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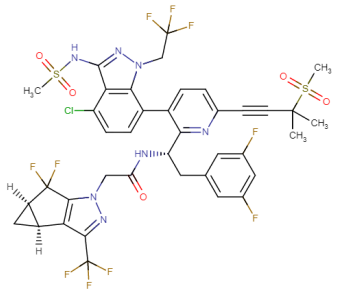


Lenacapavir (LEN)

Developer(s)

Gilead Sciences Inc.

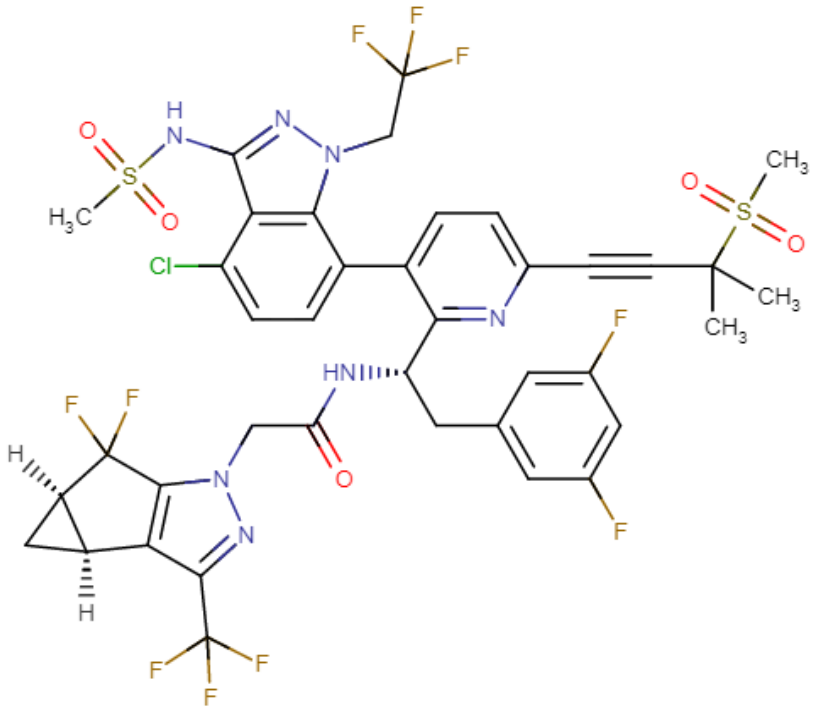
Originator

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



Lenacapavir Compound Structure

Sourced From DrugBank

Drug information

Associated long-acting platforms

Aqueous Solution, Oral solid form

Administration route

Oral, Subcutaneous, Intramuscular, To be determined

Therapeutic area(s)

HIV

Use case(s)

Pre-Exposure Prophylaxis (PrEP)
Treatment
Prevention

Use of drug

Ease of administration

Administered by a community health worker
Administered by a nurse
Administered by a specialty health worker
Self-administered
To be determined

Frequency of administration

Other/Variable/Unknown : Oral tablets 300 mg taken daily or weekly; Six-monthly injectable; Once-yearly investigational injectable.

User acceptance

Not provided

Dosage

Available dose and strength

LEN oral tablets 300 mg; each injection contains 927 mg of lenacapavir in solution. Dose for investigational Once-Yearly formulation is 5000 mg.

Maximum dose

5000 mg

Recommended dosing regimen

For PrEP: Initiation Option 1: Day 1: 927 mg by subcutaneous injection and 600 mg orally (2 x 300-mg tablets). Day 2: 600 mg orally (2 x 300-mg tablets). Initiation Option 2: Day 1: 600 mg orally (2 x 300-mg tablets). Day 2: 600 mg orally (2 x 300-mg tablets). Day 8: 300 mg orally (1 x 300-mg tablet). Day 15: 927 mg by subcutaneous injection. Maintenance: 927 mg by subcutaneous injection every 26 weeks +/- 2 weeks from date of last injection. For the treatment indication, lenacapavir is administered as part of a full treatment regimen with the relevant associated medicines.

Additional comments

Not provided

Dosage link(s)

Not provided

Drug information

Drug's link(s)

https://go.drugbank.com/drugs/DB15673

Generic name

Lenacapavir

Brand name

Sunlenca

Compound type

Small molecule

Drug class/category

Capsid inhibitor

Summary

Lenacapavir (LEN), also known as GS-6207, is a first in-class HIV-1 capsid inhibitor used in combination with other antiretrovirals for the treatment of multi-drug resistant HIV-1 infection, and has potential application as HIV pre-exposure prophylaxis. LEN is utilised combinatorially for HIV-1 treatment, as it displays excellent synergy and no known cross-resistance with any other currently approved class of antiretroviral, in addition to possessing antiviral activity at picomolar levels.

Approval status

For Treatment: Lenacapavir (SUNLENCA) 463.5mg/3ml subcutaneous injection with 300mg oral lead-in tablets are approved for use by 11 regualtory authorities (all for high income countries) for HIV-1 treatment under certain conditions. For PrEP: US FDA and South Africa has approved lenacapavir (Yeztugo) for HIV-1 prevention. It is also

under review in Brazil, EU (+EEA), Australia, and Canada. Gilead has disclosed that it is preparing additional filings in countries that rely on FDA approval for regulatory submission, including Argentina, Mexico and Peru.

Regulatory authorities

US FDA granted Breakthrough Therapy Designation for SUNLENCA in combination with other antiretroviral drugs for heavily treatment-experienced patients (HTE) adults with multi-drug resistant (MDR) HIV-1 infection failing their current antiretroviral regimen due to resistance, intolerance, or safety considerations. A European Marketing Authorization was issued for the use of SUNLENCA and it has also been classified as ‘Fast-Track Reimbursement’ by the Ministry of Health, Labour and Welfare, Japan, and ‘Part 1- Schedule 1 & Schedule 3 Poison’ by the Department of Health, Hong Kong. WHO guidelines released in July 2025 recommend offering six-monthly injectable lenacapavir as an additional PrEP option.

Delivery device(s)

No delivery device

Scale-up and manufacturing prospects

Scale-up prospects

Compound is commercially manufactured.

Tentative equipment list for manufacturing

Equipment for injectable: Stainless steel pharmaceutical reactors, glass-lined reactors, rotary evaporator (rotovap), flash chromatography columns, stainless steel autoclave, cooling bath, silica gel chromatography columns, vacuum distillation apparatus, simulated moving bed chromatography system, Chiralpak columns.

Manufacturing

Storage of injectable lenacapavir in borosilicate vials is contraindicated due to issues with chemical compatibility. Instead, it is recommended that vials are made from aluminosilicate glass.

Specific analytical instrument required for characterization of formulation

Proton nuclear magnetic resonance (1H NMR), High-performance liquid chromatography (HPLC), Ultra-Performance Liquid Chromatography (UPLC).

Clinical trials

CAPELLA

Identifier

NCT04150068

Link

https://clinicaltrials.gov/ct2/show/NCT04150068

Phase

Phase II/III

Status

Active, not recruiting

Sponsor

Gilead Sciences

More details

Not provided

Purpose

Evaluate the antiviral activity of Lenacapavir (formerly GS-6207) administered as an add-on to a failing regimen (functional monotherapy) in people living with HIV with multi-drug resistance.

Interventions

Intervention 1

Drug: Oral Lenacapavir

Intervention 2

Drug: Oral Lenacapavir Placebo

Intervention 3

Drug: Subcutaneous Lenacapavir

Intervention 4

Drug: Failing ARV Regimen

Intervention 5

Drug: Optimized Background Regimen (OBR)

Countries

Canada
France
Germany
Dominican Republic
Italy
Japan
South Africa
Spain
Thailand
United States of America

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2019-11-21 00:00:00

Anticipated Date of Last Follow-up

2024-06-26 00:00:00

Estimated Primary Completion Date

Not provided

Estimated Completion Date

2027-01-01 00:00:00

Actual Primary Completion Date

2020-10-05 00:00:00

Actual Completion Date

Not provided

Studied populations

Age Cohort

- Children
- Adolescents
- Adults
- Older Adults

Genders

- All

Accepts pregnant individuals

Unspecified

Accepts lactating individuals

Unspecified

Accepts healthy individuals

No

Comments about the studied populations

Adult aged ≥ 18 years (at all sites) or adolescent aged ≥ 12 and weighing ≥ 35 kg (at sites in North America and Dominican Republic). Currently receiving a stable failing ARV regimen for > 8 weeks. Have HIV-1 RNA ≥ 400 copies/mL at screening. Have multidrug resistance (resistance to ≥2 agents from ≥3 of the 4 main classes of ARV). Have no more than 2 fully active ARV remaining from the 4 main classes that can be effectively combined to form a viable regimen. Able and willing to receive an Optimized Background Regimen (OBR) together with Lenacapavir.

