2026 INVESTIGATOR MEETING & ANNUAL WORKSHOP

Denver, Colorado
February 21, 2026

leap Long-Acting/Extended Release Antiretroviral Research Resource Program

ABBREVIATIONS

ACA Affordable Care Act
AI Artificial Intelligence
API Active pharmaceutical ingredient
ART Antiretroviral therapy
ARV Antiretroviral
AST/ALT Aspartate aminotransferase/Alanine aminotransferase
ATQ/PGN Atovaquone/proguanil
AUC Area under the curve
AZT Zidovudine
AZT/3TC Zidovudine/Lamivudine
BDQ Bedaquiline
BE Bioequivalence
B/F/TAF Bictegravir/emtricitabine/tenofovir alafenamide
BMI Body mass index
bnAbs Broadly neutralizing antibodies
CAB Cabotegravir
CDMO Contract development and manufacturing organization
CELT Centre of Excellence for Long-acting Therapeutics
CFU Colony-forming units
CHAI Clinton Health Access Initiative
DAIDS (NIH) Division of AIDS
DCE Discrete choice experiment
DcNP Drug combination nanoparticles
DDI Drug-drug interaction
DOR Doravirine
DPV Dapivirine
DR Drug-sensitive
DS Drug-resistant
DSD Differentiated service delivery
DTG Dolutegravir
ER Extended release
FDA Food and Drug Administration
FDC Fixed-dose combination
FTC Emtricitabine
FY Fiscal year
GF Global Fund
GHSD Bureau of Global Health Security & Diplomacy
G/P Glecaprevir/pibrentasvir
GLP Good laboratory practice
GMP Good manufacturing practice
HBc HBV core
HBs HBV surface
HBsAg HBV surface antigen
HBV Hepatitis C virus
HCV Hepatitis C virus
HIV Human immunodeficiency virus
IgG Immunoglobulin G
IM Intramuscular
IND Investigational new drug
INH Isoniazid
INSTI Integrase Strand Transfer Inhibitor
IP Intellectual property
IPT Isoniazid prevention treatment
ISL Islatrovir
ISL/ULO Islatravir/ulonivirine
ISR Injection site reaction
JHU Johns Hopkins University
KP Key population
LA Long-acting
LAI Long-acting injectable
LAPaL Long-acting therapeutics, patents, and licenses
LEAP Long-acting extended release antiretroviral research program
LEN Lenacapavir
LMIC Low-middle income country
LTBI Latent TB infection
LRTI Lower respiratory tract infection
mAbs Monoclonal antibodies
MAD Multiple ascending dose
MAP Microarray patch
MMV Medicines for Malaria Venture
MPP Medicines Patent Pool
nano DDI nanofluidic drug delivery implant
NIH National Institutes of Health
NOT (NIH) Notice
NP Nanoparticle
NVP Nevirapine
N6LS Modified N6 bNAb
OAR (NIH) Office of AIDS Research
PAR (NIH) Program Announcement
PBPK Physiologically based pharmacokinetic
PD Pharmacodynamics
PEPFAR
PGLA Polyglycolic acid
PI Protease inhibitors
PIP Pediatric investigation plan
PK Pharmacokinetics
PLWH People living with HIV
PP Paliperidone palmitate
PPPY Per person per year
PrEP Pre-exposure prophylaxis
PSI Protein synthesis inhibitor
PSP Pediatric study plan
PWID People who inject drugs
Q2M Every 2 months
Q4M Every 4 months
Q6M Every 6 months
RA Regulatory authority
RAL Raltegravir
RIF/RTP Rifampin/rifapentine
ROI Return on investment
RPV Rilpivirine
RPT Rifapentine
RTI Reverse transcriptase inhibitor
SAD Single ascending dose
SC Subcutaneous
SD Single dose
SoC Standard of care
SQVr Saquinavir boosted with ritonavir
SR Sustained release
SRA Supervisory authority
SS Steady state
SSA sub-Saharan Africa
TAP Translation Accelerator Program
TB Tuberculosis
TDF Tenofovir
TE Therapeutic equivalence
TEAE Treatment-emergent AE
TLC-ART Targeted long-acting and combination antiretroviral therapy
TLD Tenofovir, lamivudine, and dolutegravir
TLE Tenofovir, lamivudine, efavirenz
TPP Target product profile
ULA Ultra-long-acting
ULO Ulonivirine
UPC User preferences core
VAS Visual analog scale
WHO World Health Organization
YRGCARE YR Gaitonde Centre for AIDS Research and Education
1HP 1 month of once-weekly INH/RPT
3HP 3 months of once-weekly INH/RPT
3TC Lamivudine

CONTENT

Where will we LEAP next?

On February 21, 2026,

On February 21, 2026, The Long-Acting Extended Release Antiretroviral Research Resource Program (LEAP) convened clinicians, investigators, developers, community advocacy groups, not-for-profit institutions, and regulatory authorities. Attendees in Denver, CO shared their perspectives and discussed updates, challenges, and future directions on the development of LA formulations. The meeting served as a forum to collectively advance the LA field. The workshop consisted of four plenary sessions and four focus groups. Over the past year, the program has achieved major scientific, organizational, and funding milestones, positioning it for the next phase of research, implementation, and global impact.

OPENING REMARKS

Carl Dieffenbach

Senior Advisor to the Office of the Director,
Fogarty International Center

Founded in 2015, LEAP has driven rapid progress in LA/ER therapies – transforming them from a conceptual challenge into a growing area of innovation for HIV prevention and treatment.

"Long-acting and sustained-release formulations improve the health of people with chronic conditions by reducing the frequency with which they must interact with their medicine."

What are pharmacologic advantages of LA therapies?

- LA therapy reframes adherence
- Daily vs episodic dosing (weekly/monthly/6-month)
- Adherence shifts from daily behavior to scheduled care interactions

ART landscape

- CAB/RPV
- LEN + mAbs (Phase 2)
- DOR/ISL (FDA review, April 2026)

What are the scientific challenges?

- Resistance (mAbs)
- Limited drug classes

PrEP pricing varies widely by setting, with oral TDF and injectable lenacapavir reaching similar low annual costs in LMICs, while in the U.S. access remains uneven due to high pricing and incomplete coverage.

Product	Setting	Annual Cost
TDF/FTC	LMICs	$40/year
TDF/FTC	U.S.	$0 under ACA, Medicaid
LEN	LMICs	$40/year
LEN	U.S.	$28,218/year

Key Takeaways

- LA therapies shift adherence models and offer major clinical advantages
- Access and delivery systems determine real-world impact
- Next phase: durable combinations, scalable delivery models, alignment between prevention and treatment strategies

OPENING REMARKS

Charles Flexner

Principal Investigator of LEAP

"Without the ability to make injectable, generic formulations of long-acting drugs for HIV treatment and prevention, we will never have an impact on this epidemic."

A year of major programmatic progress:

- First HBV LA formulations workshop, preceding the Global Hepatitis Summit
- Comprehensive review of the current state of LA/ER drugs for infectious diseases
- Meeting recap and recommendations from LEAP/CELT BE assessment + generic approvals workshop

LEAP 5-year competing renewal (funding 2026-2031) ensures continuity of the LEAP resource program and provides the foundation for expanded services and broader impact. LEAP will continue its cross-cutting infectious diseases scope: HIV, TB, and viral hepatitis.

Dr. Flexner thanked Executive Committee Vice Chair Elaine Abrams. He acknowledged NIH partners, including NIAID's Dr. Peter Kim and Dr. Marina Proto-Popova.

LEAP is now supported by an additional NIH institute: the National Institute of Mental Health (program officer Dr. Terry Sinn key contributor to establishing the new User Preferences Core).

Olagunju A et al., The Promises and Prospects of Long-Acting Therapeutics for Treatment and Prevention of Infectious Diseases. Annu Rev Pharmacol Toxicol. 2026

Arshad U et al., Accelerating Generic Long-Acting Antiretrovirals for Global HIV Treatment: Workshop Findings and a Roadmap to Access. Clin Pharmacol Ther. 2026

Strategic Directions for 2026-27

Program/Core	Institution	Lead	Role
Expanded LA/ER Modeling and Simulation Core Services	University of Liverpool	A. Owen	PK modeling, dose optimization, simulation to inform LA/ER product development + trial design
Unified Communications Core + MPP	- University of Liverpool - MPP	- A. Olagunju - L. Gaayeb	- Strategic communications, stakeholder engagement, alignment across partners + external audiences - Access strategy, voluntary licensing, generic manufacturing pathways to support global affordability and scale-up
New User Preferences Core (UPC)	University of Pennsylvania	J. Bauermeister	Behavioral science + user preference research to inform product design, acceptability, implementation
New LA/ER Translation Accelerator Program (TAP)	Johns Hopkins University	C. Flexner	Translational support to bridge preclinical discovery to clinical development and accelerate movement across the "valley of death"

Key Takeaways

- LEAP marks a transition point from convening the field to actively building infrastructure to accelerate progress.
- The past year's accomplishments and successful 5-year renewal provide a strong foundation for the next phase.
- Broader, more integrated LEAP program has new emphasis on user preferences, translation, implementation science, and multi-disease impact.

François Venter

Ezintsha, University of the Witwatersrand, South Africa

Global Access to Long-Acting HIV Therapies: A Country Perspective

"With oral treatment, we got to scale. We did not do that with PrEP."

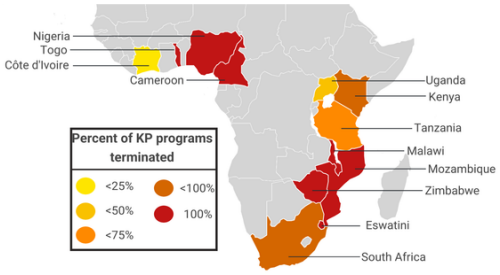
South Africa

- 6/8 million inhabitants with HIV on ART, >95% TDF/3TC/DTG FDC
- HIV incidence/mortality decrease since early 2000s
- 1.4 million have ever been on PrEP
- Weekly oral regimens are a practical, scalable near-term opportunity

What is the Reality on the Ground?

- Recent PEPFAR withdrawal destabilized testing, staffing, decimated key population programs
- Access gap despite scientific progress
- LEN approved + planned rollout, but access remains limited
- LA therapeutics mainly confined to small, non-scalable demonstration projects
- Prevention pipeline robust, but treatment less so

Impact of U.S. Funding Cuts



Global Black Gay Men Connect (GBGMC): Tracking the Freeze: Real-Time Impact on Key Populations, https://gbgmc.org/impact-us-funding-cuts/.

- Percentage of KP-serving implementing partners that have reported full or partial termination of the provision of KP services due to U.S. funding cuts as of April 2025.
- Modeling suggests that these disruptions could result in approximately 150,000 new infections annually by 2028.

