Recordati Research and Development

SOM230 (pasireotide) Signifor

Patient Information and Informed Consent
Clinical Protocol CSOM230B2412

An open label, multi-center pasireotide roll-over protocol for patients who have completed a previous Novartis sponsored pasireotide study and are judged by the investigator to benefit from continued pasireotide treatment

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Sponsor:	RECORDATI AG - Lindenstrasse 8, 6340 Baar, Switzerland Tel: + 41 (0) 61 205 61 00
CRO:	IQVIA

Informed Consent Form Summary of Changes

You may have signed a previous version of the informed consent for this study, however a new information has been made available that we need to share with you.

This summary of Changes includes the new information, and is only for ongoing patients who have been previously consented. If you have any questions please ask the study doctor and/or staff assigned to the trial to answer them.

Section	**Brief description of new change and/or-new text**
Informed consent	A new reason has been added in this Informed Consent Form to explain when the study doctor may remove you from this study: 7. The study drug has become available through specific support programmes in your country. This ICF amendment is applicable to Brazil, France, Germany, India, Italy, Malaysia, Mexico, Peru and Thailand.

Informed consent

You are invited to voluntarily join in a clinical research study that will involve taking the drug SOM230/pasireotide (Signifor®) and any medication given in combination with pasireotide (to treat Cushing's disease or acromegaly). The intention of this study is to allow continued use of pasireotide and any medication given in combination with pasireotide (to treat Cushing's disease or acromegaly), to patients who have completed their respective parent protocol (previous Novartis trial you have been participating in) and to collect long term safety data. You have recently completed a Novartis sponsored trial (parent study number…… _) and have been benefitting from treatment with pasireotide and any medication given in combination with pasireotide (to treat Cushing's disease or acromegaly) as determined by the investigator/Study Doctor.

Before you agree to join in this study, you need to know the risks and benefits so you can make an informed decision. This process is known as "informed consent".

This consent form tells you about the study that you may wish to join. Please read the information carefully and discuss it with anyone you want. This may include a friend or a relative. If you have questions please ask the Study Doctor or study staff to answer them.

Once you know about the study, you will be asked to sign this form to join this study. Your decision to take part in this study is voluntary. That means you are free to decide to join this study or not join this study and refusal to join will not affect your medical care. You are also free to leave the study at any time and without any reason. If you choose not to join in this study, or decide to withdraw you can discuss regular medical care / alternative treatments with the Study Doctor.

We may learn about new things that make you want to stop being in the study. If this happens, you will be informed. You can then decide if you want to continue to be in the study.

The Study Doctor may remove you from this study for any justified reason according to the protocol. Examples why you may be taken out of the study are:

1. Staying in the study would be harmful.
2. You need treatment not allowed in this study.
3. You fail to follow instructions.
4. The investigator feels this treatment is no longer in your best interest.
5. You become pregnant.
6. The study is cancelled.
7. The study drug has become available through specific support programmes in your country (applicable to Brazil, France, Germany, India, Italy, Malaysia, Mexico, Peru and Thailand).
8. The study drug becomes commercially available and reimbursed in your country.

If you should decide to leave the study you should tell the Study Doctor or study staff. They will make sure that proper procedures are followed and that a final visit is made for your safety.

Study Treatment

On this study you will receive pasireotide as prescribed in your parent protocol (the pasireotide study you recently completed). Your starting dose of pasireotide and any medication given in

combination with pasireotide (to treat Cushing's disease or acromegaly), will be the same as the dose that was given to you in your previous pasireotide study. During the study, your Study Doctor may change the dose depending on how you respond to pasireotide and any medication given in combination with pasireotide (to treat Cushing's disease or acromegaly).

In addition, any unused study drug and empty packages must be returned to the Study Doctors at your study visits. At the end of the study or when you leave the study you should return any study medication still in your possession to the Study Doctors.

Please tell your Study Doctor or study staff if you have any unusual symptoms.

