Global Research Collaborationfor an HIV CURE: The way forward

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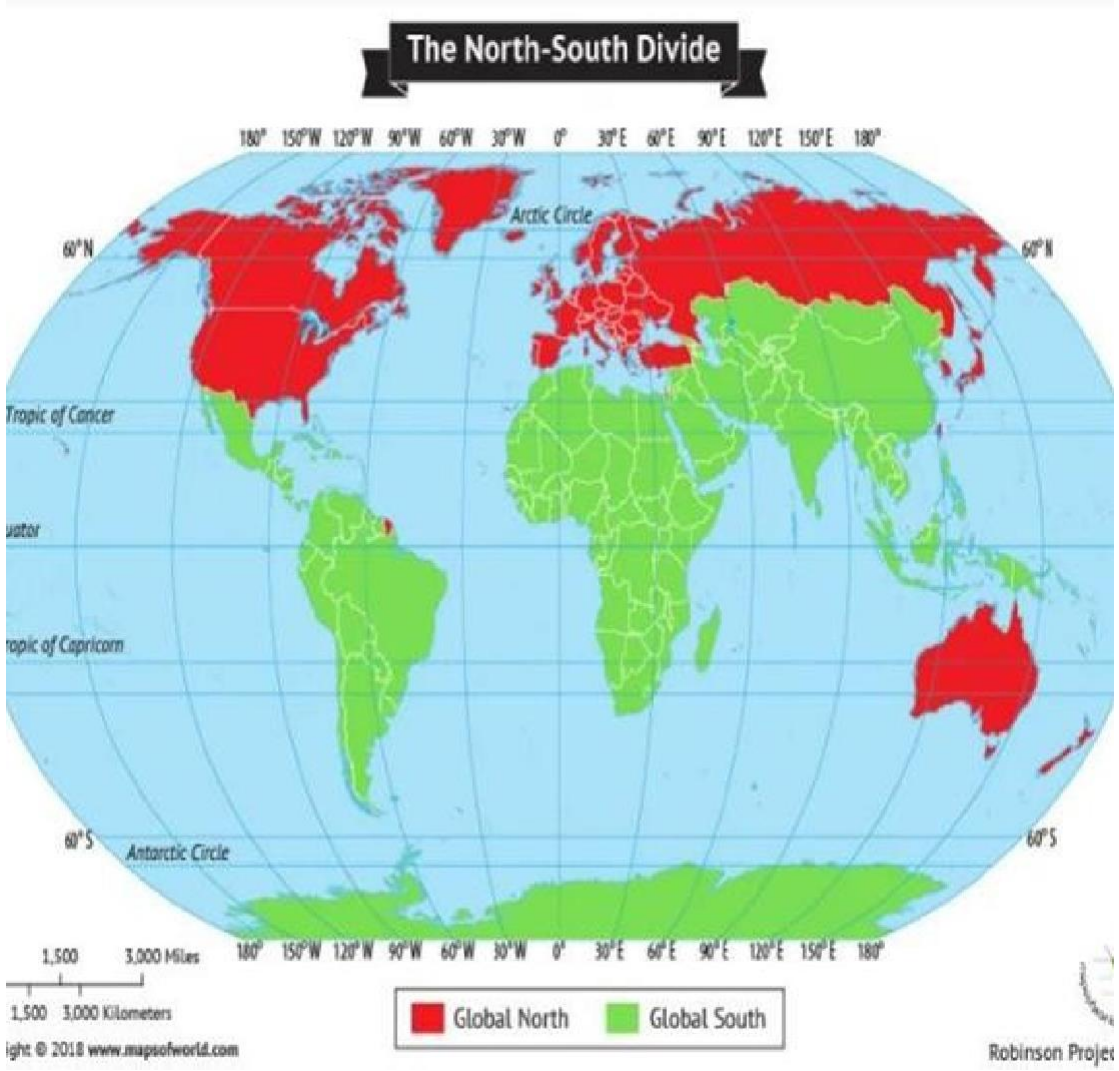
IAS Webinar – Research Priorities for an HIV CURE:
IAS Global Scientific Strategy
19th May 2022

Global North vs Global South

- Socio-economic status
- Disease prevalence
- Healthcare infrastructure
- National dedicated Research & Development support for Health
- Presence of major market players- Pharma and Funders for R&D
- HICs have supported LMICs to control the HIV epidemic this far



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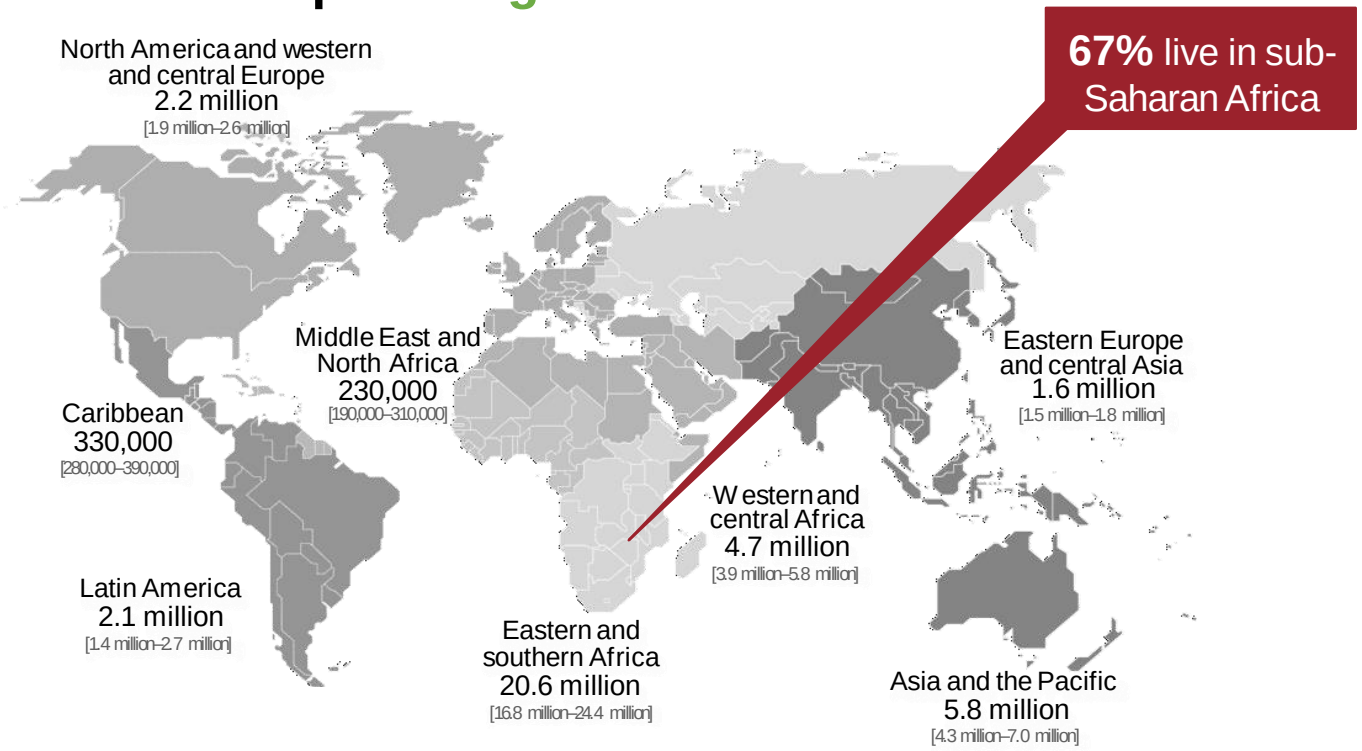
People estimated to be living with HIV

