Lenacapavir (LEN)
Gilead Sciences Inc.
https://www.gilead.com/

United States

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

Sourced from DrugBank
Drug information

Associated long-acting platforms
Aqueous drug particle suspension

Administration route
Subcutaneous, Oral

Therapeutic area(s)
HIV

Use case(s)
Pre-Exposure Prophylaxis (PrEP)
Treatment

Use of drug

Ease of administration
Administered by a nurse
Administered by a specialty health worker

User acceptance
Not provided
Drug information

Drug's link(s)
Not provided

Generic name
Lenacapavir

Brand name
Sunlenca

Compound type
Small molecule

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. Long-acting versions of LEN are administered every 26 weeks (six months) as a subcutaneous injection following an initial oral-loading period. 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 is 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.

**Regulatory authorities**

US FDA granted Breakthrough Therapy Designation for SUNLECA 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 SUNLECA 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
Drug: Oral Lenacapavir
Drug: Oral Lenacapavir Placebo
Drug: Subcutaneous Lenacapavir
Drug: Failing ARV Regimen
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**
Not provided

**Estimated Primary Completion Date**
Not provided
Estimated Completion Date
2025-12-01

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 ≥ 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**

Bi-yearly
Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Subcutaneous

Use case

Treatment

Key results

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<thead>
<tr>
<th>Type of key results</th>
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<tbody>
<tr>
<td>Article</td>
<td>Capsid Inhibition with Lenacapavir in Multidrug-Resistant HIV-1 Infection</td>
<td><a href="https://www.nejm.org/doi/10.1056/NEJMoa2115542">https://www.nejm.org/doi/10.1056/NEJMoa2115542</a></td>
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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
Drug: Oral Lenacapavir
Drug: F/TAF
Drug: Subcutaneous Lenacapavir
Drug: TAF
Drug: BIC
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
Not provided

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 ≥ 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**

Bi-yearly

**Studied LA-formulation(s)**

Injectable

**Studied route(s) of administration**

Subcutaneous

**Use case**

Treatment

**Key results**

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<tr>
<td>Abstract</td>
<td>CROI 2022: Lenacapavir: 54 week results in treatment-naive participants of CALIBRATE study</td>
<td><a href="https://i-base.info/htb/42313">https://i-base.info/htb/42313</a></td>
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<tr>
<td>Article</td>
<td>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</td>
<td><a href="https://doi.org/10.1016/S2352-3018(22)00291-0">https://doi.org/10.1016/S2352-3018(22)00291-0</a></td>
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<td>Article</td>
<td>Interim Resistance Analysis of Long-Acting Lenacapavir in Treatment-Naïve People with HIV at 28 Weeks</td>
<td><a href="https://doi.org/10.1093/ofid/ofab466.073">https://doi.org/10.1093/ofid/ofab466.073</a></td>
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**PURPOSE 1**

**Identifier**

NCT04994509

**Link**

https://clinicaltrials.gov/ct2/show/NCT04994509

**Phase**

Phase III

**Status**

Active, not recruiting

**Sponsor**

Gilead Sciences

**More details**

Not provided

**Purpose**

Evaluate the efficacy of Lenacapavir (LEN) and Emtricitabine/Tenofovir alafenamide (F/TAF) in preventing the risk of human immunodeficiency virus (HIV) infection

**Interventions**

Drug: Oral Lenacapavir (LEN)
Drug: Subcutaneous (SC) Lenacapavir (LEN)
Drug: F/TAF
Drug: F/TDF
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
Not provided

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
• Adolescents
• Adults
Genders

- Cisgender female

Accepts pregnant individuals
Unspecified

Accepts lactating individuals
Unspecified

Accepts healthy individuals
Yes

Comments about the studied populations

Specifically refers to Cisgender Adolescent Girls and Young Women (ages 16 to 25 Years) at Risk of HIV Infection. 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, and Body weight ≥ 35 kg.

