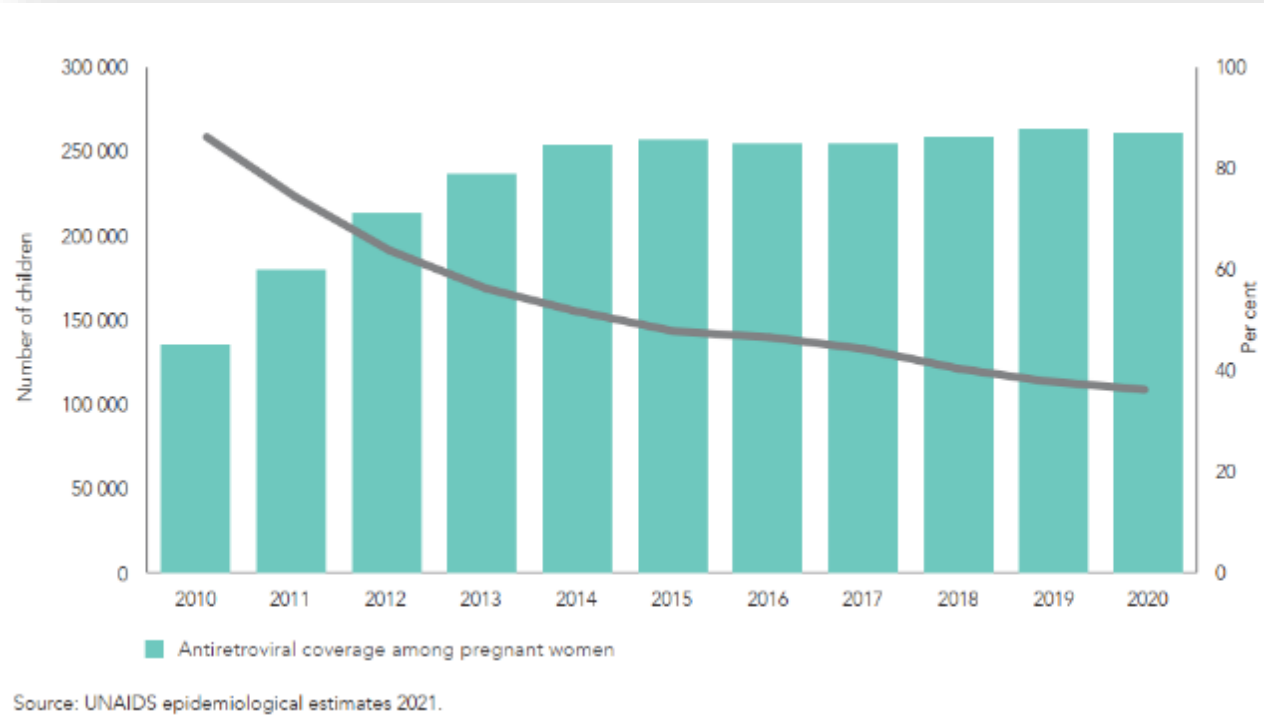


- ▶ 12% global burden
- ▶ Estimated mortality:
  - <15 years: 240,000
  - <5 years : 190,000
  - Excess TB mortality in HIV: 17%
  - TB: top 10 cause of deaths in children < 5 years
- ▶ >95% of the disease burden is DS-TB
- ▶ Diagnosis remains challenging



# High ART coverage during pregnancy but the flattening curve is associated with notable slowdown in decline of number of children living with HIV

Approximately  
1.1 million  
women living  
with HIV at start  
of their  
pregnancy



# Why Do We Need Research in Infants, Children, Adolescents and Pregnant Women?

- ▶ The immune system in fetuses and newborns is still developing. This immaturity may alter the pathogenesis and treatment of HIV and other co-occurring conditions.
- ▶ Throughout growth and in pregnant women, physiologic changes occur that may affect the use of antiretrovirals and other medications and interventions.
- ▶ Developing brains are affected by HIV, what are the effects, can they be prevented or treated?

# IMPAACT Research Agenda

2022 - 2027



Pregnant and  
PP Women



Infants



Children



Adolescents

Novel and Durable Interventions



ART-Free Remission



Tuberculosis



Complications and Co-Infections



# Current Portfolio

*includes evaluation of the following interventions/agents*

## Treatment

- DTG in Neonates, Infants, Children and Adolescents
- Selected ARV and TB drugs in Pregnant/ Postpartum Women
- ABC/DTG/3TC in Children
- LA CAB/RPV in Children & Adolescents and in Pregnancy
- DOR/3TC/TDF in Children
- Oral PrEP (TDF/FTC) in Pregnancy & Postpartum
- bNAbs in Infants

## Complications

- RSV Vaccines in Children
- Group-based Counseling Intervention in Treatment Non-adherent Adolescents
- GLE/PIB for Hepatitis C in Pregnancy

## Cure

- LPV and NVP containing early intensive treatment, RAL and NVP containing early intensive treatment, and VRC01 in Infants
- Cord Blood Transplantation with CCR5Δ32 Donor Cells
- HIVconsvX Vaccines and bNAbs in Children