In millions

Total: **37.9 million**

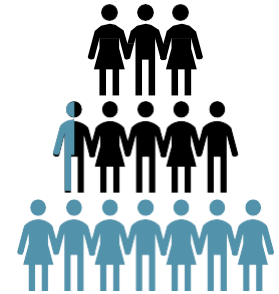
34 Years after ART was developed, HIV/AIDS remains a leading cause of death

38M
People living with HIV worldwide



Global rates are projected to remain steady through 2030[1]

47% of people living with HIV **(17.8M)** are unable to access effective antiretroviral therapy (ART)



… **11.6M** live in sub-Saharan Africa

Hard-fought progress is threatened by stagnant funding and donor fatigue

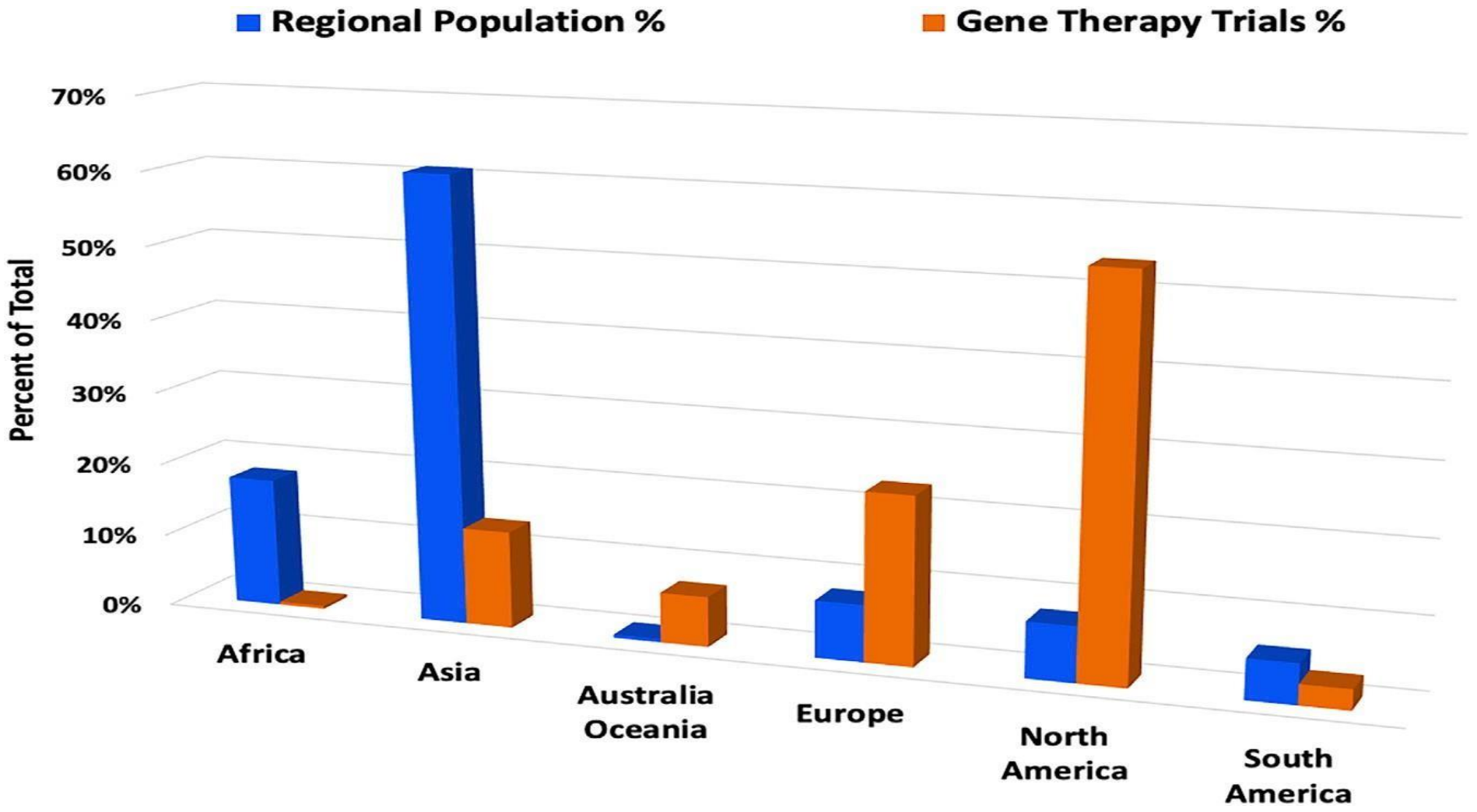
A cure could benefit 38M people living with HIV today

1. Goalkeepers Report, HIV. Map source: UNAIDS 2021 epidemiological estimates.

HIV CURE Prospects present a promising new HIV management paradigm

✓ **Curative**	Acutely focused and locally targeted on the biology of the disease
✓ **One-time**	Administered in just a single dose
✓ **Durable**	Sustained, life-long benefits
✓ **Potent**	Transformative efficacy improvements over standard of care
✓ **Safe**	Improved safety profile, avoiding adverse events and challenging medical procedures
✓ **Valuable**	High impact on quantity and quality of life, with great clinical, economic, and social value

