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THE LONG-ACTING THERAPEUTICS PATENTS AND LICENCES DATABASE

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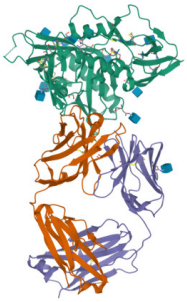


Teropavimab and Zinlirvimab

Developer(s)

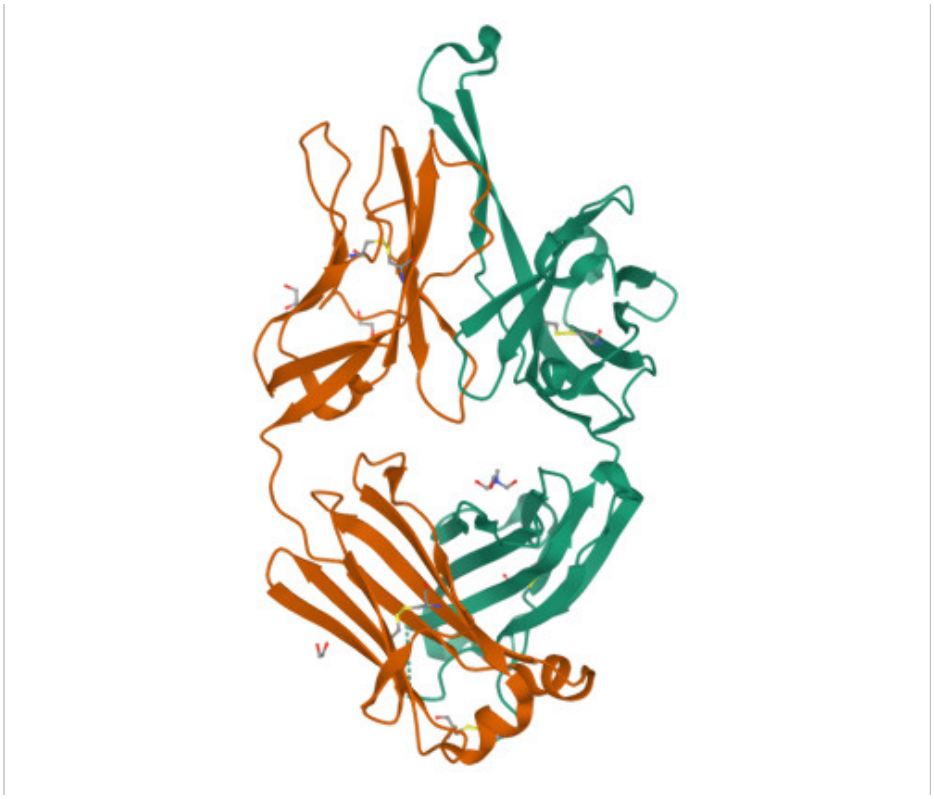
Gilead Sciences Inc.

https://www.gilead.com/

United States

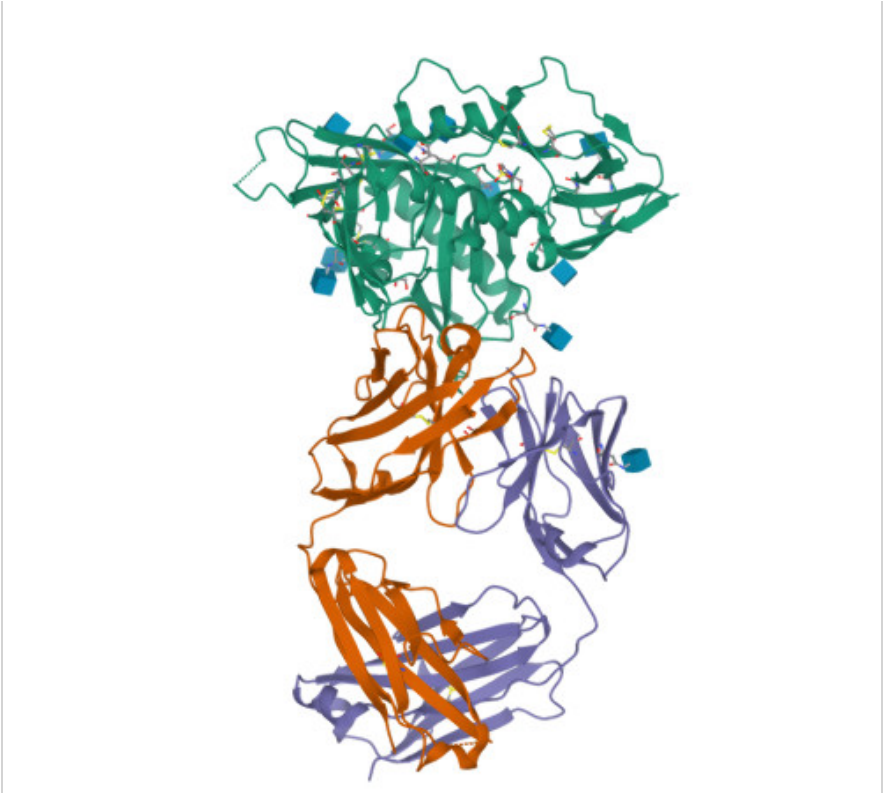
Gilead Sciences, Inc. is a multinational biopharmaceutical company that develops and manufactures innovative medicines for life-threatening diseases, including anti-viral therapeutics for HIV/AIDS, Hepatitis B, Hepatitis C and Covid-19. Headquartered in Foster City, California, Gilead was originally 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/µL 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

43

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+ T cell counts > 500 cells/µL with a nadir of CD4+ > 350 cells/µL 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 ≥ 500 cells/µL with a nadir of ≥ 350 cells/µL 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/µL at enrolment with a cell count nadir of ≥ 200 cells/µL 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/µL 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

225

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 ≥ 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-1 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