International Maternal Pediatric AIDS Clinical Trials (IMPAACT) Network

State of the Network
2016 Annual Meeting

Sharon Nachman, MD

James McIntyre, MD – Network Vice Chair

Grace Aldrovandi, MD – Laboratory Center PI

David Shapiro, PhD – Statistical & Data Management Ctr PI

Mission

- To decrease incident HIV and HIV-associated infections including mother-to-child transmission among infants, children, youth and pregnant/postpartum women
- To decrease HIV-associated mortality and morbidity among these populations

IMPAACT
International Maternal Pediatric
Adolescent AIDS Clinical Trials Network

21 US Domestic NIAID and NICHD Sites

NICHD (red)

Boston Medical Center
Jacobi Medical Center Bronx
University of Washington Children's Hospital Seattle
Emory University School of Medicine
San Juan City Hospital PR
SUNY Stony Brook
University of Southern California LA
University of Florida Jacksonville
University of Colorado Denver
South Florida CDC Ft Lauderdale
Rush University Cook County Hospital Chicago
Johns Hopkins University Baltimore
David Geffen School of Medicine at UCLA
The Children's Hospital of Philadelphia (CHOP)
Bronx-Lebanon Hospital Center

NIAID (blue)

Lurie Children's Hospital of Chicago
Pediatric Perinatal HIV, Miami
St. Jude Children's Research
Texas Children's Hospital
University of California, UC San Diego
University of Puerto Rico Pediatric

30 International NIAID and NICHD Sites

NICHD (red)

Inst of Pediatrics Fed Univ Rio de Janeiro
Hospital Federal dos Servidores Rio de Janeiro
SOM Federal University Minas Gerais Brazil
Univ of Sao Paulo Brazil
Hospital General de Agudos Buenos Aires Argentina
Hospital Geral De Nova Igaucu Brazil
Siriraj Hospital, Department of Pediatrics-Mahidol University
PHPT Chiangrai Prachanukroh Hospital
Hospital Nossa Senhora da Conceicao
KCMC Kilmanjaro Christian Medical Centre
Fundacion Huesped, Hospital Juan A Fernandez
The Henry M. Jackson Foundation for the Advancement Military Medicine, Inc.

NIAID (blue)

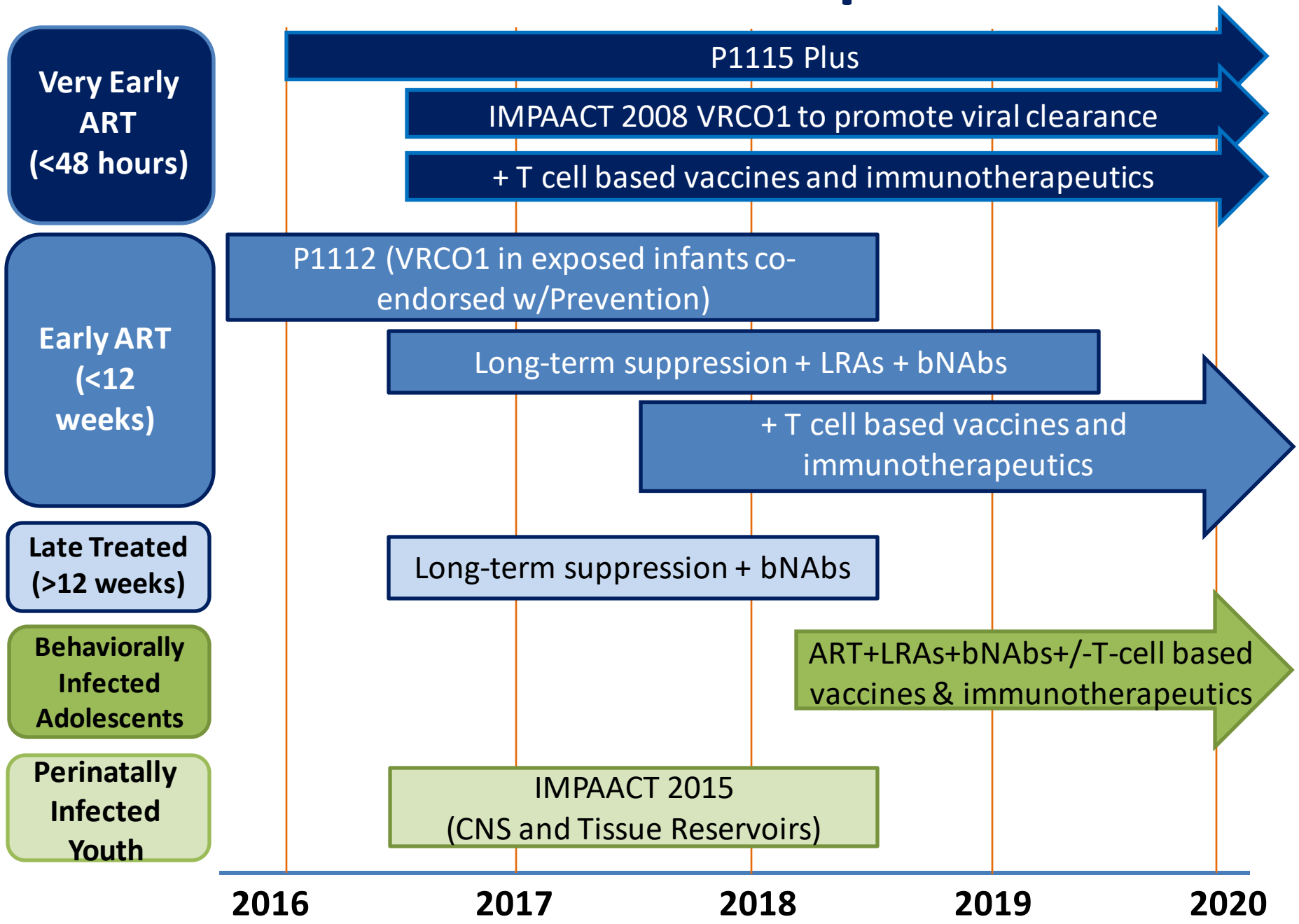
Baylor-Uganda
Blantyre
Byramjee Jeejeebhoy
Chiang Mai University
Desmond Tutu TB Centre
FAM-CRU, Cape Town
Gaborone
George
Harare Family Care
Les Centres GHESKIO
Malawi
Molepolole
MU-JHU Research Collaboration
Seke North
Shandukani
Soweto IMPAACT
St. Mary's
Umlazi

Cure Scientific Agenda

- Functional Cure: Evaluate early aggressive ART to reduce viral reservoir in neonates
- Reservoirs: Evaluate specific interventions in chronically infected-youth
  - Antiretroviral treatment
  - HIV vaccines
  - Immunomodulatory agents

- Future plans: Elucidate relationship between these reservoirs, treatments, and possibility of sterilizing cure

Cure Roadmap



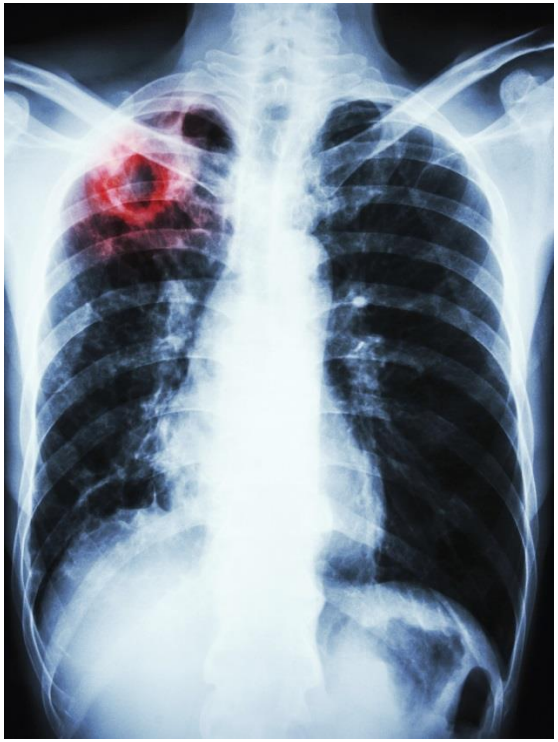
Tuberculosis

Estimated total cases in children	1,000,000 (10% global burden)
Childhood cases notified	360,000
TB deaths	136,000 (81,000 HIV-) 13.6% case fatality rate
Pediatric MDR-TB cases	32,000 (underestimate)
TB infections	6.6 million

