

State of the Network *Community Plenary*

Sharon Nachman, MD
IMPAACT Network Chair
23 September 2024



IMPAACT

International Maternal Pediatric Adolescent
AIDS Clinical Trials Network

ANNUAL MEETING
2024

State of the Network: A Snapshot



- Research Agenda
- Network Activities and Achievements
- Study Updates and Achievements
- Looking Forward

Our Mission

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



IMPAACT

International Maternal Pediatric Adolescent
AIDS Clinical Trials Network



IMPAACT Research Agenda



Pregnant & PP People



Infants



Children



Adolescents

Novel and Durable Therapeutic/Preventive Interventions



Cure and Immunotherapy



Tuberculosis



Brain and Mental Health



Scientific Aims

1

Advance **treatment during pregnancy and postpartum**, aiming to optimize maternal and child health outcomes and accelerate the evaluation (pharmacokinetics (PK), safety, antiviral efficacy), licensure and optimal use of **potent and durable ARVs and other therapeutics** for pregnant people and infants, children, and adolescents with HIV and related diseases and conditions

2

Evaluate the potential for **ART-free HIV remission** through therapeutic interventions aimed at prevention, clearance and post-treatment control of HIV reservoirs in infants, children and adolescents with HIV and leverage expertise for evaluation of **vaccines** for HIV and related/co-occurring conditions in these populations

3

Evaluate novel approaches for **TB prevention, diagnosis and treatment** in infants, children, adolescents and pregnant and postpartum people with and without HIV that will lead to optimal dosing and regimens, licensing and decreased morbidity and mortality

4

Determine optimal and feasible biological and behavioral methods for the prevention and management of **neuropsychological and mental health complications of HIV and its treatment** in infants, children, adolescents and pregnant and postpartum people

Current Portfolio

includes evaluation of the following interventions/agents

Therapeutics

- **DTG** in Neonates, Infants, Children & Adolescents
- Opportunistic, **Selected ARV and TB drugs** in Pregnant/ Postpartum People
- **LA CAB/RPV** in Children/ Adolescents & in Pregnancy
- **Oral PrEP (TDF/FTC)** in Pregnancy
- **GLE/PIB** for Hepatitis C in Pregnancy
- **Ceftriaxone & Benzathine Penicillin G** During Pregnancy

Brain & Mental Health

- **Group-based Counseling Intervention** in Treatment Non-adherent Adolescents
- **Exploring Therapeutics** in Pregnancy & Adolescence
- **Understanding Lactation & Feeding Decisions**

HIV Cure & Immunotherapy

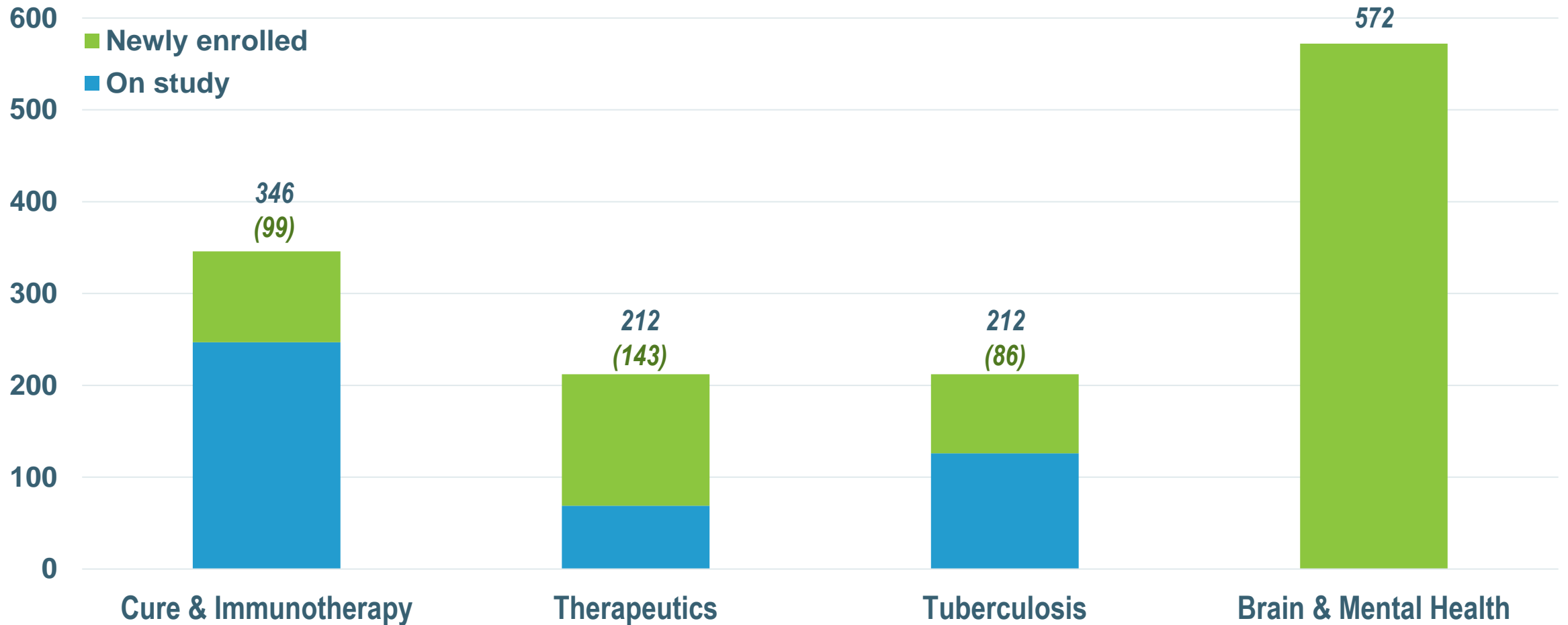
- **NVP, LPV/r, RAL, DTG, & bNAbs** for early intensive treatment in Infants
- **HIVconsvX Vaccines**
- **bNAbs** in Infants & Children