You may discuss with a doctor or health care professional, who is not directly involved in the study, health issues or medical problems related to the study treatment or disclose information related to the study treatment. In this case you should tell your doctor or health care professional that the Recordati drug, which is part of the study treatment and information relating to it, is Recordati' property and is confidential.

At the end of the study or if you stop study treatment, you should return any study treatment, that you still have remaining to the study doctors.

Trial purpose and conduct

This is a clinical research study to evaluate long term safety. This trial is sponsored by the pharmaceutical company named Recordati. Once you give your consent to join this study and are eligible to participate and enroll in the study, you will receive pasireotide either subcutaneous or long acting release formulation and any medication given in combination with pasireotide (to treat Cushing's disease or acromegaly). Recordati will make a continued supply of pasireotide and any medication given in combination with pasireotide (to treat Cushing's disease or acromegaly), available to you at no cost.

Pasireotide s.c. is a short acting formulation administered subcutaneously two or three times a day. This formulation has been tested in healthy volunteers and in patients with acromegaly, Cushing's disease and neuroendocrine tumors.

Pasireotide LAR is a long acting formulation administered intramuscularly every 28 days. It has been studied in healthy volunteers and in patients with acromegaly, Cushing's disease, and neuroendocrine tumors.

Once you enroll in the study, if you were receiving pasireotide LAR formulation in your parent protocol, you will continue to come to your Study Doctor's office/clinic/study site every month to receive your long acting release intramuscular injection. If you were receiving pasireotide subcutaneous formulation, you will be given up to a 3-month supply of the drug. You will also be given any medication that you are taking in combination with pasireotide to treat Cushing's disease or acromegaly, at your scheduled study visits. Female patients of child bearing potential will be required to have a pregnancy test at this first visit before enrolling. No other blood or medical evaluations are specifically required on this study, beside monthly at home urine pregnancy tests for women of child bearing potential. However, your Study Doctor may continue evaluations as part of the normal management of your disease and/or standard of care.

You will be asked to come to the Study Doctor's office/clinic/study site for a study visit based on the schedule that matches your parent protocol, depending on the study drug formulation netyou were receiving (i.e., monthly for LAR formulation and every three months for s.c. formulation). During this visit, general information about your health will be collected including confirmation that you are still responding to treatment, and you will receive a re-supply of study medication. Your Study Doctor will attest to you still receiving benefit.

You will be able to take the study drug(s) for as long as the Study Doctor thinks it is in your best interest. You will be taken off the study if you have intolerable side effects, if the Study Doctor no longer thinks it is in your best interest, if you are not compliant to study requirements or if you withdraw your consent.

If you stop study medication on this study or leave the study, you should tell the Study Doctor or study staff. They will ensure that proper procedures are followed and that a final visit is made for your safety.

Your Study Doctor will need to know general information about your health status up to 3

months after your last dose of study medication (30 days if you are receiving the pasireotide subcutaneous formulation and 84 days if you are receiving the pasireotide LAR formulation). Once you stop taking the study medication(s), and have had your final visit there will be no further follow-up visits. During your final safety follow up visit, female patients of childbearing potential are required to have a pregnancy test.

Patients must comply with all study requirements. If you do not or are unable to fulfill the study requirements, you will be discontinued from the study.

Patients' responsibility

It is very important that you come to all the study visits and that you follow your Study Doctor's instructions. Tell the Study Doctor about any medications you are taking during the study. This includes prescription medicines, over-the-counter medicines and vitamins. This is very important. Please tell your Study Doctor or site staff if you have any unusual symptoms.

By signing this consent form, you agree to follow your doctor's instructions and attend all study-related visits.

Study treatment discontinuation

Please inform your doctor or study staff if you decide to interrupt or stop taking the study treatment(s). You will be asked to return to the study site as soon as possible to check how you are. You should bring your study treatment(s) to the clinic. Also the Study Doctor may choose to discontinue your study treatment(s).

You may be asked to continue with study visits after stopping study treatment(s) so that all or a selection of assessments can be performed.