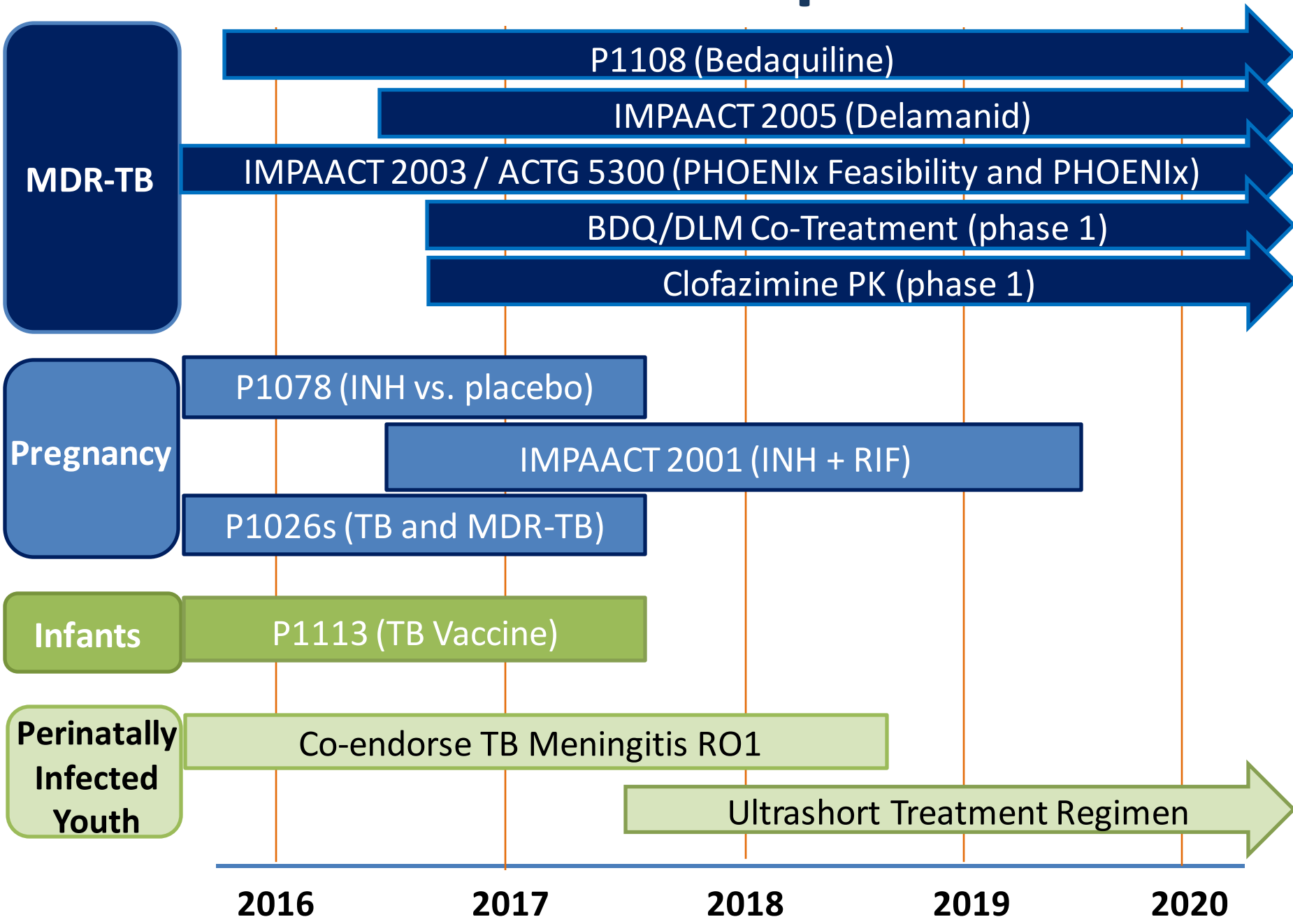
WHO 2015 Global TB report www.who.int

Tuberculosis Scientific Agenda

- In HIV-infected infants, children, and pregnant women, evaluate novel:
  - Drugs and regimens for TB treatment
    - DS and MDR TB
  - Approaches for prevention of TB
  - Tools for diagnosis of TB



TB Roadmap


MDR-TB
P1108 (Bedaquiline)
IMPAACT 2005 (Delamanid)
IMPAACT 2003 / ACTG 5300 (PHOENIx Feasibility and PHOENIx)
BDQ/DLM Co-Treatment (phase 1)
Clofazimine PK (phase 1)
Pregnancy
P1078 (INH vs. placebo)
IMPAACT 2001 (INH + RIF)
P1026s (TB and MDR-TB)
Infants
P1113 (TB Vaccine)
Perinatally Infected Youth
Co-endorse TB Meningitis RO1
Ultrashort Treatment Regimen
2016
2017
2018
2019
2020

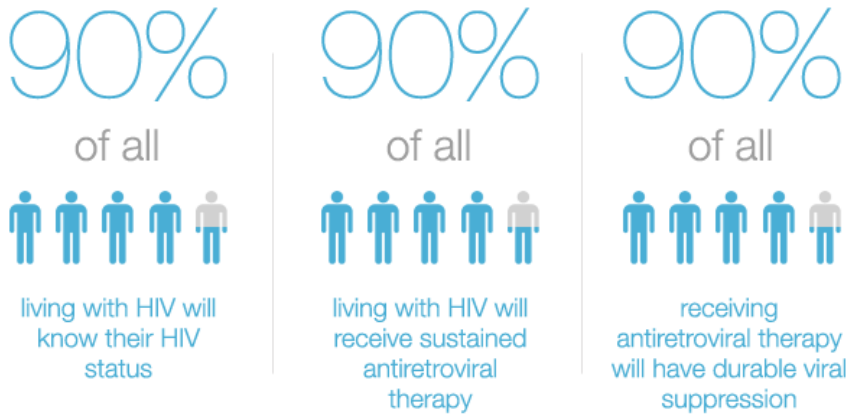
The Global Treatment Environment

Test earlier and closer to birth

Treat earlier and better

Tailor service delivery

- PEPFAR pivot; treating more with less; going faster further, including new initiatives: ACT, DREAM
- Introduction of routine viral load monitoring and ‘point of care’ technologies for early infant diagnosis and viral load monitoring



WHO 2016 Guidelines: When to Start ART

4.3 When to start ART	
4.3.1 When to start ART in adults (>19 years old)	ART should be initiated in all adults living with HIV regardless of WHO clinical stage and at any CD4 cell count *(strong recommendation, moderate quality evidence)*.
	As a priority, ART should be initiated in all adults with severe or advanced HIV clinical disease (WHO clinical stage 3 or 4) and adults with CD4 count ≤350 cells/mm³ *(strong recommendation, moderate quality evidence)*.
4.3.2 When to start ART in pregnant and breastfeeding women	AR… …V regardless of WHO clinical stage an… …erate quality evidence)*.
4.3.3 When to start ART in adolescents (10–19 years of age)	AR… …ical stage and at any CD4 cell count *(co…*
	As… …HIV clinical disease (WHO clinical stage 3 or 4) and adolescents with CD4 count ≤350 cells/mm³ *(strong recommendation, moderate quality evidence)*.
4.3.4 When to start ART in children younger than 10 years of age	ART should be initiated in all children living with HIV, regardless of WHO clinical stage or at any CD4 cell count.
	Infants diagnosed in the first year of life *(strong recommendation, moderate quality evidence)*.
	Children living with HIV one year old to less than 10 years old *(conditional recommendation, low quality evidence)*.
	As a priority, ART should be initiated in; all children ≤2 years old or children younger than 5 years with WHO HIV clinical stage 3 or 4 or CD4 count ≤750 cells/mm³ or CD percentage <25% and children 5 years and older with WHO HIV clinical stage 3 or 4 or with CD4 count ≤350 cells/mm³.