In the first year since efficacy results were reported, LEN for PrEP has achieved critical milestones in record time compared to oral PrEP, DVR, and CAB; speed, scale and equity are still needed to deliver impact.

Even though these drugs are exciting, why will almost no South Africans actually get them in the next 5 years?

- Generic licensing delays, restrictive IP frameworks
- High prices, limited availability of key drugs (CAB-LA, LEN, RILP-LA)
- Minimal access for research, implementation, guideline development
- Procurement + supply issues:
- National systems optimized for ultra-low-cost oral regimens
- Supply chains not designed for cold-chain or injectable delivery
- Supplier instability highlights system fragility

Service delivery constraints:

- Injectables require training, infrastructure, patient tracking systems
- Clinics already overstretched
- Patients prefer injectables overall, but choice remains essential
- Fewer than one PrEP user per new HIV infection globally
- Prevention programs have not achieved the scale of treatment programs
- PEPFAR withdrawal has further reversed progress

Sunil S. Solomon

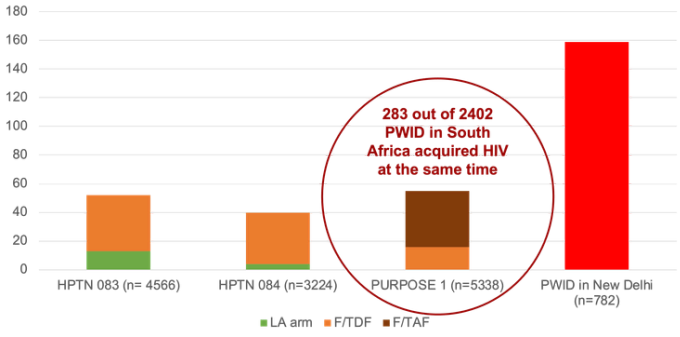
Johns Hopkins University
YRGCARE

Considerations for LA HIV Therapies in People Who Use Drugs

"We will never achieve elimination goals for HIV or hepatitis or TB without including people who use drugs – and we need to stop saying they are hard to recruit and try harder."

People who inject drugs (PWID) are a relatively small share of the global population (~14.8 million; ~0.2%) but have a disproportionate burden of infectious diseases. They account for approximately 5.5% of all people living with HIV (~27-fold higher than expected) and nearly 12% of HCV infections (~60-fold higher). Yet PWID remain largely excluded from the development, evaluation, and implementation of LA ART. Major scientific advances may bypass one of the populations most in need.

HIV incidence remains high in PWID



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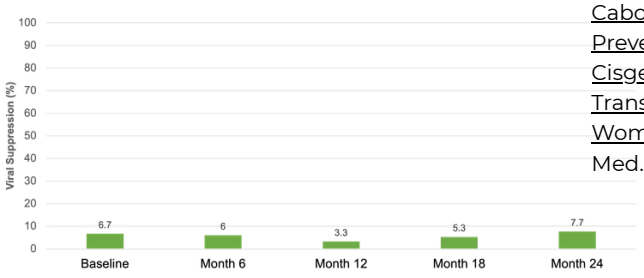


Landovitz RJ et al., Cabotegravir for HIV Prevention in Cisgender Men and Transgender Women. N Engl J Med. 2021

Biello KB et al., A missing perspective: injectable pre-exposure prophylaxis for people who inject drugs. AIDS Care. 2019

Artenie A et al., HIV incidence and factors associated with HIV risk among people who inject drugs engaged with harm-reduction programmes in four provinces in South Africa: a retrospective cohort study. Lancet HIV 2024

Critical Evidence gap

- No equivalent trials evaluating prevention of injection-related HIV acquisition and no approved PrEP indication for PWID; limited data on LA ART
- LA therapies mostly studied in stable populations, while high-incidence PWID groups remain underrepresented and viral suppression remains low
- Product design must reflect real-world use
- Clinical trials must evolve: Inclusion of real-world populations and comorbidities is essential.
  - Delivery systems matter: Integration with harm reduction, opioid treatment, and community-based care is critical; structural barriers must be addressed.
- "Giving an injection to a person who injects drugs is probably the hardest thing you can do. They don't want injections.

The global drug use landscape is evolving rapidly, with increasing use of synthetic opioids (e.g., fentanyl) and other substances (e.g., xylazine) contributing to unprecedented overdose mortality (>100,000 deaths annually in the U.S.). These shifts are frequently followed by localized HIV outbreaks, underscoring ongoing vulnerability.
Standard interventions (like incentives) aren't enough.

Key Takeaways

- Excluding PWID undermines global elimination goals
- Barriers are structural, not scientific.
- Inclusion, pragmatic design, and system integration essential

Moherndran Archary

University of KwaZulu-Natal
IMPAACT

Availability of LA Products for Children & Adolescents: When?

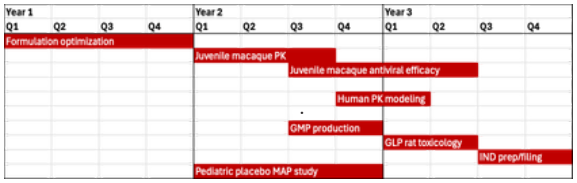
"Children and adolescents have consistently been at the back end of LA formulation development – and we need to change that paradigm."

LA formulations could transform pediatric care by addressing adherence, stigma, and treatment fatigue – particularly relevant for children and adolescents living with HIV. Yet pediatric populations continue to experience delayed access to LA innovations.

Pediatric ARV microarray patch (MAP)

- LA ARV MAPs promising for pediatric HIV
- Improve access (children, exposed infants, LMICs)

Weekly MAPs preferred; high caregiver/provider acceptability



Barriers to HIV LA in Youth

Trial / Study	Population	Intervention	Key Results	Interpretation
IMPAACT 2017 (MOCHA) – Safety	Adolescents (12-17 yrs), n≈140	CAB LA + RPV LA	- 12% of injections → ISR (mostly Grade 1-2) - 89% resolved by 7 days - No confirmed virologic failures - Few viral blips (low-level)	Strong safety + tolerability profile; supports feasibility of LA ART in adolescents
IMPAACT 2017 (MOCHA) – Acceptability	Adolescents (subset n=55)	CAB LA + RPV LA	- Injection pain decreased over time (↓55% odds by week 48) - 97-100% preferred LA over oral ART - Key benefit: reduced stigma (no visible pills) - Concern: clinic visit burden	Very high acceptability, especially for stigma reduction; clinic-based delivery is a barrier
IMPAACT 2036 (CRAYON)	Young children (2-12 yrs; 10-<40 kg; n=35)	CAB LA + RPV LA	- PK levels achieved in target range - ISRs most common AE - No major safety signals reported	Early evidence that LA ART is feasible in younger children, but ISR remains key issue
Adolescent CAB/RPV Trials	Adolescents (12-19 yrs; multiple studies)	CAB/RPV LA	- MOCHA: completed - LATA (LMICs): ongoing - CRAYON: ongoing - CROWN (unsuppressed): ongoing - Results expected ~late 2026	Field is moving from proof-of-concept → broader implementation, including LMIC and unsuppressed populations
CABNATE	Neonates exposed to HIV	CAB (oral → LA IM)	- Stepwise PK + safety design (oral → IM escalation) - Multiple cohorts to define dosing	First major effort to extend LA ART to neonates; still early-phase PK-driven development
LEN Prevention Trials	Adolescents + adults	LEN (q6 months)	- PURPOSE 1: includes small % adolescents - PURPOSE 2: large % young participants (16-25 yrs)	Strong prevention data, but limited dedicated adolescent analysis
LEN Treatment (CAPELLA + pediatric study)	Adults (MDR HIV); pediatric study ongoing	LEN + optimized regimen	- Approved for adults with MDR HIV - Pediatric study ongoing (<18 yrs, ≥35 kg)	Major advance in 6-month dosing, but pediatric data still emerging
Pipeline	Adolescents + adults	Multiple LA regimens	- LEN q12 months (Phase 3, recruiting) - CAB + LEN combo (development) - CAB ULA (Q4M) - VH-184 (new INSTI, Q6M)	Clear trajectory toward longer duration + new drug classes, but still early for pediatrics

Clinical studies in LA Formulations Injections or implants across indications

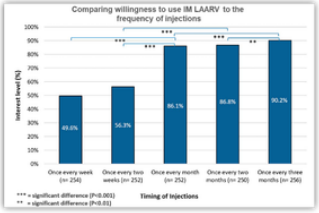
Bertagnolli L et al., Investigations of Long-Acting Formulations in Children, Adolescents, and Pregnant Women: A Systematic Review. Pharmaceutics. 2025

	Infants	Children and Infants	Children and young people	Young People
Contraception	N/A	N/A	0	18
Antipsychotics	N/A	1	0	3
Antibiotics	0	3	3	4
Other Hormone therapies	0	37	1	14
Other	3	5	2	1

Lessons from RSV Prevention

Topic	Key Points
Disease burden	RSV is the leading cause of pediatric pneumonia in Africa and Asia; PERCH study: ~31% of identified pathogens
Prevention landscape	Multiple RSV prevention strategies emerging, including long-acting monoclonal antibodies (LA-mAbs)
Effectiveness of LA-mAbs	~82% reduction in RSV LRTI; ~69% reduction in LRTI hospitalizations; ~66% reduction in all-cause hospitalizations
Policy guidance	WHO SAGE (2024): recommend passive immunization for prevention of severe RSV in infants
Access gap	Major disconnect between disease burden and access, especially in LMICs
Recent advances	Significant progress in RSV prevention, but inequities persist between high-income and LMIC settings

Youth are Interested in ART



Weld ED et al., Interest of Youth Living With HIV in Long-Acting Antiretrovirals. JAIDS. 2019

Key Takeaways

- LA formulations can transform pediatric care but delayed by development pathways
- Youth are interested in LA ART
- Early pediatric inclusion and delivery considerations are essential
- Equitable access strategies are critical for global impact

Imelda Mahaka & Ronald Ssenyonga

Pangea Zimbabwe AIDS Trust
Makerere University

Global Access to Long-Acting Formulations for HIV:
A Community Perspective | Panel Discussion

"There is no global impact without affordable, people-centered rollout."