Tuberculosis

- **Pretomanid** in Children
- **RPT/INH** in Children
- **BDQ** in Children
- **DLM** in Children
- **Combination Regimen** for RR-TB in Children
- **RPT/Mfx** in Pregnancy
- **Vaccines** in pre-adolescents

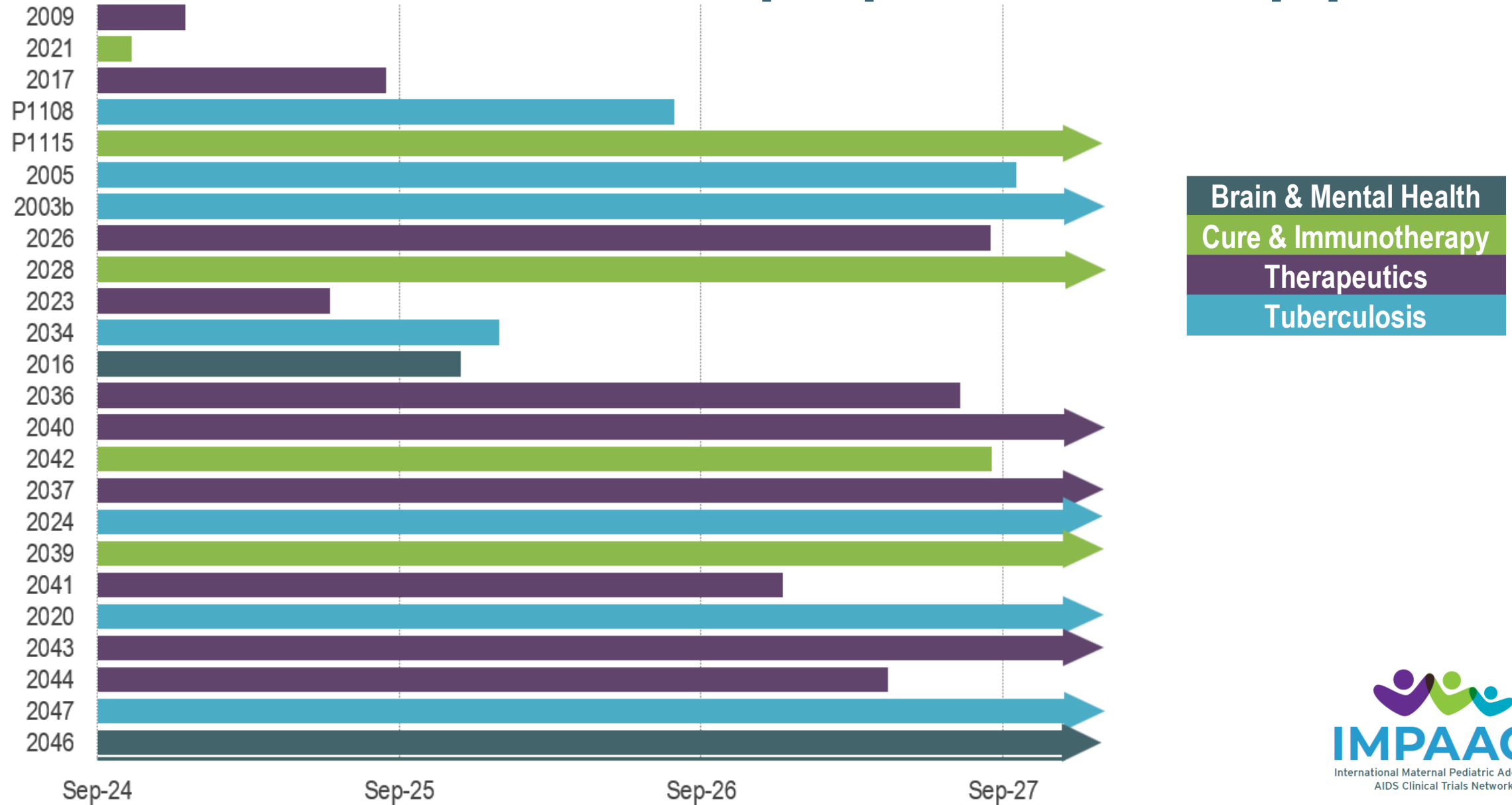
IMPAACT Participants on Study

October 2023 to August 2024



Total On Study = 1,464 participants
Newly Enrolled = 947 participant



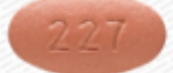







The Network has a robust and growing portfolio of current studies and new proposals in the pipeline



Network Activities and Achievements

Drug Licensure based on IMPAACT Data

11

		Birth	1 mth	2 mths	6 mths	2 yrs	6 yrs	12 yrs	18 yrs	Pregnancy		
Dolutegravir (DTG)		Dispersible tablet	Dispersible and film-coated tablets									
Abacavir (ABC)/DTG/lamivudine (3TC)*			Immediate-release and dispersible fixed-dose tablets									
Raltegravir (RAL)		Oral granules for suspension and chewable tablets										
Cabotegravir/rilpivirine (CAB/RPV)						Long-acting injectable		Long-acting injectable		Long-acting injectable		
Doravirine (DOR)/3TC/TDF								Fixed-dose tablet				
Etravirine (ETR)				Tablet							Approved	
Maraviroc (MVC)*		Oral liquid										In progress
Bedaquiline (BDQ)		Tablet										
Pretomanid (Pa)*			Immediate-release and dispersible tablets									
Remdesivir										Injection		

