

## Teropavimab and Zinlirvimab

## Developer(s)

Gilead Sciences Inc.

<https://www.gilead.com/>

United States



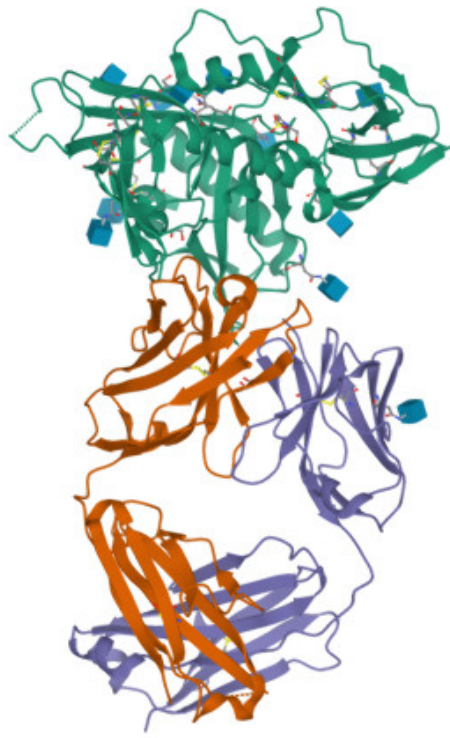
Gilead Sciences, Inc. is a multinational biopharmaceutical company that develops and manufactures innovative medicines for life-threatening diseases, including anti-viral therapeutics for HIV/AIDS, Hepatitis B, Hepatitis C and Covid-19. Headquartered in Foster City, California, Gilead was originally founded in 1987 and is currently listed on both the S&P 500 and the NASDAQ Biotechnology Index.

## Drug structure



10-1074 Fragment Antigen Binding Region

<http://doi.org/10.2210/pdb4FQ2/pdb>



3BNC117 in Complex with HIV-1 Envelope Glycoprotein GP120

<http://doi.org/10.2210/pdb4JPV/pdb>

# Drug information

## Associated long-acting platforms

Broadly neutralising monoclonal antibody

## Administration route

Intravenous, Subcutaneous

## Therapeutic area(s)

HIV

## Use case(s)

Treatment

## Use of drug

### Ease of administration

Administered by a nurse

Administered by a specialty health worker

### User acceptance

Not provided

## Dosage

### Available dose and strength

Not provided

### Frequency of administration

Not provided

### Maximum dose

Not provided

### Recommended dosing regimen

Not provided

### Additional comments

Not provided

### Dosage link(s)

Not provided

## Drug information

### Drug's link(s)

Not provided

### Generic name

Teropavimab and Zinlirvimab

### Brand name

Not provided

### Compound type

Biotherapeutic

### Summary

Teropavimab (GS-5423; 3BNC117-LS) and zinlirvimab (GS-2872; 10-1074-LS) are a long-acting combination of the broadly neutralising antibodies (bNAbs) 3BNC117 and 10-1074 currently in clinical development for the treatment of HIV-1 infection. The crystallisable fragment domains of both teropavimab and zinlirvimab contain two directed amino acid substitutions termed “LS” (residues N434S and M428L) resulting in long-acting bNAbs with improved efficacy and half-life. Teropavimab functions by targeting the CD4-binding site of the HIV-1 envelope glycoprotein gp120, while zinlirvimab targets the HIV-1 envelope V3 glycan supersite. These interactions mechanistically disrupt the initial entry of HIV-1 virions into the host CD4+ cell, which is an essential step in HIV infection.

### Approval status

Unknown

### Regulatory authorities

Unknown

**Delivery device(s)**

No delivery device



## **Scale-up and manufacturing prospects**

## **Scale-up prospects**

Production scale up and manufacturing requirements for therapeutic monoclonal antibody products are primarily related to formulation stability, pharmacokinetic suitability and maintenance of quality attributes. The industrial manufacture of high-concentration broadly neutralising antibody (bNAb) formulations for parenteral administration can introduce production challenges regarding aggregation propensity and formulation viscosity. Exploratory process optimisations such as bNAb co-formulation and multi-specific antibody composition have the potential to reduce overall manufacturing costs.

## **Tentative equipment list for manufacturing**

Industrial bioreactor vessel with a production volume capacity of between 5-25kL. Continuous disc stack centrifuges for bioreactor harvesting with subsequent membrane and depth filtration for supernatant clarification. Protein A chromatography or other suitable affinity capture apparatus followed by two chromatographic polishing steps such as cation- and anion-exchange. Ultrafiltration membrane system to concentrate and formulate the final product.

## **Manufacturing**

Biological activity of bNAbs is highly dependant on their chemical, conformational and structural stability. Reduced glycosylation of bNAbs during manufacture and chemical degradation processes such as deamidation can result in increased aggregation, loss of activity and diminished solubility. Degradation may occur at any stage throughout the manufacturing process including bioprocessing, purification, product delivery and storage. Considerations to increase formulation stability may include pH optimisation and the addition of suitable excipients (e.g. surfactants, stabilizers and buffers).