Global South is Currently Excluded from Gene Therapy Development



Kenneth Cornetta et al 2022

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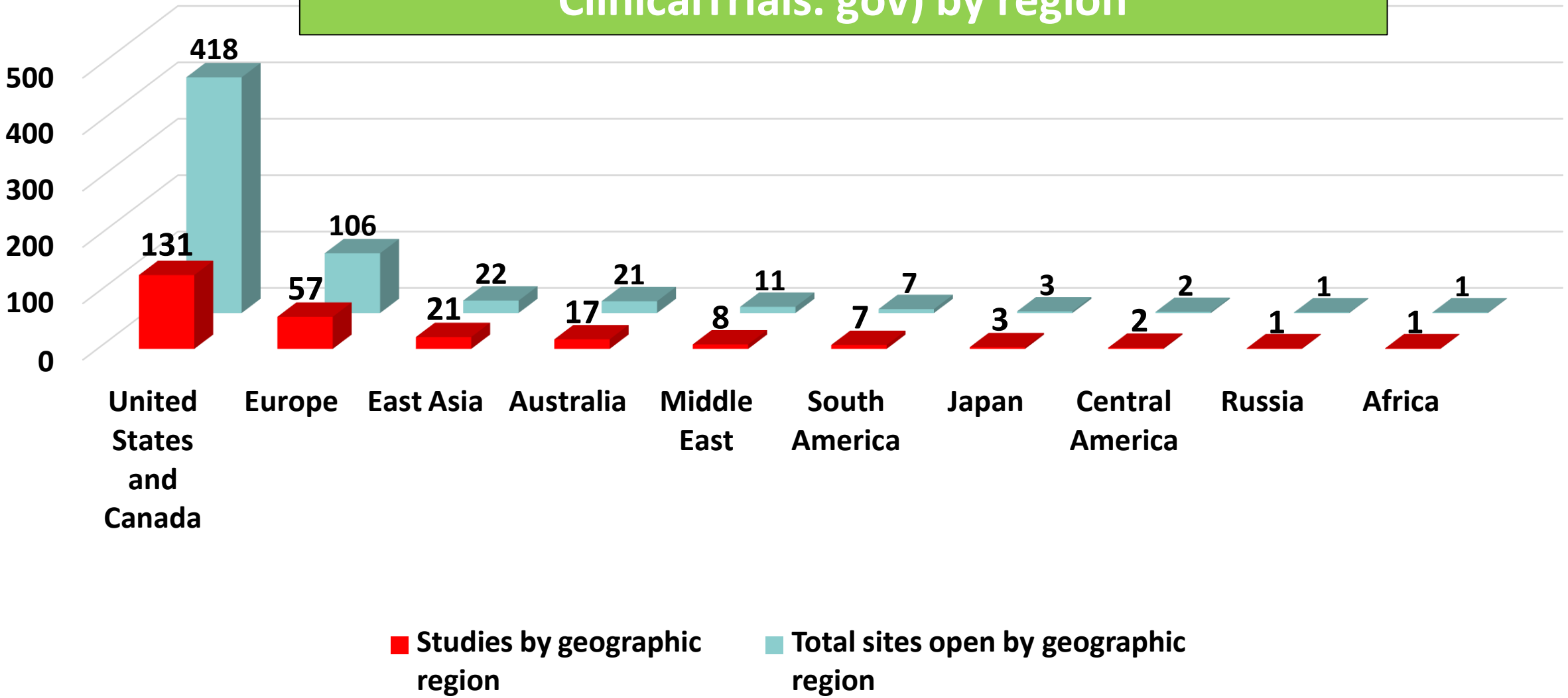
Gene Therapy Trials (accessed November 22, 2021 in ClinicalTrials. gov) by region



Kenneth Cornetta et al, 2022

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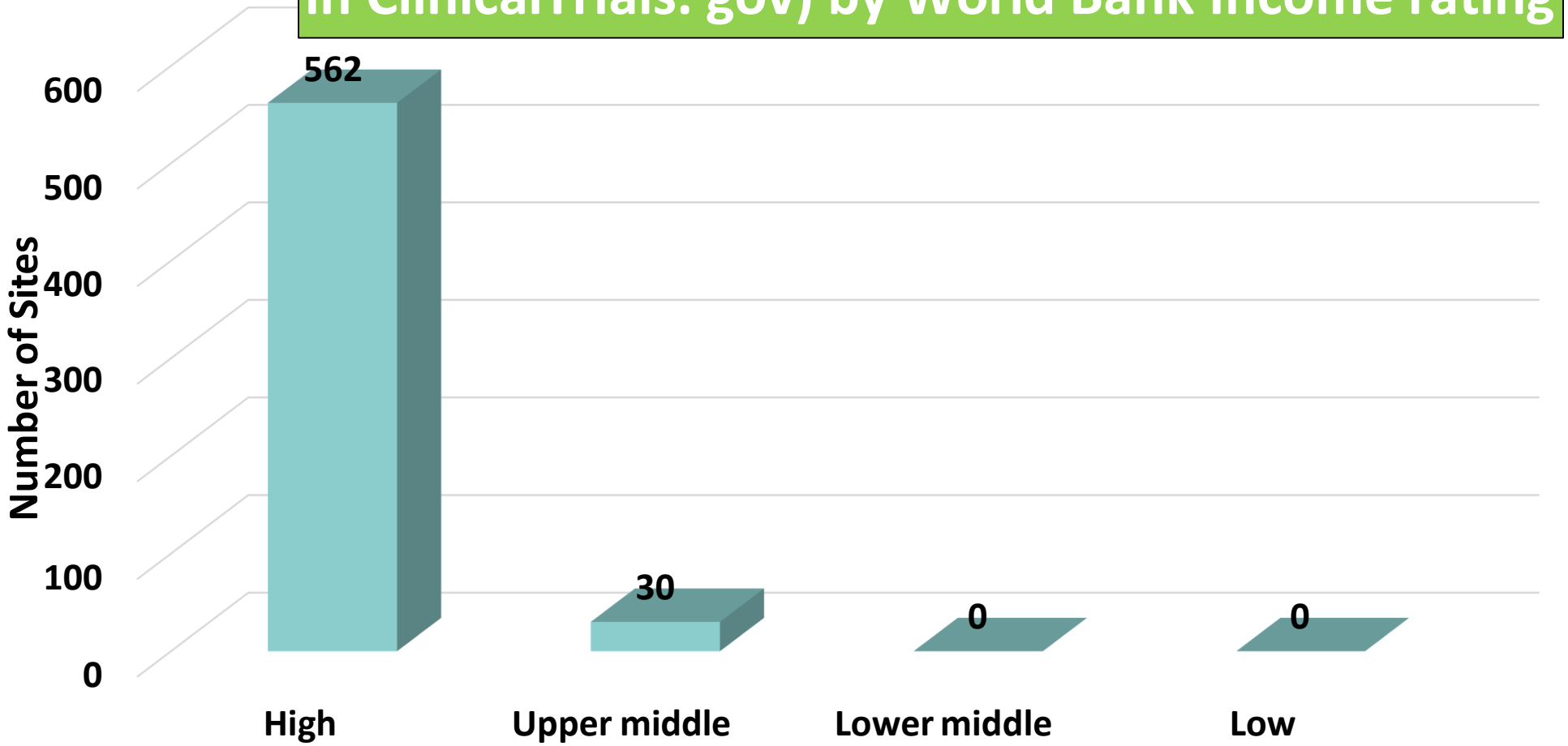
GeneTherapy Trials (accessed November 22,2021 in ClinicalTrials. gov) by World Bank Income rating