*Approved in children using weight-based dosing

Recent and Planned Contributions to Expanded Treatment Options

- ✓ Data from **IMPAACT 2019, ABC/3TC/DTG** informed EMA regulatory decision to expand approval of *Triumeq PD* to **infants and children** with HIV as young as 3 months of age who weigh at least 6 kg
- ✓ Longer term, additional data from **IMPAACT P1093** submitted to US FDA to inform **DTG** dosing in **infants and children**
- ✓ Longer term, additional data from **IMPAACT 2017** anticipated to be submitted to US FDA in 2025 to inform use of **CAB/RPV** in **adolescents**

Ongoing Collaborations to Enhance and Accelerate Research in IMPAACT's Populations

IPHASA 2023

REPUBLIC OF UGANDA
MINISTRY OF HEALTH

IAS

2nd International Paediatric HIV Symposium in Africa (IPHASA 2023)

Meeting Report

Virtual
12-14 December 2023

Platinum sponsor

Bronze sponsor

ViiV Healthcare

IMPAACT
International Maternal Pediatric Adolescent AIDS Clinical Trials Network

With support from

World Health Organization

Tuberculosis & Pregnancy

Building consensus on inclusion in research

February 2024

SANTHE
SUB-SAHARAN AFRICAN NETWORK FOR TB/HIV RESEARCH EXCELLENCE
Advanced Research Institute, Pathways PREVENT and TB

WRAIR
WORLD RESEARCH ASSOCIATION OF MILITARY HIV RESEARCH PROGRAM

Analytical Treatment Interruption (ATI) Consensus Workshop

8-10 May 2024 · Trademark Hotel, Nairobi, Kenya

PROGRAMME

MELINDA GATES foundation

NIH National Institutes of Health
Turning Discovery into Health

SCIENCE FOR AFRICA

DELIVER

Ragon Institute
RAGAN INSTITUTE FOR HEALTH CARE RESEARCH

GILEAD
Creating Possible

Guidance for best practices for clinical trials

World Health Organization

Four Children Surpass a Year of HIV Remission after Treatment Interruption:

IMPAACT P1115 Results Presented at CROI 2024

- ✓ **Four of six children remained free of detectable HIV for more than one year after their ART was interrupted to see if they could experience HIV remission.**
- ✓ The children, who acquired HIV before birth, were closely monitored in IMPAACT P1115 for safety and HIV viral suppression.
- ✓ The outcomes reported follow planned ART interruption once the children met predefined virologic and immunologic criteria.

Study Weeks off ART (no detectable plasma HIV-1 RNA)	
A	80
B	>64
C	>52
D	>48
E	8
F	3

IMPAACT Community Advisory Board

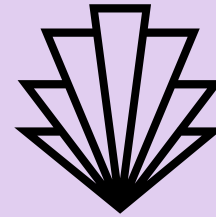
Advocating for people living with HIV/AIDS,
Protecting the interests of research participants, and
Building Community, through:



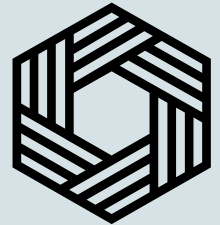
**Input on
protocol
development**



**Support for
study
implementation**



**Results
dissemination**



**Capacity
building**

IMPAACT COMMUNITY ADVISORY BOARD LEADERSHIP GROUP



Emanueli Msuya



Jayda Arrington



Ernest Moseki

Early Career Investigator Program

01 | Project Development

Develop a project using existing data or samples generated by IMPAACT Network studies.



Skills Building

Build skills to improve health outcomes for infants, children, adolescents, and pregnant & postpartum people impacted by or living with HIV, TB, & other HIV-related conditions.



02

03 | Mentorship

Work with a Network mentor to complete the research project.



Share Results

Submit manuscript to a peer-reviewed journal and present findings at the IMPAACT Annual Meeting and at one or more other scientific meetings.



