Sponsor:	Insmed Inc
Treatment Studied:	Brensocatib (INS1007)
Protocol No:	INS1007-201
Study Dates:	October 2017 to December 2019
Study Title:	A study to learn if brensocatib worked and to better understand its safety in participants with non-cystic fibrosis bronchiectasis

Thank you!

Insmed Incorporated, the sponsor of this study, thanks you for taking part in the clinical study for a new medical treatment called brensocatib. In this study, researchers learned more about the safety of brensocatib and how it may help people with non-cystic fibrosis bronchiectasis, also known as NCFBE.

Insmed Incorporated sponsored this study and thinks it is important to share the results of the study with you and the public. If you participated in the study and have questions about the results, please speak with the doctor or staff at your study center.

Why was this study done?

In people with bronchiectasis, the airways that carry air in and out of the lungs become widened and inflamed. This can lead to a buildup of mucus in the airways. The airways cannot clear the buildup of mucus, which can then cause lung infections. The main symptoms of bronchiectasis are shortness of breath and having a cough that lasts for a long time and that sometimes brings up mucus. There are different conditions that may cause bronchiectasis. One of these conditions is called cystic fibrosis. All the participants in this study had bronchiectasis, but it was not caused by cystic fibrosis. This is also known as NCFBE.

In this study, the researchers wanted to learn more about brensocatib, also known as INS1007. This treatment works by blocking a certain protein that is thought to play a role in NCFBE. Researchers think that brensocatib can help reduce inflammation in the airways and reduce the buildup of mucus. This may help decrease the symptoms of NCFBE.

Before a new medical treatment can be approved for people to take, researchers must carry out clinical studies to learn how safe the treatment is by looking at adverse reactions. Adverse reactions are unwanted medical problems that the study doctors think may be caused by the study treatment. Researchers also must learn how the treatment works in people with the disease. In this study, the researchers wanted to find out if brensocatib works in participants with NCFBE. They also wanted to find out if the participants had any adverse reactions.

Researchers in this study wanted to know:

- Did brensocatib increase how long it took before the participants had a pulmonary exacerbation?
- What adverse reactions did the participants have?

A “pulmonary exacerbation” is a symptom that is related to the lungs that has gotten worse.

Who was in this study?

To answer the questions in this study, the researchers asked for the help of 256 men and women with NCFBE. The participants were 22 to 84 years old when they joined the study.

When and where was this study done?

This study started in October 2017 and ended in December 2019. The study was done in 101 study centers in 14 countries, including:

Australia	Italy	Singapore
Belgium	Republic of Korea	Spain
Bulgaria	The Netherlands	The United Kingdom
Denmark	New Zealand	The United States
Germany	Poland	

How was this study done?

In this study, the participants were randomly assigned to take either brensocatib or the placebo. The placebo looked like brensocatib but does not have any medicine in it. Putting participants into groups by chance helps to make the groups more equal. That way, researchers can understand the results between the groups in a fairer way.

This was a "double-blind" study. This means that none of the participants, doctors, study center staff, or the sponsor of this study, knew what treatment each participant took. Knowing what treatment each participant takes could affect how the doctors or study center staff collect and understand each participant's results. Studies can be done this way so that researchers understand the true effects of the study treatment.

The doses of brensocatib were measured in milligrams, also called mg. All the participants took brensocatib or the placebo as tablets by mouth.

How the study was done

Before the study	While the participants took treatment	After treatment
• The study doctors checked to make sure the participants could join the study.	• 82 participants took 10 mg of brensocatib once a day. • 87 participants took 25 mg of brensocatib once a day. • 87 participants took the placebo once a day.	• The study doctors checked the participants' health 1 final time.
Up to 6 weeks	Up to 24 weeks	4 weeks after the last dose

Throughout this study, the study doctors:

- Checked the participants' overall health
- Took blood and urine samples
- Asked the participants how they were feeling and what medicines they were taking
- Checked the participants' NCFBE symptoms

What were the main results of the study?

Below is a summary of the main results of this study. The results each participant had are not shown here and may be different from the overall results shown below.

You can find a full list of the questions for this study on the websites listed on the last page of this summary. If there are results already available, they will also be found on these websites.