## Tuberculosis

- VPM1002/BCG in Pre-Adolescents
- Pretomanid in Children
- RPT/INH in Children
- BDQ in Children
- DLM in Children



# Current Portfolio

*26 active studies*

	2 Proposals Recently Approved	7 Protocols in Development	2 Pending and Open	9 Enrolling	3 in Follow-Up	3 Closed to Follow-Up*
Treatment		2040, 2037, 2036	2023	2026, 2017, 2009	P1093, 2019	2014, P1112
Tuberculosis		2035, 2034, 2024		2005, 2003B, P1108		
Complications	2041, 2038		2016	2021		2032 (COVID-19)
Cure		2039		2028, P1115	P1107	

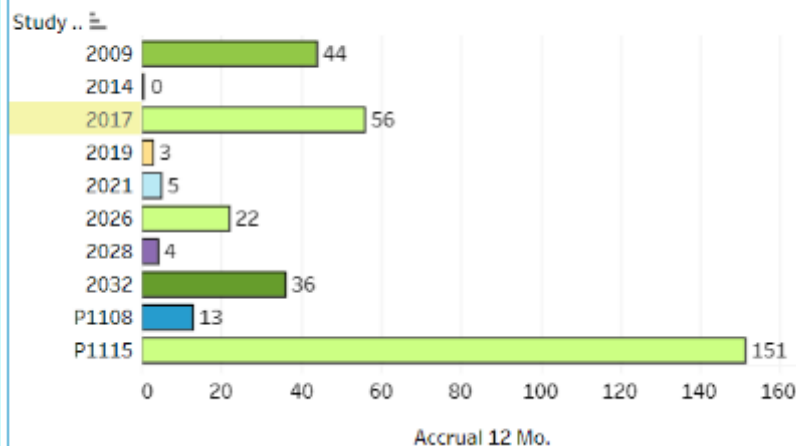
*Approximately 30 additional studies and ancillary studies (NWCS, DACS, DR) in analysis and manuscript writing phase*

\*closed to follow-up in the last year



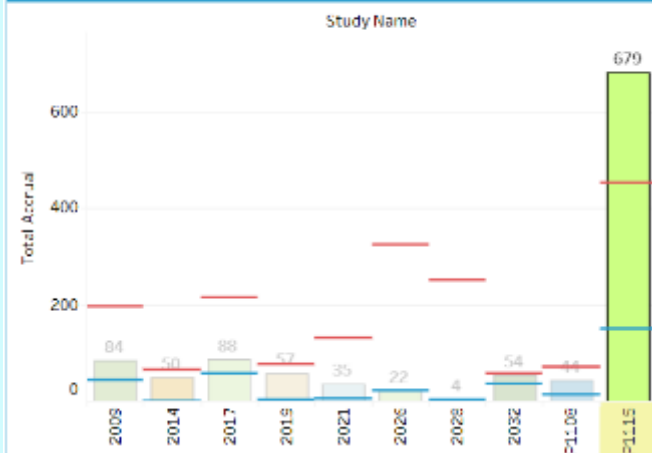
# Data Dashboards

## Accrual in Last 12 Months



## Total Accrual by Study

Red lines = Target : Blue Lines = Last 12 Months



## Approved Sites for Selected Studies

Study	Network	Site	Site Name	Site Approval Date	First Enrollment Date
2009	IMPAACT	5126	MU-JHU Care Limited CRS	10-Mar-2022	30-Mar-2022
		8051	Shandukani Research CRS	02-Apr-2019	15-Apr-2019
		30293	MU-JHU Research Collaboration (MUJHU CARE LTD) ..	04-Mar-2019	03-Apr-2019
		30301	Blantyre CRS	29-Apr-2019	06-May-2019
		30303	St Mary's CRS	26-May-2022	01-Jan-1970
		30306	Seke North CRS	11 Feb 2019	04 Mar 2019
		31798	Baylor-Uganda CRS	22-Mar-2019	09-Apr-2019
		31890	Harare Family Care CRS	26-May-2022	01-Jan-1970

# Seven Protocols Currently in Development

## *Three within the Treatment Research Area*

2040	Phase I/II Pharmacokinetics and Safety of Long-Acting <b>Injectable Cabotegravir and Rilpivirine</b> in People with Virally Suppressed HIV-1 during <b>Pregnancy and Postpartum</b>
2037	Open-Label, Phase I Study of the Safety and Pharmacokinetics of PGT121.414LS alone and in combination with VRC07-523LS in Infants Exposed to HIV-1
2036	Phase I/II Study of the Safety, Tolerability, Pharmacokinetics, and Antiviral Activity of Oral and Long-Acting <b>Injectable Cabotegravir and Rilpivirine</b> in Virologically Suppressed <b>Children</b> with HIV >2 to <12 years of age and weighing >10 kg and <40 kg