Treat All

HIV Treatment Scientific Agenda

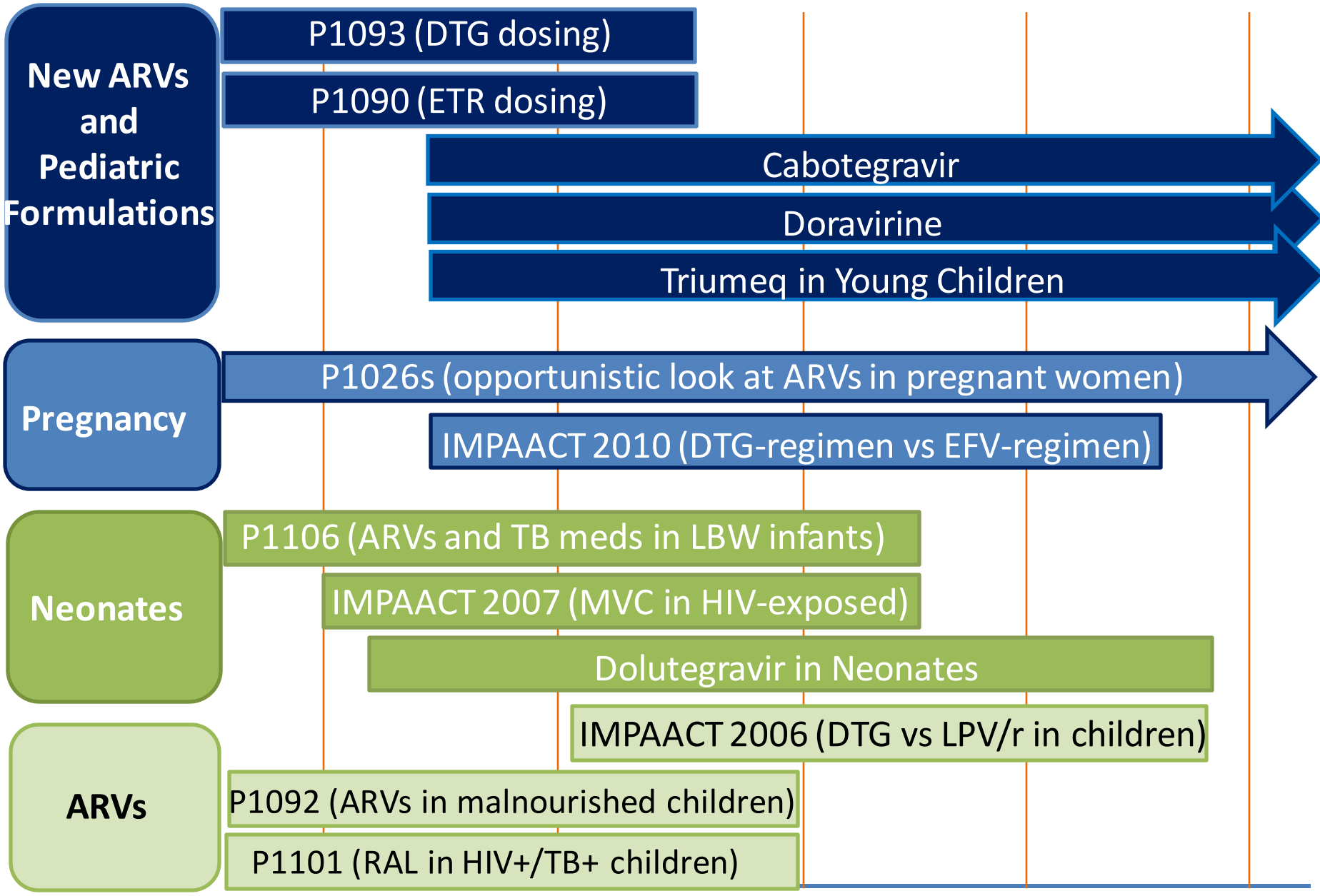
In HIV-infected infants, children and adolescents:

- Safety, pharmacokinetics (PK), and drug-drug interactions
  - new ARVs and formulations
  - novel drug combinations

In HIV-infected pregnant women:

- Safety, PK, and Efficacy of ARVs
- Drug-drug interactions (e.g., ARVs, TB drugs and contraceptives)

Treatment Roadmap

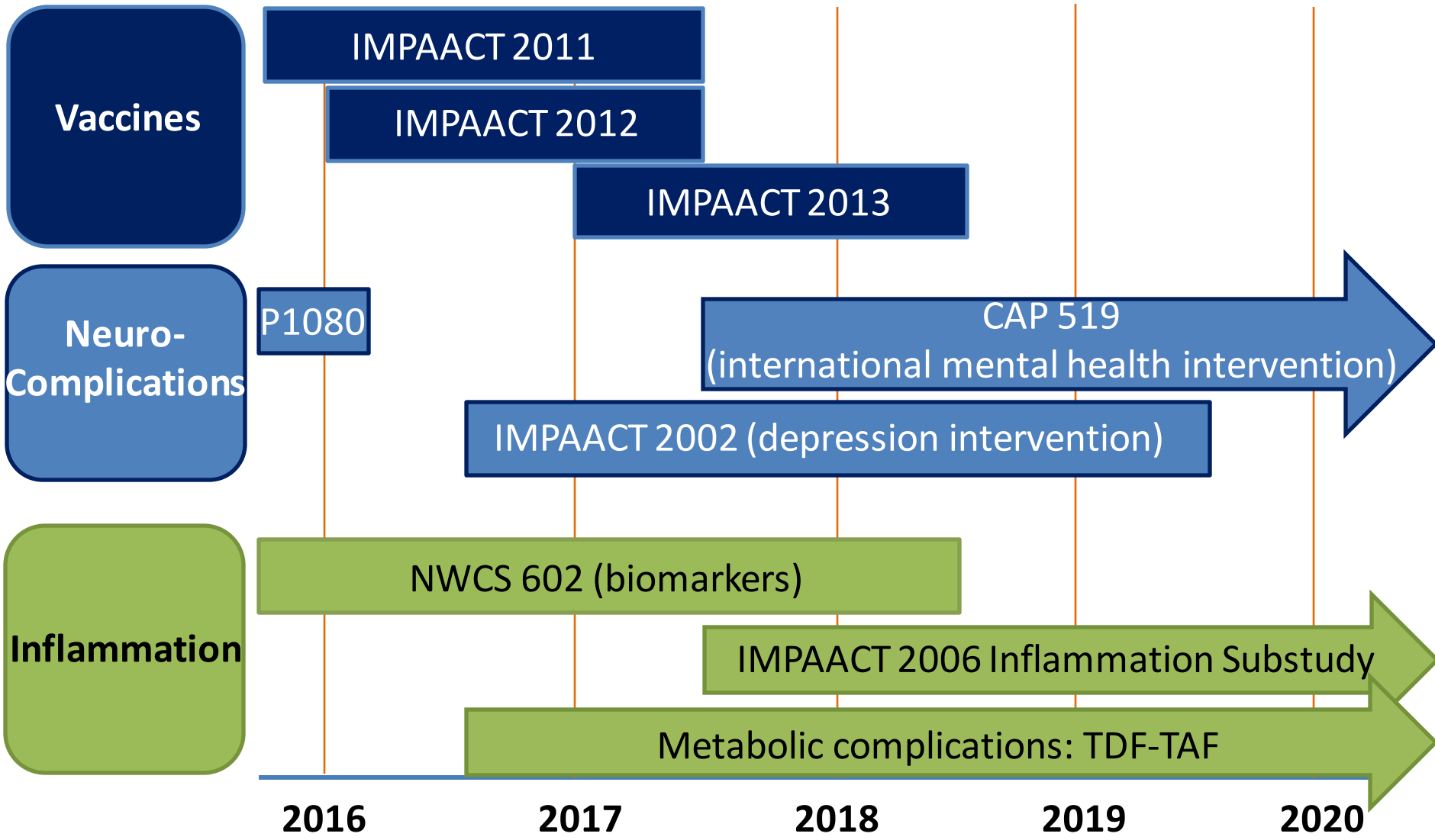


HIV/ARV Complications & Comorbidities Scientific Agenda

- Evaluate novel vaccines in HIV-exposed infants
  - Safety and immunogenicity of RSV and other vaccine candidates (building on successful collaboration with NIAID Intramural)