Did brensocatib increase how long it took before the participants had a pulmonary exacerbation?

The researchers wanted to compare how long it took before the participants had a pulmonary exacerbation in the participants who took brensocatib and those who took the placebo. A "pulmonary exacerbation" is a symptom that is related to the lungs that has gotten worse.

To answer this question, the researchers looked at the participants' NCFBE symptoms. The study doctors reviewed the participants' symptoms to see if they had a pulmonary exacerbation while they were taking the study treatments. In this study, a pulmonary exacerbation meant that they had 3 or more symptoms within 48 hours, that led to the study doctors giving the participants a medicine called an antibiotic. Antibiotics are a type of medicine which can be used to treat some infections caused by bacteria. The symptoms were:

- Increased coughing
- Increased amounts of mucus
- Changes in the color of the mucus, a sign of an infection
- Increased shortness of breath or finding it difficult to exercise
- Tiredness or feeling unwell
- Coughing up blood or coughing up blood in the mucus

The researchers then calculated the amount of time it took before the participants had a pulmonary exacerbation. This was measured in the "median" number of days. The median is the middle number in a set of numbers. It is between the lowest and highest number.

Overall, the researchers found that the median number of days before the participants had a pulmonary exacerbation was:

- 189 median number of days in the participants who took **the placebo**.
- Few participants who took either **10 mg of brensocatib** or **25 mg of brensocatib** had a pulmonary exacerbation. So, the researchers could not calculate the median number of days before the participants had a pulmonary exacerbation.

You should know that this study was designed to answer the question above. The researchers also wanted to know how many participants had a pulmonary exacerbation. But, this was not the main question the study was designed to answer.

Overall, the researchers found that fewer participants who took brensocatib had a pulmonary exacerbation compared to the participants who took the placebo:

- 31.7% of participants who took **10 mg of brensocatib** had a pulmonary exacerbation. This was 26 out of 82 participants.
- 33.3% of participants who took **25 mg of brensocatib** had a pulmonary exacerbation. This was 29 out of 87 participants.
- 48.3% of participants who took **the placebo** had a pulmonary exacerbation. This was 42 out of 87 participants.

What adverse reactions did the study participants have?

Adverse reactions are unwanted medical problems that the study doctors think may be caused by the study treatment. An adverse reaction is called "serious" if it causes long-lasting problems, puts the participant in the hospital, is life-threatening, is considered "medically important" by the study doctor, or leads to death.

Below are the adverse reactions in this study that the doctors felt may have been caused by the study treatment. But, it takes many studies for researchers to really know if an adverse reaction is caused by the study treatment. The websites listed at the end of this summary may have more information about the adverse reactions that happened in this study.

There was 1 participant who was assigned to take the placebo, but did not take the study treatment. So, the results below only include 255 participants who took the study treatments. There was 1 participant who took 10 mg of brensocatib and 1 participant who took the placebo, who both also accidently took 25 mg of brensocatib. These participants are included in the 25 mg of brensocatib results below.

How many participants had adverse reactions?

The table below shows how many participants had adverse reactions during this study.

Adverse reactions			
	10 mg brensocatib (Out of 81 participants)	**25 mg brensocatib (Out of 89 participants)**	**Placebo (Out of 85 participants)**
Overall adverse reactions	46.9% (38 participants)	41.6% (37 participants)	41.2% (35 participants)
Serious adverse reactions	3.7% (3 participants)	0% (0 participants)	5.9% (5 participants)
Left the study because of an adverse reaction	1.2% (1 participant)	1.1% (1 participant)	1.2% (1 participant)

What serious adverse reactions did the study participants have?

The table below shows the serious adverse reactions that happened in this study. 1 participant who took the placebo had 2 different serious adverse reactions.

