PLAIN LANGUAGE SUMMARY OF CLINICAL STUDY RESULTS

Study Sponsor: Gilead Sciences

Gilead Study Number: GS-US-425-6143

Date of Study: May 2022 to August 2025

Plain Language Study Title: A Study to Check the Safety of GS-8588 and how the Body Processes it in People With Well Controlled HIV-1

Date of this Plain Language Summary: June 2026

The information in this summary does not include any information available after this date.

Thank you

Thank you to the participants who contributed to the clinical study for **GS-8588**, also known as **Amtabafusp Alfa (ABF)**.

Gilead Sciences sponsored this study. This summary is prepared for study participants and the general public.

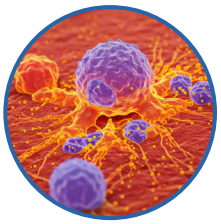
If you participated in the study and have questions about the results, please speak with a doctor or staff member at the study site.

Always talk to a doctor or healthcare provider before making any treatment changes.

This document is a short summary of this study written for a general audience. Links to scientific summaries of this study can be found at the end of this document.

General information about the study

What is Human Immunodeficiency Virus (HIV)?



HIV is a virus that attacks the immune system (body's defense system) and makes it more likely for people to get sick. HIV-1 and HIV-2 are two main types of HIV. It can be passed on to others, through bodily fluids like blood, semen, and breast milk. If HIV infection is not treated, it can lead to AIDS (acquired immunodeficiency syndrome). If a person with AIDS is not treated, they may die. There is no cure for HIV infection. Once people get it, they have it for life. But with proper treatment, it can be controlled.

There are medicines available to treat HIV called antiretroviral (ARV) medicines. These medicines stop the virus from growing or making copies of itself, helping people live longer, stay healthier, and lowering the risk of AIDS. However, people have to take these medicines for life. If they stop the medicines, the virus can come back again. Therefore, the researchers want to find new medicines that can completely remove HIV from the body to cure the infection and limit the need for lifelong treatment.

In this study, the researchers tested a new drug called GS-8588 in people with HIV-1 for the first time. They wanted to find a safe and suitable dose before further testing its effectiveness in people with HIV-1. The study participants already had well-controlled HIV-1 from taking other ARV medicines.

This is a **Phase 1b** study. This means the researchers tested the study drug in a small group of people to find a safe dose to be given to the larger population. This study did not test if the drug improves participants' health.

What was the purpose of the study?

The main purpose of this study was to learn how safe and tolerable the single and multiple doses of GS-8588 were in participants with well-controlled HIV-1. The study also measured the levels of GS-8588 to understand how much of the drug gets absorbed, distributed, and removed from the body, which is called the pharmacokinetics (PK) of the drug.

The main questions the researchers wanted to answer in this study were:

- How many participants had **unwanted medical events** during the study?
- How many participants had **abnormal** changes in their laboratory test results during the study?
- What were the PK results for GS-8588 in the blood, after taking single and multiple increasing doses of the drug?

An **unwanted medical event** is any unwanted sign or symptom that participants may have during the study. An unwanted medical event is considered "**serious**" if it:

- results in death
- is life-threatening
- is considered by the study doctor to be medically important
- causes lasting problems
- requires hospital care
- causes a birth defect

Abnormal changes mean results that are outside the normal (expected) range.

Researchers also wanted to know if there were any **side effects** that the participants had during the study.

An unwanted medical event may or may not be caused by the study treatment. **Side effects** are unwanted medical events that the study doctors thought might be caused by the study drug.

Who took part in the study?

54 participants with HIV-1 from the **United States** took part in the study.

People could take part in the study if they:

- Were at least 18 years of age
- Had very low levels (below 50 copies per ml) of HIV virus in the blood
- Were on ARV treatment for at least 6 months before entering the study, during the study treatment and follow-up

The 54 study participants were between the ages of **27** and **75** years.