Implementation Challenges and Priorities for Long-Acting HIV

Theme	Key Points
High demand, uneven access	Strong community demand (adherence, stigma reduction, flexibility); access remains limited, especially in LMICs
Structural barriers	High prices; restrictive IP; limited generic pathways; slow/fragmented regulatory processes; insufficient global financing
Health system constraints	Need for trained staff, cold chain, clinic visits, and follow-up systems limits scalability
Community concerns	Injection-related concerns; increased clinic burden; need for clear communication + user-centered design
Defining success	Scale (beyond pilots), choice (multiple options), infrastructure (sustainable delivery systems)
Speed of implementation	Policy, regulatory, supply chain, and service delivery must proceed in parallel, not sequentially
Community engagement	Communities should be partners in strategy and implementation, not just demand generation
Pediatric gap	Requires parallel development, child-friendly formulations, + market-shaping strategies
Sustainability	Integration into national systems, financing, + procurement from the outset
Policy & pricing reform	May require vaccine-like pricing, pooled procurement, + regulatory harmonization

"Global access to long-acting HIV formulations, such as injectable carbotegravia for PrEP and cabrepilvirine for treatment, represent a game-changer that could redefine HIV management and prevention and is characterized by strong demand and high enthusiasm from communities."

Key Takeaways

- LA HIV technologies will only achieve global impact if scientific innovation is matched by access innovation
- Children require parallel development pathways, child-friendly formulations, + market-shaping strategies
- Success will require intentional equity-focused rollout, strong community leadership, + coordinated global policy reform

SESSION 2

Roger Ptak

NIAID/DAIDS

Preclinical Development of LA Anti-Infective Drugs and Formulations Supported by NIH

"LEAP has accelerated this field in ways that I don't think could have been imagined when the program was started over 10 years ago."

In addition to LEAP, several NIH-supported programs aim to reduce HIV incidence, develop safer and easier-to-use next-generation therapies, and address HIV-related comorbidities and coinfections through critical preclinical and translational research resources.

NIH Application Changes

Based on the May 2025 expiration of SRATP, NIH had planned to reissue the NIAID/NIMH Notice of Special Interest (NOSI) when NIH processes changed to halt NOSIs. Now, NIH offers Highlighted Topics as centralized research priorities that aim to help align investigator-initiated proposals with NIH interests without separate funding announcements.

NIH Highlighted Topics

- No letters of intent, no pre-approval for ≥$500K applications
- Standardized submission timelines: no HIV/AIDS-specific due dates
- New international funding structure
- Linked domestic + foreign awards
- More oversight of global collaborations

Evolution of NIH-Funded Programs for Sustained Release of Antivirals for Treatment or Prevention of HIV or Treatment of Latent TB/HBV (SRATP)

Initiative	Years	Dosing Targets	Strategy
PAR-13-349	FY14-16	1/week treatment; 1/month prevention	Established weekly/monthly paradigm
PAR-16-262	FY17-19	1/week oral treatment; 1/month treatment / prevention (non-oral)	Expanded to alternative delivery routes
PAR-20-029	FY20-22	1/week oral treatment; 1/month treatment / prevention (non-oral)	Continued multi-route LA strategy
NOT-AI-22-042	FY23-25	≥3-month treatment/prevention	Shift to multi-month; added TB/HBV

DAIDS Services Program to Accelerate Drug Development

The Division of AIDS (DAIDS) maintains contracts that can potentially provide limited pre-clinical resources and services to investigators who are working on the development of therapeutics targeting HIV and HIV-associated co-infections, including B virus (HBV), hepatitis C virus (HCV) and Tuberculosis (TB). The focus of the program is to facilitate the advancement of promising drug candidates from bench to clinic and fill critical program and resources gaps in an investigator's drug development effort as they advance their product toward regulatory submissions and clinical trials.

DAIDS Services

Pediatrics/HIV Prevention Science program

- Fill preclinical gaps
  - GLP-enabling studies
  - Safety/toxicity, drug interactions, reproductive toxicology
- HIV animal models
  - PK/PD studies in nonhuman primates
- Method development
- Product manufacturing
- Scientific + regulatory support

Preclinical Resources

- In vitro testing + screening
- Chemical synthesis
- Efficacy models
  - HIV, HBV, HCV
  - TB
- Formulation + manufacturing
- Preclinical pharmacology + toxicology

Group Discussion

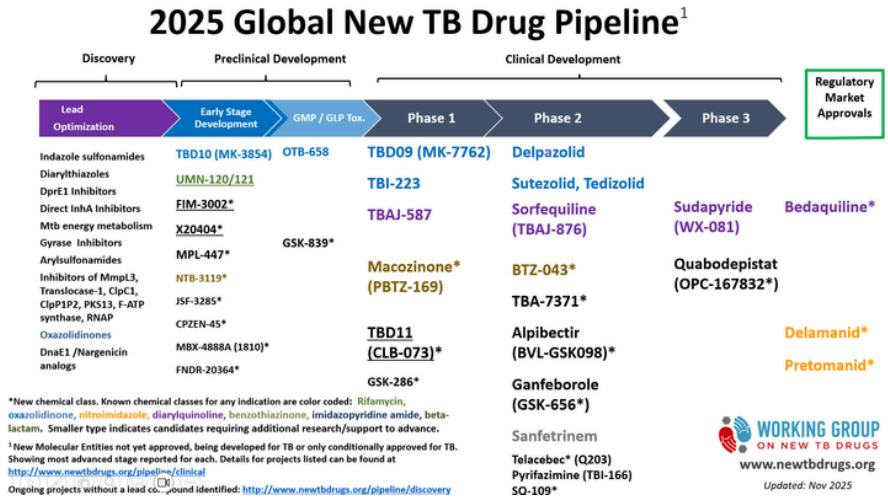
Question	Answer
How can investigators access DAIDS contract support?	Submit short description of the product and development gap; initial engagement informal and consultative; DIADS works with investigators to define needs; proposals are reviewed by a committee; selected projects may receive task order support
Will DAIDS continue supporting GMP manufacturing for early-phase studies?	Yes: continued support for GMP drug/formulation production for Phase 1 studies remains a priority. Contact: Dr. Marina Pritapova

Center for the Dissemination of Ultra-Long Acting Antiviral Release Technology (DART) aims to disseminate the nanofluidic drug delivery implant (nanoDDI), as a veterinary research tool to support animal studies in the field of HIV to replace daily dosing and reduce animal care issues.

Christopher Vinnard

Gates Medical Research Institute

LA Injectable Agents as Tools to End TB



TBD09 (MK-7762)	TBD11 (CLB073)
Oxazolidinone (PSI)	Adenylyl cyclase activator (blocks cholesterol metabolism)
Discovered by Merck/NIAID (TB Drug Accelerator)	Discovered by Calibr/Cornell (TB Drug Accelerator)
Phase 1 completed (first-in-human; up to 84-day dosing)	Phase 1 ongoing
Phase 2 in prep (safety, PK, bactericidal activity)	Phase 1 includes SAD, MAD, food effect, cross-over cohorts

Regulatory Environment for Clinical Development of LAI-TB

- Collaboration required
- PK/PD bridging from oral → LAI regimens
- Oral safety database: Clinical, preclinical

Group Discussion

Question	Answer
How should clinical trials account for people aging with HIV, including comorbidities like renal impairment?	Enroll broader, real-world populations; avoid unnecessary exclusions; generate safety/efficacy data in older and comorbid groups during trials
How are long-acting TB drugs being developed for prevention (e.g., LTBI), and how are user preferences being considered?	Current focus on active TB and treatment populations; expanding to LTBI/prevention, including user preference studies

Key Takeaways

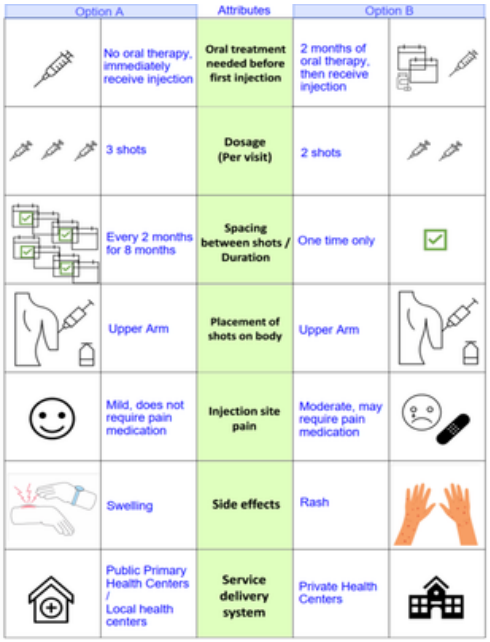
- LAIs are highly acceptable but must meet user expectations for simplicity and tolerability
- Development requires integration of user preference data, regulatory strategy, formulation science
- Future success: multi-drug regimens, partnerships, alignment with global product profiles

"We see LAI as integral to a holistic approach to ending tuberculosis."

Philippines High-Burden TB Setting Field Survey

Stage 1: Informant Consultations	Stage 2: Surveys (N ~350)
1:1 interviews with 15 national and regional TB experts	Surveys with TB patients, survivors, healthcare providers
Assessed perceived need for LAI TB regimens	Collected demographic characteristics
Explored trade-offs across LAI TB regimen scenarios	Evaluated acceptability of different LAI TB regimens
Identified facilitators and barriers to introduction	Used discrete choice experiment (DCE) to assess trade-offs between regimen attributes

Stakeholder	Most Important	Least Important
Patient	Injection site	Initial oral dosing
Survivor	Per-visit dosage	Side effects
Provider	Injection interval (duration/spacing)	Side effects



SESSION 2

David Thomas (for Andrew Owen)

CELT
University of Liverpool

LONGEVITY Formulation Development: HCV and TB

"For each of [the five programs], there's been progress in the critical chemistry of formulating the products and in proof-of-concept studies demonstrating that PK can be achieved in animal models."

What is LONGEVITY?

An integrated, multi-disease initiative aimed at developing LA therapies to address persistent gaps between the efficacy of oral regimens and real-world effectiveness. Survey data support acceptability and potential programmatic feasibility of LAI for the LONGEVITY target indications.