Health status

Positive to : HIV
Negative to : HCV

Study type

Interventional (clinical trial)

Enrollment

72

Allocation

Randomized

Intervention model

Sequential assignment

Intervention model description

Not provided

Masking

Quadruple-blind masking

Masking description

Quadruple (Participant, Care Provider, Investigator, Outcomes Assessor)

Frequency of administration

Every 6 months

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Oral

Subcutaneous

Use case

Treatment

Key resources

Type	Title	Content	Link
Link	Capsid Inhibition with Lenacapavir in Multidrug-Resistant HIV-1 Infection		https://www.nejm.org/doi/10

CALIBRATE

Identifier

NCT04143594

Link

https://clinicaltrials.gov/ct2/show/NCT04143594

Phase

Phase II

Status

Completed

Sponsor

Gilead Sciences

More details

Not provided

Purpose

Evaluate the efficacy of Lenacapavir containing regimens in people living with HIV

Interventions

Intervention 1

Drug: Oral Lenacapavir

Intervention 2

Drug: F/TAF

Intervention 3

Drug: Subcutaneous Lenacapavir

Intervention 4

Drug: TAF

Intervention 5

Drug: BIC

Countries

Dominican Republic

Puerto Rico

United States of America

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2019-11-22 00:00:00

Anticipated Date of Last Follow-up

2023-10-03 00:00:00

Estimated Primary Completion Date

Not provided

Estimated Completion Date

Not provided

Actual Primary Completion Date

2021-09-30 00:00:00

Actual Completion Date

2023-09-13 00:00:00

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

Antiretroviral (ARV) naïve with no use of any ARV within one month of screening. Use of pre-exposure prophylaxis (PrEP) (any duration), post-exposure prophylaxis (PEP) (any duration), or HIV-1 treatment (< 10 days therapy total) > 1 month prior to screening is permitted. HIV-1 RNA ≥ 200 copies/mL at screening. CD4+ cell count ≥ 200 cells/microliter at screening.

Health status

Positive to : HIV
Negative to : HCV, HBV

Study type

Interventional (clinical trial)

Enrollment

183

Allocation

Randomized

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Open label

Masking description

None (Open Label)

Frequency of administration

Every 6 months

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Oral
Subcutaneous

Use case

Treatment

Key resources

Type	Title	Content	Link
Link	CROI 2022: Lenacapavir: 54 week results in treatment-naive participants of CALIBRATE study		https://i-base.info/htb/42313
Link	Lenacapavir administered every 26 weeks or daily in combination with oral daily antiretroviral therapy for initial treatment of HIV: a randomised, open-label, active-controlled, phase 2 trial		https://doi.org/10.1016/S235 3018(22)00291-0
Link	Interim Resistance Analysis of Long-Acting Lenacapavir in Treatment-Naïve People with HIV at 28 Weeks		https://doi.org/10.1093%2Fc

GS-US-536-5816

Identifier

NCT04811040

Link

https://clinicaltrials.gov/ct2/show/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 00:00:00

Anticipated Date of Last Follow-up

2023-10-26 00:00:00

Estimated Primary Completion Date

Not provided

Estimated Completion Date

Not provided

Actual Primary Completion Date

2023-04-18 00:00:00

Actual Completion Date

2023-10-17 00:00:00

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

On first-line antiretroviral therapy (ART) for ≥ 2 years prior to screening. A change in ART regimen ≥ 28 days prior to screening for reasons other than virologic failure (VF) (eg, tolerability, simplification, drug-drug interaction profile) is allowed.

Health status

Positive to : HIV
Negative to : HCV, HBV
Other health status: No history of opportunistic infection or illness indicative of Stage 3 HIV disease; No comorbid condition(s) requiring ongoing immunosuppression.

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). Clinical pharmacologist and sponsor are not masked to treatment assignment.

Frequency of administration

Other/Variable/Unknown

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Oral
Subcutaneous

Use case

Treatment

Key resources

Not provided

GS-US-200-4072

Identifier

NCT03739866

Link

https://clinicaltrials.gov/ct2/show/NCT03739866

Phase

Phase I

Status

Completed

Sponsor

Gilead Sciences

More details

Not provided

Purpose

Separately evaluate the short-term antiviral activity of both lenacapavir and tenofovir alafenamide with respect to plasma HIV-1 RNA reduction in antiretroviral or capsid inhibitor naïve patients

Interventions

Intervention 1

Drug: Lenacapavir Subcutaneous Injection

Intervention 2

Drug: Placebo

Intervention 3

Drug: B/F/TAF

Intervention 4

Drug: TAF

Countries

United States of America

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2018-11-26 00:00:00

Anticipated Date of Last Follow-up

2021-03-16 00:00:00

Estimated Primary Completion Date

Not provided

Estimated Completion Date

Not provided

Actual Primary Completion Date

2019-11-14 00:00:00

Actual Completion Date

2020-06-15 00:00:00

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

Treatment naïve or experienced but CAI and integrase strand transfer inhibitor (INSTI) naïve, and have not received any antiretroviral therapy (ART) within 12 weeks of screening.

Health status

Positive to : HIV

Study type

Interventional (clinical trial)

Enrollment

53

Allocation

Randomized

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Double-blind masking

Masking description

Double (Participant, Investigator)

Frequency of administration

Other/Variable/Unknown : "Single dose "

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Subcutaneous

Use case

Treatment

Key resources

Type	Title	Content	Link

Link	Clinical targeting of HIV capsid protein with a long-acting small molecule	https://doi.org/10.1038/s415020-2443-1

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

Drug: Teropavimab (Formerly GS-5423)

Intervention 2

Drug: Zinlirvimab (Formerly GS-2872)

Intervention 3

Drug: Lenacapavir Tablet

Intervention 4

Drug: Lenacapavir Injection

Intervention 5

Drug: Antiretroviral Therapy

Countries

Australia

Canada

Puerto Rico

United States of America

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2023-05-15 00:00:00

Anticipated Date of Last Follow-up

2024-07-12 00:00:00

Estimated Primary Completion Date

2025-03-01 00:00:00

Estimated Completion Date

2029-12-01 00:00:00

Actual Primary Completion Date

2024-07-02 00:00:00

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

Every 6 months

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Subcutaneous

Use case

Treatment

Key resources

Not provided

IMEA 070

Identifier

NCT06289361

Link

https://clinicaltrials.gov/study/NCT06289361

Phase

Marketed

Status

Not yet recruiting

Sponsor

Institut de Médecine et d'Epidémiologie Appliquée - Fondation Internationale Léon M'Ba

More details

Immunovirological follow-up and safety of HIV-infected patients receiving lenacapavir under compassionate access in France between 01/01/2021 and 12/31/2023

Purpose

Cohort IMEA 070 -Lenacapavir Compassional

Interventions

Not provided

Countries

France

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

2024-04-01 00:00:00

Actual Start Date

Not provided

Anticipated Date of Last Follow-up

2024-03-20 00:00:00

Estimated Primary Completion Date

2024-04-15 00:00:00

Estimated Completion Date

2024-07-30 00:00:00

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

Not provided

Health status

Positive to : HIV

Study type

Observational studies (incl. patient registries)

Enrollment

58

Allocation

Not provided

Intervention model

Not provided

Intervention model description

Not provided

Masking

Not provided

Masking description

Not provided

Frequency of administration

Every 6 months

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Subcutaneous

Use case

Treatment

Key resources

Not provided

Pharmacokinetics and safety of once-yearly lenacapavir: a phase 1, open-label study

Identifier

Not provided

Link

https://doi.org/10.1016/S0140-6736(25)00405-2

Phase

Phase I

Status

Not provided

Sponsor

Gilead Sciences Inc.

