National Institute of Allergy and Infectious Diseases

Fostering Development of Pediatric-Friendly Formulations for HIV and Tuberculosis: Overview of a New NIH Contract Resource

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What are the Goals of This Presentation?

- Describe available NIH resources to advance pediatric formulations
- Demonstrate our intention to use these resources to develop a new age-appropriate formulation for HIV or TB
- Highlight the opportunity to use these resources to supplement existing efforts and strengthen partnerships across organizations

IMPAACT
International Maternal Pediatric Adolescent AIDS Clinical Trials Network

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Development of Contract Resources to Advance Pediatric Formulations

Outline of Presentation:

- Overview of a new NIAID contract to be awarded in July 2023
- Describe how contract resources to advance HIV prevention products have been expanded to include pediatric formulations for HIV treatment
- Explain how current contract resources have been used to start developing a Pediatric Formulation Roadmap
- Provide information on how to access these contract resources
- Invite interested IMPAACT colleagues to join us in this effort

Resources to Advance Pediatrics and HIV Prevention Science (RAPPS)

Purpose

- To provide drug development resources to support advancement of the next generation of HIV biomedical prevention products and **HIV treatment and prevention strategies in maternal (pregnant or breastfeeding women) and pediatric populations**

Objectives of the Program

- Advancement of promising next generation non-vaccine HIV biomedical prevention products into human clinical testing
- Expansion of user preference studies to better understand desire/choice and how best to engage women and men in HIV treatment or prevention
  - Emphasis on adolescent girls and young women (AGYW) ages 14-25 years old
  - **Potential for studies in caregivers of pediatric populations**
- Provision of gap-filling resources to support **HIV treatment and prevention strategies in maternal and pediatric/adolescent populations**
  - **Includes age-appropriate formulations and co-infections/co-morbidities**
  - **Includes treatment/prevention strategies in newborns/infants**

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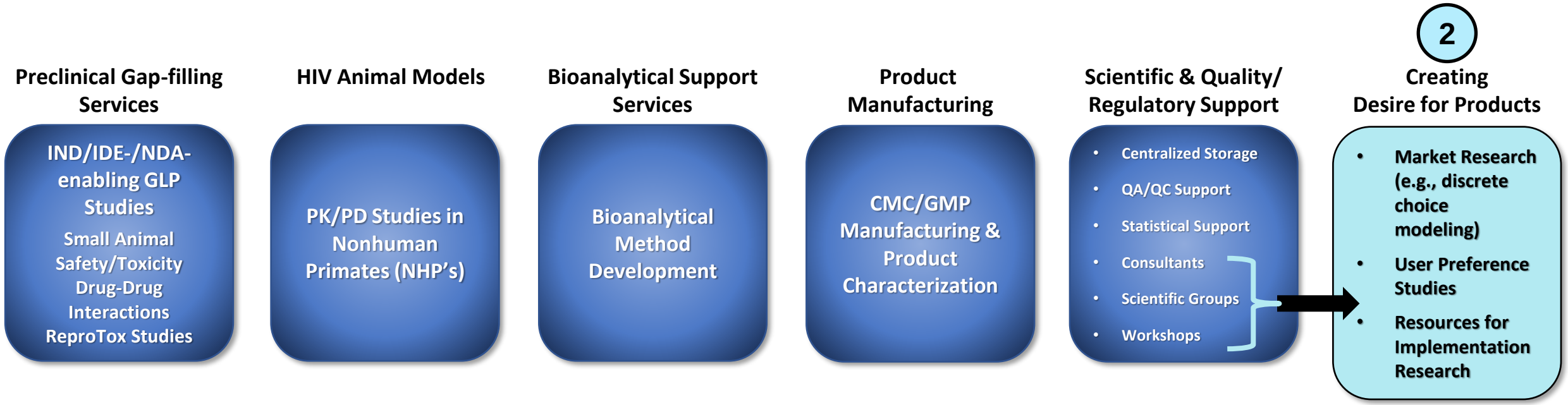
RAPPS: An Evolving Contract to Support HIV Pediatric Treatment

1. RAPPS contract resources will be based on those in a current DAIDS contract but expanded to include HIV treatment and prevention strategies/age-appropriate formulations in maternal and pediatric populations

2. RAPPS contract will include greater emphasis on use of contract resources to better understand desire/choice and how best to engage women and men in HIV treatment and prevention (e.g., caregivers for infants and adolescents)



1. The resources available in these key task areas will allow expansion of the contract to support the range of preclinical activities that are necessary to develop age-appropriate formulations.