LONGEVITY Pipeline Overview

	Research and preclinical POC	GMP/CDMO Translation	GLP Toxicology	Phase 1	Onward Licensing
LTBI (Rifapentine)	→	→		2026/27	TBD
LTBI (Isoniazid-prodrug)	→	→	Q2 2025	2026/27	TBD
LTBI (Rifapentine / isoniazid MAPs)	→		TBD	TBD	TBD
HCV (glecaprevir / pibrentasvir)	→	→	Q2 2025	2026/27	TBD
Malaria (atovaquone / proguanil MAPs)	→		TBD	TBD	TBD

Preclinical Proof-of-Concept

HCV	LTBI
Co-formulated LA G/P has favorable PK, extended exposure, dose proportionality (rodents)	LA RPT + novel INH formulations > sustained drug exposure and efficacy in preclinical models, with results comparable to standard preventive regimens

Group Discussion

Question	Answer
What is the funding outlook for these projects – will UNITAID continue support?	Current funding supports completion of Phase 1 for all 3 projects; UNITAID made early, high-risk investments and uses a stage-gated approach; future funding uncertain and depends on demonstrated value
Will liver toxicity risks require oral lead-in strategies for LA TB/HCV drugs?	For HCV: no lead-in planned (goal = one-shot cure); for TB: oral lead-in being used in Phase 1 (RPT) due to safety concerns in healthy volunteers; future need depends on Phase 1 outcomes

Regulatory Strategy

- Leveraging existing data on approved oral drugs, pursuing a 505(b)(2) pathway
- Streamlined GLP toxicology requirements + integration of existing regulatory data enable accelerated development

Manufacturing Activities

- RPT: Method transfer to CDMO complete; GMP scale-up achieved; sterilization optimized; stability confirmed; in vivo PK completed; GLP tox batches shipped
- INH: Prodrug scaled to kg; strong stability; LAI method developed and transferred to CDMO
- G/P: Method transfer complete; GMP scale-up underway; sterilization acceptable; GLP tox manufacturing planned

Key Takeaways

- LONGEVITY aims to transform infectious disease treatment through LA solutions that improve adherence and scalability
- The program demonstrates strong progress across scientific, regulatory, manufacturing domains
- Success will depend on clinical validation, safety, and sustained funding

Rodney JY Ho

University of Washington

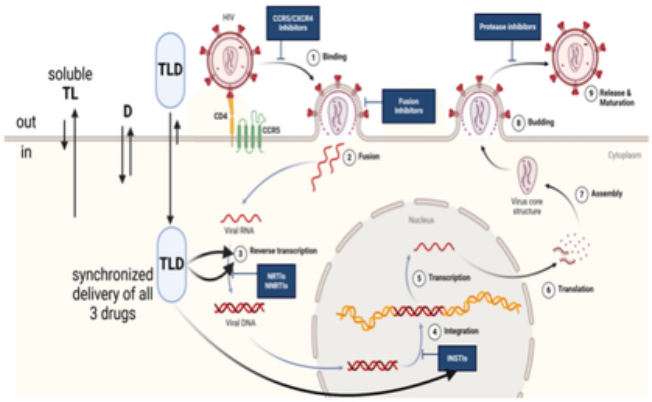
ALL-in-One Long-Acting TLD for HIV Treatment

"This cannot be done without public-private partnerships."

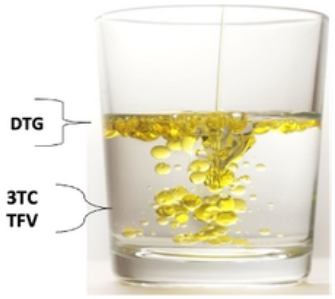
The TLC-ART public-private partnership aims to convert daily oral TLD into an LAI using a nanoparticle platform to improve adherence and treatment outcomes.

Major milestone for TLC 301: LA TLD FDA IND designation achieved in < 30 days, thanks to collaboration and early NIH funding.

TLC 101 (LA-TLR)	TLC 301 (LA-TLD)
LPV + RTV + TDF	TDF + 3TC + DTG
PI-based	INSTI-based
Phase 1 completed	Entering Phase 1
Yes (RTV)	No
GI side effects	Better tolerated



Perazzolo S et al., A novel formulation enabled transformation of 3-HIV drugs tenofovir-lamivudine-dolutegravir from short-acting to long-acting all-in-one injectable. AIDS. 2023



Mechanism: Injection site (no depot) → lymph nodes first-pass, lymphocyte exposure (70%) → PBMC/plasma (30%)

How does DcNP technology overcome solubility constraints?

- Form NPs by combining drugs + excipients into a single dry powder by spray drying at high temperature
- Nano-size DcNP in aqueous buffer at high temperature
- Cool to lock all three drug molecules in DcNP within the TLC-ART drug product
- No free drug removal step; avoids wastage and contamination risk.

Group Discussion

Question	Answer
Are large-volume SC injections too painful, and could IM delivery be preferable?	Pain driven by formulation (pH, solvent) more than volume; IM possible but may limit targeting
Is the goal to switch all patients from oral ART to LAI?	No: gradual uptake (1-5%); focus on patient choice
How might LA formulations affect dosing and supply (e.g., vs TLD)?	Likely lower drug needed, but exact dosing still unknown

Key Takeaways

- TLC-ART demonstrates feasibility of LA combination HIV therapy
- Targeted delivery may improve durability and outcomes
- Clinical studies will determine scalability and impact

Huub Gelderblom

Fred Hutchinson Cancer Center
HIV Vaccine Trials Network

Broadly Neutralizing Monoclonal Antibodies for HIV Treatment and Prevention

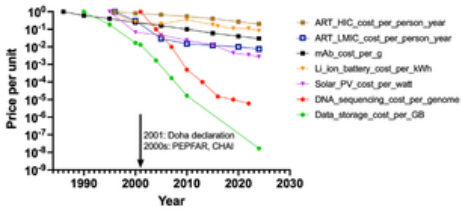
"If there have been 50 HIV treatment drugs in 9 classes since 1987, why are there only 4 HIV prevention drugs?"

Despite major ART scale-up since 2012, HIV prevention remains insufficient. PrEP uptake lags behind new infections, highlighting a persistent gap between prevention use and global HIV acquisition. HIV epidemic control by 2030 is unrealistic. Cost remains a major issue.

4 PrEP HIV drugs in 2026:

- RTIs: TDF, DPV (1996)
- INSTIs: CAB (1996)
- Capsid inhibitors: LEN (2022)
- bnAbs: Promising new option for treatment + prevention

Category	Current State
Treatment drugs	>50 across 9 classes
PrEP options	3-4 globally
PrEP uptake	~4 million users
New infections	~1.3 million annually



Randomized trial in rural Uganda and Kenya found that offering people a choice between daily oral PrEP and LAI cabotegravir significantly increased HIV prevention uptake and reduced HIV incidence compared to standard PrEP delivery.

- Multiple options increase use and effectiveness
- No single modality fits all populations
- Delivery models must evolve
- Potential for community/non-clinic delivery

Kamya MR et al. Dynamic choice HIV prevention with cabotegravir long-acting injectable in rural Uganda and Kenya: a randomised trial extension. Lancet HIV. 2024

Corey et al., Two Randomized Trials of Neutralizing Antibodies to Prevent HIV-1 Acquisition. N Engl J Med. 2021

Pharmacoequity:
How to go from clinical trial efficacy to real-world effectiveness?

Domain	Definition
Efficacy	Works in a clinical trial under controlled conditions
Approved	Authorized or recommended by regulatory bodies
Available	Produced and distributed; present in the market
Accessible	Easy for people to reach or obtain
Affordable	Priced within financial reach for broad use
Aware	People know about the product and its benefits
Appropriate	Suitable for the target population and context
Ask	Demand or interest exists for the product
Aspiration	Desire or unmet need driving uptake
Effectiveness	Produces the desired effect

bnAbs are a new drug class that target conserved Env epitopes on HIV. Proof-of-concept has been established, Q6M feasible. Expected timeline for a triple bNAb HIV product likely in the 2030s, although timing is uncertain and depends on demonstrating clear value to stakeholders.

Ogbuagu et al., Efficacy and safety of lenacapavir, teropavimab, and zinlirvimab: week-26 primary outcome results from a multicentre, open-label, randomised, active-controlled, phase 2 study. Lancet Microbe. 2026

Key Takeaways

- bnAbs are a transformative new option for HIV prevention and treatment
- Expanding choice and reducing cost are essential for impact
- Pharmacoequity must guide development and deployment

"We give monoclonal antibodies to cats and dogs here in the United States. But there are 100 countries around the world that do not have access to even the 10 monoclonal antibodies that are on the WHO essential medicine list."

Daniel R. Kuritzkes

Harvard Medical School

Broadly Neutralizing Antibodies for HIV: Why We Should Be Cautious

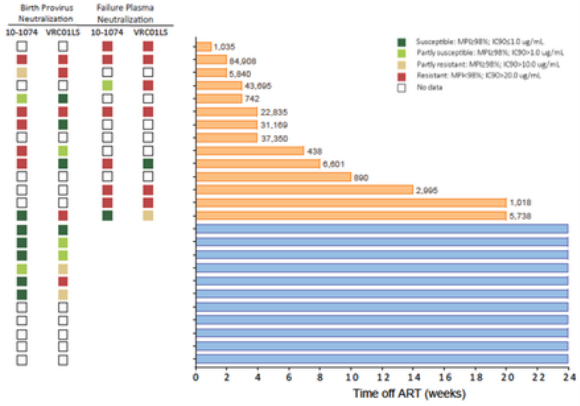
"An antibody has to be two to five times more valuable to break even with a small molecule."

bnAbs are a promising new biologic approach for HIV treatment and prevention. Early clinical data on LA combinations (LEN + bnAbs) show promising efficacy and safety, but resistance and pharmacokinetic variability remain key challenges.

bnAbs Properties and Potential Uses

- Target HIV envelope and neutralize diverse isolates
- Enhance immune effector functions
- Can be engineered for multi-specificity and longer half-life
- Prevention
- Maintenance therapy + switch strategies
- Immunotherapy for resistant/intolerant patients

Maintenance of viral suppression with VRC01-LS and 10-1074 in early-treated infants in Botswana



Shapiro et al., Broadly neutralizing antibody treatment maintained HIV suppression in children with favorable reservoir characteristics in Botswana. Sci Transl Med. 2023

What are Some of the Limitations of bnAbs?

- Target specific viral epitopes; thus don't neutralize all variants equally
- Single bnAb insufficient
- Dual combinations ~40% full coverage
- Triple combinations required for broader protection
- Preexisting resistance is common
- High proportion of people excluded from trials
- Susceptibility testing often required
- Emergent resistance
- Virologic failures with resistance to bnAbs + partner drugs

Combination Strategy	Estimated Coverage
Single bnAb	Limited
Dual bnAbs	~40% full coverage
Triple bnAbs	~75% partial, ~20% full

Draft TPP for mAb HIV prevention

Category	Details
Product	Two IgG mAbs (or one bi-/tri-specific)
Indication	Prevention of HIV infection
Efficacy profile	Prevents infection by >98% of strains
Target population	Adolescents/adults: high risk of HIV infection Infants of HIV+ mothers: at birth; during breastfeeding
Dosing	Adolescents/adults: 5 mg/kg SC every 3-6 months Infants: one dose (20 mg/kg SC) at delivery
Safety/tolerability	Adverse event frequency rare
Cost of goods	< $50 per person per year

Group Discussion

Question	Answer
Is resistance to bNAbs easier than for current HIV drugs?	Depends on antibody class; pre-existing resistance is a key issue; CD4-binding site bNAbs have higher resistance barriers, but no agent is fully resistance-proof
Do bNAbs solve key problems like acceptability, access, or feasibility?	Development driven by unmet need and potential market; bNAbs may expand options but must clearly address specific use-case gaps
Can bNAbs be affordable enough to compete with small molecules?	Currently more expensive to produce (2-5X); cost reduction requires new manufacturing approaches + market shifts
What is the role of bNAbs in infants and children?	Advantage: weight-based dosing and early use; potential for prophylaxis (e.g., during breastfeeding) + earlier pediatric studies
How do bNAbs fit into cure strategies?	May help delay viral rebound and bridge toward cure; treatment and cure pathways increasingly interconnected
Why is there strong interest in bNAbs despite challenges?	High acceptability (e.g., caregiver preference) and potential benefits beyond adherence; still early but promising trajectory
What are the key scientific limitations of bNAbs?	Main challenge is achieving durable neutralization; binding is feasible, but effective neutralization + breadth remain limiting
What is the long-term outlook (e.g., vaccines)?	bNAbs show the immune system can generate protective antibodies, supporting the feasibility of future HIV vaccines

bnAbs face significant scientific and implementation challenges despite strong biologic rationale.