04



**Clement Gascua
Adu-Gyamfi**



**Taguma Allen
Matubu**



Nyarai Soko



**Chikondi
Malamba-Banda**



Brenda Kakayi

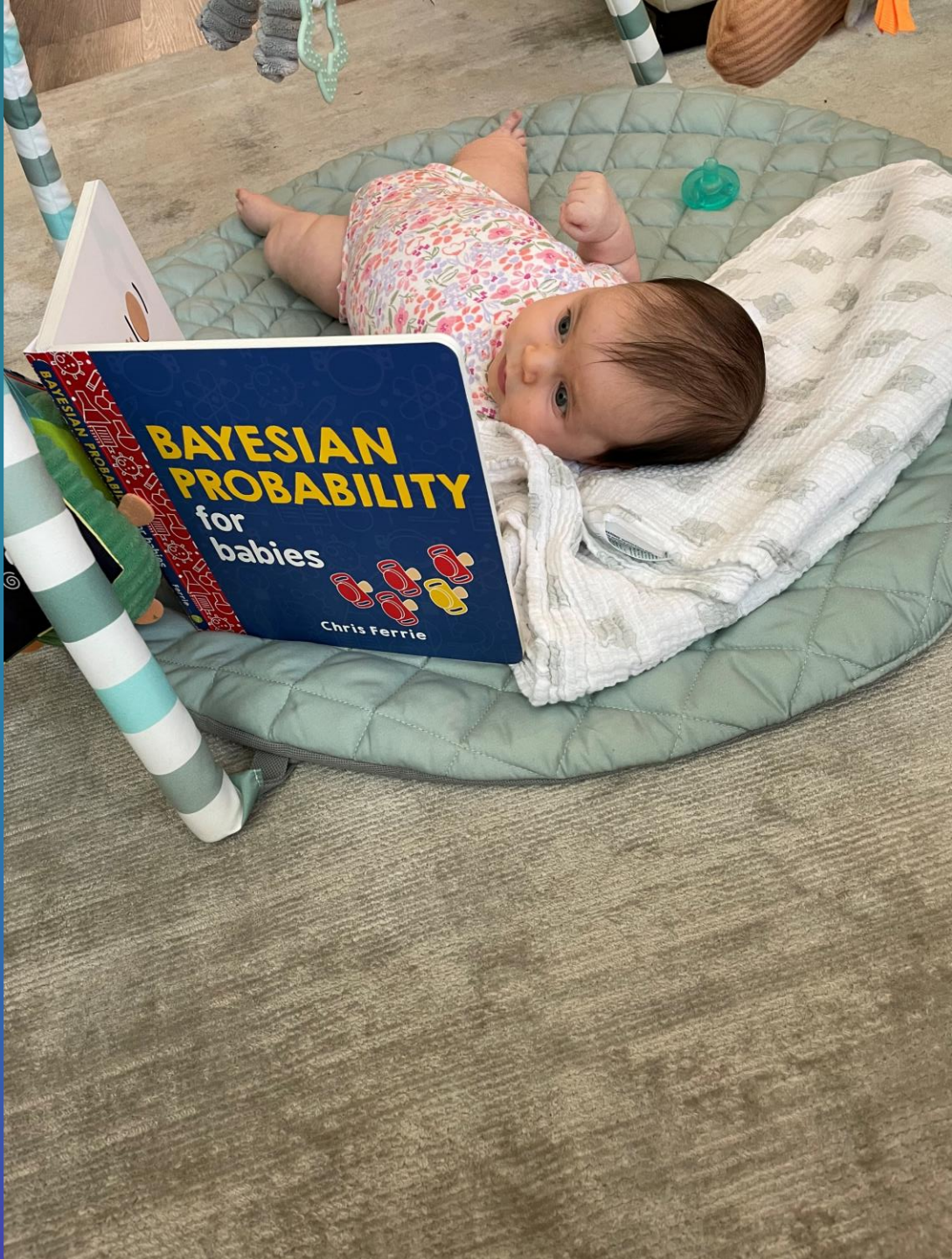
**2025 CYCLE OPEN NOW!
APPLICATIONS DUE
1 OCTOBER**



Patience Atuhaire



Violet Korutarro



A VERY EARLY CAREER INVESTIGATOR

Study Updates and Achievements

Study Highlight: P1108

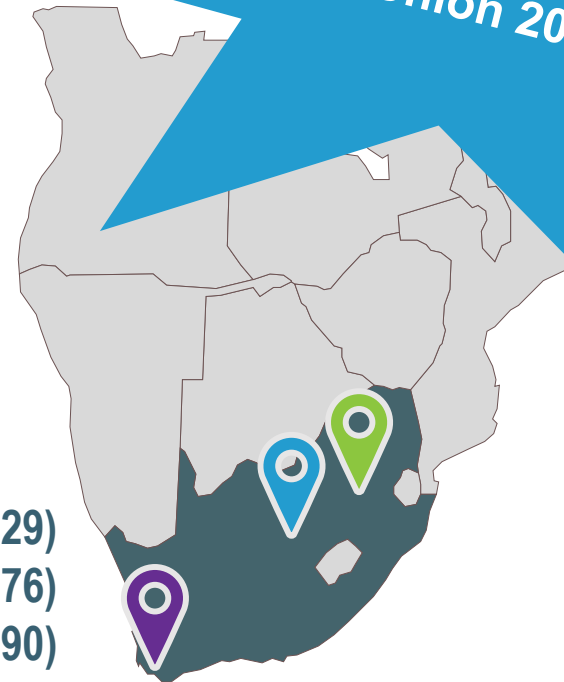
PK and Safety of Bedaquiline in Children with RR-TB

- Addressing critical need for better medications to treat children with MDR-TB
- Completed accrual of 54 children at 4 sites in Haiti and South Africa

Primary results
to be presented
at Union 2024



Sizwe (31929)
PHRU Matlosana (31976)
DTTC (31790)