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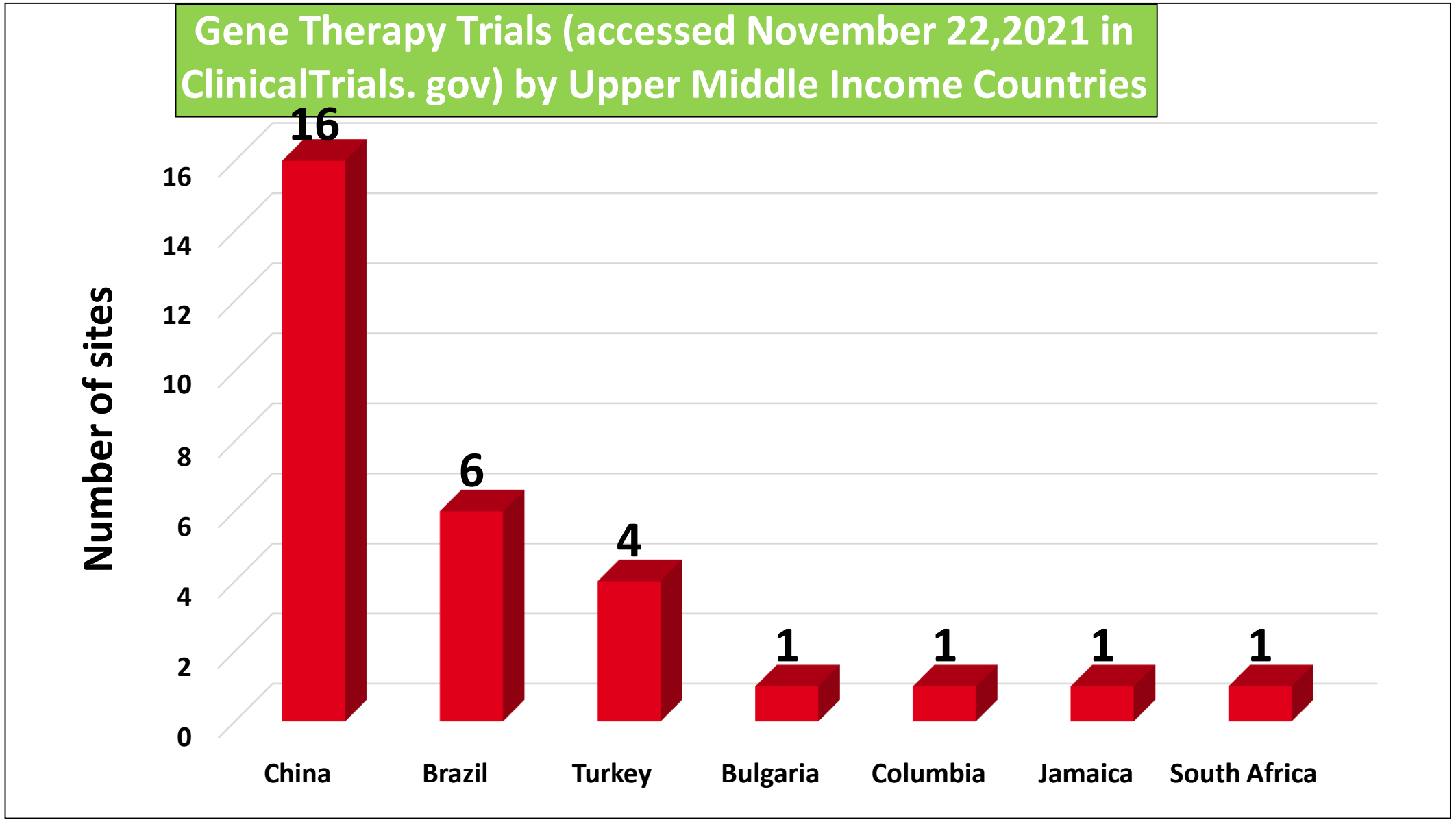
Gene Therapy Trials (accessed November 22,2021 in ClinicalTrials. gov) by Upper Middle Income Countries



WHAT IS THE WAY FORWARD ?

The need to form partnerships

Basic research | Applied research | Product development | Validation and approval | Launch and ecosystem | LMIC scaled impact

Existing

Design	Develop approaches for sustained viral suppression	$110M HIV Frontiers 1/19
Durability (Targeting & Editing)	Accelerate gene therapy for HIV	NIH
	Develop engineered B cells for HIV	Bill & Melinda Gates foundation
Detection	Discover HIV reservoir biomarkers	$100M 6/19