Lionel Tan & Alex Rinehart

ViiV Healthcare

Current Status of the ViiV LA/ER Pipeline

"We pretty much have the waterfront covered here for the life cycle of the virus."

ViiV has made a strategic shift to a fully-LA pipeline with the goal of enabling combination regimens with matched long durations.

Landovitz et al., Lancet HIV. 2023

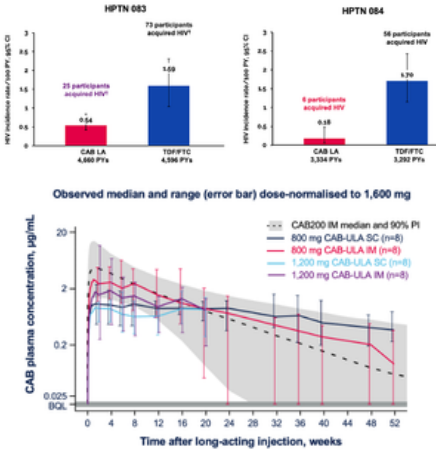
Delany-Moretlwe et al., Lancet. 2022

ViiV pipeline: Emerging LA Agents + Combinations

Drug	Class	Lifecycle	Trial Phase	Population	Findings
VH-109 (N6LS)	bNAb (CD4-binding site)	Binding + fusion	Phase IIb (EMBRACE)	Virologically suppressed adults	Maintains suppression with CAB LA; some CVF but resuppressed
VH-7079	bNAb	Binding + fusion	Phase I	Early clinical	Dual-target antibody; early-stage evaluation
VH-499	Capsid inhibitor	Nuclear entry + uncoating	Phase I/IIa (CINNAMON)	Treatment-naive adults	Potent antiviral activity; low resistance; well tolerated; no CYP3A4 interaction
VH-499	Capsid inhibitor	Assembly + budding + nuclear entry	Preclinical + Phase I	Healthy volunteers	Broad antiviral activity; exposure above target; good tolerability
CAB-ULA (Tx/PrEP)	INSTI (ULA CAB)	Integration	Phase Ia/IIb	Prevention + treatment	Established efficacy; supports extended dosing strategies
VH-184	3rd-gen INSTI	Integration	Phase I + IIa	Treatment-naive adults	Active vs INSTI-resistant virus; well tolerated; no emergent resistance
VH-310	INSTI	Integration	Non-clinical	Preclinical	Early-stage integrase inhibitor candidate
VH-109 + CAB LA	bNAb + INSTI LA combo	Entry + Integration	Phase IIb (EMBRACE Part 2)	Virologically suppressed adults	Evaluating Q6M VH-109 + CAB LA vs SoC ART

PREVENTION

- CAB LA superior to daily oral TDF/FTC at preventing new HIV acquisitions in cisgender men/transgender women
- PK bridging uses comparable drug levels for future formulations to infer efficacy without new Phase 3 trials

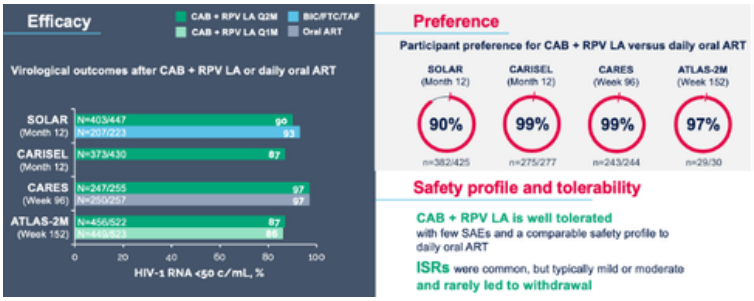


CAB ULA

- Substantially longer terminal half-life
- Slower absorption from depot
- Flatter PK profile supports Q4M dosing

TREATMENT

CAB + RPV LA Efficacy + Preference + Tolerability



CAB + RPV LA: Ongoing + Future Studies in KPs

Study	Population	Key Finding/Objective
LATITUDE	People with adherence challenges	Superior outcomes vs oral ART
MOCHA	Adolescents	High virologic suppression; strong preference for LA therapy
VOLITION	Newly diagnosed	Strong preference for LA initiation
CROWN	Adolescents + adults with viremia	Expansion to viremic populations
CRAYON	Children <12 years	Expansion to younger children
CABNATE	Neonates (postnatal prophylaxis)	CAB-only prevention strategy
CUATRO	Treatment (CAB + RPV, Q4M)	ULA regimen

Luisa Stamm

Merck Research Laboratories

Merck HIV Pipeline: LA Oral Treatment and Prevention

"The positive data with daily DOR, ISL, and weekly ISL/LEN really support the development of the LA NRTTI-based treatments for treatment and prevention."

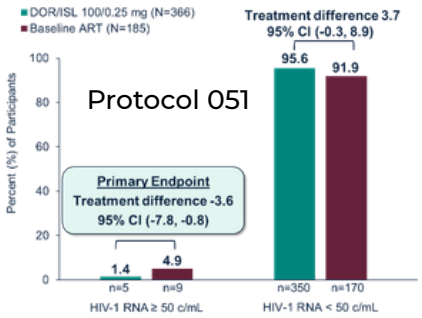
NRTTIs are Merck's foundational platform for both PrEP and treatment

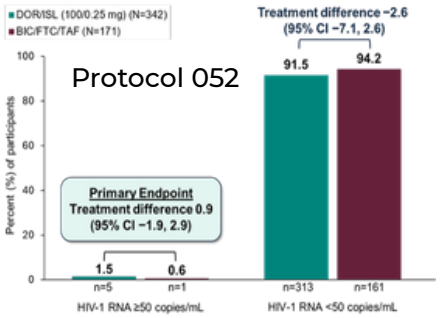
- High potency and long intracellular half-life
- Enable extended dosing intervals

Oral regimens are moving toward weekly/monthly dosing: strong early efficacy + PK data

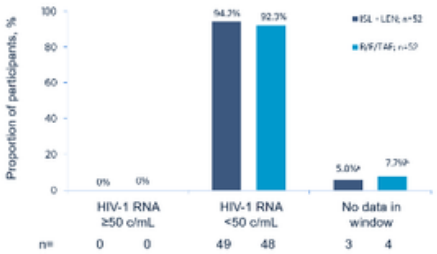
Regimen	Dosing	Indication	Phase	Results
DOR/ISL	Once-daily oral	Treatment	Phase 3	Noninferior; well-tolerated, no treatment-emergent resistance
ISL/LEN	Once-weekly oral	Treatment	Phase 3	High suppression; weekly feasible, no treatment-emergent resistance, improved patient-reported outcomes
ISL/ULO	Once-weekly oral	Treatment	Phase 2	Promising PK; active; potentially smaller pill
MK-8527	Once-monthly oral	PrEP	Phase 3	Target levels achieved; includes adolescents, pregnancy

DOR/ISL Non-inferior to Baseline ART or BIC/FTC/TAF

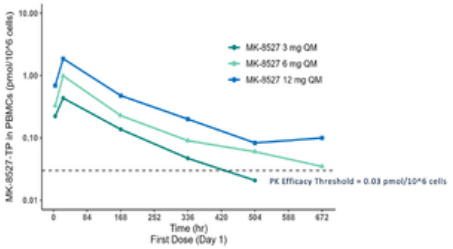




Once-weekly oral ISL+LEN maintained high virologic suppression comparable to daily B/F/TAF



MK-8527 Once-monthly oral PrEP



Key Takeaways

- LA oral regimens are a major evolution in HIV care
- NRTTI-based strategies enable flexible dosing (daily > monthly)
- Strong efficacy + safety data in the Merck pipeline

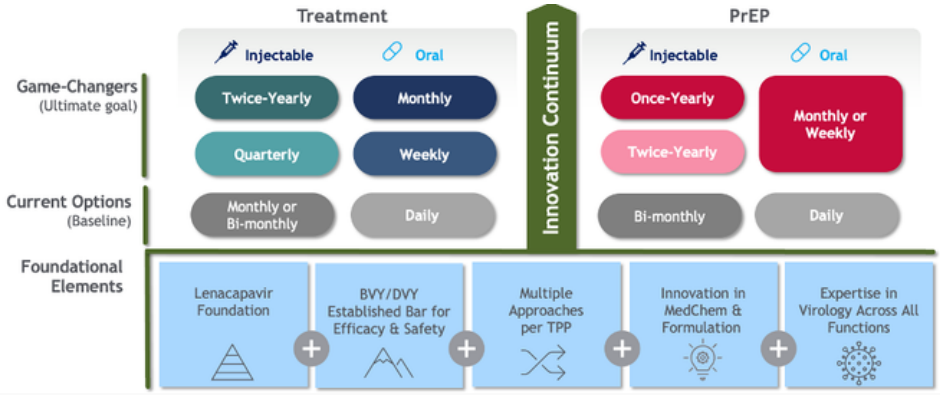
Moupali Das & Martin Rhee

Gilead Sciences

Current Status of the Gilead LA/ER Pipeline

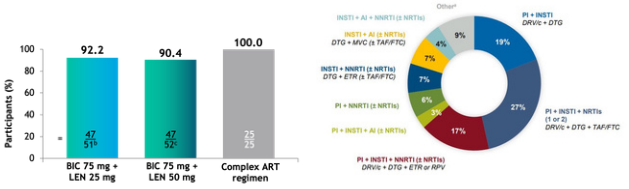
"Gilead's long-standing commitment and dedication is to end the HIV epidemic for everyone everywhere."

>16 million people have accessed a Gilead treatment or PrEP regimen, including in LMIC.



People taking complex ART regimens are typically treatment-experienced, with drug resistance, prior treatment failure, or long treatment histories. They may also have comorbidities, drug interactions, tolerability issues, or adherence challenges. As a result, they are often managed with PI-based regimens involving multiple drugs and more complicated dosing.

