

Developed by











Lenacapavir Six-Monthly

Supported by

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 Chemical Structure

Sourced from DrugBank

Drug information

Associated long-acting platforms

Aqueous Solution, Oral solid form

Administration route

Subcutaneous, Oral

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

User acceptance

Not provided

Dosage

Available dose and strength

Oral lead-in LEN tablets 300 mg; Each injection contains 927 mg of lenacapavir in solution.

Frequency of administration

Once every 26 weeks +/- 2 weeks from date of last injection.

Maximum dose

Not provided

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)

https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/215973s000lbl.pdf

Drug information

Drug's link(s)

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

Generic name

Lenacapavir

Brand name

Sunlenca

Compound type

Small molecule

Summary

Six monthly lenacapavir (LEN) is a subcutaneous injectable formulation used for the treatment of multi-drug resistant HIV-1 infection in combination with other antiretrovirals and is currently being studied as potential HIV pre-exposure prophylaxis (PrEP). Two large Phase III clinical trials (PURPOSE 1 & 2) and three Phase II trials (PURPOSE 3, 4 & 5) are currently evaluating the safety and efficacy of subcutaneous lenacapavir for PrEP. Six-monthly LEN is administered subcutaneously every 26 weeks (+/- 2 weeks from date of last injection) following an initial two day oral-loading period of 600 mg (2 x 300-mg tablets). LEN was approved in the EU for the treatment of HIV-positive adults with multidrug resistance in Aug 2022, and received approval from the U.S. FDA in Dec 2022.

Approval status

Lenacapavir (SUNLENCA) 463.5mg/3ml subcutaneous injection with 300mg oral lead-in tablets are approved for use in the United States, United Kingdom, Canada, UAE, South Korea, Hong Kong, Japan, Australia, Israel, and the European Union (27-member states of the European Union, as well as Norway, Iceland and Liechtenstein) for HIV-1 treatment under certain conditions. For PrEP: Gilead submitted an application to the US FDA for Lenacapavir in December 2024 and was granted priority review with a decision expected by June 19, 2025. It is also under review in Brazil, EU (+EEA) and South Africa.

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.

Delivery device(s)

No delivery device

Scale-up and manufacturing prospects

Scale-up prospects

Compound is commercially manufactured.

Tentative equipment list for manufacturing

Equipment: 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 Dosage: 300 mg

Intervention 2 Drug: Oral Lenacapavir Placebo Dosage: 0 mg

Intervention 3 Drug: Subcutaneous Lenacapavir Dosage: 927 mg

Intervention 4 Drug: Failing ARV Regimen

Intervention 5 Drug: Optimized Background Regimen (OBR)

Countries

United States of America Canada France Germany Italy Japan South Africa Spain Taiwan, Province of China Thailand Dominican Republic

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2019-11-21

Anticipated Date of Last Follow-up

2024-06-26

Estimated Primary Completion Date Not provided

Estimated Completion Date

2027-01-01

Actual Primary Completion Date 2020-10-05

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 \geq 18 years (at all sites) or adolescent aged \geq 12 and weighing \geq 35 kg (at sites in North America and Dominican Republic). Currently receiving a stable failing ARV regimen for > 8 weeks. Have HIV-1 RNA \geq 400 copies/mL at screening. Have multidrug resistance (resistance to \geq 2 agents from \geq 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

Once every 6 months

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Subcutaneous

Oral

Use case

Treatment

Key results

Type of key results	Title	Website link
Article	Capsid Inhibition with Lenacapavir in Multidrug-Resistant HIV-1	https://www.nejm.org/doi/10.1056/NEJM
	Infection	

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 Dosage: 600 mg and 300 mg

Intervention 2

Drug: F/TAF

Dosage: 200/25 mg

Intervention 3 Drug: Subcutaneous Lenacapavir Dosage: 927 mg

Intervention 4

Drug: TAF Dosage: 25 mg

Intervention 5

Drug: BIC Dosage: 75 mg

Countries

United States of America Puerto Rico Dominican Republic

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2019-11-22

Anticipated Date of Last Follow-up 2023-10-03

Estimated Primary Completion Date Not provided

Estimated Completion Date

Not provided

Actual Primary Completion Date

2021-09-30

Actual Completion Date

2023-09-13

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 \geq 200 copies/mL at screening. CD4+ cell count \geq 200 cells/microliter at screening.