## **Specific analytical instrument required for characterization of formulation**

Formulation characterisation for single-entity bNAb production include capillary isoelectric focusing and ion-exchange chromatography for identification of post-translational modifications, subvisible particle quantitation, thermal DSC, size-exclusion chromatography for measurement of concentration dependent aggregation

rates and capillary electrophoresis for antibody fragmentation and clipping. Co-formulated bNAbs in mixture may utilise SE-HPLC, capillary electrophoresis sodium dodecyl sulphate, dynamic light scattering, microflow imaging and multi-attribute method mass spectrometry analysis.

# Clinical trials

**YCO-0946**

## Identifier

NCT03254277

## Link

<https://clinicaltrials.gov/study/NCT03254277>

## Phase

Phase I

## Status

Completed

## Sponsor

Rockefeller University

## More details

Not provided

## Purpose

Evaluate the safety, tolerability and pharmacokinetics of a single administration of 3BNC117-LS in HIV-uninfected and HIV-1 infected participants.

## Interventions

### Intervention 1

Drug: 3BNC117-LS

## **Intervention 2**

Drug: Placebo

## **Countries**

United States of America

## **Sites / Institutions**

Not provided

## **Trials dates**

### **Anticipated Start Date**

Not provided

### **Actual Start Date**

2017-09-13

### **Anticipated Date of Last Follow-up**

Not provided

### **Estimated Primary Completion Date**

Not provided

### **Estimated Completion Date**

Not provided

### **Actual Primary Completion Date**

2020-12-31

### **Actual Completion Date**

2020-12-31

## **Studied populations**

### **Age Cohort**

- Adults
- Older Adults

### **Genders**

- All

### **Accepts pregnant individuals**

No

### **Accepts lactating individuals**

No

### **Accepts healthy individuals**

Yes

### **Comments about the studied populations**

Study participants placed into groups of HIV-infected and HIV-uninfected individuals. Inclusion criteria for HIV positive groups: Males and females aged 18-65 who have documented HIV-1 infection with CD4+ T cell counts of  $> 300$  cells/ $\mu$ L and currently receiving antiretroviral therapy (ART) with  $< 20$  copies/ml plasma HIV-1 RNA or not receiving ART for a minimum of 8 weeks with  $< 100,000$  copies/ml plasma HIV-1 RNA. Inclusion criteria for HIV negative groups: Males and females aged 18-65 who have low risk for HIV infection and agree to implement two methods of effective contraception if sexually active.

### **Health status**

Positive to : HIV

Considered at low risk of : HIV

Negative to : HBV, HCV

### **Study type**

Interventional (clinical trial)

### **Enrollment**

## **Allocation**

Non-randomized

## **Intervention model**

Parallel Assignment

## **Intervention model description**

Not provided

## **Masking**

Open label

## **Masking description**

None (open label)

## **Frequency of administration**

Other : "Single dose "

## **Studied LA-formulation(s)**

Injectable

## **Studied route(s) of administration**

Subcutaneous

Intravenous

## **Use case**

Treatment

## **Key resources**

Not provided

**A5364**

**Identifier**

NCT05079451

**Link**

<https://clinicaltrials.gov/study/NCT05079451>

**Phase**

Phase I

**Status**

Withdrawn

**Sponsor**

National Institute of Allergy and Infectious Diseases (NIAID)

**More details**

Protocol Withdrawal.

**Purpose**

Evaluate the ability and safety of the combined bNAbs 10-1074-LS and 3BNC117-LS to prevent viral rebound during an analytical antiretroviral treatment interruption.

**Interventions**

**Intervention 1**

Drug: 3BNC117-LS

**Intervention 2**

Drug: 10-1074-LS



## Countries

United States of America

## Sites / Institutions

Not provided

## Trials dates

### Anticipated Start Date

2024-01-01

### Actual Start Date

Not provided

### Anticipated Date of Last Follow-up

Not provided

### Estimated Primary Completion Date

2024-01-15

### Estimated Completion Date

2024-02-15

### Actual Primary Completion Date

Not provided

### Actual Completion Date

Not provided

## Studied populations

### Age Cohort

- Adults
- Older Adults

### Genders

All

**Accepts pregnant individuals**

No

**Accepts lactating individuals**

No

**Accepts healthy individuals**

No

**Comments about the studied populations**

Individuals aged 18-70 years with confirmed HIV-1 infection who have received a stable suppressive antiretroviral regimen (< 50 copies/ml plasma HIV-1 RNA levels) for a minimum of 48 weeks prior to enrolment with no reported continuous interruption of a treatment greater than 7 days. CD4+ T cell counts of > 450 cells/μL with a nadir of ≥200 cells μL is required for trial eligibility.

**Health status**

Positive to : HIV

Negative to : HBV, HCV, TB

**Study type**

Interventional (clinical trial)

**Enrollment**

Not provided

**Allocation**

Not provided

**Intervention model**

Single group assignment

## **Intervention model description**

Not provided

## **Masking**

Open label

## **Masking description**

None (Open Label)

## **Frequency of administration**

Other : "IV infusion of 30-60 mins duration with dosage calculated based on participants body weight "

## **Studied LA-formulation(s)**

Injectable

## **Studied route(s) of administration**

Intravenous

## **Use case**

Treatment

## **Key resources**

Not provided

# RIO

## Identifier

NCT04319367

## Link

<https://clinicaltrials.gov/study/NCT04319367>

## Phase

Phase II

## Status

Recruiting

## Sponsor

Imperial College London

## More details

Not provided

## Purpose

Evaluate whether the combination of 3BNC117-LS and 10-1074-LS can prevent HIV viral rebound after discontinuing early-initiation antiretroviral treatment in adults during primary HIV infection.