- Prevent and treat cognitive impairment
  - Evaluate long-term neurocognitive outcomes, drug-drug interactions, and relationship to specific ARV therapies
- Role of inflammation
  - Disease progression, diagnostics, and treatments

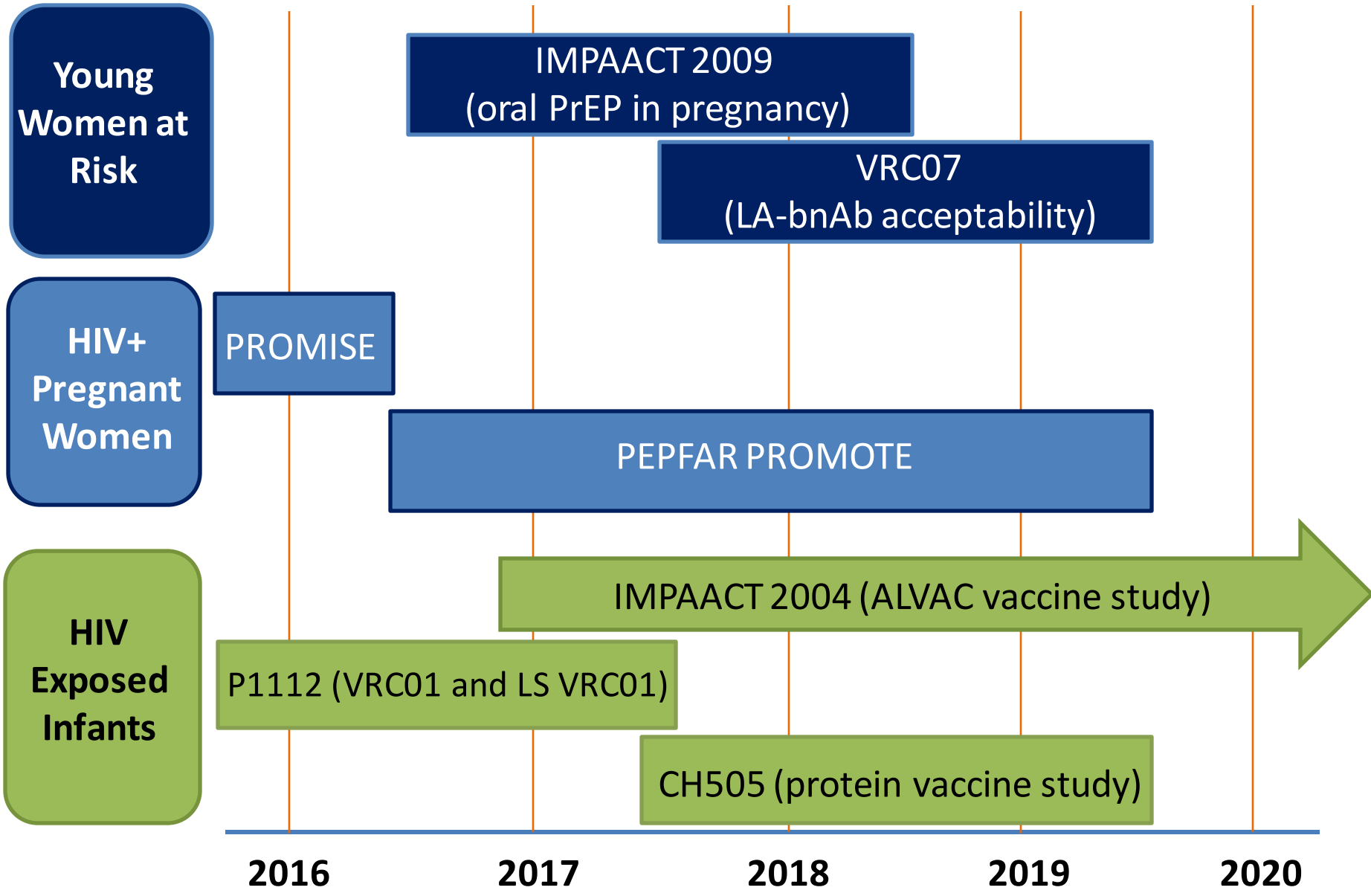
Complications & Comorbidities Roadmap



HIV Prevention Scientific Agenda

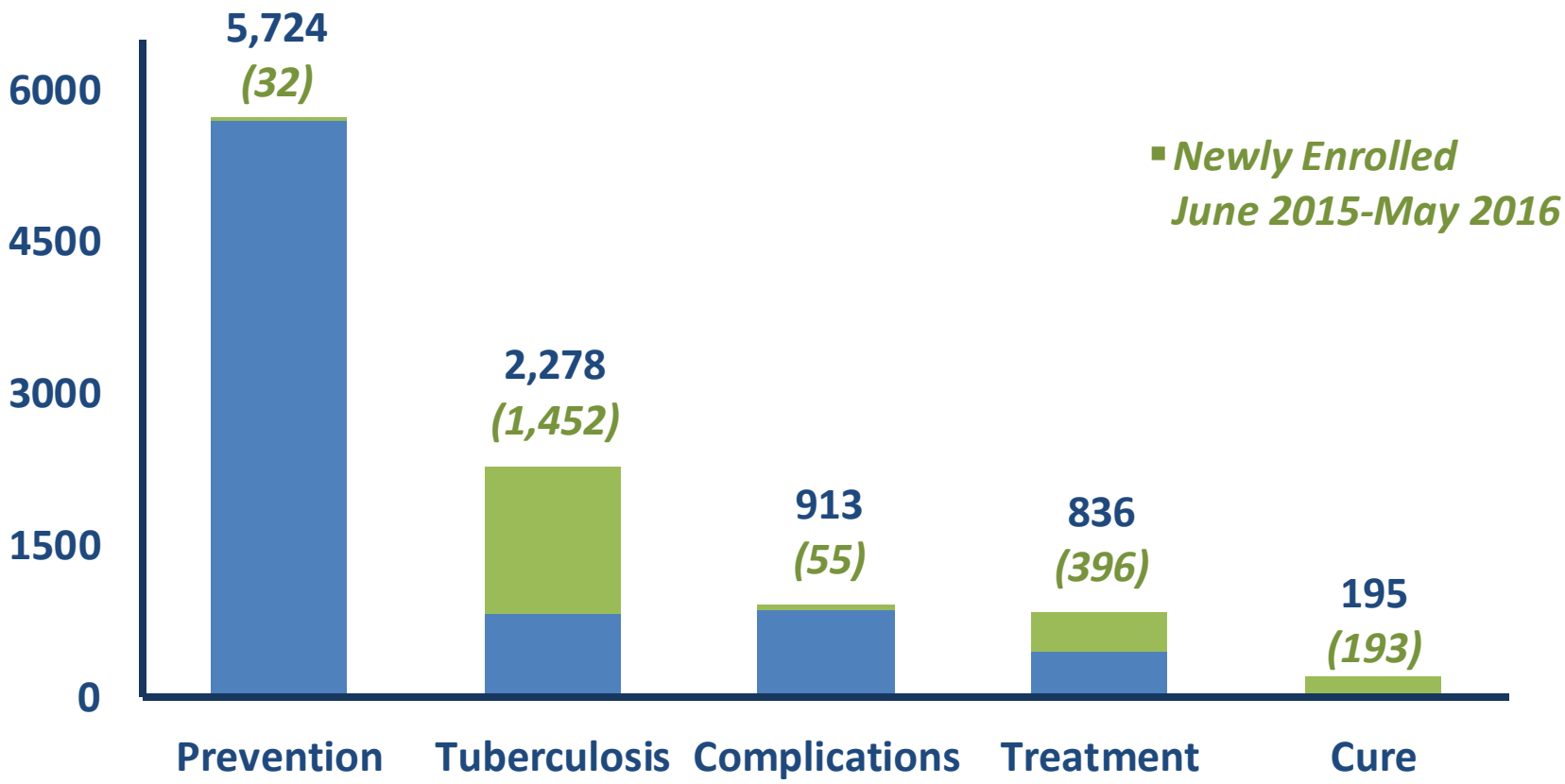
- Prevent perinatal transmission and optimize infant and maternal health outcomes
- Reduce HIV infections in youth combining behavioral and biomedical interventions
- Primary Prevention: Pre-exposure prophylaxis (PrEP)
- Secondary Prevention: Adherence to biomedical interventions, retention and care