Health status

Positive to : HIV Negative to : HBV, HCV

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

Once every 6 months

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Subcutaneous

Oral

Use case

Treatment

Key results

Type of key results	Title	Website link
Abstract	CROI 2022: Lenacapavir: 54 week results in treatment-naive participants of CALIBRATE study	https://i-base.info/htb/42313
Article	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	<u>https://doi.org/10.1016/S2352-</u> <u>3018(22)00291-0</u>
Article	Interim Resistance Analysis of Long-Acting Lenacapavir in Treatment-Naïve People with HIV at 28 Weeks	https://doi.org/10.1093%2Fofid%2Fofat

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)

Dosage: 600 mg

Intervention 2 Subcutaneous (SC) Lenacapavir (LEN) Dosage: 927 mg

Intervention 3

Oral F/TAF Dosage: 200/25 mg

Intervention 4

Oral F/TDF Dosage: 200/300 mg

Intervention 5

Placebo SC LEN Dosage: 0 mg

Countries

South Africa Uganda

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date 2021-08-30

Anticipated Date of Last Follow-up

2024-02-26

Estimated Primary Completion Date

2024-09-01

Estimated Completion Date

2027-07-01

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) \geq 60 mL/min at screening. * Body weight \geq 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

Once every 6 months

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Subcutaneous

Oral

Use case

PrEP

Key results

Type of key results	Title	Website link
Article	Various Resources related to PURPOSE trials	https://www.purposestudies.com/study- investigators/
Abstract	Twice-Yearly Lenacapavir or Daily F/TAF for HIV Prevention in Cisgender Women	https://www.nejm.org/doi/full/10.1056/N

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) Dosage: 600 mg

Intervention 2

Oral F/TDF Dosage: 200/300 mg

Intervention 3 Subcutaneous (SC) Lenacapavir (LEN) Dosage: 927 mg

Intervention 4 Placebo SC LEN Dosage: 0 mg

Intervention 5 Placebo to match F/TDF Dosage: 0 mg

Countries

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

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2021-06-28

Anticipated Date of Last Follow-up

2024-07-11

Estimated Primary Completion Date 2024-12-01

Estimated Completion Date 2028-05-01

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 \geq 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 \geq 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

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

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

Once every 6 months

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Oral

Use case

PrEP

Key results

Type of key

results	Title	Website link
Article	Proactive strategies to optimize engagement of Black, Hispanic/Latinx, transgender, and nonbinary individuals in a trial of a novel agent for HIV pre-exposure prophylaxis (PrEP)	https://pubmed.ncbi.nlm.nih.gov/35657

Type of key results	Title	Website link
Article	Gilead's Twice-Yearly Lenacapavir for HIV Prevention Reduced HIV Infections by 96% and Demonstrated Superiority to Daily Truvada® in Second Pivotal Phase 3 Trial	https://www.gilead.com/news/news- details/2024/gileads- twiceyearly-lenacapavir-for-hiv- prevention-reduced-hiv- infections-by-96-and- demonstrated-superiority-to- daily-truvada

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

Anticipated Date of Last Follow-up

2023-10-26

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

Comments about the studied populations

On first-line antiretroviral therapy (ART) for \geq 2 years prior to screening. A change in ART regimen \geq 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 : HBV, HCV 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

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

Not provided

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Subcutaneous

Oral

Use case

Treatment

Key results

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 Dosage: 20 mg, 50 mg, 150 mg, 450 mg and 750 mg

