Trial Title: A Phase 1b study in patients with acromegaly or functioning gastroenteropancreatic neuroendocrine tumors (GEP-NETs) to characterize the pharmacokinetics, pharmacodynamics, safety and tolerability of Debio 4126, a 12-week prolonged-release octreotide formulation.

Debio 4126-102 (Oxtend™-01) was an early clinical study of a new form of a medicine called **Debio 4126**. This is a long-acting version of **octreotide**, designed to be given once every 12 weeks.

The study included people with **acromegaly** - a rare condition caused by too much growth hormone, and people with **gastroenteropancreatic neuroendocrine tumors (GEP-NETs)** - rare tumors that can grow in the digestive system or pancreas. Some of them release hormones that cause certain symptoms.

Researchers looked at how much medicine stayed in the blood and how safe the medicine was. In patients with acromegaly they also looked at how the medicine affected levels of growth hormone and another hormone called insulin-like growth factor 1 (IGF-1), which induces body and/or organ growth . In GEP-NET patients they also looked at how well the medicine controlled symptoms of **carcinoid syndrome,** such as flushing or diarrhea.

This summary is based on one clinical trial. The medicine is still being studied and is not yet approved. The results may not apply to everyone and should not be used to make medical decisions.

WHO CARRIED OUT THE RESEARCH?

The trial was sponsored by Debiopharm International S.A.

THANK YOU!

Thank you to everyone who took part in this study. Your participation made this research possible. By joining the trial, you helped researchers learn more about how Debio 4126 works and how safe it may be to use. Clinical trials like this one are essential for developing new medicines and improving care for future patients.

WHAT IS DEBIO 4126?

Debio 4126 is a new form of a medicine called **octreotide**. It is given as an injection into the muscle and is designed to release slowly in the body over **12 weeks**.

Octreotide is already used in other approved medicines to treat **acromegaly** and **GEP-NETs**. One example is **Sandostatin LAR**, which is given by injection every 4 weeks. Medicines like this have been used for more than 30 years.

WHAT WAS THE PURPOSE OF THIS CLINICAL TRIAL?

This study was done to learn more about how Debio 4126 works in the body and how well it is tolerated. Researchers wanted to answer the following questions:

- How much octreotide (the active medicine in Debio 4126) was found in the blood over time after one or more injections?
- Did octreotide build up in the blood after several injections compared to just one?
- Was Debio 4126 safe and well tolerated by patients?
- For people with acromegaly: how did Debio 4126 affect levels of IGF-1 and growth hormone?

- For people with GEP-NETs: how did Debio 4126 affect symptoms of carcinoid syndrome (a group of symptoms such as flushing, diarrhea, and wheezing caused by certain hormone-producing tumors)?

HOW WAS THIS TRIAL DONE?

Who took part in this trial?

This study included two groups of participants. One group had **16 patients with acromegaly** (7 women and 9 men). The other group had **3 patients with GEP-NETs** (2 women and 1 man).

Before joining the study, all participants were already being treated with similar medicines, such as **octreotide LAR** or **lanreotide ATG**. Their condition had to be stable to be included in the trial. For people with acromegaly, this meant their levels of **IGF-1** had to be no more than **30% above the highest level considered normal** for their age and sex. For people with GEP-NETs, their **carcinoid syndrome symptoms** had to be under control.

Where did this trial take place?

This trial was carried out in **nine countries**: Denmark, France, Germany, Israel, Italy, Poland, Portugal, Spain, and the United Kingdom.

When did this trial take place?

This trial began in October 2022 and ended in December 2024.

What treatments were tested in this trial?

This trial tested **Debio 4126**, a long-acting medicine given by intramuscular injection (an injection into the muscle) every 12 weeks. It was tested at **three different dose levels**: 30 mg, 60 mg, and 90 mg.

The dose each patient received at the start of the study was based on the dose of the treatment they were already using before the trial, such as **octreotide** or **lanreotide**.

What has been completed?

In the **acromegaly group**, 16 people took part. **Fifteen completed the study as expected**, and **one person left early** for reasons not related to side effects of Debio 4126. Most people stayed on the same dose throughout the study. One person had their dose increased, but it should be noted that their **IGF-1 levels were already high before starting Debio 4126**.

In the **GEP-NET group**, 3 people were treated with Debio 4126. This part of the study was **stopped early due to a change in research strategy**, not because of safety concerns. All 3 participants in this group **left the study early**, also not due to any Debio 4126 side effects.

WHAT ARE THE MAIN RESULTS OF THIS TRIAL?

Debio 4126 released **octreotide into the blood** over the full 12-week period. Higher doses of Debio 4126 led to **higher levels of octreotide in the blood**. The medicine did **not build up in the body** over time when four doses were given, one every 12 weeks.

In most participants, the treatment helped keep hormone levels stable. **14 people** started treatment in stable condition and had results available at both the start and end of treatment. In **13 out of these 14**, levels of **IGF-1** stayed within the target range (no more than 30% above the highest level considered normal).

Debio 4126 was found to be **safe and well tolerated**. All three dose levels had **similar safety results**.

WHAT WERE THE SIDE EFFECTS?

Some people in the study experienced side effects. These are unwanted health problems that may be related to the treatment. Most of these were considered mild or moderate by the study doctor (also called the investigator), who assessed whether the side effects were likely caused by the treatment.

In the group of patients with acromegaly, gallbladder stones or sludge (also known as cholelithiasis) were reported in 4 out of 16 people. Headache, redness at the injection site (injection site erythema), hardening, and inflammation at the injection site were each reported by 2 people.

In the group of patients with GEP-NET, pain at the injection site, fever, nausea, and worsening of the underlying cancer were each reported by 1 person.

WHAT WAS LEARNED FROM THIS TRIAL?

The trial results were positive and supported the decision to move Debio 4126 forward into the next phase of clinical development.

WHERE CAN I FIND MORE INFORMATION ABOUT THIS TRIAL?

Further study details can be found by accessing www.clinicaltrials.gov, referencing the following information:

Public Trial Title	A Study to Assess the Pharmacokinetics, Pharmacodynamics, Safety, and Tolerability of Debio 4126 in Participants with Acromegaly or Functioning Gastroenteropancreatic Neuroendocrine Tumors (GEP-NETs) (OXTEND™-01)
Protocol Number	Debio 4126-102
NCT number	NCT05364944
EudraCT Number	2021-005035-23
Study Sponsor	Debiopharm https://www.debiopharm.com

Please email any questions to ClinicalTrials@debiopharm.com

ARE THERE PLANS FOR FURTHER TRIALS?

Debiopharm is starting a new Phase 3 study called Oxtend™-03. This study will include people with acromegaly who have not been treated with Debio 4126 before, have IGF-1 levels that are not elevated, and are currently receiving either octreotide or lanreotide. The goal is to learn more about how safe and effective Debio 4126 is for this group of patients. If the results continue to be positive, Debiopharm International S.A (the sponsor) plans to request an approval to make Debio 4126 available for patients.