Prevention Roadmap



Activities in the Past Year

IMPAACT Participants on Study June 2015 to May 2016

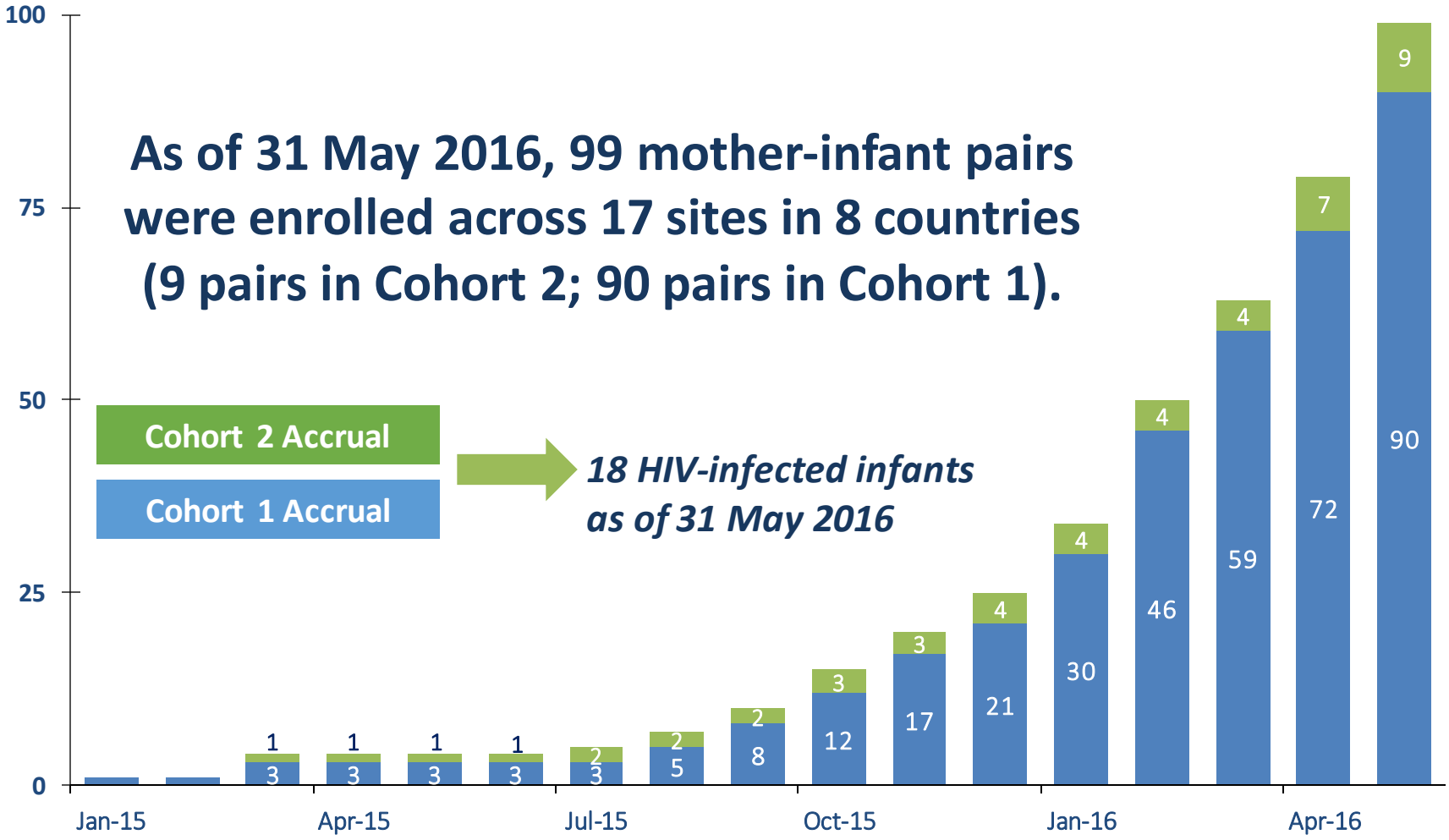


Total On Study = 9,946 participants

Newly Enrolled = 2,130 participants

Study Highlight: P1115

Very Early Intensive Treatment of HIV-Infected Infants to Achieve HIV Remission



Cure Research Agenda

Study Highlight: P1078

Antepartum vs. Postpartum INH Initiation in HIV-Infected Pregnant Women

As of 4 April 2016, accrual was completed with 956 mother-infant pairs enrolling across 13 sites in 8 countries.

Accrual was completed about 4 months ahead of schedule!

Tuberculosis Research Agenda

Study Highlight: IMPAACT 2003

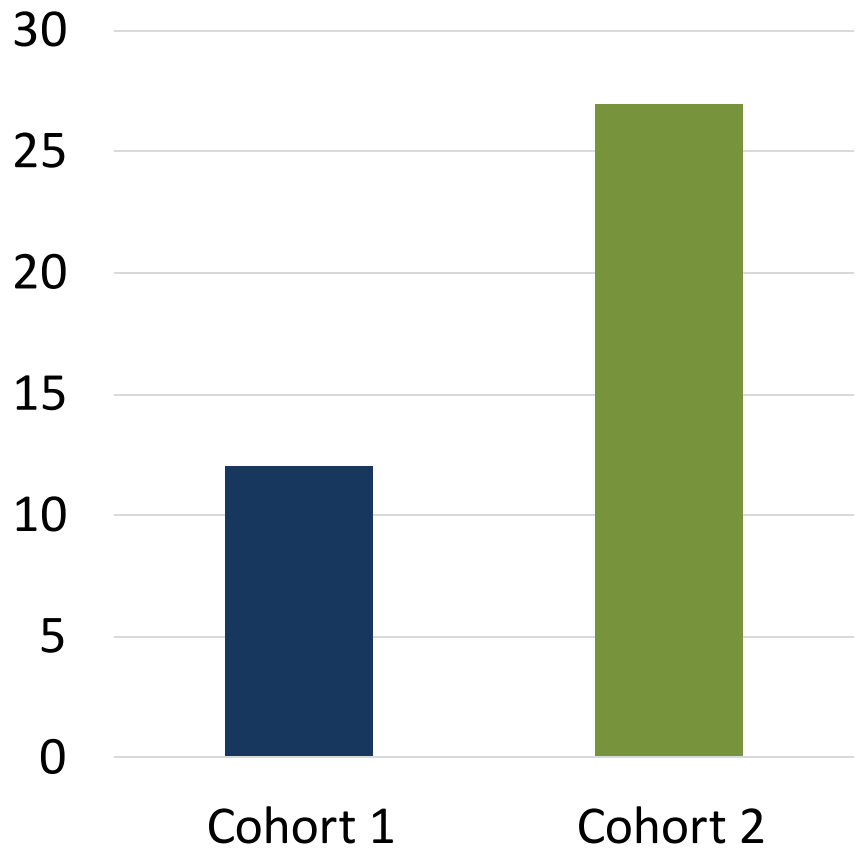
PHOENIx Feasibility, ACTG 5300

- **Tuberculosis** Research Agenda in collaboration with ACTG
- First participant enrolled October 2015
- Last participant enrolled April 2016
- 308 index cases and 1,018 household contacts enrolled