Health status

Considered high risk 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**

Bi-yearly

**Studied LA-formulation(s)**

Injectable

**Studied route(s) of administration**

Subcutaneous

**Use case**

PrEP

**Key results**

Not provided
PURPOSE 2

Identifier
NCT04925752

Link
https://clinicaltrials.gov/ct2/show/NCT04925752

Phase
Phase III

Status
Active, not recruiting

Sponsor
Gilead Sciences

More details
Not provided

Purpose
Evaluate the efficacy of Lenacapavir (LEN) in preventing the risk of HIV-1 infection.

Interventions
Drug: Oral Lenacapavir (LEN)
Drug: F/TDF & Drug: Placebo F/TDF
Drug: Sub-cutaneous (SC) Lenacapavir (LEN)
Drug: Placebo SC LEN
Drug: F/TAF (for US participants only)
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
Not provided

Estimated Primary Completion Date
2025-01-01

Estimated Completion Date
2027-04-01

Actual Primary Completion Date
Not provided

Actual Completion Date
Not provided

Studied populations
Age Cohort
- Adolescents
- Adults
- Older Adults

Genders
- 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
Specifically Cisgender Men, Transgender Women, Transgender Men, and Gender Nonbinary People ≥ 16 Years of Age Who Have Sex With Male Partners and are at risk of HIV infection.

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

Study type
Interventional (clinical trial)

Enrollment
Allocation
Randomized

Intervention model
Parallel Assignment

Intervention model description
Not provided

Masking
Double-blind masking

Masking description
Double (Participant, Investigator)

Frequency of administration
Bi-yearly

Studied LA-formulation(s)
Injectable

Studied route(s) of administration
Subcutaneous

Use case
PrEP

Key results
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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
Drug: Oral Lenacapavir
Drug: Subcutaneous Lenacapavir
Biological: Teropavimab
Biological: Zinlirvimab
Countries
United States of America

Sites / Institutions
Not provided

Trials dates

Anticipated Start Date
Not provided

Actual Start Date
2021-04-08

Anticipated Date of Last Follow-up
Not provided

Estimated Primary Completion Date
Not provided

Estimated Completion Date
Not provided

Actual Primary Completion Date
2023-04-18

Actual Completion Date
2023-10-17

Studied populations

Age Cohort
- Adults
- Older Adults

Genders
All

Accepts pregnant individuals
Unspecified

Accepts lactating individuals
Unspecified

Accepts healthy individuals
No

Comments about the studied populations
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

Not provided

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Subcutaneous

Use case

Treatment

Key results

Not provided
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
Drug: Lenacapavir
Drug: Placebo
Drug: B/F/TAF
Drug: TAF
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
Not provided

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
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(s): "Single dose"

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Subcutaneous

Use case

Treatment

Key results

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<td>Article</td>
<td>Clinical targeting of HIV capsid protein with a long-acting small molecule</td>
<td><a href="https://doi.org/10.1038/s41586-020-2443-1">https://doi.org/10.1038/s41586-020-2443-1</a></td>
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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
Drug: Lenacapavir Tablet
Drug: Long-acting Subcutaneous Lenacapavir
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
Not provided

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
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

Bi-yearly

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Subcutaneous

Use case

PrEP

Key results

Not provided
PURPOSE 4

Identifier
NCT06101342

Link
https://clinicaltrials.gov/study/NCT06101342

Phase
Phase II

Status
Recruiting

Sponsor
Gilead Sciences

More details
PWUD

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

Interventions
Drug: Long-acting Subcutaneous Lenacapavir Injection
Drug: Lenacapavir Tablet
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

*Anticipated Date of Last Follow-up*
Not provided

*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
Masking

Open label

Masking description

None (Open Label)

Frequency of administration

Bi-yearly

Studied LA-formulation(s)

Injectable
Tablet

Studied route(s) of administration

Oral
Subcutaneous

Use case

PrEP

Key results

Not provided
**GS-US-536-5939**

**Identifier**
NCT05729568

**Link**
https://clinicaltrials.gov/study/NCT05729568

**Phase**
Phase II

**Status**
Active, not recruiting

**Sponsor**
Gilead Sciences

**More details**
Not provided

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

**Interventions**
- Drug: Teropavimab (Formerly GS-5423)
- Drug: Zinlirvimab (Formerly GS-2872)
- Drug: Lenacapavir Tablet
- Drug: Lenacapavir Injection
Drug: Antiretroviral Therapy