## Interventions

### Intervention 1

Drug: Investigational Medicinal Product (3BNC117-LS and 10-1074-LS)

### Intervention 2

Drug: Placebo

## Countries

United Kingdom

Denmark

## Sites / Institutions

Not provided

## Trials dates

### Anticipated Start Date

Not provided

### Actual Start Date

2021-05-17

### Anticipated Date of Last Follow-up

Not provided

### Estimated Primary Completion Date

2027-07-31

### Estimated Completion Date

2027-07-31

### Actual Primary Completion Date

Not provided

### Actual Completion Date

Not provided

## Studied populations

### Age Cohort

- Adults

## **Genders**

- All

## **Accepts pregnant individuals**

No

## **Accepts lactating individuals**

No

## **Accepts healthy individuals**

No

## **Comments about the studied populations**

Individuals aged 18-60 who are currently receiving a stable antiretroviral therapy (ART) regimen resulting in an undetectable HIV viral load for a time period of at least one year, which commenced within three months of documented primary HIV infection. Current CD<sup>+</sup> T cell counts > 500 cells/ $\mu$ L with a nadir of CD<sup>+</sup> > 350 cells/ $\mu$ L are required. Study participants were required to be vaccinated against COVID-19 at least 28 days before enrolment.

## **Health status**

Positive to : HIV

Negative to : HBV, HCV, COVID 19

## **Study type**

Interventional (clinical trial)

## **Enrollment**

72

## **Allocation**

Randomized

## **Intervention model**

Parallel Assignment

## **Intervention model description**

Not provided

## **Masking**

Triple-blind masking

## **Masking description**

Triple (Participant, Investigator, Outcomes Assessor)

## **Frequency of administration**

Other : "Single infusions of the long-acting bNAbs 10-1074-LS and 3BNC117-LS "

## **Studied LA-formulation(s)**

Injectable

## **Studied route(s) of administration**

Intravenous

## **Use case**

Treatment

## **Key resources**

Not provided

## RHIVIERA-02

### Identifier

NCT05300035

### Link

<https://clinicaltrials.gov/study/NCT05300035>

### Phase

Phase II

### Status

Recruiting

### Sponsor

ANRS, Emerging Infectious Diseases

### More details

Not provided

### Purpose

Evaluate the efficacy of an intervention consisting of the long-acting broadly neutralising antibodies 3BNC117-LS and 10-1074-LS + ART in reducing HIV-1 replication during primary HIV-1 infection.

### Interventions

#### Intervention 1

Drug: Recombinant human monoclonal antibodies (3BNC117-LS and 10-1074-LS)

#### Intervention 2



Drug: Placebo

## Countries

France

## Sites / Institutions

Not provided

## Trials dates

### Anticipated Start Date

Not provided

### Actual Start Date

2024-04-11

### Anticipated Date of Last Follow-up

Not provided

### Estimated Primary Completion Date

2026-12-10

### Estimated Completion Date

2028-12-10

### Actual Primary Completion Date

Not provided

### Actual Completion Date

Not provided

## Studied populations

### Age Cohort

- Adults
- Older Adults

## **Genders**

- All

## **Accepts pregnant individuals**

No

## **Accepts lactating individuals**

No

## **Accepts healthy individuals**

No

## **Comments about the studied populations**

Study participants are individuals with confirmed HIV-1 infection aged 18-70 at screening and no prior history of hypersensitivity or contraindication to 10-1074-LS or 3BNC117-LS intravenous infusions.

## **Health status**

Positive to : HIV

Negative to : HCV, HBV, TB, COVID 19

## **Study type**

Interventional (clinical trial)

## **Enrollment**

69

## **Allocation**

Randomized

## **Intervention model**

Parallel Assignment

## **Intervention model description**

Not provided

## **Masking**

Triple-blind masking

## **Masking description**

Triple (Participant, Care Provider, Investigator)

## **Frequency of administration**

Other : "Dual intravenous infusion of the long-acting bNAbs 10-1074LS & 3BNC117LS between day 7 and 10. "

## **Studied LA-formulation(s)**

Injectable

## **Studied route(s) of administration**

Intravenous

## **Use case**

Treatment

## **Key resources**

Not provided

**GS-US-536-5816**

**Identifier**

NCT04811040

**Link**

<https://clinicaltrials.gov/study/NCT04811040>

**Phase**

Phase I

**Status**

Completed

**Sponsor**

Gilead Sciences

**More details**

Not provided

**Purpose**

Evaluate the safety and tolerability of a combination of the broadly neutralizing antibodies (bNAbs) teropavimab (formerly GS-5423) and GS-2872 in combination with the HIV capsid inhibitor Lenacapavir