Simplifying treatment with BIC/LEN: At week 48, BIC/LEN maintained high rates of virologic suppression, was generally well-tolerated (ARTISTRY trials)



LA Prevention Landscape

- PURPOSE studied LEN in populations most disproportionately affected by HIV
- LEN achieved rapid global approvals, including in LMICs
- Approval timelines dramatically shorter than prior PrEP technologies
- African approvals: days to weeks (mean ~51 days)
- Enabled by regulatory coordination + WHO PQ + global partnerships
- PURPOSE 3-5 expanding to underrepresented populations (e.g., PWID, Europe, North America)

Orkin C et al., Switch to single-tablet bictegravir-lenacapavir from a complex HIV regimen (ARTISTRY-1): a randomised, open-label, phase 3 clinical trial. Lancet. 2026

ISL/LEN Phase 3 studies

Study	Design	Population	Comparator	Intervention	Primary Endpoint	Notes
ISLEND-1	Phase 3, double-blind	Virologically suppressed on B/F/TAF (N~600)	Continue daily B/F/TAF	ISL/LEN once-weekly oral	HIV-1 RNA suppression at week 48	Extension: all switch to ISL/LEN through week 96
ISLEND-2	Phase 3, open-label	Virologically suppressed on standard of care (N~600)	Continue standard of care	ISL/LEN once-weekly oral	HIV-1 RNA suppression at week 48	Extension: all switch to ISL/LEN through week 96

What's Next?

- Twice-yearly treatment LA combination (LEN + TAB + ZAB) maintained high rates of viral suppression comparable to standard oral ART. Phase 3 planned for 2026.
- Next-gen LA injectable GS-3242 is a novel ER ISTI with favorable PK, safety, antiviral activity

Key Takeaways

- LEN is a key part of a broad shift toward ULA HIV care
- Treatment, prevention pipelines are converging from multi-month > annual dosing
- Global access + equity strategies are central to impact.

Vivian Cox

Johnson & Johnson

Current Status of the J&J Tuberculosis LA/ER Pipeline

"Bedaquiline has unique properties to provide a potential new TPT treatment regimen for individuals at high risk of developing active TB disease."

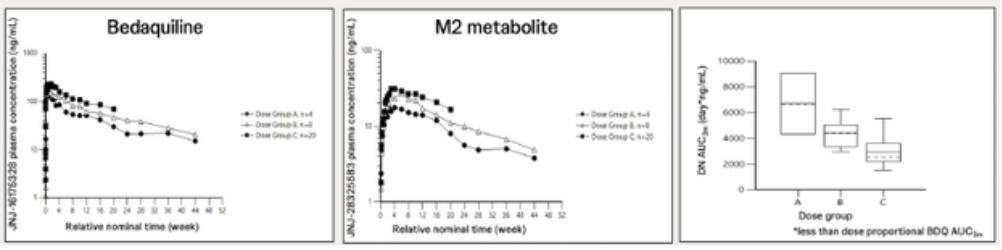
J&J conducted a first-in-human Phase 1 study evaluating LA BDQ as a potential single-dose TB preventive therapy, targeting efficacy comparable to 3HP standard of care.

Why BDQ?

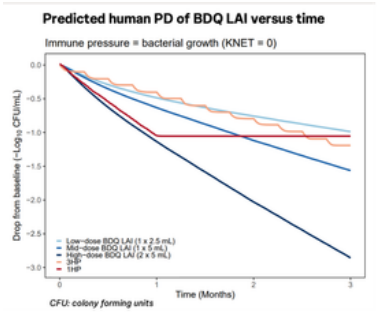
- Activity against both drug-sensitive and drug-resistant *M. tuberculosis*
- Activity in established latent TB mouse model compared to established oral TB preventive therapy
- Oral formulation has well-established safety profile
- No major DDIs with DTG or PI-based ART

Interim results: Phase 1, open-label, single ascending dose study in HIV-negative participants at single center in Austria (majority male participants; 30.5 median age, ~25 median BMI)

Category	Details
Study design	Open-label, single ascending dose; HIV(-) participants; single site (Austria); Primary endpoints: PK (Cmax, AUC, tmax) and safety; Follow-up through 52 weeks
Dose cohorts	Group A: 1 × 2.5 mL IM (low dose); Group B: 1 × 5 mL IM (mid dose); Group C: 2 × 5 mL IM (high dose)
PK	Exposure increases with dose (less than proportional); Median tmax: 4-8 days; Low/moderate variability (Cmax, AUC); Robust, sustained release; no early spikes
PK/PD modeling	Integrated mouse + human PK data; Benchmarked vs 1HP and 3HP; Mid-dose achieves ≥3HP-equivalent CFU decline; Supports Phase 3 dose selection
Safety profile	All participants had ≥1 TEAE (mostly injection-related); 72% Grade 1-2 events; 4 Grade 3 ISRs; no serious local complications; 4 SAEs (none drug-related)
Injection tolerability	Pain resolves within ~5 days; Very low VAS scores by day 5; No abscesses, nodules, severe ISR
Patient preference	Majority preferred injection vs oral regimens; Consistent preference at day 1 and day 29



- Cross-group comparison: BDQ exposure increases w/dose less than dose-proportionally
- PK/PD predicts human PD at least similar to 3HP at mid-dose BDQ LAI (Group B, mid-dose)



Strydom et al., Dose optimization of TBI-223 for enhanced therapeutic benefit compared to linezolid in antituberculosis regimen. Nat Commun. 2024

Key Takeaways

- Mid-dose BDQ LAI achieves target PD activity comparable to 3HP
- Safety profile consistent with known BDQ profile + acceptable for IM delivery
- Single-dose long-acting TB prevention is clinically feasible and moving to Phase 3

SESSION 4

Geri Donenberg

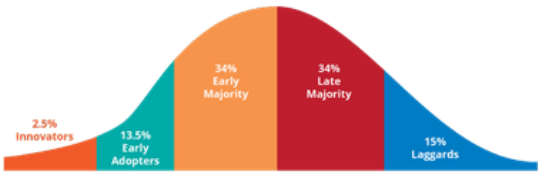
NIH DAID, OAR

What Is Implementation Science, and What Is Its Role i the NIH Research Portfolio?

"Implementation science is not implementation – it is the study of how to implement."

The NIH Office of AIDS Research (OAR) plays a central coordinating role across the agency's HIV portfolio, integrating efforts that span more than 20 NIH ICs With an annual NIH HIV/AIDS research investment of ~ $3.29 billion supporting over 3,800 research awards, OAR operates through a strategic framework often described as the "Four Cs": catalyzing new scientific opportunities, coordinating activities across NIH, convening stakeholders, and communicating priorities and progress across the field.

Innovation theory



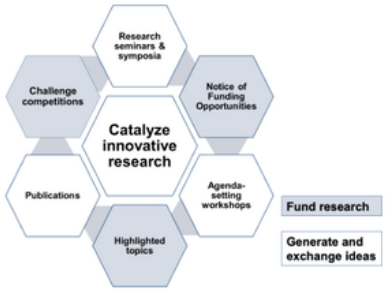
Innovation-to-impact gap

- ~17-year delay from discovery to practice
- <50% of effective interventions reach real-world use
- Scientific success does not ensure population-level impact

Domain	Barrier	Implementation Need
Acceptability	Stigma, side effects	User-centered design
Feasibility	Clinic workflow constraints	Operational redesign
Fidelity	Training variability	Standardized protocols
Reach	Limited access	Targeted outreach
Cost	Insurance barriers	Policy + payer alignment
Sustainability	Funding instability	Long-term planning

ARISE program

Accelerate implementation research to identify drivers of uptake and access, optimize delivery and scale of effective HIV interventions, and strengthen training and capacity in implementation science to help end the epidemic.



Key Takeaways

- Implementation, not discovery, is now the primary bottleneck.
- Delivery systems determine whether innovation achieves impact
- Implementation science provides a structured, actionable framework
- Early integration is essential for success at scale

mike Reid

Bureau of Global Health Security & Diplomacy/PEPFAR

The New PEPFAR: Implications for LA Treatment and Prevention

"Long-acting prevention in particular, but treatment as well, are not peripheral innovations … they are central to sustaining the epidemic response in the coming decade."

Integrated Framework: Principles and Programmatic Considerations for LEN PrEP Rollout

Domain	Area	Key Considerations	Practical Implications
Principles	Country-led	Person-centered models; align with country priorities	Design user-centered delivery; ensure national ownership
Principles	Impact	Maximize # infections averted; focus on high-incidence areas; use analytics	Target high-burden populations; optimize ROI with data
Principles	Scale	Integrate into antenatal care, primary care, DSD; build ministry capacity; align systems	Avoid parallel systems; strengthen existing platforms
Principles	Speed	Act quickly to shape price/supply; compress timelines; front-load rollout	Accelerate approvals; prioritize high-incidence settings
Programmatic	Service delivery	Integrate into primary care and community platforms; avoid LEN-only services	Leverage existing systems; prevent fragmentation
Programmatic	HIV testing	Testing before each dose; use rapid tests; nucleic acid amplification tests/self-tests not recommended	Standardize testing; align with national algorithms
Programmatic	Administration	Administered by trained individuals per policy	Enable task-shifting; expand trained workforce
Programmatic	Follow-up	Support timely return for dosing	Use reminders, tracking, community support

What are key enablers to support operational planning between GF, GHSD + country stakeholders?

- Bilateral engagement between institutions
- Participation in national Technical Working Groups coordinating LEN PrEP introduction
- Unified national introduction plan
- Uptake monitoring

Global Fund and GHSD Approaches to Financing LEN PrEP

	Global Fund	GHSD
Eswatini	✓	✓
Kenya	✓	✓
Lesotho	✓	✓
Malawi*		✓
Mozambique	✓	✓
Nigeria*	✓	
Philippines*		✓
South Africa*	✓	
Uganda	✓	✓
Ukraine*		✓
Zambia	✓	✓
Zimbabwe	✓	✓

- The GF leverages private-sector donor funding to support affordability and covers portions of product, procurement, and supply chain costs, with additional programmatic expenses managed by recipient countries.
- In contrast, GHSD uses centrally funded, market-shaping approaches to enable rapid LEN PrEP access and integration, with product procurement supported centrally and programmatic costs funded through U.S. bilateral HIV budgets.
- Procurement via wambo.org for both.

José Bauermeister

University of Pennsylvania

Introduction to the LEAP User Preferences Core

"We're not advancing the field if we just keep putting the same five variables in the model."

Why a UPC? Incorporating user perspectives results in greater uptake, equity, and sustainability.