More details

Not provided

Purpose

Not provided

Interventions

Intervention 1

Once-yearly intramuscular lenacapavir formulation 1

Dosage: 5000 mg

Intervention 2

Once-yearly intramuscular lenacapavir formulation 2

Dosage: 5000 mg

Countries

Not provided

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

Not provided

Anticipated Date of Last Follow-up

Not provided

Estimated Primary Completion Date

Not provided

Estimated Completion Date

Not provided

Actual Primary Completion Date

Not provided

Actual Completion Date

Not provided

Studied populations

Age Cohort

- Adults

Genders

- All

Accepts pregnant individuals

Unspecified

Accepts lactating individuals

Unspecified

Accepts healthy individuals

Yes

Comments about the studied populations

Not provided

Health status

Not provided

Study type

Interventional (clinical trial)

Enrollment

40

Allocation

Not provided

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Not provided

Masking description

Not provided

Frequency of administration

Yearly

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Intramuscular

Use case

PrEP

Key resources

Type	Title	Content	Link
Link	Pharmacokinetics and safety of once-yearly lenacapavir: a phase 1, open-label study		https://doi.org/10.1016/S0140-6736(25)00405-2

PURPOSE 1

Identifier

NCT04994509

Link

https://clinicaltrials.gov/study/NCT04994509

Phase

Phase III

Status

Active, not recruiting

Sponsor

Gilead Sciences

More details

The goal of this study is to evaluate the efficacy in preventing HIV infection of the study drugs, lenacapavir (LEN) and emtricitabine/tenofovir alafenamide (F/TAF), in adolescent girls and young women.

Purpose

Pre-Exposure Prophylaxis Study of Lenacapavir and Emtricitabine/Tenofovir Alafenamide in Adolescent Girls and Young Women at Risk of HIV Infection

Interventions

Intervention 1

Oral Lenacapavir (LEN)

Intervention 2

Subcutaneous (SC) Lenacapavir (LEN)

Intervention 3

Oral F/TAF

Intervention 4

Oral F/TDF

Intervention 5

Placebo SC LEN

Countries

South Africa

Uganda

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2021-08-30 00:00:00

Anticipated Date of Last Follow-up

2024-02-26 00:00:00

Estimated Primary Completion Date

2024-09-01 00:00:00

Estimated Completion Date

2027-07-01 00:00:00

Actual Primary Completion Date

Not provided

Actual Completion Date

Not provided

Studied populations

Age Cohort

- Children
- Adults

Genders

- Female

Accepts pregnant individuals

Yes

Accepts lactating individuals

Yes

Accepts healthy individuals

Yes

Comments about the studied populations

Key Inclusion Criteria: * Incidence Phase * HIV-1 status unknown at initial screening and no prior human immunodeficiency virus (HIV)-1 testing within the last 3 months. * Sexually active (has had \> 1 vaginal intercourse within the last 3 months) with cisgender male individuals (CGM). * Randomized Phase * Negative fourth generation HIV-1 antibody (Ab)/antigen (Ag) test confirmed with central HIV-1 testing. * Estimated glomerular filtration rate (GFR) ≥ 60 mL/min at screening. * Body weight ≥ 35 kg. Key Exclusion Criteria: * Prior receipt of an HIV vaccine. * Prior use of long-acting systemic HIV pre-exposure prophylaxis (PrEP) or or HIV PEP (postexposure prophylaxis). Note: Other protocol defined Inclusion/Exclusion criteria may apply.

Health status

Negative to : HIV

Study type

Interventional (clinical trial)

Enrollment

5368

Allocation

Randomized

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Double-blind masking

Masking description

Double (Participant, Investigator)

Frequency of administration

Every 6 months

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Oral

Subcutaneous

Use case

PrEP

Key resources

Not provided

PURPOSE 2

Identifier

NCT04925752

Link

https://clinicaltrials.gov/study/NCT04925752

Phase

Phase III

Status

Active, not recruiting

Sponsor

Gilead Sciences

More details

The goal of this clinical study is to test how well the study drug, lenacapavir (LEN), works in preventing the risk of HIV.

Purpose

Study of Lenacapavir for HIV Pre-Exposure Prophylaxis in People Who Are at Risk for HIV Infection

Interventions

Intervention 1

Oral Lenacapavir (LEN)

Intervention 2

Oral F/TDF

Intervention 3

Subcutaneous (SC) Lenacapavir (LEN)

Intervention 4

Placebo SC LEN

Intervention 5

Placebo to match F/TDF

Countries

Argentina
Brazil
Peru
Puerto Rico
South Africa
Thailand
United States of America

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2021-06-28 00:00:00

Anticipated Date of Last Follow-up

2024-07-11 00:00:00

Estimated Primary Completion Date

2024-12-01 00:00:00

Estimated Completion Date

2028-05-01 00:00:00

Actual Primary Completion Date

Not provided

Actual Completion Date

Not provided

Studied populations

Age Cohort

- Children
- Adults
- Older Adults

Genders

- All

Accepts pregnant individuals

Unspecified

Accepts lactating individuals

Unspecified

Accepts healthy individuals

Yes

Comments about the studied populations

Key Inclusion Criteria: Incidence Phase * CGM, TGW, TGM, and GNB who have condomless receptive anal sex with partners assigned male at birth and are at risk for HIV infection. * HIV-1 status unknown at screening and no prior HIV-1 testing within the last 3 months. * Sexually active with ≥ 1 partner assigned male at birth (condomless receptive anal sex) in the last 12 months and 1 of the following: * Condomless receptive anal sex with ≥ 2 partners in the last 12 weeks. * History of syphilis, rectal

gonorrhea, or rectal chlamydia in the last 24 weeks. * Self-reported use of stimulants with sex in the last 12 weeks. Randomized Phase * Negative local rapid fourth generation HIV-1/2 Ab/Ag, central fourth generation HIV-1/2 Ab/Ag, and HIV-1 RNA quantitative nucleic acid amplification

Health status

Negative to : HIV, HCV, HBV
Considered high risk to : HIV

Study type

Interventional (clinical trial)

Enrollment

3295

Allocation

Randomized

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Double-blind masking

Masking description

Double (Participant, Investigator)

Frequency of administration

Every 6 months

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Oral

Subcutaneous

Use case

PrEP

Key resources

Not provided

PURPOSE 3

Identifier

NCT06101329

Link

https://clinicaltrials.gov/study/NCT06101329

Phase

Phase II

Status

Recruiting

Sponsor

Gilead Sciences

More details

Not provided

Purpose

Evaluate the Pharmacokinetics, Safety, and Acceptability of Twice Yearly Long-acting Subcutaneous Lenacapavir for Pre-Exposure Prophylaxis in Cisgender Women in the United States.

Interventions

Intervention 1

Drug: Lenacapavir Tablet

Intervention 2

Drug: Long-acting Subcutaneous Lenacapavir Injection

Intervention 3

Drug: Emtricitabine/Tenofovir Disoproxil Fumarate (F/TDF)

Countries

United States of America

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2023-11-17

Anticipated Date of Last Follow-up

2024-08-12

Estimated Primary Completion Date

2028-01-01

Estimated Completion Date

2028-01-01

Actual Primary Completion Date

Not provided

Actual Completion Date

Not provided

Studied populations

Age Cohort

Adults

- Older Adults

Genders

- Cisgender female

Accepts pregnant individuals

Unspecified

Accepts lactating individuals

Unspecified

Accepts healthy individuals

Unspecified

Comments about the studied populations

Cisgender women aged 18 and older who report at least one episode of condomless vaginal or anal sex with a cisgender man in the twelve months prior to enrollment.

Health status

Considered at low risk of : HIV
Negative to : HIV, HBV

Study type

Interventional (clinical trial)

Enrollment

250

Allocation

Randomized

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Open label

Masking description

None (Open Label)

Frequency of administration

Every 6 months

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Oral
Subcutaneous

Use case

PrEP

Key resources

Not provided

PURPOSE 4

Identifier

NCT06101342

Link

https://clinicaltrials.gov/study/NCT06101342

Phase

Phase II

Status

Recruiting

Sponsor

Gilead Sciences

More details

PWUD (People Who Use Drugs).