Intervention 2

Drug: Placebo Dosage: 0 mg

Intervention 3

Drug: B/F/TAF Dosage: 50/200/25 mg

Intervention 4

Drug: TAF Dosage: 200 mg and 600 mg

Countries

United States of America

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2018-11-26

Anticipated Date of Last Follow-up

2021-03-16

Estimated Primary Completion Date

Not provided

Estimated Completion Date Not provided

Actual Primary Completion Date
2019-11-14

Actual Completion Date

2020-06-15

Studied populations

Age Cohort

- Adults
- Older Adults

Genders

• All

Accepts pregnant individuals No

Accepts lactating individuals

Accepts healthy individu	als
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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 : "Single dose "

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Subcutaneous

Use case

Treatment

Key results

Title	Website link
Clinical targeting of HIV capsid protein with a long-acting small	https://doi.org/10.1038/s41586- 020-2443-1
	Title Clinical targeting of HIV capsid protein with a long-acting small molecule

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 Dosage: 600 mg

Intervention 2

Drug: Long-acting Subcutaneous Lenacapavir Injection Dosage: 927 mg

Intervention 3

Drug: Emtricitabine/Tenofovir Disoproxil Fumarate (F/TDF) Dosage: 200/300 mg

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

2025-04-01

Estimated Primary Completion Date 2027-03-01

Estimated Completion Date 2028-10-01

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

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

Once every 6 months

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Subcutaneous

Oral

Use case

PrEP

Key results

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 Dosage: 927 mg

Intervention 2

Drug: Lenacapavir Tablet Dosage: 600 mg

Intervention 3

Drug: Emtricitabine/tenofovir disoproxil fumarate (F/TDF) Dosage: 200/300 mg

Countries

United States of America

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2023-12-13

Anticipated Date of Last Follow-up

2024-08-08

Estimated Primary Completion Date 2027-07-01

Estimated Completion Date

2027-07-01

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 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

Once every 6 months

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Subcutaneous

Oral

Use case

PrEP

Key results

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 Dosage: 600 mg

Intervention 4 Drug: Lenacapavir Injection Dosage: 927 mg

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 2024-07-12

Estimated Primary Completion Date 2025-03-01

Estimated Completion Date

2029-12-01

Actual Primary Completion Date

2024-07-02

Actual Completion Date

Not provided

Studied populations

Age Cohort

- Adults
- Older Adults

Genders

• All

Accepts pregnant individuals Unspecified

Accepts lactating individuals Unspecified

Accepts healthy individuals

No

Comments about the studied populations

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

Health status

Positive to : HIV

Negative to : HBV, HCV

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

Subcutaneous

Use case

Treatment

Key results

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

Actual Start Date Not provided

Anticipated Date of Last Follow-up 2024-03-20

Estimated Primary Completion Date 2024-04-15

Estimated Completion Date 2024-07-30

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

Once every 6 months

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Subcutaneous

Use case

Treatment

Key results

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 Dosage: 927 mg

Intervention 2 Drug: Lenacapavir Tablet Dosage: 600 mg

Intervention 3 Drug: Emtricitabine/tenofovir disoproxil fumarate (F/TDF) Dosage: 200/300 mg

Countries

France United Kingdom

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

2024-09-01

Actual Start Date

Not provided

Anticipated Date of Last Follow-up

2024-08-22

Estimated Primary Completion Date 2027-01-01

Estimated Completion Date 2029-07-01

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 \geq 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 \geq 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 (\geq 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

Once every 6 months

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Subcutaneous

Use case

PrEP

Key results

GS-US-200-6712

Identifier

NCT06749054

Link

https://clinicaltrials.gov/study/NCT06749054

Phase

Phase II

Status

Recruiting

Sponsor

Gilead Sciences

More details

The goal of this clinical study is to learn more about the study drug, lenacapavir (LEN). The study will assess the safety, tolerability, and efficacy of long-acting LEN when combined with other medicines in adolescents and children living with HIV-1 who weigh at least 35 kg and have been treated before for HIV-1. The study will also see how easy it is for participants to take LEN as injection or an oral pill. The primary objectives are to evaluate the pharmacokinetics and safety of LEN in combination with optimized background regimen (OBR) in TE pediatric participants with HIV-1.