# Seven Protocols Currently in Development

## *Three within the Tuberculosis Research Area*

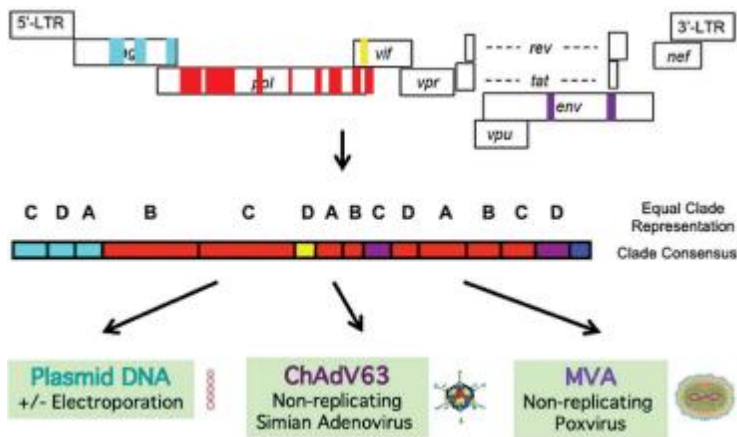
2035	Phase I/II Study of the Safety and Immunogenicity of <b>VPM1002 Vaccination or BCG Re-Vaccination</b> against Tuberculosis in South African Pre-Adolescents Living with and without HIV
2034	Phase I Study of PK, Safety, & Acceptability of <b>Pretomanid</b> in Children with Rifampicin-Resistant TB
2024	Phase I/II Dose Finding, Safety, and Tolerability Study of <b>Daily Rifapentine Combined with Isoniazid (1HP)</b> for Tuberculosis Prevention in Children 2 to <13 years of age with and without HIV

# Seven Protocols Currently in Development

## *One within the Cure Research Area*

2039

Phase I/II Study of the Safety, Immunogenicity, and Efficacy of **HIVconsvX Vaccines and Broadly Neutralizing Antibodies** in Children Living with HIV



# Protocols Planned for Development

## *Two within the Complications Research Area*

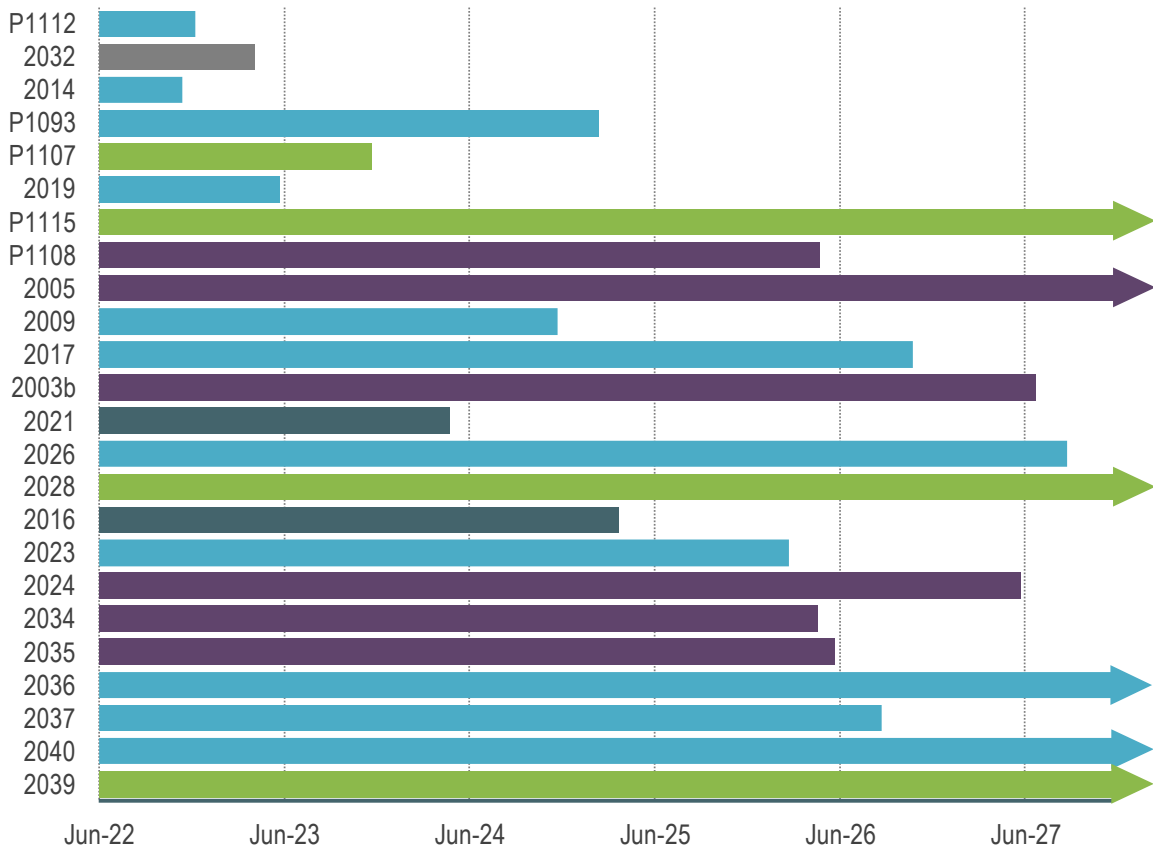
2038

Phase I Study of the Infectivity, Safety and Immunogenicity of two **Recombinant, Live-Attenuated B/HPIV3 Vector Vaccines** Expressing the Fusion Glycoprotein of **RSV** Engineered for Increased Immunogenicity, Delivered in Single Doses as **Nose Drops** to HPIV3-Seronegative Infants and Children 6 to 18 Months of Age (CAP 554)