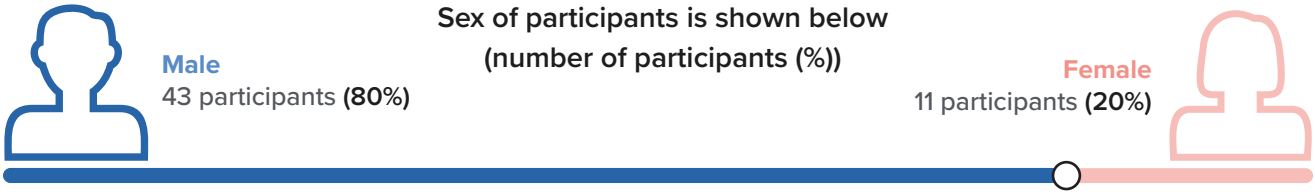
The race of participants is shown below (number of participants (%)).

Black or African American	28 (52%)
White	22 (41%)
Other or More Than One Race	3 (6%)
Asian	1 (2%)

The ethnicity of participants is shown below (number of participants (%)).

Not Hispanic or Latino	44 (81%)
Hispanic or Latino	10 (19%)

Sex of participants is shown below (number of participants (%))



What happened during the study?

This was a **randomized**, **single-blinded**, and **placebo-controlled** study.

Randomized means the researchers used a computer program to assign participants into treatment groups by chance. This helped make sure the treatments were assigned fairly. In some groups, the same number of participants (1:1) received GS-8588 or placebo. In other groups, three times more participants received GS-8588 (3:1) than placebo.

Single-blinded means that participants, doctors, and study staff did not know which treatment each participant received, but the study sponsor did. The study team closely monitored participants for side effects and had safety measures in place to manage any concerns.

Placebo-controlled means this study compared the safety and tolerability of the treatment drugs against placebo treatments. A **placebo** means a substance that looks like the treatment but does not have active drug in it.

The participants were enrolled in 9 **cohorts**.

A **cohort** is a group of individuals who share something in common. This study had 9 cohorts, participants in each cohort received the same dose levels.

Single Increasing Doses of GS-8588 and Placebo (Cohorts 1-7)

Participants in Cohorts 1–7 received a single increasing dose of GS-8588. It was given as a slow injection into a vein (intravenous [IV]) on Day 1 only.

Of 54 participants, 37 received single dose (26 received GS-8588 and 11 received placebo). The dose increased with each cohort, ranging from 0.3 mg to 3 mg (Cohorts 1 to 3) and 10 mg to 150 mg (Cohorts 4 to 7). The total study duration for participants in the single-dose cohorts was 99 days.

Multiple Increasing Doses of GS-8588 and Placebo (Cohorts 8-9)