Purpose

Evaluate the Pharmacokinetics and Safety of Twice Yearly Long-Acting Subcutaneous Lenacapavir for Pre-Exposure Prophylaxis in People Who Inject Drugs.

Interventions

Intervention 1

Drug: Long-acting Subcutaneous Lenacapavir Injection

Intervention 2

Drug: Lenacapavir Tablet

Intervention 3

Drug: Emtricitabine/tenofovir disoproxil fumarate (F/TDF)

Countries

United States of America

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2023-12-13 00:00:00

Anticipated Date of Last Follow-up

2024-08-08 00:00:00

Estimated Primary Completion Date

2027-07-01 00:00:00

Estimated Completion Date

2027-07-01 00:00:00

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

Yes

Comments about the studied populations

Participant inclusion criteria requires a positive urine drug screen for any drug of misuse including (but not limited to) opioids (eg, fentanyl, heroin), stimulants (eg, cocaine, amphetamines), psychoactive drugs (eg, benzodiazepines), or a combination of these drugs. Participants must also display evidence of recent injection(s) (eg, track marks) and self-report of injection paraphernalia sharing within the last 30 days.

Health status

Negative to : HIV, HBV, TB
Considered high risk to : HIV

Study type

Interventional (clinical trial)

Enrollment

250

Allocation

Randomized

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Open label

Masking description

None (Open Label)

Frequency of administration

Every 6 months

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Oral
Subcutaneous

Use case

PrEP

Key resources

Not provided

PURPOSE 5

Identifier

NCT06513312

Link

https://clinicaltrials.gov/study/NCT06513312

Phase

Phase II

Status

Not yet recruiting

Sponsor

Gilead Sciences

More details

The goals of this clinical study are to learn more about the study drug lenacapavir (LEN), by comparing the consistent and continuous use of LEN and emtricitabine/tenofovir disoproxil fumarate (coformulated; Truvada®) (F/TDF), then by observing the safety of LEN and F/TDF, evaluating the acceptability of LEN injections and oral F/TDF, and observe how LEN moves throughout the body in people who would benefit from pre-exposure prophylaxis (PrEP). The primary objective of this study is to compare LEN and F/TDF consistent and continuous use among people who would benefit from PrEP.

Purpose

Study of Lenacapavir Taken Twice a Year for HIV Pre-Exposure Prophylaxis (PrEP)

Interventions

Intervention 1

Drug: Lenacapavir Injection

Intervention 2

Drug: Lenacapavir Tablet

Intervention 3

Drug: Emtricitabine/tenofovir disoproxil fumarate (F/TDF)

Countries

France

United Kingdom

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

2024-09-01 00:00:00

Actual Start Date

Not provided

Anticipated Date of Last Follow-up

2024-08-22 00:00:00

Estimated Primary Completion Date

2027-01-01 00:00:00

Estimated Completion Date

2029-07-01 00:00:00

Actual Primary Completion Date

Not provided

Actual Completion Date

Not provided

Studied populations

Age Cohort

- Adults
- Older Adults

Genders

- All
- Cisgender female
- Cisgender male
- Transgender female
- Transgender male
- Gender non-binary

Accepts pregnant individuals

Unspecified

Accepts lactating individuals

Unspecified

Accepts healthy individuals

Yes

Comments about the studied populations

Key Inclusion Criteria: - Able to comprehend and provide a signed written informed consent, which must be obtained prior to initiation of study procedures. - Cisgender men who have sex with men, transgender women, transgender men, cisgender women, and nonbinary people - Increased likelihood of HIV acquisition as indicated by at least one of the following: - Condomless sex with ≥ 2 partners in the past 6 months - Diagnosis of a bacterial sexually transmitted infection (STI) in the past 12 months - Engagement in sex work or transactional sex in the past 12 months - Use of ≥ 2

courses of nonoccupational HIV post-exposure prophylaxis (nPEP) in the past 12 months - Condomless sex with a partner living with HIV who has unknown or unsuppressed viral load (≥ 200 copies/mL) in the past 12 months

Health status

Negative to : HIV

Study type

Interventional (clinical trial)

Enrollment

262

Allocation

Randomized

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Open label

Masking description

None (Open Label)

Frequency of administration

Every 6 months

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Subcutaneous

Use case

PrEP

Key resources

Not provided

10002211

Identifier

NCT06819176

Link

https://clinicaltrials.gov/study/NCT06819176

Phase

Phase I

Status

Not yet recruiting

Sponsor

National Institute of Allergy and Infectious Diseases (NIAID)

More details

Treatment intensification study designed to ascertain the effects of lenacapavir intensification in people living with HIV (PLWH) with viral suppression on daily antiretroviral therapy (ART).

Purpose

Lenacapavir Intensification to Disrupt HIV Reservoirs in Virologically Suppressed People Living With HIV Receiving Antiretroviral Therapy

Interventions

Intervention 1

Lenacapavir

Countries

United States of America

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

2025-06-05

Actual Start Date

Not provided

Anticipated Date of Last Follow-up

2025-05-30

Estimated Primary Completion Date

2028-09-01

Estimated Completion Date

2029-01-24

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

* INCLUSION CRITERIA: To be eligible to participate in this study, an individual must meet all of the following criteria: 1. Able to provide informed consent. 2. Stated willingness to comply with all study procedures and availability for the duration of the study. 3. Aged 18 years to 75 years. 4. In generally good health with an identified primary health care provider for medical management of HIV infection and willing to maintain a relationship with a primary health care provider while participating in the study. 5. Confirmed HIV-1 infection. 6. Total HIV DNA reservoir size greater than 300 copies/106 CD4+ T cells. 7. CD4+ T cell count \>200 cells/mm\^3 at screening. 8. Documentation of continuous ART treatment \>3 years with suppression of plasma viral level below the limit of quantita

Health status

Not provided

Study type

Interventional (clinical trial)

Enrollment

50

Allocation

Randomized

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Single blind masking

Masking description

Not provided

Frequency of administration

Not provided

Studied LA-formulation(s)

Not provided

Studied route(s) of administration

Not provided

Use case

Not provided

Key resources

Not provided

Excipients

Proprietary excipients used

No proprietary excipient used

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

No novel excipient or existing excipient used

Residual solvents used

No residual solvent used

Patent info

Compound patent families

Patent informations

Patent description	Representative patent	Categories	Patent holder	Licence with MPP	Patent source
Lenacapavir use to treat multidrug resistant HIV infection in heavily treatment-experienced Expiry date: 2039-07-15 The present disclosure relates to compounds of Formula (Ia) and (Ib) or a pharmaceutically acceptable salt thereof, which are useful in the treatment of an HIV infection in heavily treatment-experienced patients with multidrug resistant HIV infection.	WO2020018459	Use	Gilead Sciences, Inc	Yes	

Patent status

Patent status/countries	Low, Low- middle and upper-middle	High income
Granted		Australia, United States of America
Filed	China, Albania, Serbia, Türkiye, North Macedonia	Australia, Canada, Liechtenstein, Italy, Norway, Malta, Denmark, Belgium, United Kingdom, Greece, Netherlands, Hungary, Croatia, Switzerland, Spain, San Marino, Slovenia, Austria, Romania, Iceland, Cyprus, Finland, France, Bulgaria, Slovakia, Poland, Latvia, Ireland, Estonia, Germany, Luxembourg, Portugal, Czechia, Lithuania, Monaco, Sweden, Japan, Korea, Republic of, Taiwan, Province of China, United States of America
Not in force	World Intellectual Property Organization (WIPO), Morocco, Tunisia, Bosnia and Herzegovina, Cambodia, Montenegro, Moldova, Republic of	World Intellectual Property Organization (WIPO), Australia, Canada, Japan, Korea, Republic of

MPP Licence(s)

Bilateral licence on lenacapavir (LEN)

https://www.gilead.com/-/media/gileadcorpredesign/pdf/Other/LEN-VL.pdf

Patent informations

Patent description	Representative patent	Categories	Patent holder	Licence with MPP	Patent source
Lenacapavir manufacturing processess and intermediates Expiry date: 2039-02-15 The present disclosure relates to methods and intermediates useful for preparing a compound of formula (I): (I) or a co-crystal, solvate, salt or combination thereof.	WO2019161280	Intermediate(s), Process	Gilead Sciences, Inc	Yes	