Pediatric Formulations for HIV & TB – Activities Initiated under a Current DAIDS Contract

- Establish expertise to supplement NIAID programs in the development and optimization of age-appropriate drug formulations for infants, children, and adolescents (Drs. Dixit, Hoag, and Schaufelberger)
- Assist NIAID in planning contract activities to support development of age-appropriate formulations
- Plan NIAID-sponsored consultations to bring together relevant stakeholders to:
  - Discuss key gaps and challenges
  - Identify potential gap-filling activities for a prioritized pediatric drug formulation
  - Discuss potential ways to leverage private-public partnerships to advance pediatric HIV drug formulations
- Develop an IP strategy with originators and generic manufacturers to accelerate global access to new molecules, formulations, and drug delivery technologies

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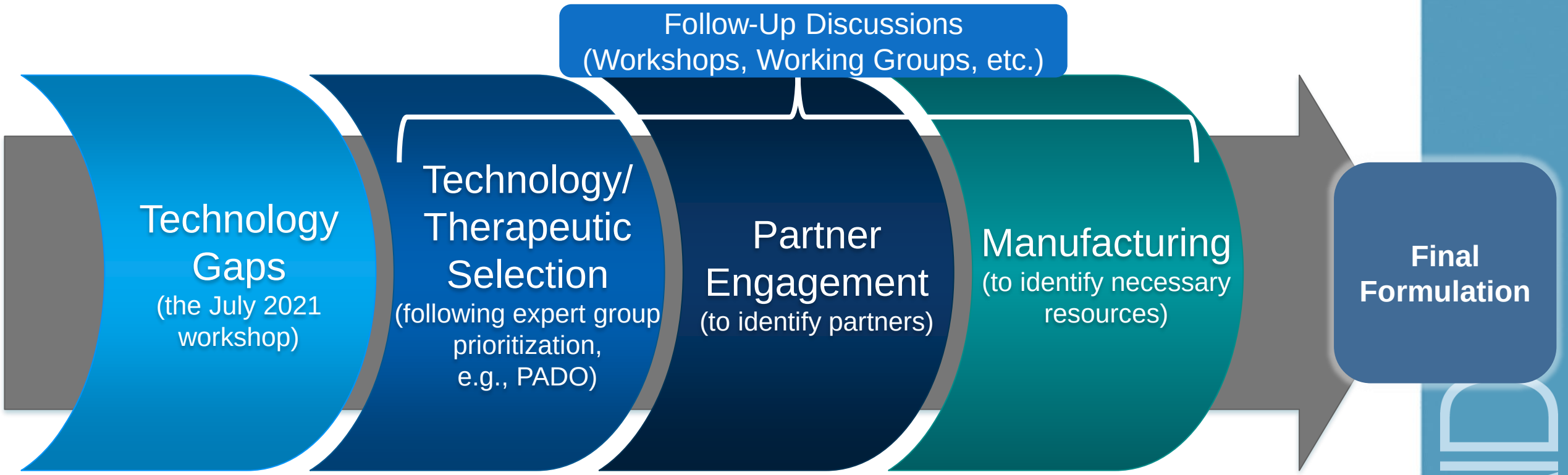
Next Steps in Planning Contract Resources to Develop and Advance a Formulation



- Feedback and recommendations from outside experts at these workshops is meant to supplement NIH expertise and aid in identification of key gaps and necessary resources to address these gaps.
- For any funding mechanisms used to support these activities, NIH Program staff will work independently to ensure a fair competition for NIH funding and avoid any potential conflicts of interest.