Serious adverse reactions			
Serious adverse reaction	**10 mg brensocatib (Out of 81 participants)**	**25 mg brensocatib (Out of 89 participants)**	**Placebo (Out of 85 participants)**
Increased amounts of lymphocytes, a type of white blood cell	1.2% (1 participant)	0.0% (0 participants)	0.0% (0 participants)
Inflammation of the large intestine	0.0% (0 participants)	0.0% (0 participants)	1.2% (1 participant)
Stomachache	0.0% (0 participants)	0.0% (0 participants)	1.2% (1 participant)
Worsening of bronchiectasis symptoms	1.2% (1 participant)	0.0% (0 participants)	1.2% (1 participant)
Lung infection caused by bacteria	0.0% (0 participants)	0.0% (0 participants)	1.2% (1 participant)
Mini stroke caused by lack of blood supply to the brain	1.2% (1 participant)	0.0% (0 participants)	0.0% (0 participants)
Fluid in the lung	0.0% (0 participants)	0.0% (0 participants)	1.2% (1 participant)
A condition called respiratory failure, where the lungs can't get enough oxygen into the blood	0.0% (0 participants)	0.0% (0 participants)	1.2% (1 participant)

None of the participants died due to a serious adverse reaction in this study.

What were the most common adverse reactions?

Gum disease and diarrhea were the most common adverse reactions. The table below shows the most common adverse reactions that happened in at least 3.0% of the participants in this study. There were other adverse reactions, but these happened in fewer participants.

Most common adverse reactions			
Adverse reaction	**10 mg brensocatib (Out of 81 participants)**	**25 mg brensocatib (Out of 89 participants)**	**Placebo (Out of 85 participants)**
Gum disease	2.5% (2 participants)	5.6% (5 participants)	0.0% (0 participants)
Diarrhea	2.5% (2 participants)	2.2% (2 participants)	3.5% (3 participants)
Painful or bleeding gums	0.0% (0 participants)	3.4% (3 participants)	0.0% (0 participants)
Tiredness	0.0% (0 participants)	3.4% (3 participants)	3.5% (3 participants)

Most common adverse reactions			
Adverse reaction	**10 mg brensocatib (Out of 81 participants)**	**25 mg brensocatib (Out of 89 participants)**	**Placebo (Out of 85 participants)**
Increased levels of a waste product called creatinine in the blood (a sign of liver disease)	3.7% (3 participants)	0.0% (0 participants)	0.0% (0 participants)
Joint pain	4.9% (4 participants)	0.0% (0 participants)	1.2% (1 participant)
Headache	1.2% (1 participant)	5.6% (5 participants)	2.4% (2 participants)
Cough	3.7% (3 participants)	1.1% (1 participant)	2.4% (2 participants)
Increased amounts of mucus	3.7% (3 participants)	1.1% (1 participant)	2.4% (2 participants)
Dry skin	1.2% (1 participant)	3.4% (3 participants)	3.5% (3 participants)
Itchy skin	1.2% (1 participant)	3.4% (3 participants)	0.0% (0 participants)
Peeling skin	3.7% (3 participants)	0.0% (0 participants)	0.0% (0 participants)
Abnormal growth or change in color of the skin	0.0% (0 participants)	3.4% (3 participants)	1.2% (1 participant)

How has this study helped people and researchers?

This study helped researchers understand more about how brensocatib worked and better understand its safety in people with NCFBE.

The results from this study will help researchers to learn more about if brensocatib helps people with NCFBE.

More studies with brensocatib are planned.

The results in this summary come from this 1 single study. Other studies may show different results. If you participated in this study and have questions about the results, please speak to the doctor or staff at your study center.

Where can I learn more about this study?

More information about this study, including any available results, can be found on the websites below:

- www.clinicaltrials.gov – Search for "**NCT03218917**"
  It is important to know that the results will not be available on this website until 2022.

- www.clinicaltrialsregister.eu – Search for "**2017-002533-32**"

The full title of your study is: A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Multi-Center Study to Assess the Efficacy, Safety and Tolerability, and Pharmacokinetics of INS1007 Administered Once Daily for 24 Weeks in Subjects with Non-Cystic Fibrosis Bronchiectasis – The WILLOW Study

The protocol number of your study is: INS1007-201

Clinical study participants help researchers make important discoveries that may lead to new medical treatments worldwide. Insmed Incorporated sponsored this study and is thankful for the help of the study participants. If you have questions about the study results, please speak with the doctors, research nurse or other team member at your study site. For more information about Insmed Incorporated:

- Their main office is located in Bridgewater, New Jersey, United States.
- Their phone number is (+)1-844-4-INSMED.
- Their website is https://insmed.com/contact-us/