**Countries**

United States of America  
Australia  
Canada  
Puerto Rico

**Sites / Institutions**

Not provided

**Trials dates**

**Anticipated Start Date**  
Not provided

**Actual Start Date**  
2023-05-15

**Anticipated Date of Last Follow-up**  
Not provided

**Estimated Primary Completion Date**  
2025-03-01

**Estimated Completion Date**  
2029-12-01

**Actual Primary Completion Date**  
Not provided

**Actual Completion Date**  
Not provided

**Studied populations**

Age Cohort
Adults
- Older Adults

Genders
- All

Accepts pregnant individuals
Unspecified

Accepts lactating individuals
Unspecified

Accepts healthy individuals
No

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

Health status
Positive to: HIV
Negative to: HCV, HBV

Study type
Interventional (clinical trial)

Enrollment
83

Allocation
Randomized
Intervention model
Parallel Assignment

Intervention model description
Not provided

Masking
Open label

Masking description
None (Open Label)

Frequency of administration
Bi-yearly

Studied LA-formulation(s)
Injectable

Studied route(s) of administration
Subcutaneous

Use case
Treatment

Key results
Not provided
IMEA 070

**Identifier**
NCT06289361

**Link**
https://clinicaltrials.gov/study/NCT06289361

**Phase**
Marketed

**Status**
Completed

**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
Not provided

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
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
Frequency of administration
Bi-yearly

Studied LA-formulation(s)
Injectable

Studied route(s) of administration
Subcutaneous

Use case
Treatment

Key results
Not provided
**ARTISTRY-2**

**Identifier**
NCT06333808

**Link**
https://clinicaltrials.gov/study/NCT06333808

**Phase**
Phase III

**Status**
Recruiting

**Sponsor**
Gilead Sciences

**More details**

The goal of this clinical study is to learn more about the effects of switching to the study drugs, bictegravir (BIC)/lenacapavir (LEN), fixed-dose combination (FDC) versus current therapy bictegravir/emtricitabine/tenofovir alafenamid (B/F/TAF) FDC in people living with HIV-1 (PWH). The primary objective of this study is to learn how effective it is to switch to BIC/LEN FDC tablets versus continuing on B/F/TAF FDC tablets in virologically suppressed PWH.

**Purpose**

Study to Compare Bictegravir/LENacapavir Versus Current Therapy in People With HIV-1 Who Are Successfully Treated With Biktarvy

**Interventions**

Bictegravir
Lenacapavir
B/F/TAF
Placebo to match B/F/TAF
Placebo to match BIC/LEN

Countries

United States of America
Puerto Rico

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date
Not provided

Actual Start Date
2024-03-25

Anticipated Date of Last Follow-up
2024-05-15

Estimated Primary Completion Date
2024-03-27

Estimated Completion Date
2024-03-27

Actual Primary Completion Date
2024-05-17

Actual Completion Date
2029-12-01

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

Key Inclusion Criteria: * Currently receiving B/F/TAF for at least 6 months prior to screening. * If plasma human immunodeficiency virus type 1 (HIV-1) ribonucleic acid (RNA) measurements in the last 6 months prior to screening are available, all levels must be \(< 50 \text{ copies/mL.} * \) At least one documented HIV-1 RNA level measured between 6 and 12 months (± 2 months) prior to screening. This and any other HIV-1 RNA measurements documented in this period must be \(< 50 \text{ copies/mL.} * \) Plasma HIV-1 RNA levels \(< 50 \text{ copies/mL at screening.} * \) No documented or suspected resistance to BIC (including integrase strand-transfer inhibitor resistant (INSTI-R) mutations T66A/I/K, E92G/Q, G118R, F121Y, Y143C/H/R, S147G, Q148H/K/R, N155H/S, or R263K in the integrase gene). * No documented or suspected resistance to BIC

Health status

Positive to : HIV

Other health status: Currently receiving B/F/TAF for at least 6 months prior to screening. If plasma human immunodeficiency virus type 1 (HIV-1) ribonucleic acid (RNA) measurements in the last 6 months prior to screening
**Study type**