**Interventions**

**Intervention 1**

Drug: Oral Lenacapavir

**Intervention 2**

Drug: Subcutaneous Lenacapavir

### **Intervention 3**

Biological: Teropavimab

### **Intervention 4**

Biological: Zinlirvimab

### **Countries**

United States of America

### **Sites / Institutions**

Not provided

### **Trials dates**

#### **Anticipated Start Date**

Not provided

#### **Actual Start Date**

2021-04-08

#### **Anticipated Date of Last Follow-up**

Not provided

#### **Estimated Primary Completion Date**

Not provided

#### **Estimated Completion Date**

Not provided

#### **Actual Primary Completion Date**

2023-04-18

#### **Actual Completion Date**

2023-10-17

## **Studied populations**

### **Age Cohort**

- Adults
- Older Adults

### **Genders**

- All

### **Accepts pregnant individuals**

Unspecified

### **Accepts lactating individuals**

Unspecified

### **Accepts healthy individuals**

No

## **Comments about the studied populations**

Study participants are required to have received an initial antiretroviral treatment regimen for two years or more prior to screening with no documented virological resistance. Individuals are permitted to change their ART regimen within 28 days prior to screening for reasons other than treatment resistance (e.g. drug-drug interactions, simplification, tolerability). Screening counts of CD4+ T cells  $\geq 500$  cells/ $\mu$ L with a nadir of  $\geq 350$  cells/ $\mu$ L are required, in addition to plasma HIV-1 RNA levels of  $< 50$  copies/ml.

## **Health status**

Positive to : HIV

Negative to : HCV, HBV

## **Study type**

Interventional (clinical trial)

## **Enrollment**

32

## **Allocation**

Randomized

## **Intervention model**

Parallel Assignment

## **Intervention model description**

Not provided

## **Masking**

Double-blind masking

## **Masking description**

Double (Participant, Investigator)

## **Frequency of administration**

Not provided

## **Studied LA-formulation(s)**

Injectable

## **Studied route(s) of administration**

Intravenous

## **Use case**

Treatment

## **Key resources**

Not provided



# MCA-1031

## Identifier

NCT05245292

## Link

<https://clinicaltrials.gov/study/NCT05245292>

## Phase

Phase I

## Status

Recruiting

## Sponsor

Rockefeller University

## More details

Not provided

## Purpose

Evaluate the antiretroviral activity and safety of the broadly neutralising antibodies 3BNC117-LS and 10-1074-LS in combination with IL-15 superagonist complex N-803.

## Interventions

### Intervention 1

Drug: 3BNC117-LS

### Intervention 2

Drug: 10-1074-LS

## **Intervention 3**

Drug: N803

## **Countries**

United States of America

## **Sites / Institutions**

Not provided

## **Trials dates**

### **Anticipated Start Date**

Not provided

### **Actual Start Date**

2022-12-07

### **Anticipated Date of Last Follow-up**

Not provided

### **Estimated Primary Completion Date**

2025-12-31

### **Estimated Completion Date**

2025-12-31

### **Actual Primary Completion Date**

Not provided

### **Actual Completion Date**

Not provided

## **Studied populations**

### **Age Cohort**

- Adults

Older Adults

### **Genders**

- Male
- Female

### **Accepts pregnant individuals**

No

### **Accepts lactating individuals**

No

### **Accepts healthy individuals**

No

### **Comments about the studied populations**

Study participants are males and females aged 18-70 with a confirmed HIV-1 infection who are currently receiving a stable antiretroviral treatment regimen ( $< 50$  copies/ml plasma HIV-1 RNA) for at least 48 weeks with no reported continuous interruption of treatment greater than 7 days. CD4+ T cell counts were required to be  $> 450$  cells/ $\mu\text{L}$  at enrolment with a cell count nadir of  $\geq 200$  cells/ $\mu\text{L}$  and HIV-1 RNA plasma levels at  $< 20$  copies/ml.

### **Health status**

Negative to : HBV, HCV

Positive to : HIV

### **Study type**

Interventional (clinical trial)

### **Enrollment**

36

### **Allocation**

Not provided

## **Intervention model**

Single group assignment

## **Intervention model description**

Not provided

## **Masking**

Open label

## **Masking description**

None (Open Label)

## **Frequency of administration**

Other : "Single intravenous infusions of the long-acting bNAbs 10-1074-LS (dosed at 10mg/kg) and 3BNC117-LS (dosed at 30mg/kg) on day zero. "

## **Studied LA-formulation(s)**

Injectable

## **Studied route(s) of administration**

Intravenous

## **Use case**

Treatment

## **Key resources**

Not provided

**MCA-0994**

**Identifier**

NCT04250636

**Link**

<https://clinicaltrials.gov/study/NCT04250636>

**Phase**

Phase I

**Status**

Completed

**Sponsor**

Rockefeller University

**More details**

Not provided

**Purpose**

Evaluate the antiviral activity, pharmacokinetics and safety of single intravenous infusions of the bNAbs 3BNC117-LS and 10-1074-LS in HIV-infected individuals who are not currently receiving ART.