If you cannot or do not want to continue to attend study visits while off study treatment(s), your Study Doctor or study staff may ask if they can contact you by telephone until the end of the study to check on how you are doing. You may decline contact by telephone if you so choose.

Withdrawal of your consent to participate in this study

You may decide that you not only want to stop study treatment(s) but also don`t want to come to any further visits, and don`t want to have any further assessments or contact by the study staff. This is considered as withdrawal of your consent from participation in this study. It is important that you inform your Study Doctor of your decision to withdraw your consent in writing or in a manner compatible with local laws, cultures, and norms.

Recordati will continue to retain and use all research results and any biological samples that have already been collected for the study evaluation (as per local regulations).

You can discuss further regular medical care with the Study Doctor. The choice to withdraw from research participation will not affect your medical care.

Risks and inconveniences

Risks are possible side effects of the study medicine. Pasireotide could cause side effects like abdominal pain, nausea, vomiting, loose stools, diarrhea, mild dizziness and headache. It could also affect hormones, like insulin, which regulate blood sugar levels and the glucose in your blood may increase during treatment. Therefore, your doctor may monitor your blood glucose during this study if he/she feels it necessary.

A small number of cases of QT prolongation have been reported in some participants in pasireotide clinical trials. QT is one of the measurements taken during the ECG (heart tracing) and increases (prolongation) in QT may lead to an irregular heartbeat which in rare instances can develop into a sudden, life-threatening condition. The majority of cases that were reported in the pasireotide clinical trials resolved or improved spontaneously without discontinuation of the study drug.

A small number of cases of concomitant increases in blood liver enzymes and bilirubin have been reported in some participants in pasireotide clinical trials. Blood liver enzymes and bilirubin are important measurements to evaluate liver health and function and a concomitant increase may lead to liver damage which in rare instances can progress to liver failure, a life-threatening condition. In the pasireotide clinical trials, subjects and patients were generally asymptomatic and remained clinically well and liver function returned to normal after discontinuation of pasireotide. However, if you were to experience abnormal yellowing of the skin or eyes, or dark colored urine while in this study, you should notify your doctor immediately as these could be symptoms of liver problems. Though the risk is small, these findings may indicate a potential risk for liver failure associated with the treatment of pasireotide.

Problems or side effects that are not now known could also occur. You will be given any new information that may affect your willingness to start or continue in the study.

Your injection under the skin may cause pain at the injection site or cause local irritation such as swelling and redness. If any irritation occurs, it is expected to disappear after a short time.

The safety profile of any other drugs that are given to you in combination with pasireotide, to treat Cushing's disease or acromegaly, can be given to you as applicable. Please ask your Study Doctor for possible side effects regarding any combination medications that you are given in your parent study.

Contraception and pregnancy

Women who are pregnant or nursing a child cannot participate in this trial. You must confirm, to the best of your knowledge, that you are not now pregnant, and that you do not intend to become pregnant during the trial. You will be required to take monthly at home urine pregnancy tests if you are a woman of child bearing potential, and report the results to your Study coordinator/Study doctor.

The risks to an unborn human fetus or a nursing child from the medications you are required to take in this study are not known.

As a female participant in the study it is therefore important that you use a highly effective form of birth control method (contraception) if you are sexually active and may become pregnant. Highly effective methods of birth control have a less than 1% chance of unwanted pregnancy during one year, if used appropriately according to the instructions of the manufacturer. Please discuss with your Study Doctor the most appropriate birth control method for you that also respect your cultural and religious situation. Examples of highly effective birth control methods are:

- Total abstinence (no sexual relations), when this is in line with your preferred and usual lifestyle. Periodic abstinence like calendar, ovulation, symptothermal, post-ovulation methods, and withdrawal are not acceptable methods of contraception.
- Female sterilization, when you have been already surgically sterilized prior to the study by surgical removal of both ovaries (woman's reproductive system that stores and releases eggs for fertilization and produces female sex hormones), total hysterectomy (surgical removal of the uterus and cervix) or tubal ligation (getting your "tubes tied") at least six weeks before taking study treatment.
- Your male partner has already been sterilized with the appropriate documentation. The sterilized male partner should be your sole partner.
- Use of oral, injected or implanted hormonal methods of contraception or placement of an intrauterine device (IUD) or intrauterine system (IUS) or other forms of hormonal contraception that have comparable efficacy (failure rate <1%), for example hormone vaginal ring or transdermal hormone contraception (in case of oral contraception you should have been using the same pill on a stable dose for a minimum of 3 months before taking study treatment).
- In case of use of oral contraception you should have been stable on the same pill for a minimum of 3 months before taking study treatment.