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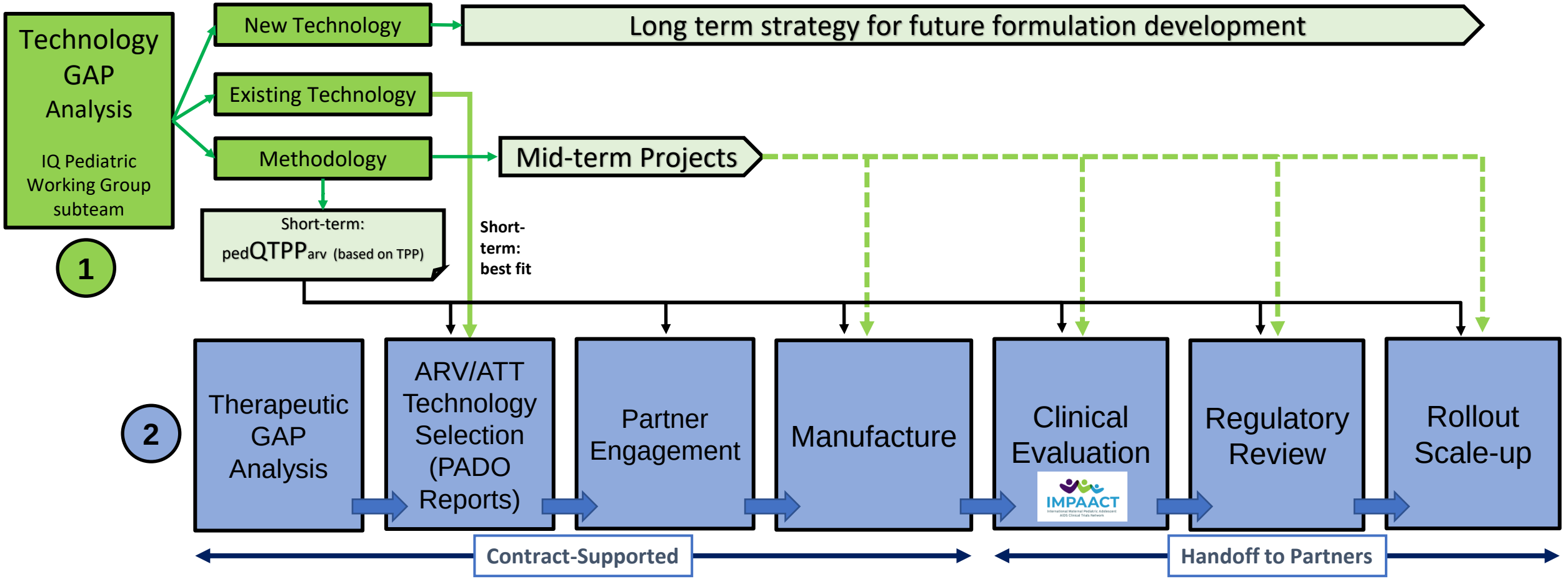
Development of a Pediatric Formulation Roadmap: Technical & Therapeutic Gap Analysis



pedQTTParv = Pediatric Quality (=CMC) Target Product Profile for antiretrovirals
PADO: WHO Pediatric Antiretroviral Drug Optimization Group
ARV = Antiretroviral drug
ATT = Antituberculosis therapeutic

Identifying Partners & Relevant Stakeholders

Past Partners
(HIV Prevention)

MTN microbicide trials network

ALLIANCE FOR MICROBICIDE DEVELOPMENT

INTERNATIONAL PARTNERSHIP FOR MICROBICIDES

CONRAD
Leaders in Reproductive Health and HIV Prevention

POPULATION COUNCIL
Ideas. Evidence. Impact.