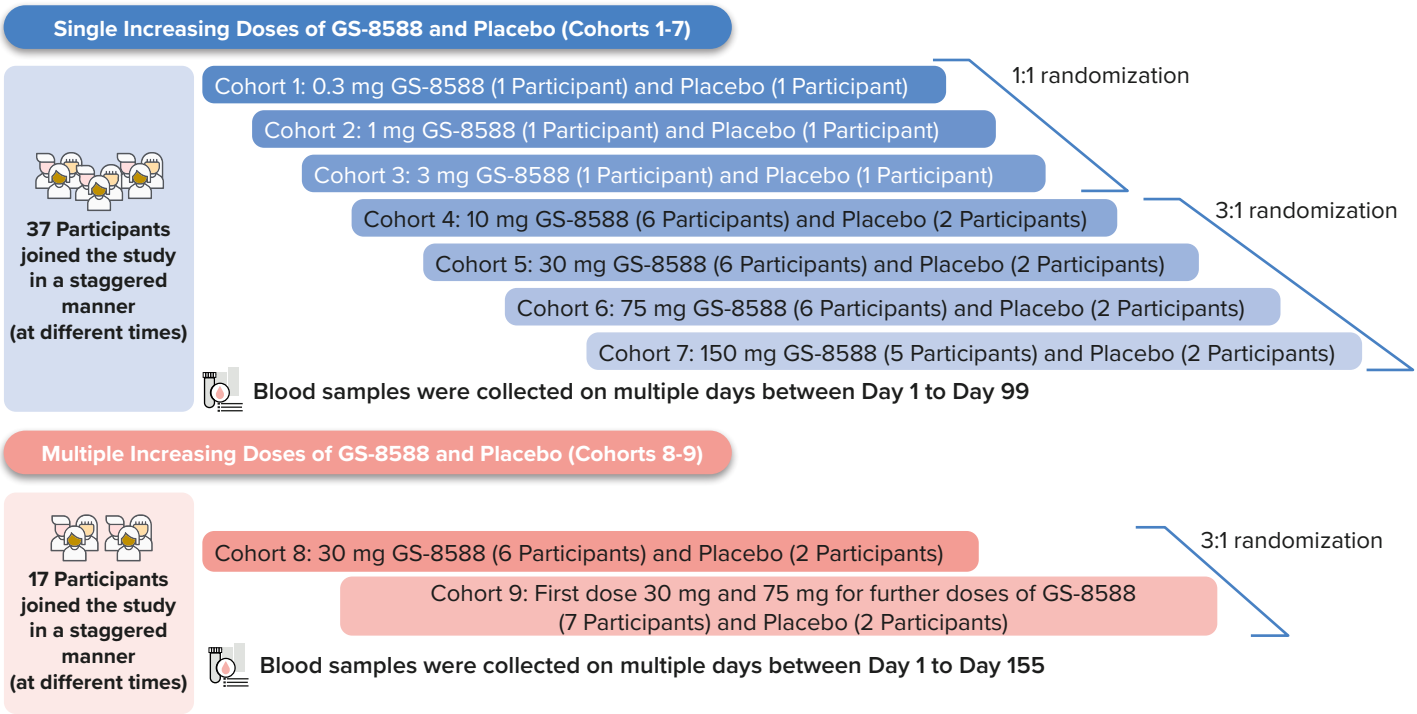
Participants in Cohorts 8–9 received multiple doses of GS-8588. It was given as a slow injection into a vein (IV) on Days 1, 15, 29, 43, and 57. The participants in Cohort 9 received 30 mg for the first dose, and 75 mg for further doses.

Of 54 participants, 17 participants received multiple doses (13 received GS-8588 and 4 received placebo). The dose increased between the two cohorts, from 30 mg in Cohort 8 to 75 mg in Cohort 9. The total study duration for participants in the multiple-dose cohorts was up to 155 days.

For both the single-dose and multiple-dose cohorts, researchers enrolled participants at a higher dose only after reviewing safety information (such as serious side effects) from the previous, lower-dose cohort.

They collected blood samples at different time points to measure the level of GS-8588 in the blood. Participants' safety was monitored throughout the study.

The graphics below show the study plan:



Of the 54 participants who took part, 49 participants completed the study. Five participants discontinued because: 2 did not follow the study procedure, 1 left based on study doctors' decision, 1 chose to stop participating, and 1 could not be contacted.

What were the results of the study?

This is a summary of the main results from this study. The individual results of each participant might be different and are not mentioned in this summary. A detailed presentation of the results can be found on the website listed at the end of this summary.

When the data was analyzed, all participants who received single dose placebo were grouped in one Placebo Single Dose Cohort and those who received multiple doses of placebo were grouped in Placebo Multiple Dose Cohort.

How many participants had unwanted medical events during the study?

The researchers kept track of any unwanted medical events that the participants may have had during the study.

The table below shows how many participants had unwanted medical events during the study.

Overall Unwanted Medical Events

	Cohort 1	Cohort 2	Cohort 3	Cohort 4	Cohort 5	Cohort 6	Cohort 7	Placebo	Cohort 8	Cohort 9	Placebo
	GS-8588 Single Increasing Doses								GS-8588 Multiple Increasing Doses		
	0.3 mg 1 participant	1 mg 1 participant	3 mg 1 participant	10 mg 6 participants	30 mg 6 participants	75 mg 6 participants	150 mg 5 participants	 11 participants	30 mg 6 participants	75 mg 7 participants	 4 participants
	Number of participants (%)										
How many participants had **any** unwanted medical events?	1 (100%)	1 (100%)	1 (100%)	5 (83%)	5 (83%)	6 (100%)	5 (100%)	8 (73%)	5 (83%)	7 (100%)	2 (50%)

1 participant each in Cohorts 1, 6, and, 9 had serious unwanted medical events. The study doctors did not think that any of these serious unwanted medical events were caused by the study drug.