2041

Safety and Pharmacokinetics of **GLE/PIB** in **Pregnant Persons with Hepatitis C** with or without HIV (CS 5032)

# The Network has a robust and growing portfolio of current studies and new proposals in the pipeline



Complications
Cure
Treatment
Tuberculosis
COVID-19



# Network Activities and Achievements

# Contributions to Expanded Treatment Options

Data from three studies informed recent US FDA decisions for ART in children living with HIV

- ✓ **P1093/DTG:** expanded approval of *Trumeq* and *Trumeq PD* for children 10-25 kg
- ✓ **IMPAACT 2014/DOR and DOR/3TC/TDF:** expanded approval of *Destrigo* and *Pifeltro* for children 35 kg and more
- ✓ **IMPAACT 2017/CAB/RPV:** expanded approval of *Cabenuva* for children aged 12 years and older, 25 kg and more



## IMPAACT 2017 (MOCHA) Data Informs U.S. FDA Approval of Cabenuva for HIV Treatment in Virologically Suppressed Adolescents

MARCH 2022

ANNOUNCEMENTS

SHARE 

The IMPAACT Network is pleased to announce that interim data from [IMPAACT 2017/MOCHA](#) (More Options for Children and Adolescents) has informed the U.S. Food and Drug Administration's (FDA) decision to approve Cabenuva (cabotegravir, CAB; rilpivirine, RPV) for the treatment of HIV-1 in adolescents who are virologically suppressed, 12 years of age or older, and weigh at least 35 kg. Adolescents must be on a stable antiretroviral regimen with no history of treatment failure, and with no known or suspected resistance to either



First time a long-acting HIV treatment is available for adolescents

**ViiV HEALTHCARE ANNOUNCES US FDA APPROVAL OF *CABENUVA* (CABOTEGRAVIR, RILPIVIRINE) FOR VIROLOGICALLY SUPPRESSED ADOLESCENTS LIVING WITH HIV WHO ARE 12 YEARS OF AGE OR OLDER AND WEIGH AT LEAST 35 KG**

# Contributions to Expanded Treatment Options

Additional data from four studies anticipated to be submitted to regulatory authorities:

- ▶ IMPAACT 2014 – DOR and DOR/3TC/TDF
- ▶ IMPAACT 2017 – CAB/RPV
- ▶ IMPAACT 2019 – ABC/DTG/3TC
- ▶ IMPAACT 2032 – RDV



*Group of children, Getty Images*



# IMPAACT P1107 Team Presents First Known Case of a Woman with HIV Remission

FEBRUARY 2022

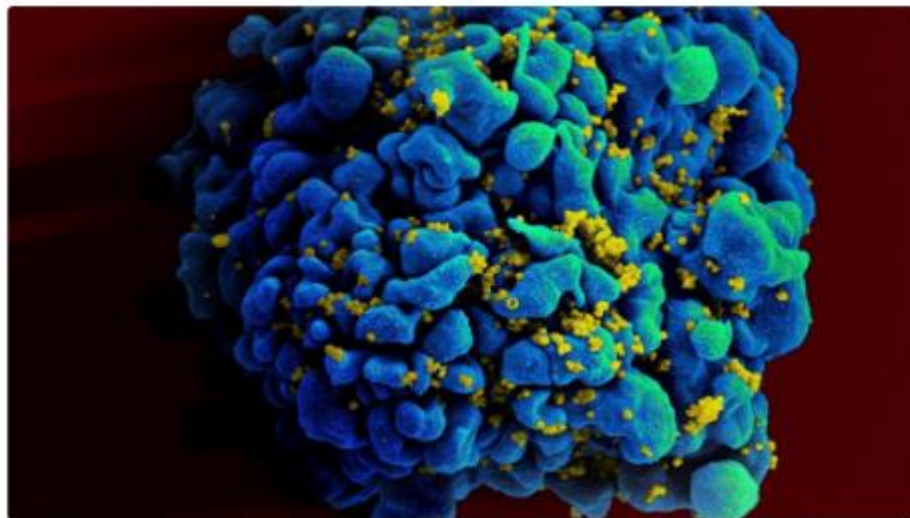
STUDY RESULTS

SHARE



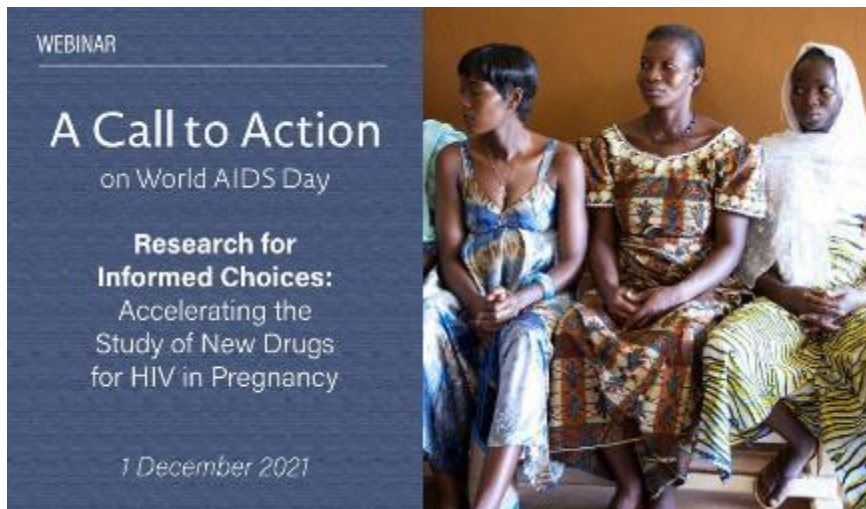
The [IMPAACT P1107](#) protocol team presented the **first known case of a woman with HIV remission** following a stem cell transplant for treatment of acute myelogenous leukemia (AML) at CROI 2022 on 15 February. The transplant consisted of cord blood stem cells with the CCR5 $\Delta$ 32 genetic mutation and haploidentical peripheral blood stem cells from a relative. Since having the stem cell transplant, the participant has been in remission for AML.

>> [See Latest Press Coverage](#)



HIV-infected T cell, NIAID

# Call to Action: Accelerating Study of New Drugs for HIV in Pregnancy



Three major conceptual shifts that will facilitate inclusion of pregnant women in research:

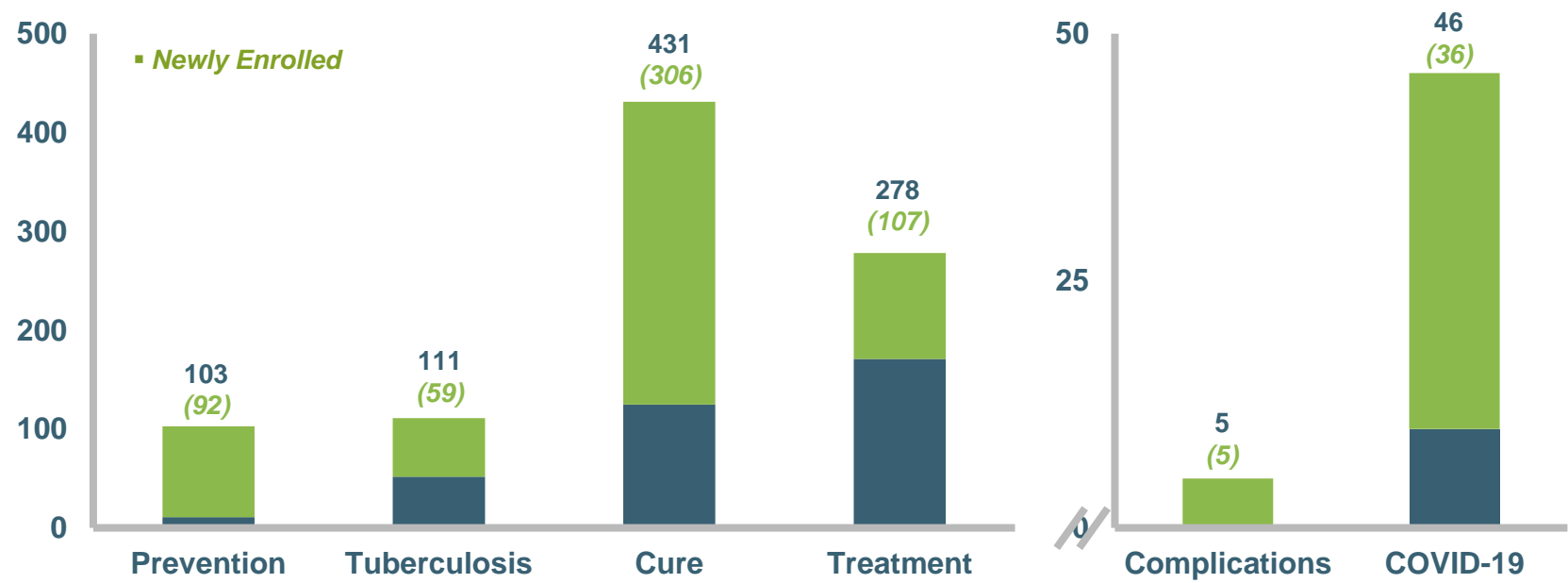
- ✓ Considering pregnant women as a **complex population** rather than a vulnerable population
- ✓ Moving from protecting from research to **protecting through research**
- ✓ **Promoting fair inclusion in**, rather than presumptive exclusion from, clinical drug trials

Source: WHO and IMPAACT: A Call to Action Webinar on World AIDS Day. 1 December 2021. <https://www.impaactnetwork.org/who-and-impaact-call-action-webinar-world-aids-day>. Accessed 08 June 2022.