New Funding Announced: $200M

PUBLIC HEALTH

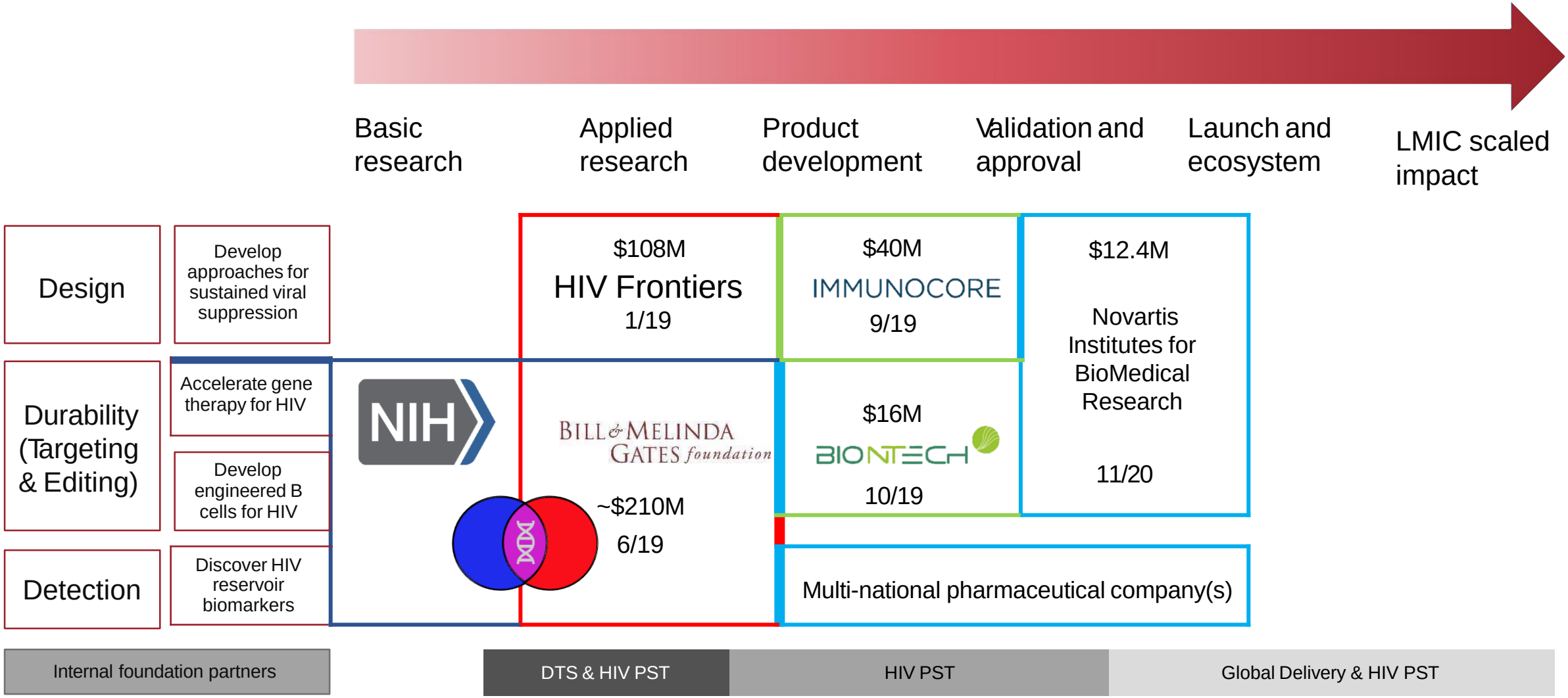
Gates and NIH join forces on HIV and sickle cell diseases

A unique marriage aims to speed development of simple DNA-based cures

By **Jon Cohen** and **Jocelyn Kaiser** 11/19

Internal foundation partners | DTS & HIV PST | HIV PST | Global Delivery & HIV PST

The need to form partnerships



The HIV Frontiers program is laying the groundwork to reach a bold new goal

THE GOAL: In the next 10-15 years, achieve effective, long-lasting, and safe "single-shot" cures for HIV (i.e., durable ART-free suppression of viremia) that could ultimately be scaled and implemented globally, including in under-resourced parts of the world

Two research platforms have emerged as frontrunners:

gene therapy and therapeutic vaccination

Either platform could lead to new treatments with a target product profile including:

- "Single-shot" (administered as an outpatient in a single encounter)
- Lowers the viral load to <50 copies/ml without ART, resulting in remission of disease and prevention of transmission
- Prevents or controls reinfection of the treated individual
- Safe
- Affordable: amortized cost including monitoring at $1-2k in sub-Saharan Africa, $50-100k in US/Europe, $25-50k in the rest of the world[1]

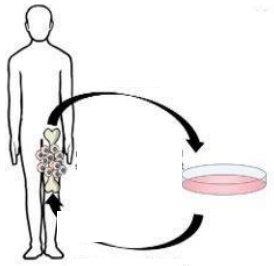
1. Phillips et al., J Inf Dis 2016

The research platforms may provide “CURES” - not only for Hiv but FOR other diseases AS WELL

PLATFORM A : GENE THERAPY

Targeting and editing of long-lived cells *in vivo*, e.g., using viral or nonviral vectors to modify hematopoietic stem cells (HSCs), T stem central memory (TSCM) cells, and memory B cells

Ex vivo gene therapy can now cure sickle cell disease, but the technology is not accessible



Can the technology be adapted to develop an affordable “*in vivo*” approach to gene therapy to combat HIV?

Platform A will build on current *ex vivo* gene therapy approaches for sickle cell disease to develop single shot treatments that result in a “cure” for both HIV and sickle cell disease

PLATFORM B: THERAPEUTIC VACCINATION

Creation of a therapeutic vaccine against HIV by harnessing the “vaccinal effect” to generate durable T cell responses against HIV and/or by using an mRNA vaccine to induce T cell responses against highly-networked epitopes

A fraction (<1%) of people infected with HIV suppress virus in the bloodstream without ART. Could a treatment be developed that converts more people into this type of “elite virus controller”?

Could a vaccine given after a person is infected trigger an immune response that has a long-lasting, suppressive effect against HIV?

Platform B will leverage new technology in mRNA vaccines - developed for SARS-CoV-2, the virus that causes COVID-19 - to trigger a long-lasting immune response to suppress HIV in the body

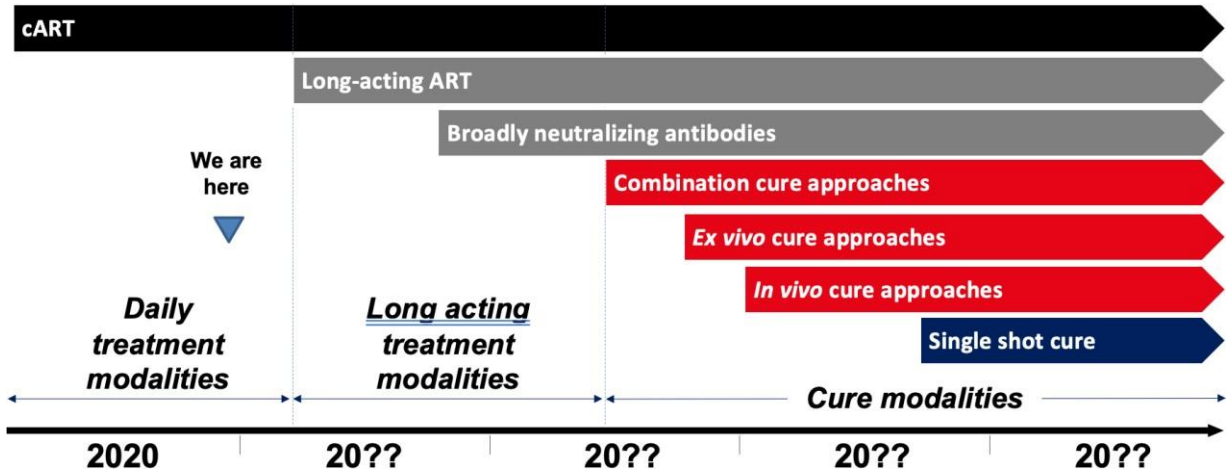
Bringing curative interventions into sub-Saharan Africa