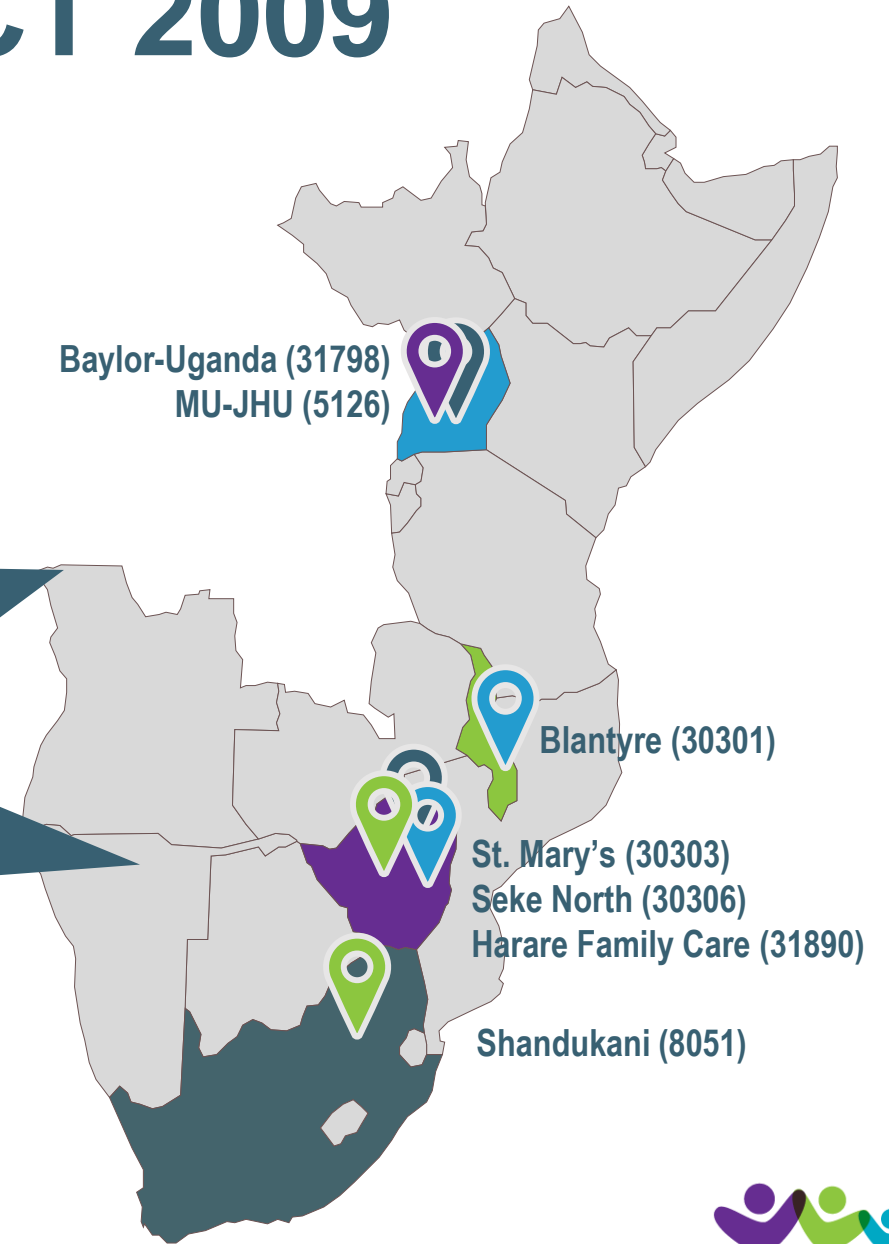


Study Highlight: IMPAACT 2009

PrEP in Pregnancy

22

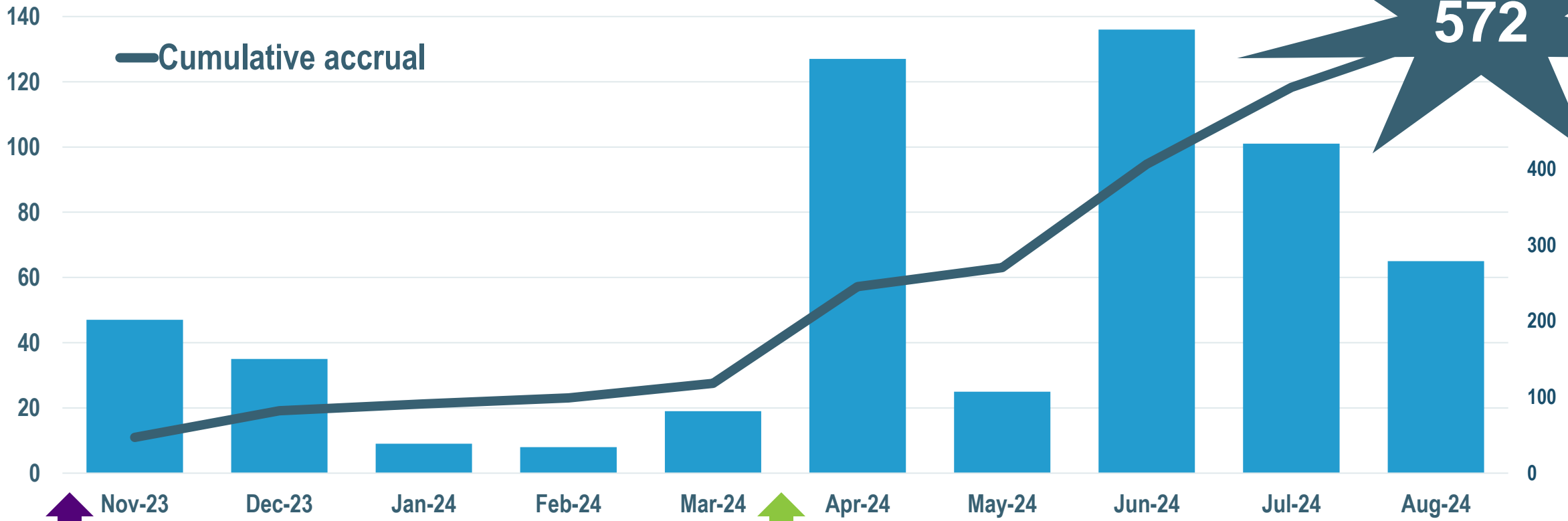
Completed
follow-up of 350
mother-infant pairs in
the PrEP Comparison
Component as of
24 Feb 2024