No serious unwanted medical events were reported in the other cohorts.

How many participants had abnormal changes in their laboratory test results during the study?

Laboratory tests were done before and after the study drug or placebo were given to check whether any values changed to outside the normal range. They classified the abnormal changes in laboratory test results as mild, moderate, severe, and potentially life-threatening.

The table below shows participants with abnormal changes in their laboratory test results.

Abnormal Changes in Laboratory Test Results

	Cohort 1	Cohort 2	Cohort 3	Cohort 4	Cohort 5	Cohort 6	Cohort 7	Placebo	Cohort 8	Cohort 9	Placebo
	GS-8588 Single Increasing Doses								GS-8588 Multiple Increasing Doses		
	0.3 mg 1 participant	1 mg 1 participant	3 mg 1 participant	10 mg 6 participants	30 mg 6 participants	75 mg 6 participants	150 mg 5 participants	11 participants	30 mg 6 participants	75 mg 7 participants	4 participants
	Number of participants (%)										
Mild changes	1 (100%)	0	1 (100%)	2 (33%)	2 (33%)	1 (17%)	0	5 (46%)	0	2 (29%)	1 (25%)
Moderate changes	0	0	0	4 (67%)	3 (50%)	2 (33%)	3 (60%)	4 (36%)	6 (100%)	4 (57%)	0
Severe changes	0	0	0	0	0	3 (50%)	1 (20%)	0	0	1 (14%)	1 (25%)
Potentially life-threatening changes	0	1 (100%)	0	0	0	0	1 (20%)	0	0	0	0

Abnormal changes in laboratory test results were seen in some participants. Most changes were mild or moderate. At higher doses, more participants had moderate changes, and a few had severe changes.

Some participants who received placebo also had abnormal results. This can happen due to normal body changes or natural variation in test results.

What were the PK results for GS-8588 in the blood, after taking single and multiple increasing doses of the drug?

To answer this question, researchers collected blood samples from the participants at different time intervals.

The researchers looked at the following important measures:

- The highest level of the drug in the blood after dosing (called maximum concentration [C_{max}])
- The total amount of drug absorbed in the body over time (called area under the curve [$AUC_{infinity}$])
- How long it takes for half of the drug to leave the body (called half-life)
- How quickly the body removes the drug (called clearance)
- The extent to which the drug spreads in the body (called volume of distribution)

Single Increasing Doses of GS-8588

After participants received single increasing doses of GS-8588 (from 0.3 mg to 3 mg and from 10 mg to 150 mg), the researchers studied how drug levels changed with dose:

- When the dose increased from 0.3 mg to 10 mg, the drug levels increased more than expected. This means that doubling the dose led to more than double the drug levels
- When the dose increased further from 10 mg to 150 mg, the drug levels increased in line with the dose. This means that doubling the dose led to approximately double the drug levels

After single doses of 10 mg to 150 mg:

- It took about 6 to 10 days for half of the drug to leave the body (half-life)
- The body removed the drug at a rate of about 1 to 2 liters per day (clearance), meaning it was cleared slowly over time
- The drug spread through the body in a moderate way (volume of distribution: about 7 to 9 liters)

Multiple Increasing Doses of GS-8588

After participants received multiple increasing doses of GS-8588 (from 30 mg to 75 mg every 2 weeks), the researchers studied how drug levels changed over time:

- The total amount of drug in the body over each dosing period (AUC_{tau}) increased slightly (about 10%) over time
- The level of the drug in the blood just before the next dose (C_{tau}) also increased (about 50%) over time
- However, the highest level of the drug in the blood after dosing (C_{max}) did not increase over time

After multiple doses:

- It took about 10 to 11 days for half of the drug to leave the body (half-life)
- The body removed the drug at a rate of about 1 to 2 liters per day (clearance), meaning it was cleared slowly over time
- The drug spread through the body in a moderate way (volume of distribution: about 7 to 9 liters)

Overall, taking single or multiple doses of GS-8588 was generally safe in people with well-controlled HIV-1.

What side effects did participants have during the study?

The researchers also checked if participants had any side effects during the study. The results from several studies in larger population are usually needed to help decide if a study drug actually causes a side effect.