Sunnylands Summit: The Path Towards Ending HIV February, 2019

Objective:
To consider what it will take to develop and ensure the widest possible access to a cure for HIV, specifically in sub-Saharan Africa

Goals:
- To align on a Target Product Profile for an HIV cure
- To agree what it will take to ensure that a cure with this profile is **widely accessible** to the **largest number** of people in sub-Saharan Africa

Multi-stakeholder Consensus on the Target Product Profile for an HIV Cure



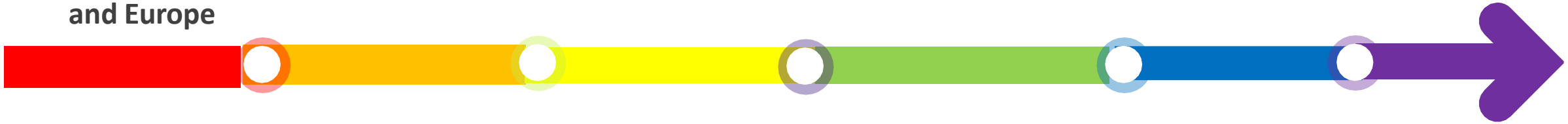
Lewin et al., Lancet HIV, 2020

HIV Cure Africa Acceleration Partnership (HCAAP): The case for an HIV cure and how to get there

Dybul et al., Lancet HIV, 2020

Gene Therapy Development: How Long Before Access in LMICs ?

2017
Approval in US and Europe



2024
Goal to have first Phase 1 trials initiated

Global Gene Therapy Initiative (GGTI) Working Group was formed in 2020 to work towards enabling access and implementation of gene therapies as curative medicines in LMICs initially focusing on HIV and SCD.

GGTI works by advocating for appropriate research, clinical development, capacity-building, training, community adoption, regulatory pathway approval and sustainability

GGTI
GLOBAL GENE THERAPY INITIATIVE

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Cofounders of GGTI

Prof Jennifer Adair, FredHutch, Seattle

Dr Cissy Kityo Mutuluuza, Joint Clinical Research Centre, Uganda


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Port Sudan
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Omdurman
Massawa
Medina
Riyadh
Jidda
PERSIAN GULF
RUB AL KHALI
Gondar
Djibouti
Hargeisa

Emphasis: patients and advocates at the table

Michael Louella
Community Engagement Project Manager defeatHIV Community Advisory Board, Co-Chair, DARE CAB

Olabimpe Olayiwola
Research Assistant, NIH NHLBI Grant Recipient, Case Western Reserve University

Moses Supercharger
Chair, Joint Clinical Research Centre's Community Advisory Board

Evelyn Harlow Mwesigwa
Program Officer, Uganda MoH; Director, Sickle Cell Network Uganda

Jeff Sheehy
Consultant
Former: CIRM Executive Board
District 8 Representative, San Francisco

Lynda Dee
Attorney
Founder: AIDS Action Baltimore

HOW ARE WE DOING IT ?

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Clinical Readiness & Implementation

Training & Capacity Building

Regulation & Policy

Infrastructure for Commercialization

New Technology Development

Sustainability

Community Outreach & Education

Adoption

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Collaboration is integral to this project's success

Bolster transformative clinical gene therapy research,

accelerating the development of curative therapies for SCD, β-Thalassemia, HIV, and other debilitating conditions.

GGTI Access to Gene Therapy Products for HIV and SCD

GGTI
GLOBAL GENE THERAPY INITIATIVE

NIH National Heart, Lung, and Blood Institute

CaringCross

Multispecific anti-HIV duoCAR-T cells display broad in vitro antiviral activity and potent in vivo elimination of HIV-infected cells in a humanized mouse model

KIM ANTHONY-GONDA, ARIOLA BARDHI, ALEX RAY, NINA FLERIN, MENGYAN LI, WEIZAO CHEN, CHRISTINA OCHSENBAUER, JOHN C. KAPPES, WINFRIED KRUEGER, [...]
BORO DROPULIĆ +7 authors Authors Info & Affiliations

SCIENCE TRANSLATIONAL MEDICINE · 7 Aug 2019 · Vol 11, Issue 504 · DOI: 10.1126/scitranslmed.aav5685

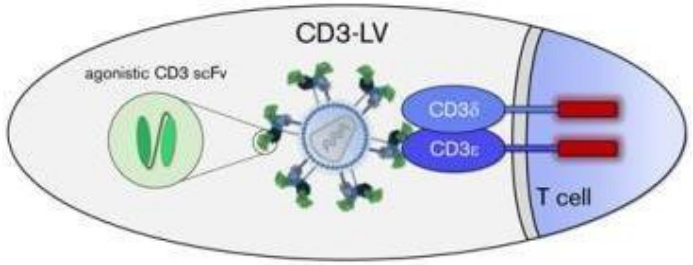
Article | Open Access | Published: 02 October 2019

Development of a forward-oriented therapeutic lentiviral vector for hemoglobin disorders

Naoya Uchida, Matthew M. Hsieh, Lydia Raines, Juan J. Haro-Mora, Selami Demirci, Aylin C. Bonifacino, Allen E. Krouse, Mark E. Metzger, Robert E. Donahue & John F. Tisdale

Nature Communications **10**, Article number: 4479 (2019) | Cite this article

Inserm



Frank, A.M. et al. *Blood Advances*, 2020

A viral vector which delivers T cell gene therapies in peripheral blood.

Licensed to Sana Biotechnology

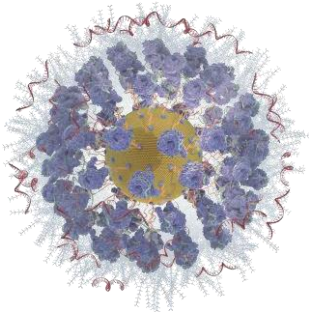
New Technology Development

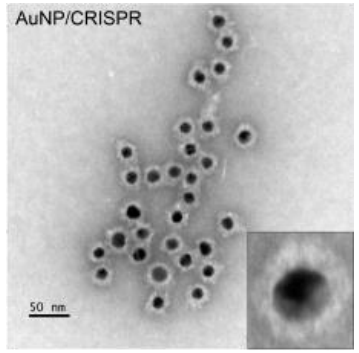
Sustainability

GGTI GLOBAL GENE THERAPY INITIATIVE

FRED HUTCH CURES START HERE®

A nanoparticle to deliver CRISPR gene edits to blood stem cells in the bone marrow.