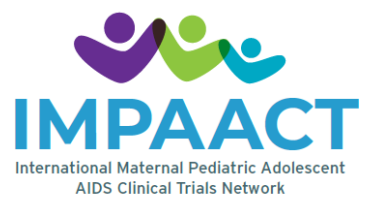
Study Highlight: IMPAACT 2016

Group-Based Intervention to Improve Mental Health and ART Adherence among Youth



Pilot Tests Began

Randomized Control Trial Enrollment of Youth and Caregivers Began

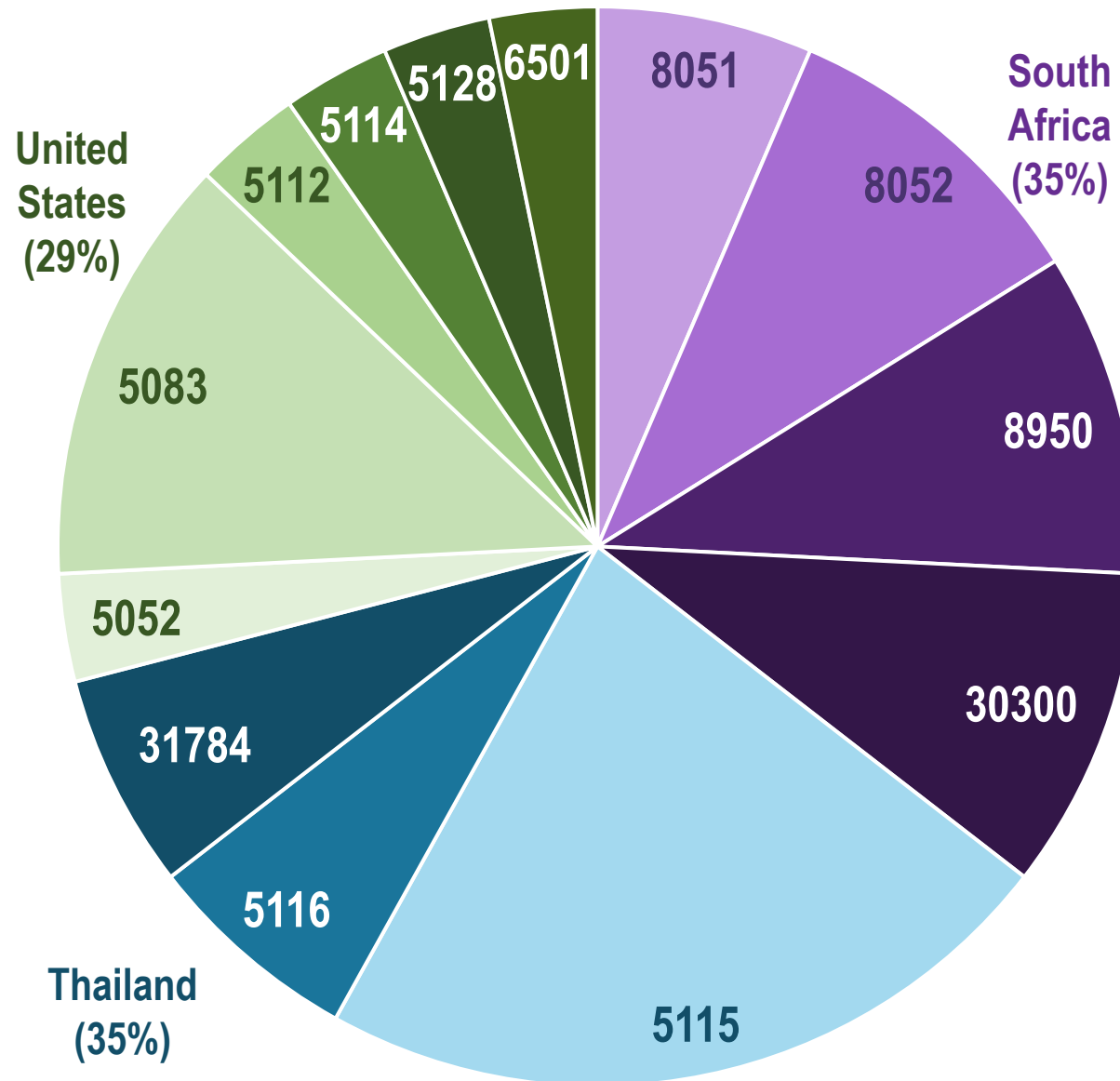


Study Highlight: IMPAACT 2023

Safety & PK of DTG in Neonates Exposed to HIV

24

Therapeutics



- Completed enrollment into Cohort 1
- Cohort 2 is ~50% enrolled
- Cohort 2 interim analysis ongoing

FIRSTS IN IMPAACT 2028

Long-Term Study of Children who
Received Early Treatment for HIV

FIRST

phase of accrual has
been completed

FIRST

batches of specimens
have been shipped for
protocol-specified testing
and repository storage

FIRST

round of proposals
for use of study data
and specimens will
be solicited in 2025

CRAYON

IMPAACT 2036

Cabotegravir and Rilpivirine
Long-Acting Injections in Young Children

- Continued successful collaboration from IMPAACT 2017 with ViiV/Janssen to study long-acting, injectable regimens in children
- Children age two to less than 12 years old
- Interim analysis ongoing

12 SITES IN BOTSWANA,
BRAZIL, SOUTH AFRICA,
THAILAND, & THE US

9 SITES ACTIVATED

8 SITES
ENROLLED

35 PARTICIPANTS
ENROLLED!

And Many Other Studies

IMPAACT 2034
Enrolling
(3 Oct 2023)

P1041
Concluded
(20 Feb 2020)

IMPAACT 2037
pending
(13 Jun 2024)

P1093 Closed
to follow-up
and POS/PAC
(18 Oct 2023)

P1107
Concluded
(16 Mar 2023)

MOCHA
Closed to accrual
(27 Oct 2023)

Tatelo Plus
pending
(9 May 2024)

P1080
Concluded
(20 Sep 2023)

IMPAACT 2015
Concluded
(23 May 2024)

IMPAACT 2014
Concluded
(18 Dec 2023)

P1092
Concluded
(19 Apr 2024)

IMPAACT 2021
closed to accrual
(20 Nov 2023) and
closed to follow-up
(25 Apr 2024)

Looking Forward

Protocols Currently in Development

Three within the Tuberculosis Research Area

2020

A Phase II Study of **Shortened Oral Novel Treatment** for Rifampicin-Resistant Tuberculosis **in Children**

2024

Phase I/II Dose Finding, Safety, and Tolerability Study of **Daily Rifapentine Combined with Isoniazid (1HP)** for Tuberculosis Prevention in Children 2 to <13 years of age with and without HIV

2047

Pharmacokinetics, Safety and Tolerability of **High Dose Rifapentine** Given with Moxifloxacin for **Tuberculosis During Pregnancy** (Radiant-Moms Plus)

Protocols Currently in Development

One within the Cure & Immunotherapy Research Area

2039

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

One within the Brain & Mental Health Research Area

2046

Understanding Parental Lactation and Infant Feeding Decisions Tailored to People with HIV (**UPLIFT Study**)