Study Highlight: P1092

PK of ZDV, 3TC, and LPV/r in Severely Malnourished HIV-Infected Children

- **Treatment** Research Agenda
- Completed enrollment into Cohort 2 in March 2016
- Sites in Malawi, Tanzania, Uganda, and Zimbabwe



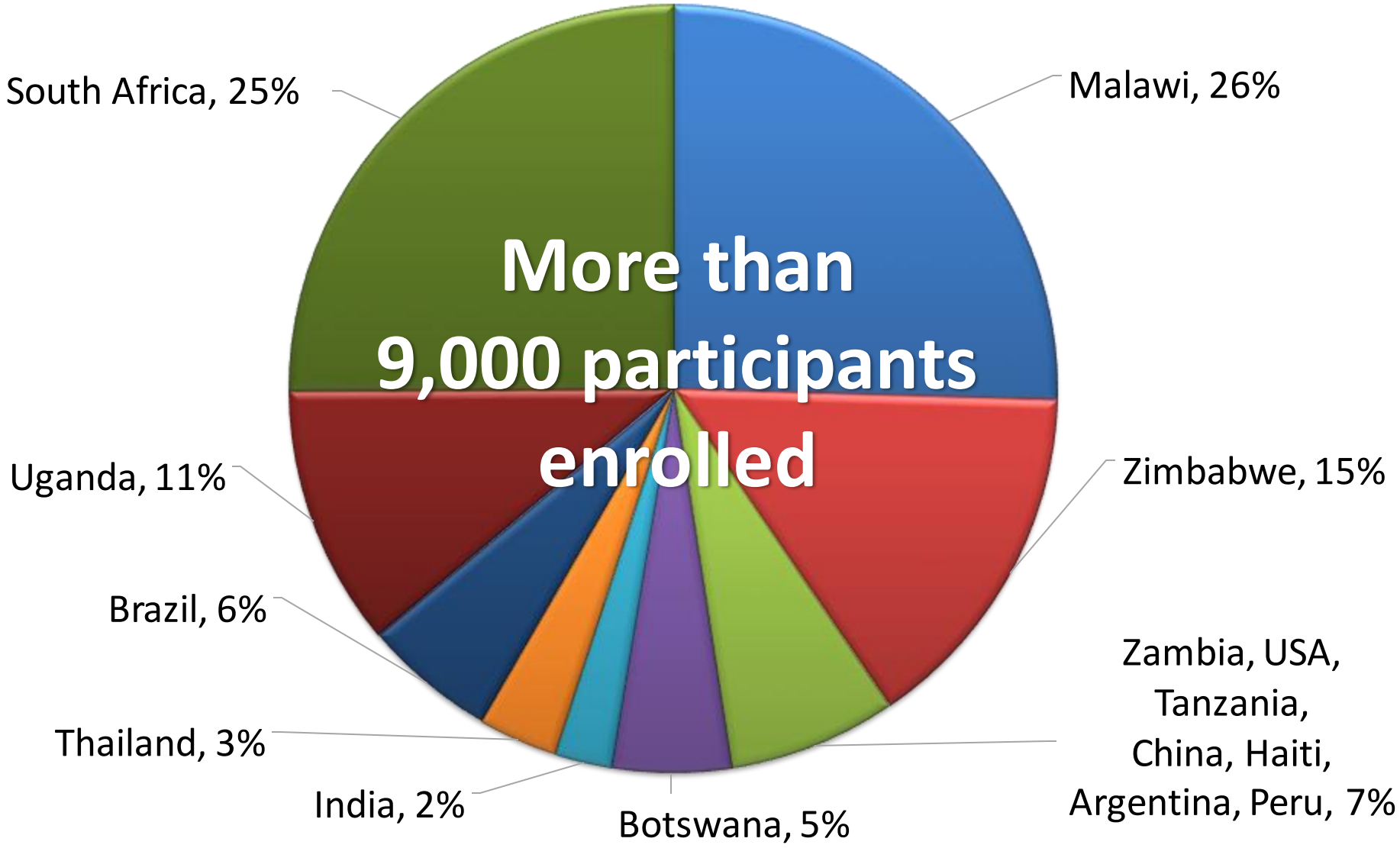
Study Highlight: P1106

PK Characteristics of ARVs & TB Medications in LBW Infants

- **Treatment** Research Agenda
- Completed enrollment into Arm 1 (HIV-exposed infants on NVP) in May 2016
- Two sites in South Africa

Study Highlight: IMPAACT 1077

PROMISE Studies



Study Highlight: IMPAACT 1077

PROMISE
IMPAACT 1077
Promoting Maternal and Infant Survival Everywhere

by the Numbers

4	studies (1077BF, 1077FF, P1084s, 1077HS)
15	countries
65	sites
>9,000	participants enrolled
155,946	visits completed*
2,434,824	CRFs completed*
1,223,910	samples stored*
8	sites continuing with PROMOTE
>2,500	lab queries*
39,472	data queries*
11	DSMB reviews
8	abstracts presented to accepted to CROI, AIDS, or Pads Workshop*
1	manuscript accepted to NEJM