Shahbazi, R. et al. *Nature Materials*, 2019

Founded a new biotech company in 2021 (Auraeda, Inc.)

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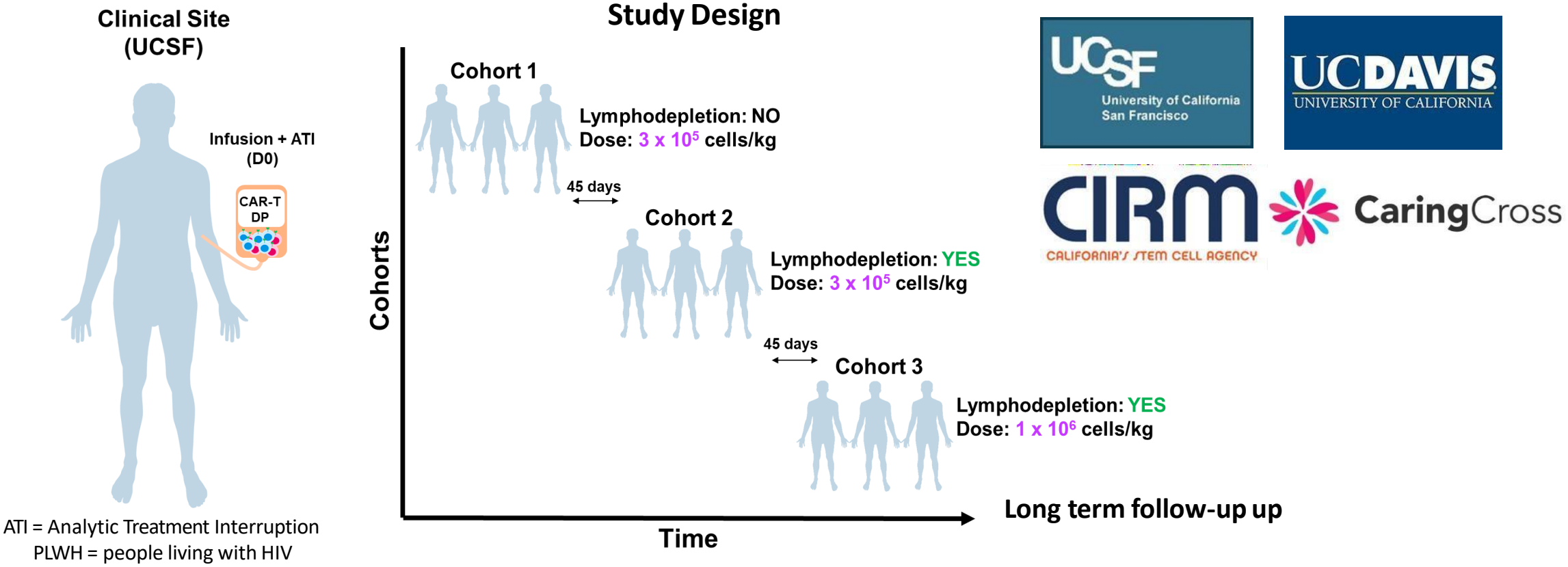
Collaboration is integral to this project's success

Enable access to advanced therapies in LMIC, disrupting the current philosophy that access to advanced therapies in LMIC is a decade away from possible

Clinical trial design: Translating anti-HIV duoCAR-T cell therapy to PWH

- First-in-human phase I/II study to evaluate the **safety** and **efficacy** of duoCAR-T cell therapy in ART-suppressed PLWH (NCT04648046, PI: Dr. Steven Deeks)