Purpose

Evaluation of Long-Acting Lenacapavir for the Treatment of HIV-1 in Treatmentexperienced Adolescents and Children

Interventions

Intervention 1 Oral Lenacapavir

Intervention 2 Subcutaneous Lenacapavir

Intervention 3 Optimized Background Regimen (OBR)

Countries

United States of America South Africa

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2025-03-26

Anticipated Date of Last Follow-up 2025-05-07

Estimated Primary Completion Date 2026-06-01

Estimated Completion Date

2026-12-01

Actual Primary Completion Date

Actual Completion Date

Not provided

Studied populations

Age Cohort

- Children
- Adolescents

Genders

• All

Accepts pregnant individuals Unspecified

Accepts lactating individuals Unspecified

Accepts healthy individuals

Comments about the studied populations

Key Inclusion Criteria: * Body weight at screening \geq 35 kg. * On a stable failing antiretroviral (ARV) regimen for \geq 8 weeks before screening and willing to continue the regimen until Day 1. * Plasma HIV-1 RNA \geq 400 copies/mL on at least 2 consecutive occasions spanning at least 6 months, including at screening. * Have previously changed their ARV regimen due to treatment failure. * ARV treatment options limited due to resistance, tolerability, contraindications, safety, drug access. * Able and willing to commit to taking LEN in combination with their OBR. * The following laboratory parameters at screening: 1. Estimated glomerular filtration rate (eGFR) \geq 60 mL/min/1.73 m\^2 using Bedside Schwartz Formula. 2. Absolute neutrophil count \geq 0.50 GI/L (\geq 500 cells/mm\^3). 3. Hemoglob

Health status

Negative to : TB, HBV, HCV

Study type

Interventional (clinical trial)

Enrollment

12

Allocation

Not provided

Intervention model

Single group assignment

Intervention model description

Not provided

Masking

Open label

Masking description

Not provided

Frequency of administration

Once every 6 months

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Subcutaneous

Use case

Treatment

Key results

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

Pending...

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

2025-05-26

Actual Start Date Not provided

Anticipated Date of Last Follow-up 2025-05-20

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

Once every 6 months

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Subcutaneous

Use case

Treatment

Key results

223616

Identifier

NCT06970223

Link

https://clinicaltrials.gov/study/NCT06970223

Phase

Phase I

Status

Recruiting

Sponsor

ViiV Healthcare

More details

This study will evaluate the tolerability and acceptability of injection site reactions (ISRs) of two long-acting (LA) injectables. Additional characteristics of the ISRs will be investigated and described as well as safety outcomes.

Purpose

A Study to Investigate if Long Acting Cabotegravir (CAB) and Lenacapavir (LEN) Injections Are Tolerable and Acceptable When Administered to Healthy Adults Without HIV

Interventions

Intervention 1 Cabotegravir long-acting

Intervention 2

Lenacapavir long-acting

Countries

United States of America

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date Not provided

Actual Start Date

2025-04-22

Anticipated Date of Last Follow-up 2025-05-05

Estimated Primary Completion Date 2025-07-30

Estimated Completion Date 2026-07-07

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

Inclusion Criteria: Participants are eligible to be included in the study only if all the following criteria apply: 1. At the time of obtaining informed consent, 18 years of age. 2. Body weight 50 kg and BMI within the range 18 to 32 kg/m2 (inclusive). 3. Participants who are overtly healthy as determined by medical evaluation by a responsible and experienced physician, including medical history, physical examination, laboratory tests and cardiac monitoring. 4. A participant with a significant clinical abnormality or laboratory parameter(s) which is/are not specifically listed in the inclusion or exclusion criteria, outside the reference range for the population being studied may be included if the investigator determines and documents that the finding is unlikely to introduce additional

Health status

Not provided

Study type

Interventional (clinical trial)