**and counting!*

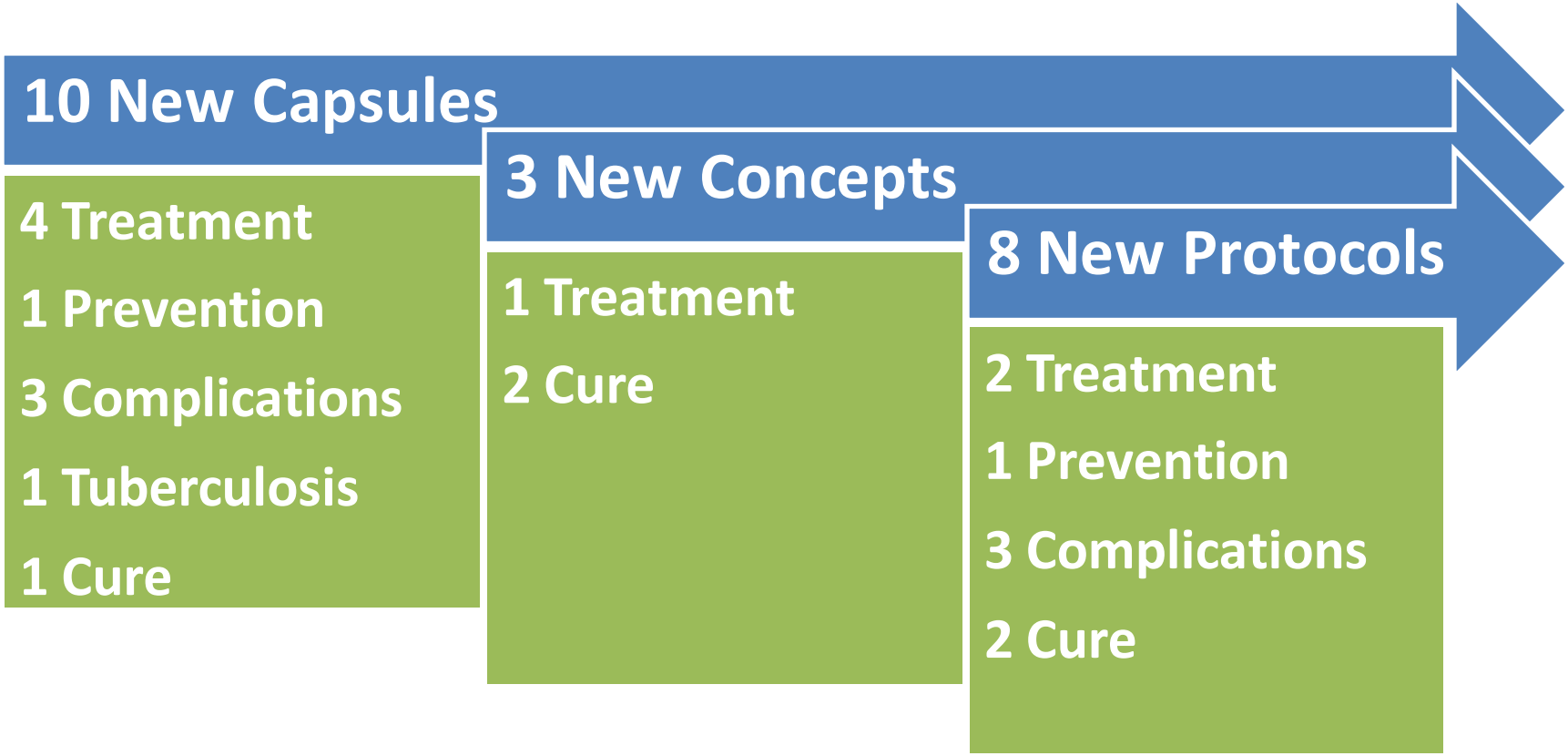
30 Active Studies

May 2015 to June 2016

	3 Pending and Open	13 Enrolling	10 In Follow-up	3 Closed to Follow-up*
Treatment	2007	P1026s, P1090, P1092, P1093, P1097, P1101, P1106, P1110	P1060, P1066, P1102	P1070
Prevention		P1112	1077HS, 1077BF, 1077FF	
Complications		P1080	P1076, P1104s	P1084s, P1114
Tuberculosis	P1108, 2001	P1113	P1078, 2003/5300	
Cure		P1107, P1115		

*closed to follow-up in the last year

IMPAACT Science Generation
June 2015 to May 2016



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Seven New Protocols Currently in Development

2015	Evaluating the HIV Reservoir in the CNS in Perinatally-Infected Individuals on ART
2014	Phase I/II Trial of the Pharmacokinetics, Safety, and Efficacy of MK-1439 (Doravirine or DOR) and MK-1439A (FDC of DOR + lamivudine + TDF) in HIV-infected Adolescents

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New Protocols Currently in Development (cont'd)

2013	Phase I Placebo-Controlled Study of the Infectivity, Safety & Immunogenicity of a Single Dose of a Recombinant Live-Attenuated Respiratory Syncytial Virus Vaccine, RSV/NS2/N/ΔM2-2-HindIII, Lot RSV#011A , Delivered as Nose Drops to RSV-Seronegative Infants 6 to 24 Months of Age
2012	Phase I Placebo-Controlled Study of the Infectivity, Safety & Immunogenicity of a Single Dose of a Recombinant Live-Attenuated Respiratory Syncytial Virus Vaccine, LID cp ΔM2-2, Lot RSV#009A, Delivered as Nose Drops to RSV-Seronegative Infants 6 to 24 Months of Age

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New Protocols Currently in Development (cont'd)

2010	Phase III Study of the Virologic Efficacy and Safety of Dolutegravir-Containing versus Efavirenz-Containing Antiretroviral Therapy Regimens in HIV-1-Infected Pregnant Women and their Infants
2009	PK, Feasibility, Acceptability, & Safety of Oral PrEP for Primary HIV Prevention during Pregnancy & Postpartum in Adolescents & Young Women
2008	Phase I/II Multisite Randomized Controlled Study of Monoclonal Antibody VCR01 Combined with ART to Promote Clearance of HIV-1 Infected Cells in Infants

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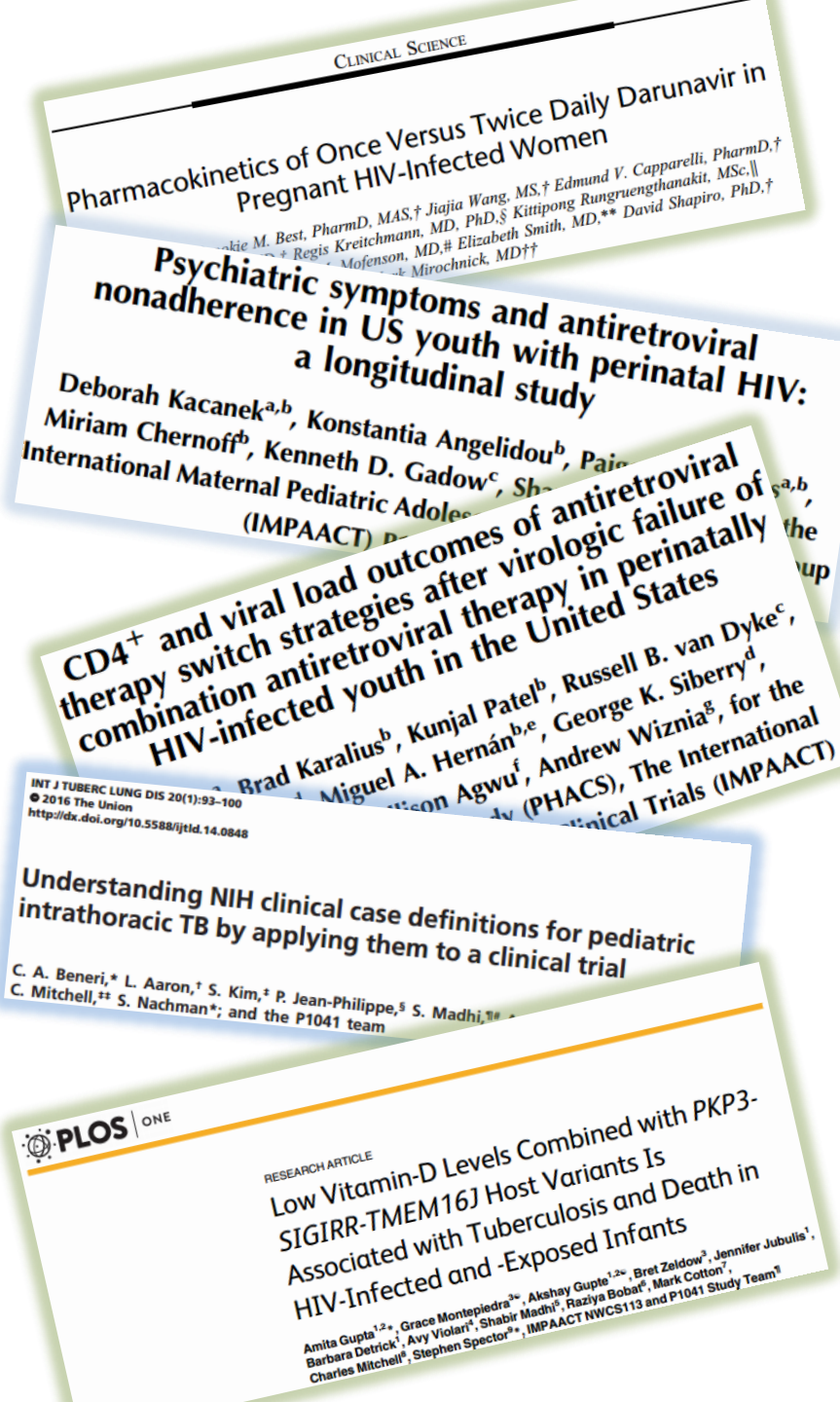
Publications

- **27** publications submitted in past 12 months
- **25** manuscripts published in JAIDS, Journal of Clinical Pharmacology, PIDJ, CID, TB and Lung Disease, PLoS One



Abstracts

15 abstracts at CROI 2016

- DTG PK in HIV-infected Pregnant and Postpartum Women
- NVP Dosing for Treatment in First Months of Life
- Impact of Maternal TDF Use on HIV-Exposed Newborn BMC
- Breast Milk and In Utero HIV-1 Transmission Select for Unique Envelope Signatures

8 IMPAACT abstracts at AIDS 2016

- 3 abstracts from PROMISE (with 6 abstracts for the HIV Pediatrics Workshop)

Additional abstracts accepted to ICAAC, ICAAP, ICASA, and ID week

Cross Network Study Initiatives

- MDR-TB Prevention (PHOENIx)
- TB and HIV Vaccine Studies
  (Aeras/P1113 and IMPAACT 2004)
- RSV and VRC01 Studies
  (IMPAACT 2011/2012/2013 and P1112)