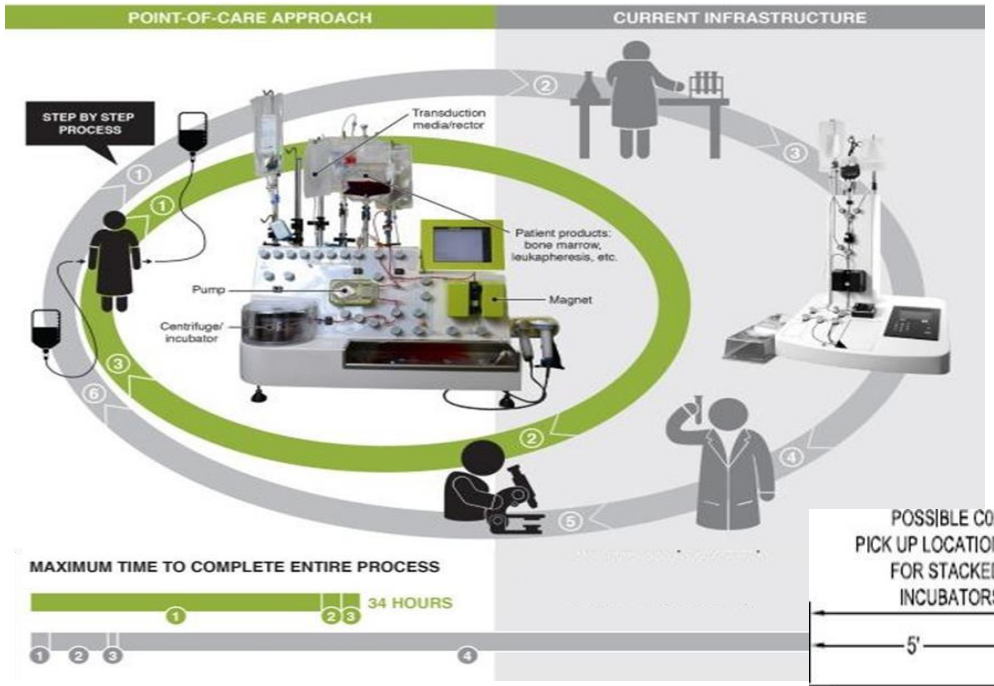


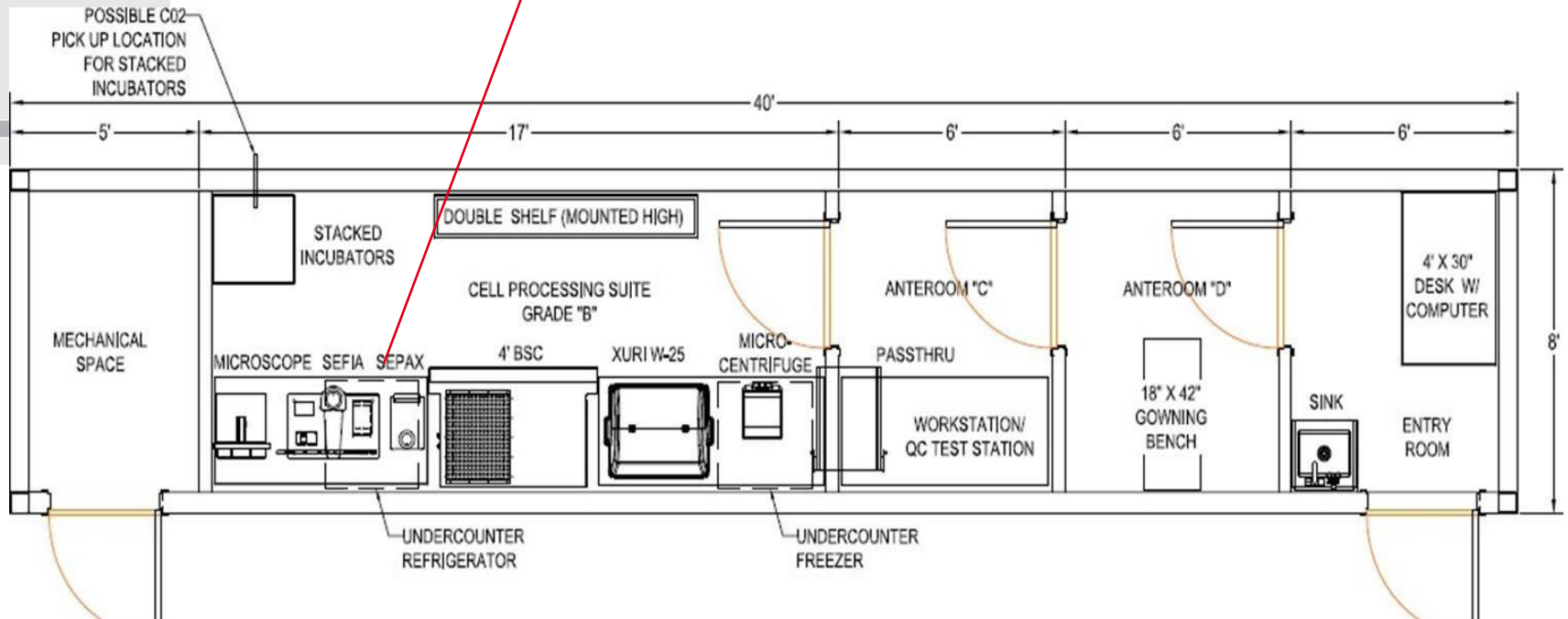
ATI = Analytic Treatment Interruption
PLWH = people living with HIV

Collaboration is integral to this project's success

Refine manufacturing processes involved in the production of advanced therapies, iterating over technology and driving down costs across the field

Production and Manufacturing: Place-of-Care





Decentralized Manufacturing
Container Facility
cGMP Cell Therapy Processing Suite

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Collaboration is integral to this project's success

Develop infrastructure, institutional voids, and ecosystems, paving the path for large-scale international collaborations and similar projects

Funding Success: Training the 1st Generation of Ugandan Gene Therapists

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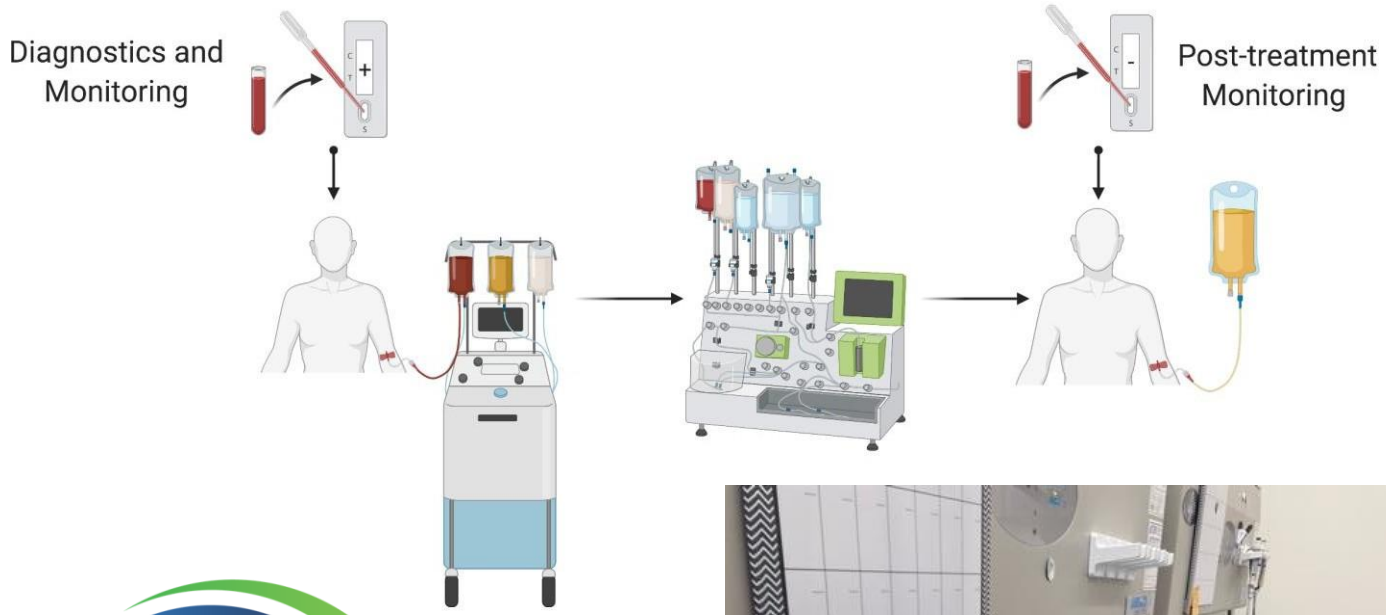
Clinical Readiness & Implementation

Training & Capacity-building



CaringCross
CREATING ACCESS TO CURES

GGTI
GLOBAL GENE THERAPY INITIATIVE

BILL & MELINDA GATES foundation

Dr. Lois Bayigga, JCRC as she learns the process of blood stem cell transduction in the Adair Lab.

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FDA

Regulation & Policy

Infrastructure for Commercialization

GGTI
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EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

World Health Organization