Enrollment

60

Allocation

Randomized

Intervention model

Cross-over assignment

Intervention model description

Not provided

Masking

Open label

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 results

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 in HIV pre- exposure prophylaxis (PrEP) Expiry date: 2040-11-25	WO2021108544	Use	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, 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, Japan, Taiwan, Province of China, Hong Kong
Not in force	World Intellectual Property Organization (WIPO), Morocco, Tunisia, Bosnia and Herzegovina, Cambodia, Montenegro, Moldova, Republic of	World Intellectual Property Organization (WIPO), Japan, Korea, Republic of, United States of America

MPP Licence(s)

Bilateral licence on lenacapavir (LEN)

			Licence	
	Representative		with	Patent
Patent description	patent	Categories Patent holder	MPP	source
Longoppyinuse to treat multidrug	W02020018450		Vac	
Lenacapavir use to treat multidrug	02020018459		res	
resistant HIV infection in heavily				
treatment-experienced				
Expiry date: 2039-07-15				

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), Canada, Japan, Korea, Republic of

MPP Licence(s)

Bilateral licence on lenacapavir (LEN)

		Licence		
	Representative		with	Patent
Patent description	patent	Categories Patent holder	МРР	source
Lenacapavir manufacturing	WO2019161280	Intermediate(s),	Yes	
processess and intermediates		Process		
Expiry date: 2039-02-15				

Patent status

Patent status/countries	Low, Low- middle and upper-middle	High income
Granted	China, Albania, Türkiye, North Macedonia, India	Australia, Liechtenstein, Italy, Norway, Malta, Denmark, Belgium, United Kingdom, Greece, Netherlands, Switzerland, Spain, Slovenia, Austria, Cyprus, 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
Not in force	World Intellectual Property Organization (WIPO), Argentina, Morocco, Tunisia, Serbia, Bosnia and Herzegovina, Cambodia, Montenegro, Moldova, Republic of	World Intellectual Property Organization (WIPO), Hungary, Croatia, San Marino, Romania, Iceland, Lithuania, Monaco, Japan, Korea, Republic of, Bahamas

MPP Licence(s)

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	Low, Low- middle and upper-middle	High income 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, Malta, Norway, San Marino, 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, United States of America, 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)

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

Patent status/countries

Filed

Low, Low- middle and upper-middle Hig

Türkiye, North Macedonia, Albania, Serbia, Morocco, Argentina, Costa Rica, Jordan, Philippines, India, Uganda, Egypt, Guatemala, Indonesia, Nigeria, Thailand, Ukraine, Viet Nam

High income

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, Japan, Singapore, Taiwan, Province of China, United States of America, Saudi Arabia, Panama

World Intellectual Property Organization (WIPO), Monaco, Malta, San Marino, Chile, Japan, Korea, Republic of, Uruguay, Trinidad and Tobago

Not in force

World Intellectual Property Organization (WIPO), North Macedonia, Albania, Bosnia and Herzegovina, Montenegro, Serbia, Moldova, Republic of, 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)

MPP Licence(s)

Bilateral licence on lenacapavir (LEN)

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	WO2014134566	Compound	Gilead Sciences, Inc	Yes	
virus.					

Patent status

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

Patent status/countries	Low, Low- middle and upper-middle	High income
Filed	Türkiye, North Macedonia, Albania, Serbia, Argentina, Costa Rica, 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, Hong Kong, Japan, New Zealand, Singapore, United States of America, Uruguay, Bahamas

MPP Licence(s)

Bilateral licence on lenacapavir (LEN)