All sexually active male patients should use a condom during intercourse while taking study drug and for 30 days after pasireotide s.c. last dose and 84 days after pasireotide LAR last dose. Male patients should not father a child in this period. A condom is also required to be used by vasectomized men in order to prevent delivery of the drug via seminal fluid.

If you become pregnant or suspect being pregnant during study treatment and within the 30 day follow up period you must inform the Study Doctor immediately, and if on study treatment, you have to stop immediately. You will not be allowed to continue study treatment if you are pregnant. Your Study Doctor will medically follow your pregnancy until delivery to monitor you and your child`s safety.

General information on pregnancy and contraception

85 out of 100 sexually active women who do not use birth control can expect to become pregnant in a year. No matter which birth control you are using from the list above, it is important to follow the manufacturer directions. If you don't, you raise your chance of getting pregnant.

Hormonal contraception is available in the form of pills which need to be taken every day, injections, which lasts approximately 3 months and as implanted devices. Hormonal methods are associated with some risks like changes in your cycle, nausea, headache, changes in mood, weight gain, breast tenderness, and blood clots.

Implanted devices are inserted into the uterus and can stay there for several years. They can cause cramps, bleeding, and infertility. It is important to know that not all women experience all of the adverse effects listed above.

Benefits of treatment

You may receive no direct benefit from being in this study. However, your taking part may help patients get better care in the future.

Costs and compensation for participation in this study

There will be no monetary costs to you for participating in this study. You will not be charged for the study drug(s) or any of the tests and procedures performed solely for research purposes.

Compensation for injury resulting from the study

It is important that you follow carefully all the instructions given by the Study Doctor and his/her staff regarding this study.

If you become ill or are physically injured as a result of participation in this study, please contact the Study Doctor right away *[investigator's name and contact information]*; (s)he will treat you or refer you for treatment.

The reasonable costs of such treatment beyond that provided by your insurance will be covered by the Sponsor, Recordati. Recordati will provide payment for medical expenses for injuries:

- if you received reasonable medical care,
- if you followed instructions,
- if the injury is related to the study drug or to properly performed study procedures that are not part of your usual medical care,
- that are not the result of the natural course of any underlying disease and/or pre-existing disease process present prior to the proper administration of pasireotide.

In no way does signing this consent form waive your legal rights, nor does it relieve the investigators, Sponsor or involved institutions from their legal and professional responsibilities.

Alternative procedures or treatment

Other procedure and/or medicines may be available to you. Listed below are all the diseases that are being treated in this trial and alternative treatment options for those diseases.

Acromegaly: surgery, radiotherapy, medical therapy (e.g. other somatostatin analogs; GH receptor antagonists, dopamine agonist)

Cushing's disease: surgery, radiotherapy, medical therapy (e.g. other somatostatin analogs dopamine agonists, steroidogenesis inhibitors, glucocorticoid receptor antagonists)

Dumping syndrome: octreotide, surgery

Melanoma, NET and carcinoid: surgery, radiation, chemotherapy, immunotherapy

You can ask your doctor about their potential benefits and risks of each of these treatment options.

What will happen to my Personal Data?