ViiV Healthcare

USAID FROM THE AMERICAN PEOPLE

CDC

Leveraging Relationships

Identifying Opportunities

Future Partners
(HIV Prevention & Pediatric Formulations)

HPTN HIV Prevention Trials Network

IMPAACT International Maternal Pediatric Adolescent AIDS Clinical Trials Network

IQ INTERNATIONAL CONSORTIUM FOR INNOVATION & QUALITY IN PHARMACEUTICAL DEVELOPMENT

GAP·f Global Accelerator for Paediatric formulations WHO Hosted Network

ViiV Healthcare

MERCK INVENTING FOR LIFE

Future Contract Expansion

- **Pediatrics**
  - Age-appropriate formulations
  - Co-morbidities (TB)
  - Cure research
- **Marketing Science/Human Centered Design**
  - Integrating concepts into product development

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How Do You Learn More about These Resources?

Details on the new contract:

https://www.niaid.nih.gov/grants-contracts/pediatrics-and-hiv-prevention-science-rfp

Website for requesting services under DAIDS contracts:

https://www.niaid.nih.gov/research/requesting-access-daids-services-program

DAIDS Program Contact for more information:

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IMPAACT Colleagues: Come Meet Us and Join the Effort!

NIH Contract Resource Drop-In Room

Room #: Columbia 2

Topic: DAIDS Contract Resources for Pediatric Formulation

Time: 2:00 – 4:00 pm EDT

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DAIDS

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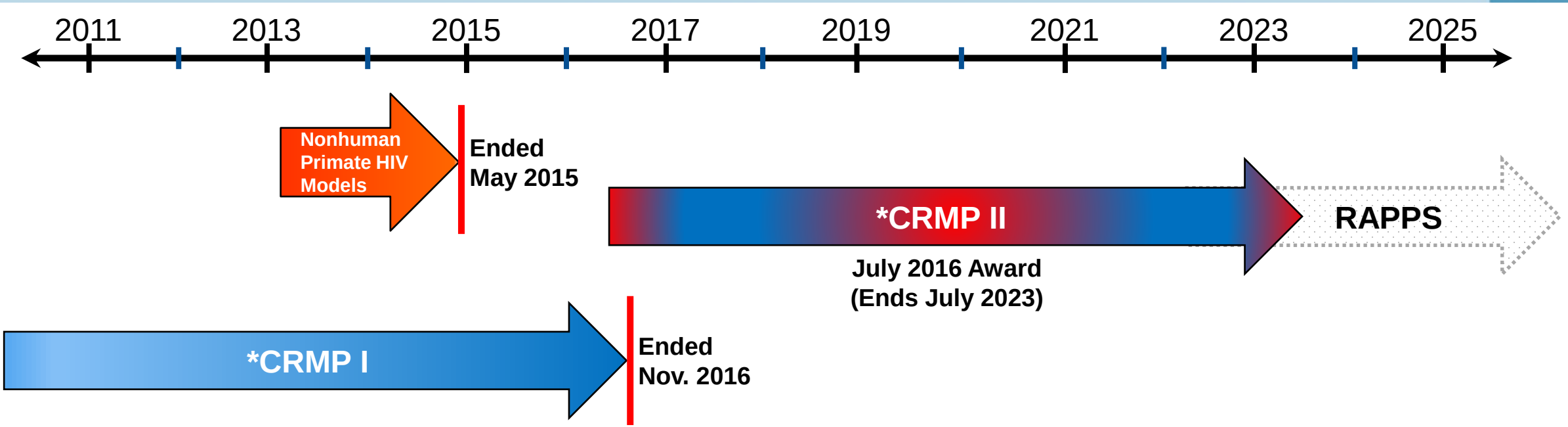
Backup Slides/Slides for DAIDS Drop-in Session

RAPPS: An Evolving Contract to Support HIV Prevention and Pediatric Treatment



***CRMP I**
Gap-Filling Services (IND-enabling)

Product Development Plans

Best Practices Working Groups

\+

Nonhuman Primate (NHP) HIV Models

NHP Safety, Efficacy, and Pharmacokinetic Studies

=

CRMP II:

Task Area A: Gap-Filling (IND-, IDE-, or NDA-enabling)