Supporting material

Publications

Link JO, Rhee MS, Tse WC, Zheng J, Somoza JR, Rowe W, Begley R, Chiu A, Mulato A, Hansen D, Singer E, Tsai LK, Bam RA, Chou CH, Canales E, Brizgys G, Zhang JR, Li J, Graupe M, Morganelli P, Liu Q, Wu Q, Halcomb RL, Saito RD, Schroeder SD, Lazerwith SE, Bondy S, Jin D, Hung M, Novikov N, Liu X, Villasenor AG, Cannizzaro CE, Hu EY, Anderson RL, Appleby TC, Lu B, Mwangi J, Liclican A, Niedziela-Majka A, Papalia GA, Wong MH, Leavitt SA, Xu Y, Koditek D, Stepan GJ, Yu H, Pagratis N, Clancy S, Ahmadyar S, Cai TZ, Sellers S, Wolckenhauer SA, Ling J, Callebaut C, Margot N, Ram RR, Liu YP, Hyland R, Sinclair GI, Ruane PJ, Crofoot GE, McDonald CK, Brainard DM, Lad L, Swaminathan S, Sundquist WI, Sakowicz R, Chester AE, Lee WE, Daar ES, Yant SR, Cihlar T: 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.

Zhuang S, Torbett BE: Interactions of HIV-1 Capsid with Host Factors and Their Implications for Developing Novel Therapeutics. Viruses. 2021 Mar 5;13(3). pii: v13030417. doi: https://doi.org/10.3390/v13030417

The Human Immunodeficiency Virus type 1 (HIV-1) virion contains a conical shell, termed capsid, encasing the viral RNA genome. After cellular entry of the virion, the capsid is released and ensures the protection and delivery of the HIV-1 genome to the host nucleus for integration. The capsid relies on many virus-host factor interactions which are regulated spatiotemporally throughout the course of infection. In this paper, we will review the current understanding of the highly dynamic HIV-1 capsid-host interplay during the early stages of viral replication, namely intracellular capsid trafficking after viral fusion, nuclear import, uncoating, and integration of the viral genome into host chromatin. Conventional anti-retroviral therapies primarily target HIV-1 enzymes. Insights of capsid structure have resulted in a first-in-class, long-acting capsid-targeting inhibitor, GS-6207 (Lenacapavir). This inhibitor binds at the interface between capsid protein subunits, a site known to bind host factors, interferes with capsid nuclear import, HIV particle assembly, and ordered assembly. Our review will highlight capsid structure, the host factors that interact with capsid, and highthroughput screening techniques, specifically genomic and proteomic approaches, that have been and can be used to identify host factors that interact with capsid. Better structural and mechanistic insights into the capsid-host factor interactions will significantly inform the understanding of HIV-1 pathogenesis and the development of capsid-centric antiretroviral therapeutics.

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.

Singh K, Gallazzi F, Hill KJ, Burke DH, Lange MJ, Quinn TP, Neogi U, Sonnerborg A: GS-CA Compounds: First-In-Class HIV-1 Capsid Inhibitors Covering Multiple Grounds. Front Microbiol. 2019 Jun 20;10:1227. doi: https://doi.org/10.3389/fmicb.2019.01227

Recently reported HIV-1 capsid (CA) inhibitors GS-CA1 and GS-6207 (an analog of GS-CA1) are first-in-class compounds with long-acting potential. Reportedly, both compounds have greater potency than currently approved anti-HIV drugs. Due to the limited access to experimental data and the compounds themselves, a detailed mechanism of their inhibition is yet to be delineated. Using crystal structures of capsid-hexamers bound to well-studied capsid inhibitor PF74 and molecular modeling, we predict that GS-CA compounds bind in the pocket that is shared by previously reported CA inhibitors and host factors. Additionally, comparative modeling suggests that GS-CA compounds have unique structural features contributing to interactions with capsid. To test their proposed binding mode, we also report the design of a cyclic peptide combining structural units from GS-CA compounds, host factors, and previously reported capsid inhibitors. This peptide (Pep-1) binds CA-hexamer with a docking score comparable to GS-CA compounds. Affinity determination by MicroScale thermophoresis (MST) assays showed that CA binds Pep-1 with a ~7-fold better affinity than well-studied capsid inhibitor PF74, suggesting that it can be developed as a possible CA inhibitor.