# IMPAACT Participants on Study

June 2021 to May 2022



*Total On Study = 974 participants*  
*Newly Enrolled = 605 participants*

# Community Engagement

- ▶ Community representation and input on all network groups and levels – clinical research sites, leadership groups, scientific and other committees, protocol teams, cross-network activities
- ▶ ICAB ensures that the principles of community participation and partnership are at the foundation of all community engagement activities and provides community input throughout the research process (concept development, study implementation, and results dissemination)



# 29 Early Career Investigators Program

Overall goal: to prepare the next generation of health care professionals with skills to maintain and strengthen HIV programs for IMPAACT's populations of interest, experience the collaborative nature of network research, hone presentation skills, and develop a scholarly work that is suitable for publication.

More  
details  
to come  
soon!

## Key Dates:

- ▶ July 2022: Application announcement
- ▶ 1 October 2022: submission deadline
- ▶ 1 December 2022: funding initiated

# Study Updates and Achievements

# Study Highlight: P1108

## PK and Safety of Bedaquiline in Infants, Children, and Adolescents with MDR-TB Disease and with or without HIV

- ▶ Addressing critical need for better medications to treat children with MDR-TB
- ▶ Interim study data informed 2022 WHO consolidated guidelines on tuberculosis, Module 5: management of tuberculosis in children and adolescents
- ▶ 43 evaluable participants enrolled of 54 total at sites in Haiti and South Africa



*Child with mask, Getty Images*

Anticipate Version 2.0 issued  
by August 2022

# Study Highlight: IMPAACT 2014

## Doravirine as Fixed-Dose Combination for Adolescents

Closed to  
follow-up and  
POS/PAC  
25 May 2022

- ▶ New fixed-dose, one-pill/once-a-day combination for adolescents
- ▶ 55 participants enrolled at 8 sites in South Africa, Thailand, and the US in Cohort 2
- ▶ Data informed recent US FDA and EMA decisions to approve DOR and fixed-dose combination of DOR/3TC/TDF in adolescents living with HIV



Group of adolescents inside, Getty Images



# Study Highlight: IMPAACT 2021

## RSV Vaccine Candidate Study

Resumed  
Accrual  
01 Apr 2022

- ▶ Randomized, Phase I/II placebo-controlled study among healthy RSV-seronegative children 6-24 months of age to assess safety and immunogenicity of candidate vaccines
- ▶ 30 of 160 participants enrolled at 10 sites in the US prior to accrual pause due to COVID-19
- ▶ 5 participants enrolled since accrual resumed at 2 sites!



*Babies holding hands, Getty Images*

# Study Highlight: IMPAACT 2028

## Long-Term Clinical, Immunologic, and Virologic Profiles of Children who Received Early Treatment for HIV

- ▶ Enable long-term follow-up of infants who received early or very early treatment for HIV in other cure-related studies
- ▶ Establish a biorepository for investigations related to the clinical, immunologic, and virologic effects of early treatment with priority for early career investigators
- ▶ Six of 35 sites activated, with four participants enrolled at sites in the US

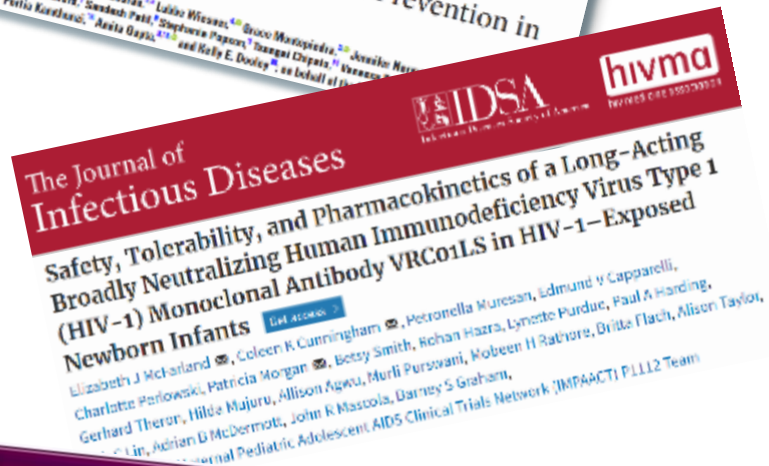
Opened to accrual  
(8 Nov 2021) with  
first enrollment  
2 February 2022

# More to come at tomorrow's plenary!

<b>IMPAACT 2032</b>	Remdesivir for COVID-19 Treatment in Pregnancy	Kristina Brooks
<b>IMPAACT 2017/ MOCHA</b>	Long-Acting CAB & RPV in Adolescents Living with HIV	Carolyn Bolton & Aditya Gaur
<b>IMPAACT 2010/ VESTED</b>	ARV Regimens for Pregnant People Living with HIV and Their Infants	Lameck Chinula
<b>IMPAACT 2019</b>	Fixed-Dose Combination of ABC/DTG/3TC in Children Living with HIV	Pat Flynn
<b>IMPAACT P1115</b>	Very Early ART Treatment for Neonates Exposed to HIV	Ellen Chadwick

# Publications

- ▶ **59** publications submitted for IMPAACT review in past 12 months
- ▶ **41** manuscripts published in Lancet HIV, CID, JID, Antimicrobial Agents and Chemotherapy, AIDS, JAIDS, Journal of Clinical Pharmacology, among others



# Abstracts

**17** at CROI 2022, **3** at IAS 2021, **5** at HIV Peds 2021

- ▶ 6 abstracts from IMPAACT 2010/VESTED
- ▶ 4 abstracts from P1078/TB APPRISE, 3 from IMPAACT 2019, and 3 from PROMISE 1077BF/1077FF/P1084s
- ▶ Additional results from P1041/P1106, NICHD P1081, P1107, P1112, P1115, IMPAACT 2017/MOCHA, IMPAACT 2032 among others!