Patent status

Patent status/countries	Low, Low- middle and upper-middle	High income
Granted	China, Türkiye, India	Australia, Liechtenstein, Italy, Norway, Malta, Denmark, Belgium, United Kingdom, Greece, Netherlands, Switzerland, Spain, Slovenia, Austria, Finland, France, Bulgaria, Slovakia, Poland, Latvia, Ireland, Estonia, Germany, Luxembourg, Portugal, Czechia, Sweden, Japan, Korea, Republic of, Taiwan, Province of China, United States of America, Hong Kong
Filed	China, Albania, Serbia, Türkiye, North Macedonia, India	Australia, Canada, Liechtenstein, Italy, Norway, Malta, Denmark, Belgium, United Kingdom, Greece, Netherlands, Hungary, Croatia, Switzerland, Spain, San Marino, Slovenia, Austria, Romania, Iceland, Cyprus, Finland, France, Bulgaria, Slovakia, Poland, Latvia, Ireland, Estonia, Germany, Luxembourg, Portugal, Czechia, Lithuania, Monaco, Sweden, Korea, Republic of, Taiwan, Province of China, United States of America

Patent status/countries	Low, Low- middle and upper-middle	High income
Not in force	World Intellectual Property Organization (WIPO), Argentina, Morocco, Tunisia, Albania, Serbia, Bosnia and Herzegovina, Cambodia, Montenegro, Moldova, Republic of, North Macedonia	World Intellectual Property Organization (WIPO), Hungary, Croatia, San Marino, Romania, Iceland, Cyprus, Lithuania, Monaco, Bahamas

MPP Licence(s)

Bilateral licence on lenacapavir (LEN)

https://www.gilead.com/-/media/gileadcorpredesign/pdf/Other/LEN-VL.pdf

Patent informations

Patent description	Representative patent	Categories	Patent holder	Licence with MPP	Patent source
Crystalline forms of Lenacapavir sodium salt Expiry date: 2038-08-16 Lenacapavir solid forms, including pharmaceutically acceptable salts and cocrystals of the inhibitor, as well as crystalline forms of the salts and cocrystals, for use in the treatment of a Retroviridae viral infection including an infection caused by the HIV virus. The present disclosure also relates to pharmaceutical compositions containing the novel salts, cocrystals, and crystalline forms thereof, and methods of treating or preventing a Retroviridae viral infection.	WO2019035904	Polymorphs	Gilead Sciences, Inc	Yes	

Patent status

Patent status/countries	Low, Low- middle and upper-middle	High income
Granted	Türkiye	Belgium, Germany, France, Luxembourg, Netherlands, Switzerland, United Kingdom, Sweden, Italy, Austria, Liechtenstein, Greece, Spain, Denmark, Portugal, Ireland, Finland, Cyprus, Bulgaria, Czechia, Estonia, Slovakia, Poland, Malta, Norway, Romania, Latvia, Lithuania, Slovenia, Australia, Canada, Japan, Korea, Republic of, Taiwan, Province of China, United States of America, Hong Kong

Patent status/countries	Low, Low- middle and upper-middle	High income
Filed	Türkiye, North Macedonia, Albania, Serbia, China, India	Belgium, Germany, France, Luxembourg, Netherlands, Switzerland, United Kingdom, Sweden, Italy, Austria, Liechtenstein, Greece, Spain, Denmark, Monaco, Portugal, Ireland, Finland, Cyprus, Bulgaria, Czechia, Estonia, Slovakia, Hungary, Poland, Iceland, Malta, Norway, San Marino, Croatia, Romania, Latvia, Lithuania, Slovenia, Canada, Hong Kong
Not in force	World Intellectual Property Organization (WIPO), North Macedonia, Albania, Bosnia and Herzegovina, Montenegro, Serbia, Moldova, Republic of, Morocco, Tunisia, Cambodia, Argentina, Bangladesh	World Intellectual Property Organization (WIPO), Luxembourg, Denmark, Monaco, Finland, Cyprus, Bulgaria, Estonia, Hungary, Iceland, Malta, San Marino, Croatia, Romania, Latvia, Lithuania, Japan, Taiwan, Province of China

MPP Licence(s)

Bilateral licence on lenacapavir (LEN)

https://www.gilead.com/-/media/gileadcorpredesign/pdf/Other/LEN-VL.pdf

Patent informations

Patent description	Representative patent	Categories	Patent holder	Licence with MPP	Patent source
Lenacapavir compound and its use in HIV (oral and parenteral) Expiry date: 2037-08-17 The present disclosure relates to novel compounds for use in the treatment of a Retroviridae viral infection including an infection caused by the HIV virus. The present disclosure also relates to intermediates for its preparation and to pharmaceutical compositions containing said novel compound.	WO2018035359	Compound	Gilead Sciences, Inc	Yes	

Patent status

Patent status/countries	Low, Low- middle and upper-middle	High income
Granted	Türkiye, Morocco, Brazil, China, Colombia, Dominican Republic, Turkmenistan, Belarus, Tajikistan, Kazakhstan, Azerbaijan, Kyrgyzstan, Armenia, Mexico, Peru, Philippines, Botswana, Gambia (the), Ghana, Kenya, Lesotho, Malawi, Mozambique, Namibia, Sierra Leone, Liberia, Sao Tome and Principe, Sudan, Eswatini, Tanzania, United Republic of, Zambia, Zimbabwe, Indonesia, Malaysia, Ukraine, South Africa, Uzbekistan	Belgium, Germany, France, Luxembourg, Netherlands, Switzerland, United Kingdom, Sweden, Italy, Austria, Liechtenstein, Greece, Spain, Denmark, Portugal, Ireland, Finland, Cyprus, Bulgaria, Czechia, Estonia, Slovakia, Hungary, Poland, Iceland, Malta, Norway, Croatia, Romania, Latvia, Lithuania, Slovenia, Australia, Canada, Costa Rica, Russian Federation, Hong Kong, Israel, Japan, Korea, Republic of, New Zealand, Singapore, Taiwan, Province of China, United States of America, Bahamas, Bahrain, Kuwait, Qatar, Saudi Arabia, Oman, United Arab Emirates, Macao, Panama

Patent status/countries	Low, Low- middle and upper-middle	High income
Filed	Türkiye, North Macedonia, Albania, Serbia, Morocco, Argentina, China, Jordan, Philippines, India, Uganda, Egypt, Guatemala, Indonesia, Nigeria, Thailand, Ukraine, Viet Nam	Belgium, Germany, France, Luxembourg, Netherlands, Switzerland, United Kingdom, Sweden, Italy, Austria, Liechtenstein, Greece, Spain, Denmark, Monaco, Portugal, Ireland, Finland, Cyprus, Bulgaria, Czechia, Estonia, Slovakia, Hungary, Poland, Iceland, Malta, Norway, San Marino, Croatia, Romania, Latvia, Lithuania, Slovenia, Australia, Hong Kong, Korea, Republic of, Singapore, Taiwan, Province of China, United States of America, Saudi Arabia, Panama
Not in force	World Intellectual Property Organization (WIPO), North Macedonia, Albania, Bosnia and Herzegovina, Montenegro, Serbia, Moldova, Republic of, Morocco, Argentina, Colombia, Dominican Republic, Ecuador, Peru, Rwanda, Uganda, Bangladesh, Bolivia (Plurinational State of), Cuba, Egypt, Benin, Cameroon, Burkina Faso, Chad, Guinea-Bissau, Comoros, Mali, Senegal, Congo, Guinea, Gabon, Niger, Equatorial Guinea, Mauritania, Togo, Côte d'Ivoire, Central African Republic, Pakistan, Paraguay, El Salvador, Venezuela (Bolivarian Republic of)	World Intellectual Property Organization (WIPO), Monaco, Malta, San Marino, Chile, Japan, Korea, Republic of, Uruguay, Trinidad and Tobago

MPP Licence(s)