Margot N, Ram R, Rhee M, Callebaut C: Absence of Lenacapavir (GS-6207) Phenotypic Resistance in HIV Gag Cleavage Site Mutants and in Isolates with Resistance to Existing Drug Classes. Antimicrob Agents Chemother. 2021 Feb 17;65(3). pii: AAC.02057-20. doi: https://doi.org/10.1128/aac.02057-20. Print 2021 Feb 17

Lenacapavir (LEN; GS-6207) is a potent first-in-class inhibitor of HIV-1 capsid with longacting properties and the potential for subcutaneous dosing every 3 months or longer. In the clinic, a single subcutaneous LEN injection (20 mg to 750 mg) in people with HIV (PWH) induced a strong antiviral response, with a >2.3 mean log10 decrease in HIV-1 RNA at day 10. HIV-1 Gag mutations near protease (PR) cleavage sites have emerged with the use of protease inhibitors (PIs). Here, we have characterized the activity of LEN in mutants with Gag cleavage site mutations (GCSMs) and mutants resistant to other drug classes. HIV mutations were inserted into the pXXLAI clone, and the resulting mutants (n = 70) were evaluated using a 5-day antiviral assay. LEN EC50 fold change versus the wild type ranged from 0.4 to 1.9 in these mutants, similar to that for the control drug. In contrast, reduced susceptibility to PIs and maturation inhibitors (MIs) was observed. Testing of isolates with resistance against the 4 main classes of drugs (n = 40) indicated wild-type susceptibility to LEN (fold change ranging from 0.3) to 1.1), while reduced susceptibility was observed for control drugs. HIV GCSMs did not impact the activity of LEN, while some conferred resistance to MIs and PIs. Similarly, LEN activity was not affected by naturally occurring variations in HIV Gag, in contrast to the reduced susceptibility observed for MIs. Finally, the activity of LEN was not affected by the presence of resistance mutations to the 4 main antiretroviral (ARV) drug classes. These data support the evaluation of LEN in PWH with multiclass

resistance.

Swanstrom, A.E. *et al.* (2023). Long-acting lenacapavir protects macaques against intravenous challenge with simian-tropic HIV. *eBioMedicine*, 95, p. 104764. DOI: 10.1016/j.ebiom.2023.104764.

Background

Long-acting subcutaneous lenacapavir (LEN), a first-in-class HIV capsid inhibitor approved by the US FDA for the treatment of multidrug-resistant HIV-1 with twice yearly dosing, is under investigation for HIV-1 pre-exposure prophylaxis (PrEP). We previously derived a simian-tropic HIV-1 clone (stHIV-A19) that encodes an HIV-1 capsid and replicates to high titres in pigtail macaques (PTM), resulting in a nonhuman primate model well-suited for evaluating LEN PrEP in vivo.

Methods

Lenacapavir potency against stHIV-A19 in PTM peripheral blood mononuclear cells in vitro was determined and subcutaneous LEN pharmacokinetics were evaluated in naïve PTMs in vivo. To evaluate the protective efficacy of LEN PrEP, naïve PTMs received either a single subcutaneous injection of LEN (25 mg/kg, N = 3) or vehicle (N = 4) 30 days before a high-dose intravenous challenge with stHIV-A19, or 7 daily subcutaneous injections of a 3-drug control PrEP regimen starting 3 days before stHIV-A19 challenge (N = 3).

Findings

In vitro, LEN showed potent antiviral activity against stHIV-A19, comparable to its potency against HIV-1. In vivo, subcutaneous LEN displayed sustained plasma drug exposures in PTMs. Following stHIV-A19 challenge, while all vehicle control animals became productively infected, all LEN and 3-drug control PrEP animals were protected from infection.

Interpretation

These findings highlight the utility of the stHIV-A19/PTM model and support the clinical development of long-acting LEN for PrEP in humans.

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)
- <u>Global Fund</u>, PEPFAR Announce Coordinated Effort to Reach 2 Million People with Lenacapavir for PrEP to Significantly Reduce Global HIV Infections - Dec 2024

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

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