Interventional (clinical trial)

**Enrollment**

546

**Allocation**

Randomized

**Intervention model**

Not provided

**Intervention model description**

Not provided

**Masking**

Double-blind masking

**Masking description**

Not provided

**Frequency of administration**

Daily

**Studied LA-formulation(s)**

Tablet

**Studied route(s) of administration**

Oral

**Use case**
Treatment

**Key results**

Not provided
ARTISTRY-1

Identifier
NCT05502341

Link
https://clinicaltrials.gov/study/NCT05502341

Phase
Phase II/III

Status
Recruiting

Sponsor
Gilead Sciences

More details
The goal of this clinical study is to learn more about the effects of switching to the study drugs, bictegravir (BIC) plus lenacapavir (LEN), versus current therapy (Phase 2) and BIC/LEN fixed-dose combination (FDC) versus current therapy (Phase 3) in people living with HIV (PWH).

Purpose
Study to Compare Bictegravir/Lenacapavir Versus Current Therapy in People With HIV-1 Who Are Successfully Treated With a Complicated Regimen

Interventions
Bictegravir
Lenacapavir
BIC/LEN fixed dose combination
Stable Baseline Regimen

**Countries**

United States of America  
South Africa  
United Kingdom  
Taiwan, Province of China  
Spain  
Puerto Rico  
Korea, Republic of  
Japan  
Italy  
Germany  
France  
Dominican Republic  
Canada  
Australia  
Argentina

**Sites / Institutions**

Not provided

**Trials dates**

**Anticipated Start Date**
Not provided

**Actual Start Date**
2022-08-16

**Anticipated Date of Last Follow-up**
2024-05-02

**Estimated Primary Completion Date**
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

Key Inclusion Criteria: * If plasma HIV-1 RNA measurements in the 6 months prior to screening are available, all levels must be \( \leq 50 \) copies/mL. * At least one documented plasma HIV-1 RNA level measured between 6 and 12 months (± 2 months) prior to screening. This and any other HIV-1 RNA measurements documented in this period must be \( \leq 50 \) copies/mL * Plasma HIV-1 RNA levels \( \leq 50 \) copies/mL at screening. *
Currently receiving a complex antiretroviral (ARV) regimen due to previous viral resistance, or intolerance, or contraindication to existing single-tablet regimens (STR), and on this regimen for at least 6 months prior to the screening visit. The criteria to define a complex regimen in this study are as follows: * A regimen containing a boosted protease inhibitor or a nonnucleos(t)id

**Health status**

Negative to: HBV, TB

**Study type**

Interventional (clinical trial)

**Enrollment**

671

**Allocation**

Randomized

** Intervention model**

Parallel Assignment

**Intervention model description**

Not provided

**Masking**

Open label

**Masking description**

Not provided

**Frequency of administration**
Daily

**Studied LA-formulation(s)**

Tablet

**Studied route(s) of administration**

Oral

**Use case**

Treatment

**Key results**

Not provided
The primary objective of this study is to evaluate the efficacy of oral weekly islatravir (ISL) in combination with lenacapavir (LEN) in virologically suppressed people with HIV (PWH) at Week 24.

**Purpose**

Study Evaluating the Safety and Efficacy of Islatravir in Combination With Lenacapavir in Virologically Suppressed People With HIV