HIV-1 REMISSION WITH CCR5 $\Delta$ 32 $\Delta$ 32  
HAPLO-CORD TRANSPLANT IN A U.S.  
WOMAN: IMPAACT P1107

Yvonne Bryson, MD

David Geffen School of Medicine at UCLA and Mattel  
Children's Hospital, Los Angeles, California, USA

Growth of infants with perinatal exposure  
to maternal DTG vs EFV and TDF vs TAF:  
the randomized IMPAACT 2010 trial

Lynda Stranix-Ghibanda, Lauren Zimba, Sean Brummel,  
Benjamin Johnston, Tapwa Mbengeranwa, Haseena Cassim,  
Gerhard Theron, Sherika Hanley, Mavisio Owar, Katie McCarthy,  
Nathica Oekiloune, Patrick Jean-Philippe, Lameck Chinua,  
Shahin Lockman, for the IMPAACT 2010/VESTED study team and investigators

TWO YEAR VIROLOGIC OUTCOMES  
OF VERY EARLY ART FOR INFANTS  
IN THE IMPAACT P1115 STUDY

Deborah Persaud, MD

Johns Hopkins University School of Medicine, Baltimore, Maryland, USA

[www.croiconference.org/abstract/1107](https://www.croiconference.org/abstract/1107)

Oral presentation: CROI 2022 - 3-8 February 2022



USA: Perinatal HIV is now mostly prevented by ART  
Oral presentation: HIV 2022 - 19-23 July 2022



[www.hivpreventionworkshop.org/abstract/1115](https://www.hivpreventionworkshop.org/abstract/1115)

Oral presentation: HIV Peds 2021 - 12-14 February 2021



*Additional abstracts accepted to upcoming meetings  
at AIDS 2022 and the HIV Pediatrics Workshop*

# Looking Forward



# Study Highlight: IMPAACT 2023

Safety & PK of Dolutegravir in Neonates Exposed to HIV

Version 2.0  
to sites  
30 March 2022

- ▶ Study to determine DTG dosing for children from birth through the first 4-6 weeks of life
- ▶ Planned at 17 sites in Brazil, South Africa, Thailand, and the US

Anticipate open to accrual  
by July 2022



*Baby feet, Getty Images*



# Study in Development: IMPAACT 2034

PK and Safety of Pretomanid in Infants, Children, and Adolescents with RR-TB with or without HIV

- ▶ Addressing critical need for better medications to treat children with drug resistant tuberculosis
- ▶ Collaborative study with TB Alliance
- ▶ Planned at 7 sites in India, South Africa, Tanzania, and Thailand

Anticipate Version 1.0  
by July 2022



*Child with mask, Getty Images*

# Study in Development: IMPAACT 2035

Safety and Immunogenicity of VPM1002 Vaccination or BCG Revaccination against TB in Pre-Adolescents with and without HIV

- ▶ Addressing critical need for vaccinations against tuberculosis
- ▶ Collaborative study with HVTN

Anticipate Version 1.0  
within the next few weeks!



*Adolescent with mask getting vaccinated, Getty Images*

# Study in Development: IMPAACT 2036

Safety & PK of Oral and Long-Acting Injectable Cabotegravir and Rilpivirine in Virologically Suppressed Children with HIV

- ▶ Continued successful collaboration from IMPAACT 2017 with ViiV/Janssen to study long-acting, injectable regimens in children
- ▶ Children will be two to less than 12 years old
- ▶ Planned at 12 sites in Brazil, Botswana, South Africa, Thailand, Uganda, and the US

Anticipate protocol to sites  
by September 2022



*Child with celebratory soccer/football gear,  
Getty Images*

# Study in Development: IMPAACT 2037

## Safety and PK Parameters of Potent Anti-HIV Neutralizing Monoclonal Antibodies

- ▶ Building on work from IMPAACT P1112, evaluating two potent anti-HIV neutralizing monoclonal antibodies
- ▶ Will be administered soon after birth to infants at high risk for peripartum or breastfeeding HIV transmission

Anticipate protocol to sites by Q4 2022



*Clinician administering shot to infant on lap, Getty Images*

# Study in Development: IMPAACT 2040

PK & Safety of Long-Acting Injectable Cabotegravir and Rilpivirine in People with Virally Suppressed HIV-1 during Pregnancy and Postpartum

- ▶ Continued successful collaboration from IMPAACT 2017 and 2036 with ViiV/Janssen to study long-acting, injectable regimens
- ▶ Enrolling participants who are pregnant and living with HIV (and their infants)