UPC Objectives

- Establish a multidisciplinary and community engaged core committed to integrating a robust user preference research agenda within LEAP-supported protocols
- Design and support the implementation of user preference objectives and endpoints for LEAP-supported protocols through rigorous, cutting-edge science
- Synthesize best practices in user preferences research specific to LA/ER products and set priorities for best practices in user preferences research involving LA/ER products

UPC Members


Jose Bauermeister (UPENN)


Sybil Hosek (UIC)


Sarit Golub (CUNY)


Karine Dubé (UPENN)


Douglas Krakower (Harvard/BIDMC)


Alexandra Minnis (RTI)


Christine Rael (U Colorado)


Willey Lin (UPENN)

Pillar	Focus	Key Activities
1: Community engagement	Ensure user perspectives shape development	- Embed human-centered design principles to include patients, providers, policymakers - Conduct focus groups, interviews, community forums across diverse settings -Prioritize underserved, high-burden, KPs
2: Methods development	Standardize and strengthen research approaches	-Align methodologies across LEAP-supported protocols for comparability -Harmonize stated-preference techniques (e.g., DCEs, conjoint analysis) -Strengthen rigor of social and behavioral data collection and analysis
Pillar 3: Knowledge synthesis	Generate and share evidence and best practices	- Conduct iterative landscape analyses of user preference research in LA/ER - Produce systematic reviews and consensus statements - Disseminate best practice recommendations tailored to infectious diseases - Share outputs via LEAP website, workshops, and peer-reviewed publications
4: Technical assistance & capacity building	Support implementation and global capacity	- Offer consultative services via LEAP "NEED HELP" portal - Provide rapid, tailored support at national and international meetings - Build global capacity through mentorship and collaboration

What is behavioral congruence and why does it matter?

Consistency between the aims, attitudes, and values professed by an individual or group and their observable behaviors. In personality research, for example, behavioral congruence occurs when individuals' self-ratings are consistent with their actions.

ViiV, Merck, Gilead, J&J & Generics Representatives

"I think one thing we're going to have to talk about is shared risk."

The Industry Roundtable convened representatives from pharmaceutical companies, generic manufacturers, and global health partners to discuss how to accelerate the development, approval, and equitable access of LA HIV and TB therapies. Discussion focused on bridging persistent gaps between innovation and real-world impact, including earlier inclusion of key populations (adolescents, pregnant individuals, children), strategies for speeding parallel development and regulatory activities, and the critical role of generic partnerships, technology transfer, and shared-risk models.

Below is a condensed, topical recap of the discussion.

Q4M CAB is a PK-driven option designed to expand choice, with uptake determined by factors beyond dosing frequency.

Dosing intervals are largely determined by PK and may occupy a middle ground between Q2M and Q6M, though the optimal "sweet spot" will ultimately depend on real-world uptake and user preference. Importantly, dosing frequency is only one factor shaping adoption. Access, DDIs, tolerability, and delivery also matter, reinforcing the need for multiple options rather than a one-size-fits-all approach.

Pregnancy data are increasingly generated by allowing participants to remain on a study drug, with growing evidence but continued caution for newer LA agents.

There is increasing use of "continue-on-pregnancy" designs, allowing participants to re-consent and remain on a study drug, with emerging but still limited pregnancy data from ISL programs and more robust data expected from MK-8527 following the PURPOSE 1 model. CAB already has substantial pregnancy data (e.g., HPTN 084), while newer LA agents are taking a more cautious approach, often relying on extension studies and modeling to build the evidence base.

Adolescent inclusion is planned for BDQ, with efforts to start studies early, though not fully in parallel with adult Phase 3 trials.

Adolescent (12-18) studies are planned and intended to begin as early as feasible, although they may not run fully in parallel with adult Phase 3 trials. There is a continued push to minimize delays and accelerate access for adolescents.

INDUSTRY ROUNDTABLE (cont'd)

LEN neonatal prophylaxis is in early development, focused on defining formulation and dosing given unique infant pharmacology.

Active pediatric drug development is underway across programs, with a focus on optimizing formulation, route of administration, duration, and dosing frequency. A key challenge is the rapidly changing neonatal metabolism in the context of LA exposure, and while many efforts are currently in the preclinical and translational phases, human studies are planned, supported by extensive engagement with global experts to define optimal study designs.

CAB is currently limited to CAB/RPV for treatment, with interest in broader use but no confirmed expansion plans.

The current treatment indication for CAB is limited to CAB/RPV, which restricts flexibility for generics, clinical trials, and pediatric use. Despite strong stakeholder demand for alternative drug partners and combinations, discussions are ongoing and no expansion plans have been confirmed.

LA BDQ pediatric development will use modeling and staged inclusion, alongside a partnership-driven access strategy.

LA BDQ pediatric strategy builds on extensive oral BDQ data, including use in infants, and will use PK/PD modeling to define dosing for LA formulations in children. Development is expected to follow a staged approach, starting with adolescents (≥12 years, ≥30 kg) and expanding to younger populations. Simultaneously, operational challenges will need to be addressed, including identifying appropriate cohorts and managing injection tolerability and volume. Access will likely rely on a non-traditional, partnership-driven model (e.g., with Gates), with the goal of avoiding the slow uptake seen after oral BDQ approval in 2012.

Faster access to LA HIV products requires early generic engagement, strong tech transfer, regulatory alignment, and shared-risk, parallel development.

Accelerating access requires prioritizing a small number of high-impact products and engaging generic manufacturers before Phase 3 readout. Success also depends on selecting capable partners with LMIC reach, providing robust technology transfer to avoid delays, and addressing regulatory barriers, which remain a major bottleneck. A shared-risk model, beginning work roughly two years pre-approval, and parallel clinical, regulatory, and access workstreams (supported by originator bridge supply) have emerged as a proven approach.

Accelerating prevention timelines (e.g., pre-efficacy filing) is being explored but constrained by market uncertainty and risk tolerance.

A central constraint is the uncertain size of the PrEP market, which limits at-risk investment and delays early licensing decisions. While earlier filing and development decisions (prior to full efficacy data) are being explored, these approaches require greater risk tolerance and alignment across regulators, industry, and partners; the LEN example highlights the benefits of early licensing and parallelization.

While HIV treatment scaled through coordinated demand and clear economics, LA prevention requires new models for scale, incentives, and delivery.

ART scale-up has been a major success, driven by coordinated global strategy, clear demand, and aligned policy, whereas PrEP uptake has lagged due to uncertain demand and fragmented implementation. These differences reflect underlying economic challenges: treatment markets are more predictable, while prevention is harder to forecast. Also, LA products, which disrupt traditional scale and margin models, require new approaches to pricing, incentives, and delivery.

FOCUS GROUPS

Toward a collective agenda to advance the long-acting field.

Four 15-minute Focus Groups preceded the 2026 Annual LEAP Workshop and were intended to foster informative and provocative discussion of strategically selected topics, listed below. Highlights and recommendations from each focus group were presented. Attendance for these sessions was limited.

Focus Group 1
Managing HIV/HBV Coinfection

Focus Group 2
Bridging the Valley of Death

Focus Group 3
Ending HIV: Is LEN the Answer?

Focus Group 4
User Preferences Research

FOCUS GROUP 1

Rapporteur

Monica Gandhi

UCSF

Co-Chairs

Chloe Thio

JHU

Jordan Feld

University Health Network Rseearch

Managing HIV/HBV Coinfection

- Simplified HBV testing
- Integrated HBV management
- Resource-adapted guidelines

Baseline HBsAg testing is essential for defining a decision algorithm for switching treatment.

This focus group discussed what should be tested before switching off TDF-containing ART, how to monitor LA therapy, how to manage chronic HBV when there is a strong case for LA HIV therapy, and how to approach HBV vaccination amid variable testing capacity. HBsAg testing is the standard first-line screening test (low-cost) for active HBV infection globally.

Participants repeatedly contrasted resource-rich settings (where triple serologies and HBV DNA test after positive result may be possible) with LMIC scenarios, where HBsAg testing is commonly available but core antibody (anti-HBc), surface antibody (anti-HBs), and HBV DNA testing are often limited by cost and infrastructure.

"What do we do in LMIC settings for screening when you move to two-drug ART that doesn't cover hepatitis B or you use LA ART?"

HBV DNA testing is not scalable for routine use, although it may be appropriate in select contexts such as suspected occult HBV. Monitoring can instead rely on HBsAg and AST/ALT every 6 months, as supported by CARES trial results. Vaccination strategies should be adapted to reflect testing constraints, and CAB/RPV should be avoided unless concurrent HBV-active therapy is maintained.

Draft Recommendations

- Make HBsAg testing a non-negotiable baseline step before switching off TDF-containing ART
- Where feasible, test for anti-HBc and anti-HBs at baseline to identify prior HBV exposure without immunity and guide vaccination
- Use AST/ALT monitoring and repeat HBsAg as a practical surveillance tool while on LA therapy; escalate work-up if enzymes rise
- Recognize that HBV DNA testing is not scalable in many programs; prioritize simpler algorithms that can be implemented broadly.

FOCUS GROUP 2

Rapporteur

Keith Crawford

NIH DAIDS

Co-Chairs

Brian Kearney

Exavir Therapeutics

Paul Domanico

CHAI

Preclinical Discovery & Development to Industry Collaboration – Bridging the "Valley of Death"

- Clear value and alignment
- Multiple valleys of death
- Early planning for global access

"Industry has clear go and no-go criteria … academia could operate that way if it had more flexible sources of funding."

How should stakeholders align on value when developing LA products?

Value differs across stakeholders: industry may prioritize ROI and niche positioning, while others emphasize access, publications, or community acceptability. Early alignment is essential, beginning with clear conversations and development of a TPP and roadmap to guide engagement with regulators, investors, and partners.

What are the key "valleys of death" in development, and how can they be addressed?

Rather than a single barrier, multiple valleys exist, driven by uncertainty around maturity, risk, and regulatory pathways. LA formulations face added complexity from regulatory cycles and BE requirements. These challenges can be mitigated by generating strong data packages to clarify safety, PK, and regulatory strategy, and by leveraging modeling and pre-competitive platforms where possible and acceptable.

"Design potent products, good PK profiles that are safe, and these will be more appealing to industry."

Bridging the Valley of Death

This focus group discussed practical "how-to" issues for translating LA concepts into products: aligning a clear value proposition across stakeholders, navigating multiple "valleys of death" (financing, technical, regulatory, and strategic), and managing culture gaps between academia and industry. Participants repeatedly emphasized that success depends on early clarity about what is required (and why), disciplined communication related to timelines and deliverables, and deliberate inclusion of community and global-access considerations so products can ultimately be delivered at scale to the people who need it and are used by those people.