**Interventions**

**Intervention 1**

Drug: 3BNC117-LS

**Intervention 2**

Drug: 10-1074-LS

## Countries

United States of America

## Sites / Institutions

Not provided

## Trials dates

### Anticipated Start Date

Not provided

### Actual Start Date

2020-10-13

### Anticipated Date of Last Follow-up

Not provided

### Estimated Primary Completion Date

Not provided

### Estimated Completion Date

Not provided

### Actual Primary Completion Date

2022-01-21

### Actual Completion Date

2022-02-11

## Studied populations

### Age Cohort

- Adults
- Older Adults

## **Genders**

- All

## **Accepts pregnant individuals**

No

## **Accepts lactating individuals**

No

## **Accepts healthy individuals**

No

## **Comments about the studied populations**

Study participants are individuals with HIV-1 infection who have not received antiretroviral therapy (either by choice, intolerance or ART-naïvety) for at least 28 days prior to study enrolment with plasma HIV-1 RNA levels between 500 - 100,000 copies/mL and CD4+ T cell counts > 300 cells/μl.

## **Health status**

Positive to : HIV

Negative to : HBV, HCV

## **Study type**

Interventional (clinical trial)

## **Enrollment**

6

## **Allocation**

Not provided

## **Intervention model**

Single group assignment

### **Intervention model description**

Not provided

### **Masking**

Open label

### **Masking description**

None (Open Label)

### **Frequency of administration**

Other : "Single intravenous infusions of the long-acting bNAbs 10-1074-LS and 3BNC117-LS dosed at 30mg/kg. "

### **Studied LA-formulation(s)**

Injectable

### **Studied route(s) of administration**

Intravenous

### **Use case**

Treatment

### **Key resources**

Not provided



**YCO-0971**

**Identifier**

NCT03554408

**Link**

<https://clinicaltrials.gov/study/NCT03554408>

**Phase**

Phase I

**Status**

Completed

**Sponsor**

Rockefeller University

**More details**

Not provided

**Purpose**

Evaluate the pharmacokinetic profile, tolerability and safety of 10-1074-LS in the first clinical study administered individually or in combination with 3BNC117-LS to individuals with and without HIV.

**Interventions**

**Intervention 1**

Drug: Subcutaneous 10-1074-LS

**Intervention 2**

Drug: Subcutaneous 3BNC117-LS

### **Intervention 3**

Drug: Intravenous 10-1074-LS

### **Intervention 4**

Drug: Intravenous 3BNC117-LS

### **Countries**

United States of America

### **Sites / Institutions**

Not provided

### **Trials dates**

#### **Anticipated Start Date**

Not provided

#### **Actual Start Date**

2018-06-20

#### **Anticipated Date of Last Follow-up**

Not provided

#### **Estimated Primary Completion Date**

Not provided

#### **Estimated Completion Date**

Not provided

#### **Actual Primary Completion Date**

2021-02-04

#### **Actual Completion Date**

2021-02-04

## **Studied populations**

### **Age Cohort**

- Adults
- Older Adults

### **Genders**

- All

### **Accepts pregnant individuals**

No

### **Accepts lactating individuals**

No

### **Accepts healthy individuals**

Yes

## **Comments about the studied populations**

Study participants placed into groups of HIV-infected and HIV-uninfected individuals.

Inclusion criteria for HIV positive groups: Males and females aged 18-65 who have documented HIV-1 infection and are currently receiving antiretroviral therapy with < 50 copies/ml plasma HIV-1 RNA levels and CD4+ T cell count of > 300 cells/μL.

Inclusion criteria for HIV negative groups: Males and females aged 18-65 who have low risk for HIV infection and agree to implement two methods of effective contraception if sexually active.

## **Health status**

Positive to : HIV

Considered at low risk of : HIV

Negative to : HIV, HBV, HCV

## **Study type**

Interventional (clinical trial)

## **Enrollment**

77

## **Allocation**

Randomized

## **Intervention model**

Parallel Assignment

## **Intervention model description**

Not provided

## **Masking**

Double-blind masking

## **Masking description**

Double (Participant, Investigator)

## **Frequency of administration**

Other : "Dose escalation study "

## **Studied LA-formulation(s)**

Injectable

## **Studied route(s) of administration**

Subcutaneous

Intravenous

## **Use case**

Treatment

## **Key resources**

Not provided

**NCT05612178**

**Identifier**

NCT05612178

**Link**

<https://clinicaltrials.gov/study/NCT05612178>

**Phase**

Phase I

**Status**

Recruiting

**Sponsor**

National Institute of Allergy and Infectious Diseases (NIAID)

**More details**

Not provided

**Purpose**

Evaluate the safety and effects of repeated doses of 3BNC117-LS and 10-1074-LS on persistent viral reservoirs in people living with HIV who are currently receiving suppressive antiretroviral therapy.