Task Area B: HIV Animal Models

Task Area C: Bioanalytical Support Services

Task Area D: Product Manufacturing

Task Area E: Scientific & Quality/Regulatory Support

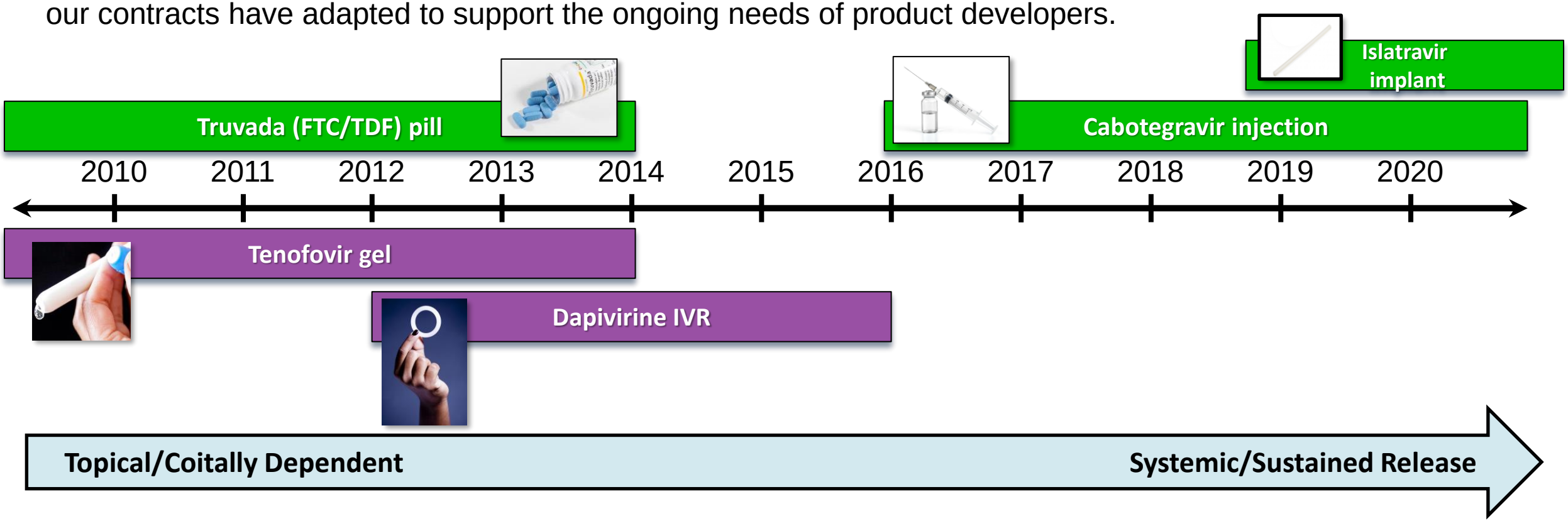
RAPPS:

- Similar Task Area structure as CRMP II
- Available contract resources will allow <u>expansion to support pediatric formulation development</u>

***Comprehensive Resources for HIV Microbicides and Biomedical Prevention (CRMP)**

PSP Contract Resources to Advance HIV Prevention Products

- Over the past 12 years, PSP contracts have supported the development of 12 product IND's – leading to the activation of multiple clinical trials.
- Supported formulation types have included topical gels, films, intravaginal rings, a long-acting injectable, and an implant.
- As products have evolved from early topical microbicides to more advanced sustained-release formulations, our contracts have adapted to support the ongoing needs of product developers.



Example: HIV Prevention Pharmacology Best Practices Working Group (BPWG)

Contract Activities

<u>August 2011 meeting</u>:

Identified key research areas of research for the HIV pharmacology field

<u>June 2012 meeting</u>:

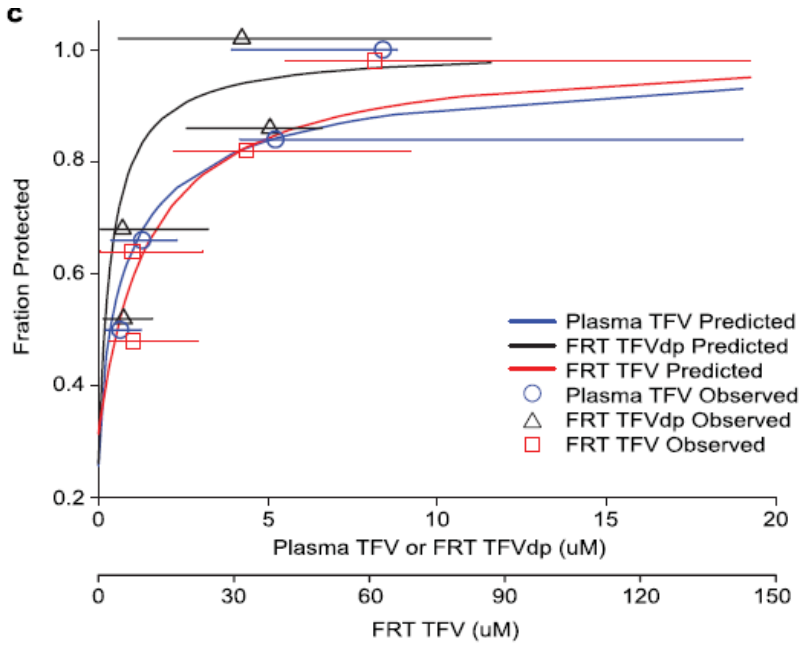
Discussed development of protocols to support pharmacokinetic (PK)/ pharmacodynamic (PD) studies in relevant animal models

<u>Follow-on studies in female BLT Mice (2013-2015)</u>:

To establish correlations between TDF drug concentrations and protective efficacy in a vaginal model of HIV transmission

Example Outcome

PK-PD modeling of systemic TDF PrEP



Predicting HIV Pre-exposure Prophylaxis Efficacy for Women using a Preclinical Pharmacokinetic-Pharmacodynamic *In Vivo* Model. 2017. *Scientific Reports* 7:41098

Impact to HIV Prevention

- First comprehensive review of available data in HIV pharmacology from animal models and human studies
- Identified gaps, challenges, and future directions for selecting and advancing PrEP candidate and strategies
- BPWG Recommendations:
  - Extensive dose ranging and fractionization studies in animal models to establish predictive PK/PD models
  - Collection of PK samples across multiple compartments to bridge animal and human studies

Other PSP Programs to Advance Long-Acting Technologies in Pediatric Populations

RFA AI-18-057: Long-Acting Drug Delivery Systems for ART Optimization in HIV-1 Infected Children (R61/R33 Clinical Trial Not Allowed)

- 3 Applications Funded*

Project**	Long-Acting Technology	Targeted Minimum Dosing Frequency	PI, Institution
MAPs for Peds: Development of a Microarray Patch for Delivery of Long-Acting Antiretrovirals for Treatment of Pediatric HIV Infection	Microarray Patches	Monthly	Darin Zehrung, PATH
NextGen Long-Acting and Targeted Combination ART for Children with HIV	Drug Combination Nanoparticles	Every 4 Weeks	Rodney Ho, Univ. Washington
LA HIV Treatment in Pediatrics	Implant System	Every 6 Months	Leah Johnson, RTI

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*With NICHD co-funding
**All projects using end-user informed approach