The table below shows how many participants had side effects during the study.

Overall Side Effects

	Cohort 1	Cohort 3	Cohort 5	Cohort 6	Cohort 7	Placebo	Cohort 8	Cohort 9	Placebo	Total
	GS-8588 Single Increasing Doses						GS-8588 Multiple Increasing Doses			
	0.3 mg 1 participant	3 mg 1 participant	30 mg 6 participants	75 mg 6 participants	150 mg 5 participants	11 participants	30 mg 6 participants	75 mg 7 participants	4 participants	54 participants
	Number of participants (%)									
How many participants had **any** side effects?	1 (100%)	1 (100%)	4 (67%)	5 (83%)	5 (100%)	2 (18%)	3 (50%)	7 (100%)	1 (25%)	29 (54%)

Only Cohorts with any side-effects are presented in the above table.

2 out of 7 participants (29%) in Cohort 9 stopped treatment due to side effects.

The study participants did not have any serious side effects during the study. No deaths were reported due to side effects.

What were the non-serious side effects?

The table below lists the most common non-serious side effects that occurred in **at least 15%** of the total number of study participants. These side effects were not serious in nature and did not meet the definition of 'serious side effects' mentioned in this summary.

Most Common Non-Serious Side Effects

	Cohort 1	Cohort 5	Cohort 6	Cohort 7	Placebo	Cohort 8	Cohort 9	Placebo	Total
	GS-8588 Single Increasing Doses					GS-8588 Multiple Increasing Doses			
	0.3 mg	30 mg	75 mg	150 mg		30 mg	75 mg		
	1 participant	6 participants	6 participants	5 participants	11 participants	6 participants	7 participants	4 participants	54 participants
	Number of participants (%)								
Headache	0	1 (17%)	5 (83%)	3 (60%)	0	2 (33%)	3 (43%)	1 (25%)	15 (28%)
A group of symptoms associated with inflammation (Cytokine release syndrome)	0	2 (33%)	4 (67%)	3 (60%)	0	2 (33%)	2 (29%)	0	13 (24%)
Fever (Pyrexia)	0	2 (33%)	4 (67%)	3 (60%)	0	1 (17%)	3 (43%)	0	13 (24%)
A feeling of being cold without an apparent cause (Chills)	1 (100%)	1 (17%)	3 (50%)	3 (60%)	0	2 (33%)	0	0	10 (19%)
Feeling sick to the stomach (Nausea)	0	1 (17%)	2 (33%)	2 (40%)	0	1 (17%)	3 (43%)	0	9 (17%)
Peeling of the skin on palms and/or soles of feet (Skin exfoliation)	0	0	2 (33%)	2 (40%)	1 (9%)	1 (17%)	2 (29%)	0	8 (15%)
Vomiting	0	1 (17%)	1 (17%)	3 (60%)	0	0	3 (43%)	0	8 (15%)

Only Cohorts with any side-effects are presented in the above table.

There were other non-serious side effects, but those occurred in fewer participants. Some participants may have had more than 1 non-serious side effects.

How has this study helped researchers?

The researchers learned about the safety of the tested doses of GS-8588 to find which doses could be given safely without causing too many side effects. They also learned about the levels of the drug in the participants' bodies after taking single and multiple increasing doses of GS-8588.

The results from several studies are needed to help decide which treatments work and are safe. This summary shows only the main results from this one study. Other studies may provide new information or different results.

Gilead Sciences may have further studies with GS-8588.

Where can I learn more about this study?

You can find more information about this study on the website listed below.

Gilead Website	GS-US-425-6413
www.gileadclinicaltrials.com	

Full Study Title: A Phase 1b Randomized, Blinded, Placebo-Controlled, Single and Multiple Ascending Dose Study to Evaluate the Safety, Tolerability, and Pharmacokinetics of GS-8588 in People With HIV-1 Who are Virologically Suppressed on Antiretroviral Therapy

To learn more about clinical trials in general,
please visit this page on www.clinicaltrials.gov website

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Clinical study participants belong to a large community of people who take part in clinical research around the world. They help researchers answer important health questions and find medical treatments for patients.

GILEAD