Bilateral licence on lenacapavir (LEN)

https://www.gilead.com/-/media/gileadcorpredesign/pdf/Other/LEN-VL.pdf

Patent informations

Patent description	Representative patent	Categories	Patent holder	Licence with MPP	Patent source
Lenacapavir and analogues (Markush formula) and their use in HIV Expiry date: 2034-02-28 Compounds of formula (I) or salts thereof are disclosed. Also disclosed are pharmaceutical compositions comprising a compound of formula I, processes for preparing compounds of formula I, intermediates useful for preparing compounds of formula I and therapeutic methods for treating a Retroviridae viral infection including an infection caused by the HIV virus.	WO2014134566	Compound	Gilead Sciences, Inc	Yes	

Patent status

Patent status/countries	Low, Low- middle and upper-middle	High income
Granted	Türkiye, North Macedonia, Albania, Bosnia and Herzegovina, Montenegro, Serbia, Brazil, China, Cuba, Turkmenistan, Belarus, Tajikistan, Kazakhstan, Azerbaijan, Kyrgyzstan, Armenia, Mexico, Peru, Philippines, Ukraine, Botswana, Gambia (the), Ghana, Kenya, Lesotho, Malawi, Mozambique, Namibia, Sierra Leone, Liberia, Rwanda, Sudan, Eswatini, Tanzania, United Republic of, Zambia, Zimbabwe, Benin, Cameroon, Burkina Faso, Chad, Guinea-Bissau, Comoros, Mali, Senegal, Congo, Guinea, Gabon, Niger, Equatorial Guinea, Mauritania, Togo, Côte d'Ivoire, Central African Republic, Colombia, Indonesia, Malaysia, Viet Nam, South Africa	Belgium, Germany, France, Luxembourg, Netherlands, Switzerland, United Kingdom, Sweden, Italy, Austria, Liechtenstein, Greece, Spain, Denmark, Monaco, Portugal, Ireland, Finland, Cyprus, Bulgaria, Czechia, Estonia, Slovakia, Hungary, Poland, Iceland, Malta, Norway, San Marino, Croatia, Romania, Latvia, Lithuania, Slovenia, Australia, Canada, Chile, Costa Rica, Russian Federation, Hong Kong, Israel, Japan, Korea, Republic of, New Zealand, Singapore, Taiwan, Province of China, United States of America, Bahrain, Kuwait, Qatar, Saudi Arabia, Oman, United Arab Emirates, Macao, Panama

Patent status/countries	Low, Low- middle and upper-middle	High income
Filed	Türkiye, North Macedonia, Albania, Serbia, Argentina, Ukraine, India, Egypt, Thailand	Belgium, Germany, France, Luxembourg, Netherlands, Switzerland, United Kingdom, Sweden, Italy, Austria, Liechtenstein, Greece, Spain, Denmark, Monaco, Portugal, Ireland, Finland, Cyprus, Bulgaria, Czechia, Estonia, Slovakia, Hungary, Poland, Iceland, Malta, Norway, San Marino, Croatia, Romania, Latvia, Lithuania, Slovenia, United States of America
Not in force	World Intellectual Property Organization (WIPO), North Macedonia, Albania, Bosnia and Herzegovina, Montenegro, Serbia, Argentina, Brazil, China, Moldova, Republic of, Peru, Uganda, Bolivia (Plurinational State of), Colombia, Ecuador, Malaysia, Paraguay, Pakistan, El Salvador, Venezuela (Bolivarian Republic of), Viet Nam, South Africa	World Intellectual Property Organization (WIPO), Luxembourg, Denmark, Monaco, Finland, Cyprus, Bulgaria, Estonia, Malta, San Marino, Croatia, Romania, Latvia, Lithuania, Australia, Canada, Costa Rica, Hong Kong, Japan, New Zealand, Singapore, United States of America, Uruguay, Bahamas

MPP Licence(s)

Bilateral licence on lenacapavir (LEN)

https://www.gilead.com/-/media/gileadcorpredesign/pdf/Other/LEN-VL.pdf

Supporting material

Publications

Link JO, et al. Clinical targeting of HIV capsid protein with a long-acting small molecule. Nature. 2020 Aug;584(7822):614-618. doi: https://doi.org/10.1038/s41586-020-2443-1. Epub 2020 Jul 1.

Oral antiretroviral agents provide life-saving treatments for millions of people living with HIV, and can prevent new infections via pre-exposure prophylaxis1-5. However, some people living with HIV who are heavily treatment-experienced have limited or no treatment options, owing to multidrug resistance6. In addition, suboptimal adherence to oral daily regimens can negatively affect the outcome of treatment-which contributes to virologic failure, resistance generation and viral transmission-as well as of pre-exposure prophylaxis, leading to new infections1,2,4,7-9. Long-acting agents from new antiretroviral classes can provide much-needed treatment options for people living with HIV who are heavily treatment-experienced, and additionally can improve adherence10. Here we describe GS-6207, a small molecule that disrupts the functions of HIV capsid protein and is amenable to long-acting therapy owing to its high potency, low in vivo systemic clearance and slow release kinetics from the subcutaneous injection site. Drawing on X-ray crystallographic information, we designed GS-6207 to bind tightly at a conserved interface between capsid protein monomers, where it interferes with capsid-protein-mediated interactions between proteins that are essential for multiple phases of the viral replication cycle. GS-6207 exhibits antiviral activity at picomolar concentrations against all subtypes of HIV-1 that we tested, and shows high synergy and no cross-resistance with approved antiretroviral drugs. In phase-1 clinical studies, monotherapy with a single subcutaneous dose of GS-6207 (450 mg) resulted in a mean log10-transformed reduction of plasma viral load of 2.2 after 9 days, and showed sustained plasma exposure at antivirally active concentrations for more than 6 months. These results provide clinical validation for therapies that target the functions of HIV capsid protein, and demonstrate the potential of GS-6207 as a long-acting agent to treat or prevent infection with HIV.

Bester SM, Wei G, Zhao H, Adu-Ampratwum D, Iqbal N, Courouble VV, Francis AC, Annamalai AS, Singh PK, Shkriabai N, Van Blerkom P, Morrison J, Poeschla EM, Engelman AN, Melikyan GB, Griffin PR, Fuchs JR, Asturias FJ, Kvaratskhelia M: Structural and mechanistic bases for a potent HIV-1 capsid inhibitor. Science. 2020 Oct 16;370(6514):360-364. doi: https://doi.org/10.1126/science.abb4808

The potent HIV-1 capsid inhibitor GS-6207 is an investigational principal component of long-acting antiretroviral therapy. We found that GS-6207 inhibits HIV-1 by stabilizing and thereby preventing functional disassembly of the capsid shell in infected cells. X-ray crystallography, cryo-electron microscopy, and hydrogen-deuterium exchange experiments revealed that GS-6207 tightly binds two adjoining capsid subunits and promotes distal intra- and inter-hexamer interactions that stabilize the curved capsid lattice. In addition, GS-6207 interferes with capsid binding to the cellular HIV-1 cofactors Nup153 and CPSF6 that mediate viral nuclear import and direct integration into gene-rich regions of chromatin. These findings elucidate structural insights into the multimodal, potent antiviral activity of GS-6207 and provide a means for rationally developing second-generation therapies.

Marrazzo J. Lenacapavir for HIV-1 - Potential Promise of a Long-Acting Antiretroviral Drug. *N Engl J Med*. 2022;386(19):1848-1849. doi:10.1056/NEJMe2204376

As we walk through the lobby of a modern clinic for the treatment of patients with human immunodeficiency virus (HIV) infection or review antiretroviral regimens in the electronic medical record, it is easy to forget the days when managing multidrug-resistant HIV-1 was routine. Although the advent of protease inhibitors has saved lives, [1] many patients already had resistance mutations to then-available nucleoside reverse-transcriptase inhibitors (NRTIs). For these patients and for others who contracted HIV infection with primary resistance, the subsequent iterative availability of new drug classes, including non-NRTIs and integrase-strand transferase inhibitors, essentially offered functional monotherapy against a background of complex resistance mutations. These patients continue to be among the most challenging to treat, even in well-resourced settings. At worst, treatment options may be exhausted;

even if a suitable regimen can be designed, survival and quality of life are often compromised.[2] Globally, among adults in whom non–NRTI-based first-line antiretroviral therapy has failed, 50 to 97% have evidence of resistance to these drugs.[3]

In this issue of the *Journal*, Segal-Maurer and colleagues[4] describe a potentially new option for addressing this topic in the CAPELLA trial. Lenacapavir is a first-in-class capsid inhibitor with several important characteristics. First, it has two mechanisms of action at separate stages of the viral life cycle, thus posing a barrier to resistance that may be intrinsically higher. Second, it can be administered subcutaneously in infrequent injections up to every 6 months, which minimizes the pill burden and may improve adherence. Third, adverse events appear to be uncommon except for the formation of injection-site nodules or indurations in the small number of patients who have been evaluated. Finally, although resistance to lenacapavir was noted in 8 of 72 patients in the CAPELLA trial (mainly in those with M66I mutations), such resistance largely occurred early in the trial, and half these patients had poor adherence to their optimized background therapy. The early timing is reassuring because emergence of late resistance poses greater challenges to monitoring of the efficacy of antiretroviral therapy, especially in resource-limited settings. Moreover, some patients had viral suppression while continuing to receive lenacapavir, which suggests that reduced replication capacity of these mutants may translate into less fitness in maintaining infection.