**Interventions**

**Intervention 1**

Biological: 3BNC117-LS

**Intervention 2**

Biological: 10-1074-LS

### **Intervention 3**

Other: Sterile Saline

### **Countries**

United States of America

### **Sites / Institutions**

Not provided

### **Trials dates**

#### **Anticipated Start Date**

Not provided

#### **Actual Start Date**

2023-07-26

#### **Anticipated Date of Last Follow-up**

Not provided

#### **Estimated Primary Completion Date**

2025-12-31

#### **Estimated Completion Date**

2025-12-31

#### **Actual Primary Completion Date**

Not provided

#### **Actual Completion Date**

Not provided

### **Studied populations**

#### **Age Cohort**

Adults

- Older Adults

### **Genders**

- All

### **Accepts pregnant individuals**

No

### **Accepts lactating individuals**

No

### **Accepts healthy individuals**

No

### **Comments about the studied populations**

Adult persons of any sex or gender, aged 18 years to 70; with confirmed HIV-1 infection and receiving antiretroviral therapy with plasma HIV-1 RNA levels of < 50 copies/mL and no reported interruption of ART for 7 consecutive days or longer for at least 96 weeks.

### **Health status**

Positive to : HIV

Negative to : HBV, HCV

### **Study type**

Interventional (clinical trial)

### **Enrollment**

200

### **Allocation**

Randomized



## **Intervention model**

Parallel Assignment

## **Intervention model description**

Not provided

## **Masking**

Triple-blind masking

## **Masking description**

Triple (Participant, Care Provider, Investigator)

## **Frequency of administration**

Other : "Administered 3 times at 20-week intervals. "

## **Studied LA-formulation(s)**

Injectable

## **Studied route(s) of administration**

Intravenous

## **Use case**

Treatment

## **Key resources**

Not provided

# PAUSE

## Identifier

NCT06031272

## Link

<https://clinicaltrials.gov/study/NCT06031272>

## Phase

Phase I

## Status

Not yet recruiting

## Sponsor

AIDS Clinical Trials Group

## More details

Not provided

## Purpose

Evaluate the safety, antiviral activity, and immunomodulatory effects of co-administered 3BNC117-LS-J and 10-1074-LS-J in ART-treated adults in Sub-Saharan Africa.

## Interventions

### Intervention 1

Drug: 3BNC117-LS-J

### Intervention 2

Drug: 10-1074-LS-J

### **Intervention 3**

Drug: Placebo for 3BNC117-LS-J

### **Intervention 4**

Drug: Placebo for 10-1074-LS-J

### **Countries**

Botswana

Malawi

South Africa

### **Sites / Institutions**

Not provided

### **Trials dates**

#### **Anticipated Start Date**

2024-05-15

#### **Actual Start Date**

Not provided

#### **Anticipated Date of Last Follow-up**

Not provided

#### **Estimated Primary Completion Date**

2025-06-30

#### **Estimated Completion Date**

2026-06-30

#### **Actual Primary Completion Date**

Not provided

#### **Actual Completion Date**

Not provided

## **Studied populations**

### **Age Cohort**

- Adults
- Older Adults

### **Genders**

- All

### **Accepts pregnant individuals**

No

### **Accepts lactating individuals**

No

### **Accepts healthy individuals**

No

## **Comments about the studied populations**

Participants are individuals aged 18 to 70 years with a confirmed HIV-1 infection and who have received stable suppressive ART for at least 96 weeks prior to study entry. Eligible participants must also display a CD4+ cell count of >450 cells/ $\mu$ L obtained within the previous 56 days and plasma HIV-1 RNA levels of <50 copies/mL for at least 96 weeks prior to study entry.

## **Health status**

Positive to : HIV

Negative to : HBV, HCV, TB

## **Study type**

Interventional (clinical trial)

## **Enrollment**

48

## **Allocation**

Randomized

## **Intervention model**

Parallel Assignment

## **Intervention model description**

Not provided

## **Masking**

Double-blind masking

## **Masking description**

Double (Participant, Investigator)

## **Frequency of administration**

Other : "Single intravenous infusions of 3BNC117-LS-J (30 mg/kg) and 10-1074-LS-J (10 mg/kg) administered on Day 0. "

## **Studied LA-formulation(s)**

Injectable

## **Studied route(s) of administration**

Intravenous

## **Use case**

Treatment

**Key resources**

Not provided

# IAVI C100

## Identifier

NCT04173819

## Link

<https://clinicaltrials.gov/study/NCT04173819>

## Phase

Phase I/II

## Status

Active, not recruiting

## Sponsor

International AIDS Vaccine Initiative

## More details

Not provided

## Purpose

Evaluate the safety and pharmacokinetics of the combination broadly neutralizing antibodies, 3BNC117-LS-J and 10-1074-LS-J, in healthy American and African Adults.

## Interventions

### Intervention 1

Biological: 3BNC117-LS-J

### Intervention 2

Biological: 10-1074-LS-J

### **Intervention 3**

Biological: Combination 3BNC117-LS-J and 10-1074-LS-J

### **Intervention 4**

Biological: Placebo

### **Countries**

United States of America

Kenya

Rwanda

South Africa

Uganda

### **Sites / Institutions**

Not provided

### **Trials dates**

#### **Anticipated Start Date**

Not provided

#### **Actual Start Date**

2019-01-25

#### **Anticipated Date of Last Follow-up**

Not provided

#### **Estimated Primary Completion Date**

2023-09-01

#### **Estimated Completion Date**

2023-09-01

#### **Actual Primary Completion Date**

Not provided



**Actual Completion Date**

Not provided

**Studied populations****Age Cohort**

- Adults

**Genders**

- All

**Accepts pregnant individuals**

No

**Accepts lactating individuals**

Unspecified

**Accepts healthy individuals**

Yes

**Comments about the studied populations**

Healthy male and female individuals aged between 18-45 who are willing to undergo HIV testing, risk reduction counselling and receive HIV test results; in addition to maintaining low-risk behaviour for the entire trial duration.