**Interventions**

ISL
LEN
B/F/TAF
Countries
United States of America

Sites / Institutions
Not provided

Trials dates

Anticipated Start Date
Not provided

Actual Start Date
2021-10-05

Anticipated Date of Last Follow-up
2024-01-17

Estimated Primary Completion Date
2021-09-22

Estimated Completion Date
2021-09-22

Actual Primary Completion Date
2024-01-19

Actual Completion Date
2027-11-01

Studied populations

Age Cohort
- Adults
- Older Adults

Genders
Accepts pregnant individuals
Unspecified

Accepts lactating individuals
Unspecified

Accepts healthy individuals
No

Comments about the studied populations
Key Inclusion Criteria: * Received bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) for ≥ 24 weeks at screening. * Documented plasma human immunodeficiency virus type 1 (HIV-1) ribonucleic acid (RNA) \(< 50 \text{ copies/mL} \) or undetectable HIV-1 RNA level according to the local assay being used if the limit of detection is \( \geq 50 \text{ copies/mL} \) for \( \geq 24 \text{ weeks} \) before and at screening. * Plasma HIV-1 RNA \( \leq 50 \text{ copies/mL} \) at screening. Key Exclusion Criteria: * History of prior virologic failure while receiving treatment for HIV-1. * Prior use of, or exposure to, islatravir (ISL) or lenacapavir (LEN). * Active, serious infections requiring parenteral therapy \(< 30 \text{ days} \) before randomization. * Active or occult hepatitis B virus (HBV) coinfection, defined as hepatitis B core antibody (HBcAb) posi

Health status
Positive to: HIV
Negative to: HCV, HBV

Study type
Interventional (clinical trial)

Enrollment
142

Allocation
Randomized

**Intervention model**
Parallel Assignment

**Intervention model description**
Not provided

**Masking**
Open label

**Masking description**
Not provided

**Frequency of administration**
Weekly

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

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

**Use case**
Treatment

**Key results**
Not provided
PURPOSE 5

**Identifier**
Not provided

**Link**
Not provided

**Phase**
Phase II

**Status**
Recruiting

**Sponsor**
Gilead Sciences

**More details**

**Purpose**
PURPOSE 5 will evaluate the persistence of the therapy against emtricitabine/tenofovir disoproxil fumarate (F/TDF) in individuals who could benefit from PrEP but are not currently using it.

**Interventions**
Countries

France
United Kingdom

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date
2024-08-01

Actual Start Date
Not provided

Anticipated Date of Last Follow-up
Not provided

Estimated Primary Completion Date
2027-05-01

Estimated Completion Date
2027-05-01

Actual Primary Completion Date
Not provided

Actual Completion Date
Not provided

Studied populations

Age Cohort

• Adults
Older Adults

Genders

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

Accepts pregnant individuals
Unspecified

Accepts lactating individuals
Unspecified

Accepts healthy individuals
Unspecified

Comments about the studied populations

PWBP: people who would benefit from PrEP but are not currently using it.

Health status

Negative to : HIV

Study type

Not provided

Enrollment

262

Allocation

Not provided

Intervention model
Not provided

**Intervention model description**

Not provided

**Masking**

Not provided

**Masking description**

Not provided

**Frequency of administration**

Bi-yearly

**Studied LA-formulation(s)**

Not provided

**Studied route(s) of administration**

Subcutaneous

**Use case**

PrEP

**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
### Compound patent families

#### Patent informations

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Crystalline forms of Lenacapavir sodium salt</td>
<td>WO2019035904</td>
<td>Polymorphs</td>
<td>Gilead Sciences, Inc</td>
<td>No</td>
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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.

#### Patent status

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<td>World Intellectual Property Organization (WIPO), Luxembourg, Denmark, Monaco, Finland, Cyprus, Estonia, Hungary, Iceland, Malta, San Marino, Croatia, Romania, Latvia, Lithuania, Japan, Taiwan, Province of China</td>
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**Patent informations**

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<td>Lenacapavir compound and its use in HIV (oral and parenteral)</td>
<td>WO2018035359</td>
<td>Compound</td>
<td>Gilead Sciences, Inc</td>
<td>No</td>
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<td>Expiry date: 2037-08-17</td>
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<td>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.</td>
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**Patent status**

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</table>
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.

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<td>World Intellectual Property Organization (WIPO), Luxembourg, Denmark, Monaco, Finland, Estonia, San Marino, Croatia, Romania, Latvia, Lithuania, Australia, Canada, Hong Kong, Japan, New Zealand, Singapore, United States of America, Uruguay, Bahamas</td>
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Supporting material
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.


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 high-throughput 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.
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.

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.


Lenacapavir (LEN; GS-6207) is a potent first-in-class inhibitor of HIV-1 capsid with long-acting 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

**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**

- [PURPOSE PrEP Studies Overview: Prevention With a Purpose](https://www.avac.org/research/campaigns/overview-prepepr)
Comment & Information

Not provided