Segal-Maurer et al. enrolled a highly treatment-experienced group of patients who had a median CD4+ count of 150 cells per cubic millimeter. The population notably included persons who are not always embraced in trials of new agents: adolescents (≥12 years of age) and patients with a relatively high body-mass index. The investigators used a rigorous definition of multidrug resistance and a two-cohort design that provided the opportunity to study lenacapavir in patients who were receiving different regimens. Cohort 1 included 36 patients who had stable viremia (i.e., a decrease of <0.5 log10 copies per milliliter between the screening and cohort-selection visits) and an HIV-1 RNA level of 400 copies or more per milliliter. These patients were randomly assigned in a 2:1 ratio to receive oral lenacapavir or matching

placebo for the first 14 days, with the initiation of subcutaneous lenacapavir on day 15 and day 29, respectively. Cohort 2 included 36 patients (3 with reduced viremia and 33 who were enrolled after cohort 1 had been closed) who all received open-label oral lenacapavir with optimized background therapy on day 1 and started to receive subcutaneous lenacapavir once every 6 months on day 15. Follow-up occurred through week 52. Finally, the patients included an ethnically and racially diverse group that was representative of patients with HIV-1 infection — notably, 25% were women, 38% were Black, and 21% were Hispanic or Latinx. However, representation from Africa and Asia was limited.

The majority of patients in both cohorts had suppression of viremia, which was defined as a reduction of at least 0.5 log10 copies per milliliter in plasma HIV-1 RNA by day 15 (the primary efficacy end point measured at the end of the functional monotherapy period) and a viral load of less than 50 copies per milliliter and less than 200 copies per milliliter at week 26 after the initiation of subcutaneous lenacapavir. By day 15 in cohort 1, viral suppression had occurred in 88% of the patients in the lenacapavir group as compared with 17% of those in the placebo group. In cohort 2, the patients also had similar viral suppression, with a mean change from baseline in viral load of −2.49 log10 copies per milliliter by 26 weeks. Finally, lenacapavir treatment resulted in a least-squares mean increase from baseline in the CD4+ count of 75 cells per cubic millimeter in cohort 1 and 104 cells per cubic millimeter in cohort 2.

Although the number of patients in this trial was small, the CAPELLA trial offers support for HIV-1 treatment with long-acting agents with mechanisms of action that may minimize the development of resistance mutations. Equally exciting is the potential for the use of such agents as HIV-1 preexposure prophylaxis, for which lenacapavir is currently being evaluated. That said, several challenges remain — most notably, obstacles to establishing the safety and efficacy of very long-acting products in women of reproductive age (15 to 49 years) who are pregnant, are breast-feeding, or wish to become pregnant.[5,6] The number of such women was projected to increase by 54% between 2015 and 2030 in sub-Saharan Africa, where the incidence of HIV-1 infection remains unacceptably high and access to modern contraceptives remains subpar.[7] Nearly half of all infants born to women with HIV infection have resistance to one or

more non-NRTIs.3 To truly change the trajectory of the global HIV pandemic, we must ensure expanded access to safe and effective life-changing medications for all patients.

Segal-Maurer S, DeJesus E, Stellbrink HJ, et al. Capsid Inhibition with Lenacapavir in Multidrug-Resistant HIV-1 Infection. *N Engl J Med*. 2022;386(19):1793-1803. doi:10.1056/NEJMoa2115542

Background:

Patients with multidrug-resistant human immunodeficiency virus type 1 (HIV-1) infection have limited treatment options. Lenacapavir is a first-in-class capsid inhibitor that showed substantial antiviral activity in a phase 1b study.

Methods:

In this phase 3 trial, we enrolled patients with multidrug-resistant HIV-1 infection in two cohorts, according to the change in the plasma HIV-1 RNA level between the screening and cohort-selection visits. In cohort 1, patients were first randomly assigned in a 2:1 ratio to receive oral lenacapavir or placebo in addition to their failing therapy for 14 days; during the maintenance period, starting on day 15, patients in the lenacapavir group received subcutaneous lenacapavir once every 6 months, and those in the placebo group received oral lenacapavir, followed by subcutaneous lenacapavir; both groups also received optimized background therapy. In cohort 2, all the patients received open-label oral lenacapavir with optimized background therapy on days 1 through 14; subcutaneous lenacapavir was then administered once every 6 months starting on day 15. The primary end point was the percentage of patients in cohort 1 who had a decrease of at least 0.5 log10 copies per milliliter in the viral load by day 15; a key secondary end point was a viral load of less than 50 copies per milliliter at week 26.

Results:

A total of 72 patients were enrolled, with 36 in each cohort. In cohort 1, a decrease of

at least 0.5 log10 copies per milliliter in the viral load by day 15 was observed in 21 of 24 patients (88%) in the lenacapavir group and in 2 of 12 patients (17%) in the placebo group (absolute difference, 71 percentage points; 95% confidence interval, 35 to 90). At week 26, a viral load of less than 50 copies per milliliter was reported in 81% of the patients in cohort 1 and in 83% in cohort 2, with a least-squares mean increase in the CD4+ count of 75 and 104 cells per cubic millimeter, respectively. No serious adverse events related to lenacapavir were identified. In both cohorts, lenacapavir-related capsid substitutions that were associated with decreased susceptibility developed in 8 patients during the maintenance period (6 with M66I substitutions).

Conclusions:

In patients with multidrug-resistant HIV-1 infection, those who received lenacapavir had a greater reduction from baseline in viral load than those who received placebo. (Funded by Gilead Sciences; CAPELLA ClinicalTrials.gov number, NCT04150068.).

Łupina K, Nowak K, Lorek D, et al. Pharmacological advances in HIV treatment: from ART to long-acting injectable therapies. *Arch Virol*. 2025;170(9):195. Published 2025 Aug 19. doi:10.1007/s00705-025-06381-8

Human immunodeficiency virus (HIV) remains a global public health challenge, affecting millions worldwide despite significant advancements in antiretroviral therapy (ART). While ART has transformed HIV into a manageable chronic condition, long-term adherence, drug resistance, and access disparities continue to hinder treatment success. Recent research has focused on developing alternative therapeutic strategies, particularly long-acting injectable (LAI) therapies and immunotherapeutic approaches to improve adherence and potentially achieve viral remission. This review explores the evolution of pharmacological advancements in HIV treatment, highlighting the transition from daily oral ART to long-acting formulations such as cabotegravir, rilpivirine, and lenacapavir. LAI therapies reduce the burden of daily adherence, enhance treatment efficacy, and decrease stigma, particularly in

vulnerable populations. Additionally, novel immunotherapeutic strategies such as broadly neutralizing antibodies, immune checkpoint inhibitors, and chimeric antigen receptor T cell therapy are being investigated for their potential to induce long-term viral suppression or cure. Despite these promising developments, several challenges remain, including resistance-associated mutations, accessibility issues, and long-term safety concerns. This review summarizes recent clinical trials, discusses the benefits and limitations of emerging HIV therapies, and outlines future research directions. The continued advancement of LAI therapies and immunotherapeutics holds great potential to improve treatment outcomes, expand global access to care, and move closer to a functional cure for HIV.