Protocols Currently in Development

Two within the Therapeutics Research Area

2041

Phase I/II Study of the Pharmacokinetics and Safety of **Glecaprevir/Pibrentasvir** Initiated **During Pregnancy in People with Hepatitis C** with and without HIV

2044

Phase IV Study of the Pharmacokinetics and Safety of **Ceftriaxone and Benzathine Penicillin G** **During Pregnancy**

IMPAACT has a range of studies on broadly neutralizing antibodies, exploring innovative approaches to treatment, prevention, and remission

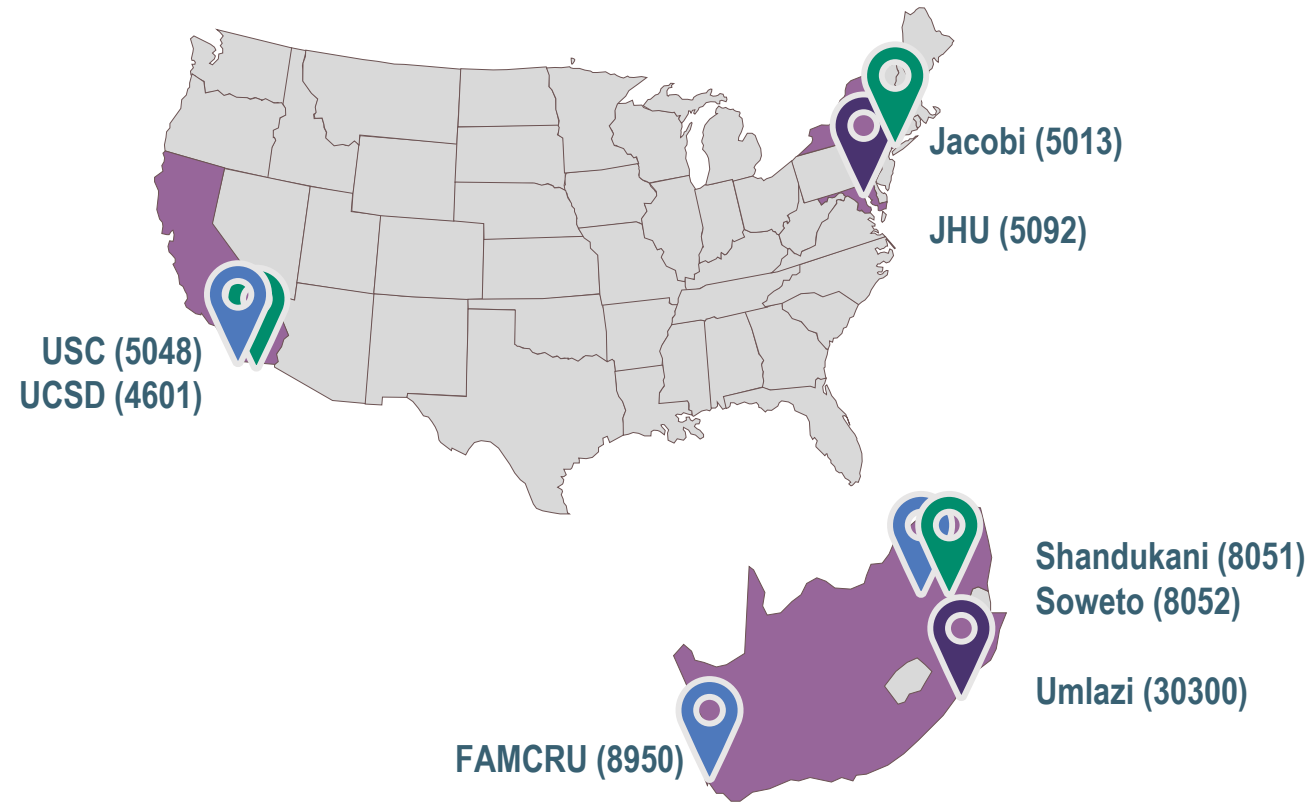
Study	P1115 Version 3.0	IMPAACT 2037	IMPAACT 2039	Tatelo Plus (IMPAACT 2042)
Purpose	Early intensive therapy for remission	Prevention	HIV control and remission	HIV control and remission
Population	Neonates and infants	Neonates	Children	Infants and children
bNAbs	VRC07-523LS	VRC07-523LS	VRC07-523LS	VRC07-523LS
			PGDM1400LS	PGDM1400LS
		PGT121.414.LS	PGT121.414.LS	PGT121.414.LS



CREATE

IMPAACT 2040 Cabotegravir & Rilpivirine
Antiretroviral Therapy in Pregnancy

- 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)