**Health status**

Considered at low risk of : HIV

Negative to : HIV, HCV, HBV, TB

**Study type**

Interventional (clinical trial)

**Enrollment**

## **Allocation**

Randomized

## **Intervention model**

Parallel Assignment

## **Intervention model description**

Not provided

## **Masking**

Double-blind masking

## **Masking description**

Double (Participant, Investigator)

## **Frequency of administration**

Other : "Single infusions of the long-acting bNAbs 10-1074-LS-J and 3BNC117-LS-J (either alone or in-combination at differing ratios). "

## **Studied LA-formulation(s)**

Injectable

## **Studied route(s) of administration**

Subcutaneous

Intravenous

## **Use case**

PrEP

## **Key resources**

Not provided

**GS-US-536-5939**

**Identifier**

NCT05729568

**Link**

<https://clinicaltrials.gov/study/NCT05729568>

**Phase**

Phase II

**Status**

Active, not recruiting

**Sponsor**

Gilead Sciences

**More details**

Not provided

**Purpose**

Evaluate the Safety and Efficacy of bNAbs GS-5423 and GS-2872 in Combination With Lenacapavir as Long-Acting Treatment Dosed Every 6 Months in Virologically Suppressed Adults With HIV-1 Infection.

**Interventions**

**Intervention 1**

Teropavimab (Formerly GS-5423)

**Intervention 2**

Zinlirvimab (Formerly GS-2872)

### **Intervention 3**

Drug: Lenacapavir Tablet

### **Intervention 4**

Drug: Lenacapavir Injection

### **Intervention 5**

Drug: Antiretroviral Therapy

### **Countries**

United States of America

Australia

Canada

Puerto Rico

### **Sites / Institutions**

Not provided

### **Trials dates**

#### **Anticipated Start Date**

Not provided

#### **Actual Start Date**

2023-05-15

#### **Anticipated Date of Last Follow-up**

Not provided

#### **Estimated Primary Completion Date**

2025-03-01

#### **Estimated Completion Date**

2029-12-01

**Actual Primary Completion Date**

Not provided

**Actual Completion Date**

Not provided

**Studied populations****Age Cohort**

- Adults
- Older Adults

**Genders**

- All

**Accepts pregnant individuals**

Unspecified

**Accepts lactating individuals**

Unspecified

**Accepts healthy individuals**

No

**Comments about the studied populations**

Participants are required to be receiving a stable ART regimen with no clinically significant documented resistance (except isolated NRTI mutations). Plasma HIV-1 RNA < 50 copies/mL at screening visit 2 and documented plasma HIV-1 RNA < 50 copies/mL for  $\geq$  12 months preceding screening visit 2.

**Health status**

Positive to : HIV

Negative to : HCV, HBV

**Study type**

Interventional (clinical trial)

## **Enrollment**

83

## **Allocation**

Randomized

## **Intervention model**

Parallel Assignment

## **Intervention model description**

Not provided

## **Masking**

Open label

## **Masking description**

None (Open Label)

## **Frequency of administration**

Once every 6 months

## **Studied LA-formulation(s)**

Injectable

## **Studied route(s) of administration**

Intravenous

## **Use case**

Treatment

**Key resources**

Not provided



# Excipients

## **Proprietary excipients used**

Not provided

## **Novel excipients or existing excipients at a concentration above Inactive Ingredients Database (IID) for the specified route of administration**

Not provided

## **Residual solvents used**

Not provided

# Patent info

## Description

Zinlirvimab+Teropamivimab combination

## Brief description

Zinlirvimab variants + combination with Teropamivimab (Heavy chain e.g. SEQ 59-61)

## Representative patent

WO2020056145

## Category

Combination of active substances

## Patent holder

The Rockefeller University

## Exclusivity

Not provided

## Expiration date

September 12, 2039

## Status

Filed in China, India, Us, EP

## **Description**

Zinlirvimab- Broadly neutralising anti-HIV antibodies

## **Brief description**

The invention relates to anti-HIV antibodies. Also disclosed are related methods and compositions.