Anticipate protocol to sites by May 2023



*Group of people who are pregnant, Getty Images*

# And Many Other Studies Met Key Milestones!

45

IMPAACT 2008  
POS/PAC  
15 Apr 2022

IMPAACT 2015  
POS/PAC  
02 Nov 2021

IMPAACT 2019  
Closed to  
accrual  
28 Jun 2021

IMPAACT 2026  
1<sup>st</sup> Enrollment  
01 Sep 2021

IMPAACT 2005  
Version 3.0  
issued  
30 Jul 2021

IMPAACT P1093  
data published &  
support reg  
submission

IMPAACT 2009 PrEP  
Comp opened  
(13 Jan 2022) and  
1<sup>st</sup> Enrollment  
08 Mar 2022

IMPAACT P1112  
Close to follow-up  
18 Dec 2021

IMPAACT 2010  
published  
primary results



# Cross Network Study Initiatives



- ▶ MDR-TB Prevention (PHOENIX)
- ▶ TB Vaccine Studies (IMPAACT 2036)
- ▶ Dolutegravir (P1093/ODYSSEY)
- ▶ RSV and VRC Studies (IMPAACT 2011/2012/2013, IMPAACT 2018, IMPAACT 2021; P1112, IMPAACT 2008, IMPAACT 2037)



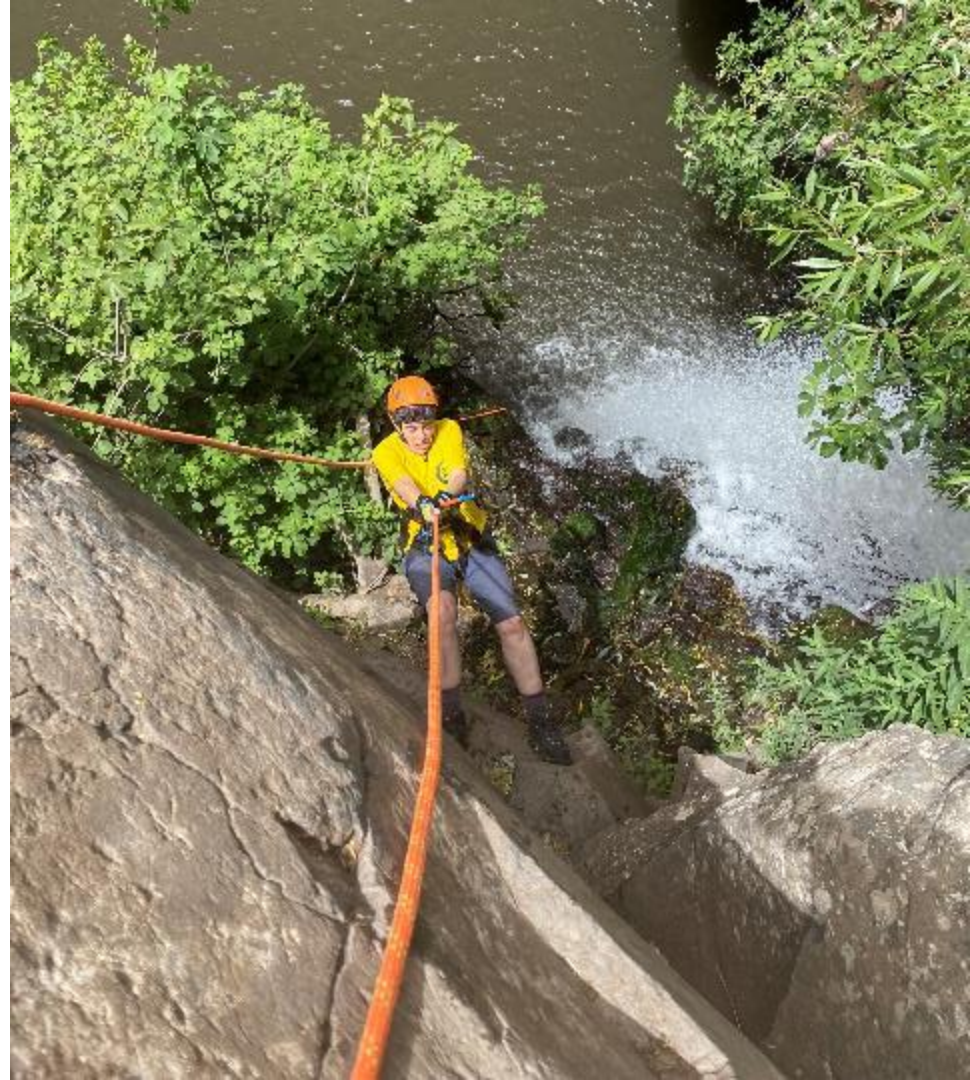


# Pharma and Other Collaborations



**We have had a great  
year with excellent  
work and significant  
accomplishments!**

**Let's prepare for the  
coming year of  
IMPAACT work and  
keep climbing to  
greater heights!**



# THANKS!



*Children smiling on a playground, Getty Images*

**Thank you to site staff, to the communities, and to all of the individuals and families engaged in clinical research!**

**Let's continue to move the science forward!**