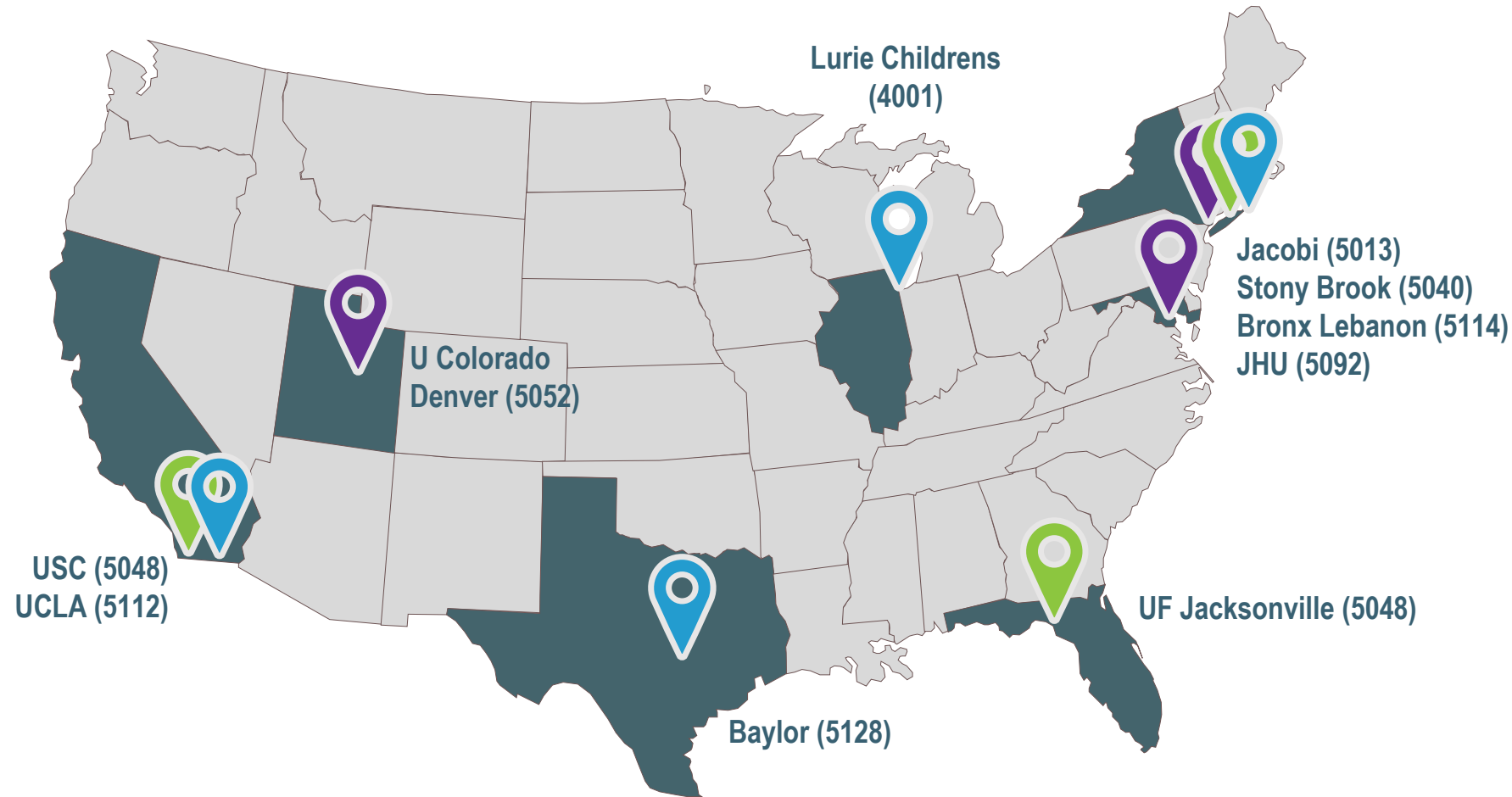


Anticipate opening to accrual by April 2025

Study Highlight: IMPAACT 2041

PK & Safety of Glecaprevir/Pibrentasvir during Pregnancy in People with Hepatitis C

- Collaboration with AbbVie and CDC
- Enrolling participants who are pregnant with Hepatitis C (and their infants)

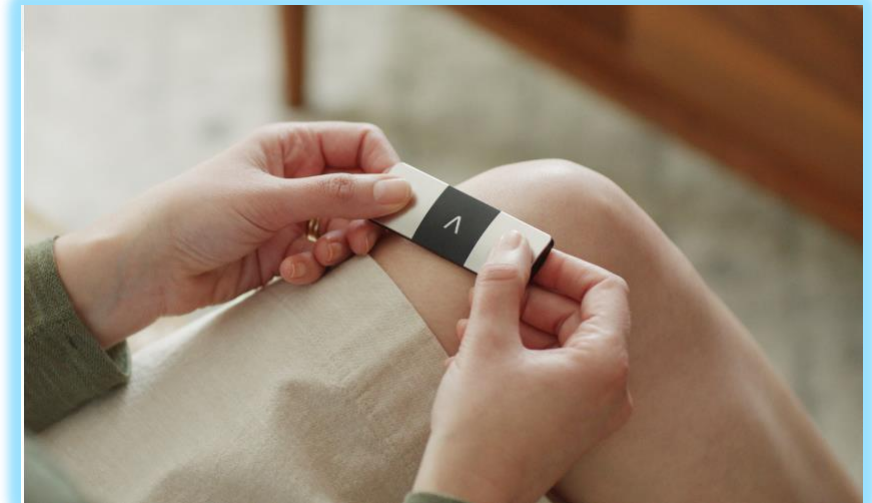


Looking ahead

- Population/simulation modeling to bridge gaps between research and implementation
- Ultra long-acting ARVs for children and during pregnancy
- New methods and tools to improve clinical trial efficiency:
 - AI for document development (for example, ICFs)
 - AI technology for ultrasounds
 - Mobile ECG machine
 - Tools to evaluate depression and other neuropsychological events



Using AI technology for ultrasounds. Image from Jeffrey Stringer, et al.



KardiaMobile® 6L portable ECG machine

- Publish remaining P1093 results

Initiate

- Tatelo Plus
- IMPAACT 2037
- CREATE
- IMPAACT 2041
- IMPAACT 2024

Complete Accrual:

- IMPAACT 2005
- IMPAACT 2016
- IMPAACT 2023
- CRAYON

Finalize Protocol:

- IMPAACT 2020
- IMPAACT 2039
- IMPAACT 2044
- UPLIFT

Complete Follow Up:

- P1108
- MOCHA

- Begin enrolling into P1115 Version 3.0

Coming up in the next year

SAVE THE DATE

UPCOMING IMPAACT
ANNUAL MEETING

7-12 SEPTEMBER 2025

THANKS!

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!