Pharma Collaborations:
New Formulations/Products

ViiV Healthcare

AERAS

Cipla

GILEAD

SANOFI

gsk

MERCK

abbvie

Otsuka

Abbott

janssen

IMPAACT
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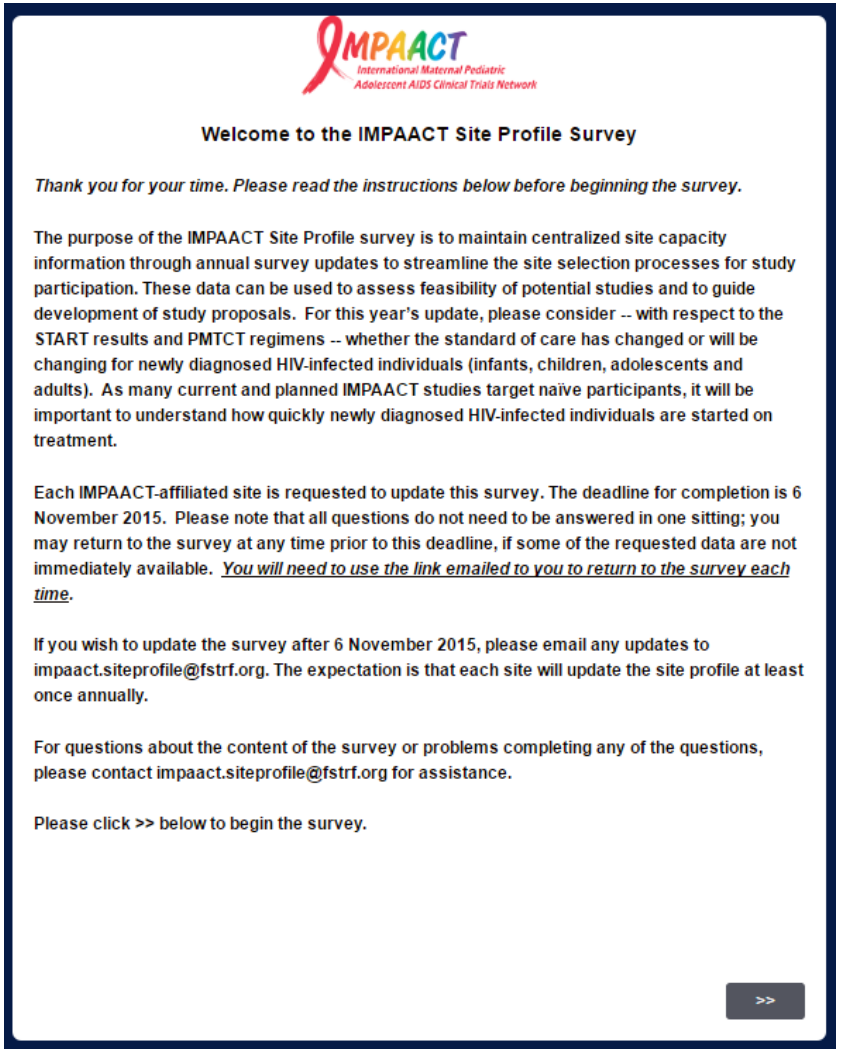
Site Information

- Updated site profiles including site capacity August 2015
- Aids in network-wide planning, rapidly identifying sites with specific capabilities for specific studies
- Avoids duplication of data collected for site selection
- Includes drug regulatory and ethical review requirements



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Welcome to the IMPAACT Site Profile Survey

Thank you for your time. Please read the instructions below before beginning the survey.

The purpose of the IMPAACT Site Profile survey is to maintain centralized site capacity information through annual survey updates to streamline the site selection processes for study participation. These data can be used to assess feasibility of potential studies and to guide development of study proposals. For this year's update, please consider -- with respect to the START results and PMTCT regimens -- whether the standard of care has changed or will be changing for newly diagnosed HIV-infected individuals (infants, children, adolescents and adults). As many current and planned IMPAACT studies target naïve participants, it will be important to understand how quickly newly diagnosed HIV-infected individuals are started on treatment.

Each IMPAACT-affiliated site is requested to update this survey. The deadline for completion is 6 November 2015. Please note that all questions do not need to be answered in one sitting; you may return to the survey at any time prior to this deadline, if some of the requested data are not immediately available. *You will need to use the link emailed to you to return to the survey each time*.

If you wish to update the survey after 6 November 2015, please email any updates to impaact.siteprofile@fstrf.org. The expectation is that each site will update the site profile at least once annually.

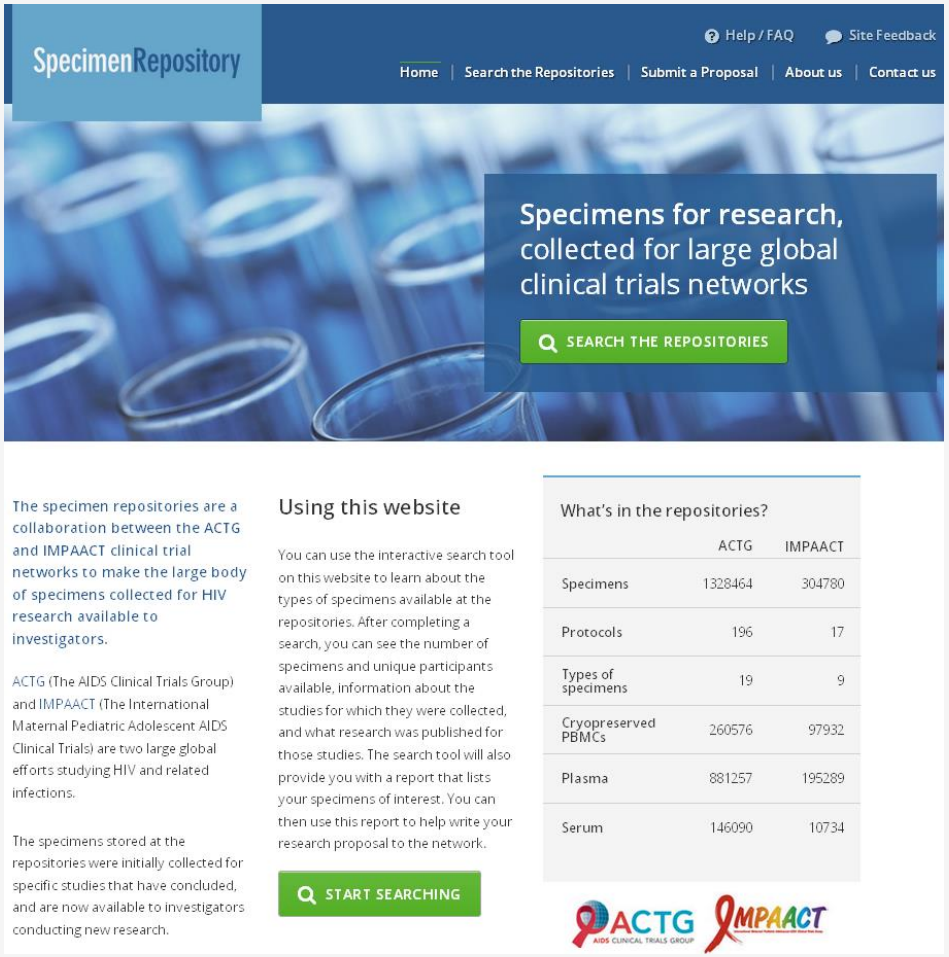
For questions about the content of the survey or problems completing any of the questions, please contact impaact.siteprofile@fstrf.org for assistance.

Please click >> below to begin the survey.

>>

www.specimenrepository.org

Collaboration between IMPAACT and ACTG to make the large body of specimens collected for HIV research available to investigators



frontier science

Plans for the Upcoming Year… What is on the horizon?

- Continue to work with other networks, partners, community, and scientific experts to develop robust collaborations
- Prioritize new capsules/concept sheets
- Continue Early Career Investigator Program

Plans for the Upcoming Year…

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Thank you to the sites, to the community, and to all the individuals and families engaged in clinical research

Let's continue to move the science forward!