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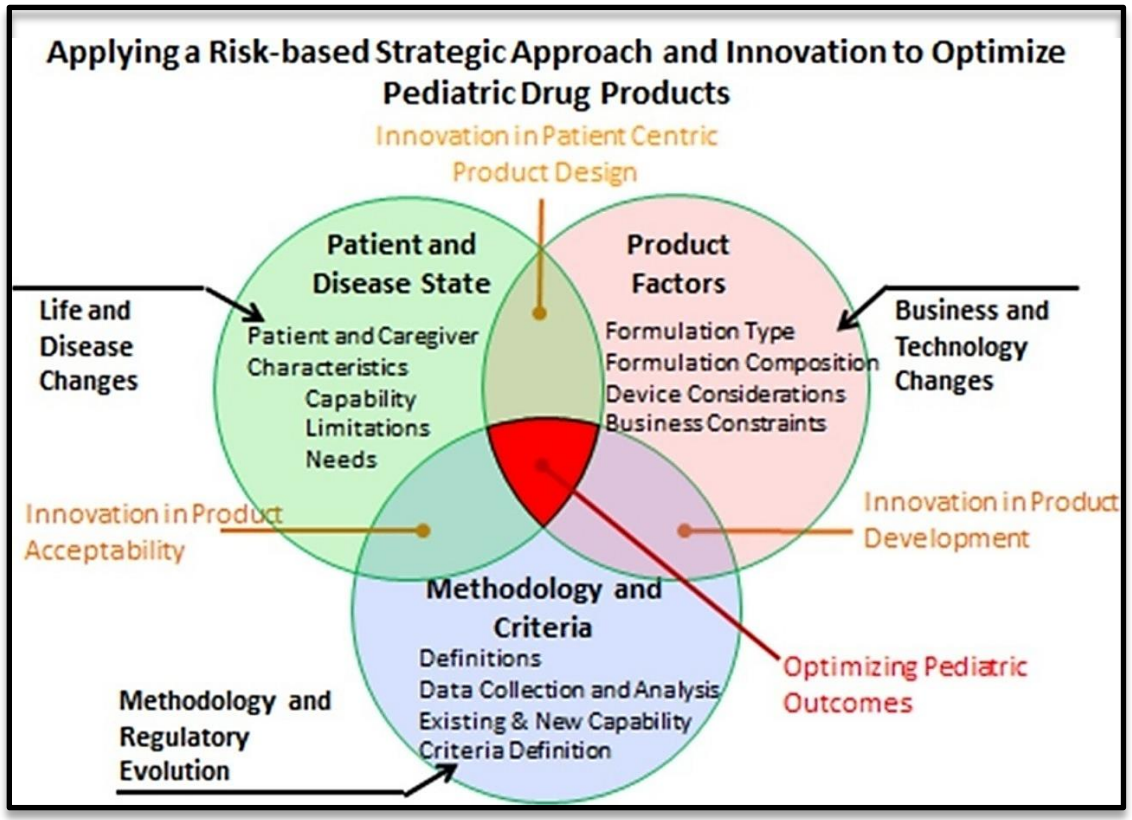
Development of Contract Resources to Advance Pediatric Formulations



*Ternik et al. 2018. Assessment of swallowability and palatability of oral dosage forms in children. Int. J. Pharmaceutics. 536(2):570-81

Outcomes of 1st Workshop (CMC Focused)

Pre-Workshop	Prioritization at Workshop	Recommendations	Post-Workshop
Gap Assessment: • Acceptability, general • Acceptability, mini-tablets/ multi-particulates • Taste masking • Fixed-dose combinations • Long-acting oral • Long-acting injectables • Needle-free injection • Dosage forms for PrEP • Neonates • Knowledge management • Development tools • Technology transfers • Supply chain stability	1. Long-acting injectables, implants 2. Neonates 3. Long-acting, oral 4. Taste masking 5. Acceptability mini-tablets, multi-particulates	• Apply learnings to PADO5 proposals (formulations) • Propose “neonate formulation platform” • Organize workshop “long-acting” • Advance basic sensory sciences, e.g., bitter blockers with foundational studies • White paper ped QTPP for ARVs	• PADO5 preliminary report: limited opportunities for specific product development • NIH Preclinical/Early Development “hub” to partner with developers for acceleration of pediatric medicines development • Foundational studies, e.g., bitter blockers, AI/ML, neonates • Other: IQ Pediatric Working Group survey “mini-tablets” (ongoing)

Glossary of Terms

IND: Investigational New Drug Application

IDE: Investigational Device Exemption

NDA: New Drug Application

ARV = Antiretroviral drug

ATT = Antituberculosis therapeutic

CMC: Chemistry Manufacturing Controls

CRMP: Comprehensive Resources for HIV Microbicides and Biomedical Prevention

GLP: Good Laboratory Practices

GMP: Good Manufacturing Practices

QA/QC: Quality Assurance/Quality Control

PADO: WHO Pediatric Antiretroviral Drug Optimization

RAPPS: Resources to Advance Pediatrics and HIV Prevention Science

pedQTTParv = Pediatric Quality Target Product Profile for antiretrovirals