Valley	Where it Occurs	Core Problem	Key Drivers	Potential Solutions
Scientific/Translational	Discovery → early development	Promising compounds lack sufficient data to advance	Misalignment on readiness (academia vs industry); weak models (esp. pediatrics); limited understanding of industry needs	Design early for safety + PK; align expectations; early academia-industry conversations; define handoff points
Business	Development prioritization	Projects dropped due to lack of commercial viability	ROI constraints; dynamic industry priorities; delays; rigid funding structures; limited pediatric market	Understand industry incentives; define go/no-go criteria; flexible funding; earlier partnership planning
Regulatory	Preclinical → clinical → approval	Regulatory complexity slows or blocks progress	Nonstandard excipients (LA products); PK/PD uncertainties; BE challenges; evolving pathways	Use modeling (PK/PD); engage regulators early; develop alternative BE strategies; standardize approaches
Stakeholder/Access	Post-approval → implementation	Approved products not used or accessible	Cost; inequitable access (LMICs); lack of demand shaping; misaligned user preferences	Engage end users early; plan for access; incorporate end-user preferences; apply global access strategies

How do culture and communication gaps affect development?

Industry timelines are tightly linked to deliverables, and poor communication or missed expectations can have cascading consequences. Clear roles, defined expectations for outputs, and effective translation between stakeholders (often via intermediaries) are critical to maintaining momentum and avoiding delays.

How should community engagement and inclusion of vulnerable populations be approached?

Community input should begin early, even as drug developers balance the constraints of early-phase trials with the need for inclusive participation in high-burden settings. Engaging community advisory boards early, intentionally including diverse populations, and running trials in parallel can help accelerate access once early risks are addressed.

Why does a pediatric gap persist, and how can it be addressed?

Despite incentives, pediatric development often lags behind adult programs. Past successes have relied on early data sharing and parallel development. Moving forward, early collaboration on pediatric study plans (PSPs/PIPs), use of modeling approaches such as PBPK, and staged inclusion strategies can help accelerate availability for adolescents and children.

"Pediatrics is not a major market for most industries, but there are certain strategies that are improving the situation."

FOCUS GROUP 3

Rapporteur

Ethel Weld

JHU

Co-Chairs

Sinead Delany-Moretlwe

Wits Reproductive Health and HIV Institute

Angela Colbers

Radboud University Medical Center

Ending HIV: Is LEN the Answer?

- LA design/implementation uncertainty
- End-user needs vs feasibility gap
- Early engagement, structured tools

"Identifying people at risk and sustaining them on care and engaging them on prevention is challenging, and sustaining people on treatment who are positive is a known fraught and difficult prospect."

Can LEN prevent HIV infection?

Yes: efficacy has already been demonstrated at near-perfect levels. Ongoing work focuses on optimizing formulation and delivery.

Will people start and stay on LEN?

Uptake will depend on acceptability, including concerns about nodules and perceived risk, which can be addressed through counseling, peer influence, and improved formulations.

Can coverage reach those at highest risk?

Coverage remains challenging due to dynamic risk, mobility, and engagement gaps, requiring targeted outreach and more adaptive eligibility frameworks.

Can health systems deliver LEN at scale?

Scaling will likely depend on overcoming retention, tracking, and infrastructure challenges. Solutions may inlcude digital tools, decentralized care, and peer support.

Can LEN help end HIV transmission at the epidemic level?

Potentially: but only if it is integrated with ART, testing, and stronger health systems, combining prevention and treatment at scale.

"Cross-company collaborations [are] not only desirable but possible in this world."

This focus group discussed where uncertainty arises when designing and implementing LA/ER products. Key tensions include: i) variability in how LA is defined across modalities and indications; ii) the gap between ideal end-user desires and formulation/technology feasibility; and iii) real-world implementation constraints such as strict dosing windows, payer/insurance barriers, and LMIC access. Participants emphasized the need for earlier and more continuous engagement of end users (including adolescents and transgender women) and providers throughout development, and for structured frameworks (e.g., target product/regimen profiles) and iterative processes that translate preferences into feasible design decisions.

Theme	Emphasis	Practical Actions
Efficacy vs effectiveness	Efficacy is "a slam dunk" (near-100% in PURPOSE-1), but effectiveness depends on persistence, missed doses, real-world adherence	Study persistence and discontinuation; develop strategies for missed injections and re-engagement; monitor breakthrough infections
Resistance & breakthrough risk	Concern about capsid resistance emerging during prolonged sub-therapeutic exposure	Strengthen surveillance for breakthrough infections; define testing strategies; study transmissibility and fitness of resistant virus
Acceptability and tolerability	Injection site nodules can drive discontinuation in some populations (e.g., visible nodules in thin people)	Optimize formulations; provide patient counseling; tailor approaches for different populations
DDIs	Limited real-world data for LA formulations; complex interactions with opioids + psychiatric medications	Conduct clinical DDI studies (not just simulations); generate real-world evidence; prioritize high-risk populations
Population targeting and uptake	Many people at risk do not perceive themselves as such; PrEP eligibility is dynamic	Improve risk identification strategies; integrate with testing and outreach programs; tailor messaging
Population-level impact	Modeling suggests substantial but incomplete epidemic control; impact depends on coverage + mobility	Combine LEN with ART scale-up; prioritize high-incidence populations; incorporate mobility into models
Pregnancy and early life	Limited PK data but ongoing rollout in pregnancy; emerging neonatal strategies (e.g., microneedle patches)	Use PBPK modeling; collect real-world pregnancy data; accelerate neonatal prevention approaches
LMIC implementation	Retention, tracking, follow-up are major challenges; peer support critical	Deploy reminder systems; leverage peer networks (e.g., mentor mothers); decentralize delivery
Prevention vs system dependency	LEN reduces daily adherence burden but increases reliance on health systems	Invest in delivery infrastructure; integrate with existing HIV programs; ensure continuity of care

How can the LEAP UPC save time?

- Standardized templates for qualitative and quantitative user-preference instruments
- Centralized resource library synthesizing evidence across diseases, geographies, modalities
- Decision-support tools to match options to patient/provider circumstances
- Guidance on applying AI to streamline transcription, translation, rapid debriefing, analysis
- Marketing expertise + guidance for adapting commercial marketing methods to academic/public health contexts
- Approaches to determine when a project has sufficient input (sampling/coverage metrics; potentially borrowing epidemiologic principles)

FOCUS GROUP 4

Rapporteur

Karine Dubé
U Penn

Co-Chairs

José Bauermeister
U Penn

Rachel Bender Ignacio
Fred Hutch Cancer Center

User Preferences Research

- Dynamic, context-driven acceptability
- Design–feasibility gap
- Evolving user preferences

"We need to know which problem we're trying to solve, is it acceptability, access, or feasibility, and plan accordingly."

Defining LA and Aligning Expectations

A lack of consistent definitions for "long-acting" (e.g., weekly vs monthly vs 6-month dosing) shapes expectations and uptake. Standardizing terminology and aligning messaging across duration and modality are essential to reduce confusion and support adoption.

Understanding Layered and Evolving Preferences

User preferences operate across individual, social, and technical domains and evolve over time and context. Research and product design must account for this complexity by capturing multiple layers of influence and building flexibility into both products and delivery systems.

Bridging Ideal Design and Real-World Feasibility

There is a persistent tension between ideal user preferences (e.g., minimal burden) and practical constraints related to PK, safety, and manufacturing. Developers must define acceptable trade-offs early and incorporate feasibility into design decisions from the outset.

USER PREFERENCE RESEARCH

"I don't think we've ever resolved the conundrum of the tight versus elephant pants. But we agree that pants should be comfortable and forgiving, just like LA products."

Improving Research Approaches and Inclusion

Abstract research questions often yield limited insight; experiential methods such as prototypes, simulations, and early engagement with user advisory boards are more informative. At the same time, gaps in data - particularly for adolescents and other underrepresented groups - highlight the need for broader inclusion and earlier generation of relevant PK and safety data.

Managing Delivery Constraints and System Realities

While LA products reduce daily burden, they introduce new constraints such as strict dosing windows and re-initiation challenges. Programs must incorporate flexibility, backup options, and patient-centered delivery approaches. Cost remains a dominant factor in decision-making, requiring affordability and access strategies to be integrated early in development.

Addressing Pipeline, Measurement, and Implementation Gaps

Uncertainty often emerges between late-stage trials and real-world implementation, underscoring the need to integrate implementation science earlier and test delivery models in parallel with efficacy. Standardized tools and shared frameworks can improve comparability of preference data across studies.

Expanding the Definition of End Users

What do end-users really want?

- Flexible, infrequent dosing;
- Minimal clinic burden
- No/limited side effects
- Affordability
- Simple, invisible products

Many key populations - and even stakeholders such as providers, payers, and implementers - are often excluded from early design decisions. Expanding the definition of end users is critical to ensure products are usable, scalable, and relevant in real-world settings.

FINAL DISCUSSION

Charles Flexner

Principal Investigator of LEAP

"The thing that surprised me the most about this meeting is we, at the end of the planning, I felt we were far too focused on HIV and kind of left tuberculosis and viral hepatitis in the dust … and they managed to claw themselves back to the top."

Scientific progress has outpaced implementation readiness

- LA prevention + treatment options now highly effective
- Tools alone will not change the epidemic trajectory
- Success depends on uptake, persistence, + equitable access
- Integration into existing systems is essential for sustainability
- Delivery systems + implementation strategies remain underdeveloped

Coordination across stakeholders is critical

- Governments, donors, industry, + communities must align early
- High-burden + underserved populations must be prioritized
- Global access strategies must be embedded from the outset
- Community engagement is essential to ensure relevance + uptake
- Market shaping, financing, + delivery must be synchronized
- Fragmented approaches risk slowing scale-up + reducing impact

Speed matters – but pace must be strategic

- There is a limited window to shape markets, pricing, + supply
- Early action in high-incidence settings can maximize impact
- Delays risk widening disparities and slowing progress toward epidemic control

User-centered approaches are foundational

- Acceptability, preferences, + real-world constraints shape uptake
- Products must align with lived experiences + system realities
- Behavioral + social factors are as important as biomedical efficacy

Group Discussion

Question	Answer
Should implementation science be R01-driven?	Yes, NIH is encouraging investigator-driven proposals without fixed funding targets.
Who is the "user?"	Not just patients: also clinicians, policymakers, and system-level decision-makers.
What's missing in current IS efforts?	Greater clarity, rigor, and differentiation from existing work.
How are LEN lessons being shared?	Iteratively – learning in real time and adapting during rollout.
Does implementation science slow access?	It shouldn't: when done well, it accelerates scale-up.
Why aren't effective products reaching people?	Delivery and uptake systems, not the products, are the gap.
Can implementation and learning happen together?	Yes, through rapid, iterative approaches during rollout.

Key Takeaways

- Implementation, not innovation, is now the primary bottleneck
- LA tools require strong health systems + coordinated delivery
- Equity and user preferences must be incorporated early
- Speed and alignment are essential to maximize impact
- System-level solutions are required for sustained epidemic control

leap

Long-Acting/Extended Release
Antiretroviral Research Resource Program