## **Representative patent**

WO2014063059

## **Category**

Active substance

## **Patent holder**

The Rockefeller University; California Institute of Technology

## **Exclusivity**

Not provided

## **Expiration date**

October 18, 2033

## **Status**

Granted in China, US, EAPO, EP

## **Description**

Teropavimab - HIV neutralizing antibodies and methods of use thereof

## **Brief description**

The invention provides broadly neutralizing antibodies directed to epitopes of Human Immunodeficiency Virus, or HIV. The invention further provides compositions containing HIV antibodies used for prophylaxis, and methods for diagnosis and treatment of HIV infection. Claims include antibody comprising aa 1-112 teropavimab H chain and 1-89 of L chain

## **Representative patent**

WO2012158948

## **Category**

Active substance

## **Patent holder**

The Rockefeller University; California Institute of Technology

## **Exclusivity**

Not provided

## **Expiration date**

May 17, 2032

## **Status**

Granted in US, EAPO, EP

## **Supporting material**

## Publications

Gautam, R., Nishimura, Y., Gaughan, N. *et al.* A single injection of crystallizable fragment domain-modified antibodies elicits durable protection from SHIV infection. *Nat Med* **24**, 610–616 (2018). <https://doi.org/10.1038/s41591-018-0001-2>

In the absence of an effective and safe vaccine against HIV-1, the administration of broadly neutralizing antibodies (bNAbs) represents a logical alternative approach to prevent virus transmission. Here, we introduced two mutations encoding amino acid substitutions (M428L and N434S, collectively referred to as 'LS') into the genes encoding the crystallizable fragment domains of the highly potent HIV-specific 3BNC117 and 10-1074 bNAbs to increase their half-lives and evaluated their efficacy in blocking infection following repeated low-dose mucosal challenges of rhesus macaques (*Macaca mulatta*) with the tier 2 SHIVAD8-EO. A single intravenous infusion of 10-1074-LS monoclonal antibodies markedly delayed virus acquisition for 18 to 37 weeks (median, 27 weeks), whereas the protective effect of the 3BNC117-LS bNAb was more modest (provided protection for 11–23 weeks; median, 17 weeks). Serum concentrations of the 10-1074-LS monoclonal antibody gradually declined and became undetectable in all recipients between weeks 26 and 41, whereas the 3BNC117-LS bNAb exhibited a shorter half-life. To model immunoprophylaxis against genetically diverse and/or neutralization-resistant HIV-1 strains, a combination of the 3BNC117-LS plus 10-1074-LS monoclonal antibodies was injected into macaques via the more clinically relevant subcutaneous route. Even though the administered mixture contained an amount of each bNAb that was nearly threefold less than the quantity of the single monoclonal antibody in the intravenous injections, the monoclonal antibody combination still protected macaques for a median of 20 weeks. The extended period of protection observed in macaques for the 3BNC117-LS plus 10-1074-LS combination could translate into an effective semiannual or annual immunoprophylaxis regimen for preventing HIV-1 infections in humans.

Mendoza P, Gruell H, Nogueira L, Pai JA, Butler AL, Millard K, Lehmann C, Suárez I,

Oliveira TY, Lorenzi JCC, Cohen YZ, Wyen C, Kümmerle T, Karagounis T, Lu CL, Handl L, Unson-O'Brien C, Patel R, Ruping C, Schlotz M, Witmer-Pack M, Shimeliovich I, Kremer G, Thomas E, Seaton KE, Horowitz J, West AP Jr, Bjorkman PJ, Tomaras GD, Gulick RM, Pfeifer N, Fätkenheuer G, Seaman MS, Klein F, Caskey M, Nussenzweig MC.

Combination therapy with anti-HIV-1 antibodies maintains viral suppression. *Nature*. 2018 Sep;561(7724):479-484. DOI: 10.1038/s41586-018-0531-2. Epub 2018 Sep 26. PMID: 30258136; PMCID: PMC6166473.

Individuals infected with HIV-1 require lifelong antiretroviral therapy, because interruption of treatment leads to rapid rebound viraemia. Here we report on a phase 1b clinical trial in which a combination of 3BNC117 and 10-1074, two potent monoclonal anti-HIV-1 broadly neutralizing antibodies that target independent sites on the HIV-1 envelope spike, was administered during analytical treatment interruption. Participants received three infusions of 30 mg kg<sup>-1</sup> of each antibody at 0, 3 and 6 weeks. Infusions of the two antibodies were generally well-tolerated. The nine enrolled individuals with antibody-sensitive latent viral reservoirs maintained suppression for between 15 and more than 30 weeks (median of 21 weeks), and none developed viruses that were resistant to both antibodies. We conclude that the combination of the anti-HIV-1 monoclonal antibodies 3BNC117 and 10-1074 can maintain long-term suppression in the absence of antiretroviral therapy in individuals with antibody-sensitive viral reservoirs.

## Additional documents

No documents were uploaded

## Useful links

There are no additional links

# Access principles

## Collaborate for development



Consider on a case by case basis, collaborating on developing long acting products with potential significant public health impact, especially for low- and middle-income countries (LMICs), utilising the referred to long-acting technology

Not provided

## Share technical information for match-making assessment



Provide necessary technical information to a potential partner, under confidentiality agreement, to enable preliminary assessment of whether specific medicines of public health importance in LMICs might be compatible with the referred to long-acting technology to achieve a public health benefit

Not provided

## Work with MPP to expand access in LMICs



In the event that a product using the referred to long-acting technology is successfully developed, the technology IP holder(s) will work with the Medicines Patent Pool towards putting in place the most appropriate strategy for timely and affordable access in low and middle-income countries, including through licensing

Not provided



## Comment & Information

Not provided