Saidi F, Hosseinipour MC, Chi BH. Long-Acting Injectable Antiretroviral Drugs for Pregnant and Breastfeeding Women: Current Advances, Challenges, and Future Directions. *Curr HIV/AIDS Rep*. 2025;22(1):44. Published 2025 Aug 15. doi:10.1007/s11904-025-00751-2

This review explores the promise and challenges of integrating long-acting antiretroviral agents-cabotegravir, lenacapavir, and cabotegravir-rilpivirine-into HIV prevention and treatment programs for pregnant and breastfeeding populations. It aims to examine current evidence, implementation experiences, and barriers to equitable access.

Emerging data support the efficacy and safety of long-acting agents during pregnancy and breastfeeding. Recent clinical trials have begun to include pregnant women by design, and national demonstration projects have successfully introduced injectable PrEP in maternal health settings. These developments signal growing recognition of the need for inclusive research and service delivery models. Long-acting antiretrovirals have the potential to transform maternal HIV prevention and treatment. However, challenges such as delayed inclusion in trials, policy constraints, limited product choice, high costs, and funding limitations persist. Addressing these gaps is critical to ensuring equitable access and informing future research and implementation strategies.

Pebody R. WHO recommends lenacapavir for HIV prevention. *Lancet HIV*. Published online August 5, 2025. doi:10.1016/S2352-3018(25)00224-3

WHO issued guidelines supporting the use of lenacapavir for pre-exposure prophylaxis (PrEP) on July 14, 2025, less than 13 months after the first press release announcing 100% efficacy in the PURPOSE-1 study.

Anderer S. WHO Recommends Lenacapavir for HIV Prevention in New Guidelines. *JAMA*. Published online August 1, 2025. doi:10.1001/jama.2025.10988

New guidelines released by the World Health Organization (WHO) recommend the use of injectable lenacapavir, the first twice-yearly preexposure prophylaxis (PrEP) option for HIV prevention.

The US Food and Drug Administration (FDA) recently approved the long-acting antiretroviral lenacapavir, marketed as Yeztugo, as an effective alternative to daily oral pills and other shorter-acting PrEP. Requiring only 2 doses per year, lenacapavir could be useful for people who face challenges with daily adherence, stigma, or access to health care, WHO noted.

The guidelines also state that rapid HIV diagnostic tests, which deliver results in less than 30 minutes, may be used to inform treatment decisions for long-acting PrEP. Assays of blood or saliva can reduce costs and minimize delays compared with nucleic acid testing techniques.

Access to lenacapavir remains limited in clinical settings, but WHO urges governments, donors, and global health partners to begin using the drug to diversify HIV prevention efforts as the infection continues to spread. In 2024, an estimated 1.3 million people were newly diagnosed with HIV, with a disproportionate risk among men who have sex with men, people who inject drugs, people in prisons, sex workers, and transgender individuals.

Kirby T.New lenacapavir guidelines from WHO. *Lancet Infect Dis*. Published online August 4, 2025. doi:10.1016/S1473-3099(25)00490-6

WHO has announced that twice-yearly injections of lenacapavir should be included as an additional HIV prevention option and that rapid diagnostic tests (RDTs) can be used for HIV testing for initiation, continuation, and discontinuation of lenacapavir and other long-acting and daily-oral pre-exposure prophylaxis (PrEP).

Lynch S, Cohen RM, Kavanagh M, et al. Lessons for long-acting lenacapavir: catalysing equitable PrEP access in low-income and middle-income countries. *Lancet HIV*. Published online July 11, 2025. doi:10.1016/S2352-3018(25)00161-4

Despite substantial advances in biomedical HIV prevention, including long-acting injectable pre-exposure prophylaxis (PrEP) options such as cabotegravir, barriers to widespread adoption and scale-up persist in low-income and middle-income countries. Long-acting injectable lenacapavir is a potentially transformative HIV prevention tool, providing an unprecedented opportunity to accelerate progress. However, the global HIV response is under threat like never before, with drastic funding cuts undermining the gains of the past 25 years. The challenges of introducing and scaling up long-acting lenacapavir and other PrEP innovations are numerous. Without deliberate policy, programmatic, and financing interventions, new prevention technologies risk following slow adoption patterns of previous innovations, weakening a needed transformation of the HIV response. Drawing on lessons from the scale-up of antiretroviral therapy, and experience with previous biomedical prevention tools, a new ten-point framework should be adopted to accelerate individual and epidemiological impact-even at this time of extraordinary uncertainty.

Vail RM, Cantor A, Shah SS, et al. *Interim Guideline on the Use of Twice-Yearly Lenacapavir for HIV Prevention*. Baltimore (MD): Johns Hopkins University; July 2025.

Subcutaneous Lenacapavir as PrEP

- Clinicians should recommend SC LEN as a preferred PrEP regimen for protection against HIV through sexual exposure for individuals who are willing to receive subcutaneous injections every 6 months and have no contraindications or barriers to its use. For other preferred PrEP regimens, see the NYSDOH AI guideline PrEP to Prevent HIV and Promote Sexual Health.
- Clinicians should discuss potential risks and benefits and engage individuals who are or may become pregnant in shared decision-making when considering SC LEN as PrEP.

Cantos VD, Ramírez BC, Kelley CF, Rio CD, Grinsztejn B. Lenacapavir: a potential game changer for HIV prevention in the Americas, if the game is played equitably. *Lancet Reg Health Am*. 2025;47:101146. Published 2025 Jun 10. doi:10.1016/j.lana.2025.101146

Lenacapavir, a first in class long-acting capsid inhibitor has near 100% efficacy in preventing HIV. As such, it has the potential to curb the rising HIV incidence in Latin America, a region with stark intra- and inter-country PrEP uptake disparities. In this viewpoint, we summarize the current efforts to scale up lenacapavir access globally and the necessary steps to include Latin America in these endeavours.

van Zyl G, Prochazka M, Schmidt HA, et al. Lenacapavir-associated drug resistance: implications for scaling up long-acting HIV pre-exposure prophylaxis. *Lancet HIV*. Published online June 18, 2025. doi:10.1016/S2352-3018(25)00128-6

Although drug resistance could emerge if lenacapavir is initiated during undiagnosed acute infection or if infection occurs during the drug's pharmacokinetic tail, these cases will not compromise the effectiveness of WHO-recommended therapies, as there is no cross-resistance between lenacapavir and other licensed antiretroviral drugs. Lenacapavir pre-exposure prophylaxis (PrEP) is also unlikely to drive population-level

lenacapavir resistance given the rarity of breakthrough infections and the reduced replication capacity of most lenacapavir-resistant variants, which most likely reduces their transmission potential. Conversely, the risk of acquiring lenacapavir-resistant HIV-1 while receiving lenacapavir PrEP is likely to remain extremely low, as lenacapavir-associated drug-resistance mutations are rare among individuals without previous lenacapavir exposure, and widespread use of lenacapavir-based regimens remains years away. Nonetheless, as the number of lenacapavir PrEP programmes increase, surveillance for emerging lenacapavir resistance should also be implemented.

Additional documents

No documents were uploaded

Useful links

- Gilead Announces First Global Regulatory Approval of Sunlenca® (Lenacapavir)
- PURPOSE PrEP Studies Overview: Prevention With a Purpose
- An Overview of Lenacapavir for PrEP Trials (AVAC)
- Pharmacokinetics and safety of once-yearly lenacapavir: a phase 1, open-label study
- Capsid Inhibition with Lenacapavir in Multidrug-Resistant HIV-1 Infection
- CROI 2022: Lenacapavir: 54 week results in treatment-naive participants of CALIBRATE study
- Lenacapavir administered every 26 weeks or daily in combination with oral daily antiretroviral therapy for initial treatment of HIV: a randomised, open-label, active-controlled, phase 2 trial
- Interim Resistance Analysis of Long-Acting Lenacapavir in Treatment-Naïve People with HIV at 28 Weeks
- Clinical targeting of HIV capsid protein with a long-acting small molecule
- Guidelines on lenacapavir for HIV prevention and testing strategies for long-acting injectable pre-exposure prophylaxis
- Will long-lasting HIV preventive be a game changer—or a missed opportunity? Kupferschmidt K. , Science. 2025

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