Data Protection laws vary by country. Many countries have very specific requirements regarding the informed consent of the data subject. The elements required to be included in the following subsections of the informed consent are:

- *definition of Personal Data. Please note with respect to Personal Data that in adult studies the code used to de-identify subjects should not display subject's full date of birth (DD/MM/YY). However, in pediatric studies MM/YY may be a possibility especially for studies conducted in infants.*
- *identification of individuals that will review medical records that will identify the subject by name;*
- *that records identifying the subject will be kept confidential and that any published results will not reveal the identity of the subject ;*
- *that by signing the informed consent the subject or his/her legal guardian authorizes access to medical records;*
- *identification of types of data collected and a simple and thorough explanation of the purposes of collection and processing of data;*
- *identification of categories of third parties that may have access to the data or to whom the data may be transferred, in particular persons or organization that are acting as data processors (Recordati affiliates, CROs, outsourcing companies, labs, etc.). In some EU countries, this data may need to be specific. Please contact your data privacy legal representative to determine level of specificity in your country; a statement, if appropriate, that the data may be transferred to countries that do not provide an adequate level of data protection as in the study country (generally any country outside of the EEA, Canada, Argentina, Switzerland, Israel, New Zealand, Uruguay, Andorra, Faroe, or Guernsey).;*
- *explanation of the extent to which study participants have the right to access information held about them to correct inaccuracies and any limits to those rights;*
- *date or event upon which the consent may not be considered to be valid anymore.*

What is Personal Data?

The study doctor will collect your Personal Data meaning your name, initials, address, gender, age/date of birth and health information.

If necessary, the study doctor may contact your doctor to collect more medical information. He/she may check your health information on public records if allowed by local law.

The study doctor will replace your name and other general information about you, excluding age/date of birth and gender, with a special code that identifies you. The study doctor will associate this code with the study information and any biological samples to make it unlikely that anyone will be able to identify you.

Recordati, which has appointed as its data processing representative in the European Union Recordati Rare Diseases Italy s.r.l. with registered office in Civitali 1, 20148 Milan (Italy), will receive the Personal Data below from your study doctor for the purpose of the study:

- Your assigned code and age/date of birth, gender
- Study information

Recordati is the data controller for the processing of personal data you provided in the past to Novartis, and of personal data which you may provide in the future to Recordati. Recordati has contracted the Clinical Research Organizations IQVIA and PPD for the data processing activities for the purpose of this study.

How will my Personal Data be used?

Your Personal Data will be examined to see whether the study is done accurately and to see if the study drug is safe and effective. It will be examined with the Personal Data from all of the other participants in this study to learn more about the effects of the drug.

Your Personal Data may also be combined with data from other studies. This is to analyze and better understand the safety and efficacy of the study drug. Personal Data may be used to check that the study is accurate and conducted correctly. Some of the processing of your Personal Data may be automated meaning that Recordati may use computers and other technology based solutions to process the Personal Data.

Although you already consented to the processing by Novartis of the personal data you had provided, Recordati wishes to obtain your renewed consent to the processing of your personal data already collected by Novartis and of the additional data that Recordati may collect directly from you during the study. Your decision to provide your consent is completely free. However, if you decide not to renew your consent to the processing of your personal data by Recordati, you will no longer be able to take part in this study, and therefore the staff and the doctors of the study will not be able to collect the necessary information, If you give your consent, you authorize such access to your Personal Data including your original medical records.

(USE THE FOLLOWING TEXT FOR TRIALS IN THE US)

The individuals mentioned in bullets 2 & 3 of the Section 'Who Can see my Personal Data' may use your Personal Data, including any of your remaining coded biological samples, for

additional medical and/or scientific research and development projects that are outside of the current study purpose and objectives.

Where are Personal Data kept and secured?

Upon the renewal of your consent to the processing of past and future data, Recordati will keep your personal data for a period of 25 years from the last follow-up relating to this clinical study. This retention period may be extended if this should prove necessary for Recordati in relation to any dispute, investigation or proceedings or if this should be required by new legislation. In the absence of the renewal of your consent, Recordati will store the data collected by Novartis for the period of time prescribed by the law.

The Personal Data collected in this study by Novartis and Recordati will be entered in' Recordati secure electronic systems, and the companies who work with Recordati may operate these systems. Your Personal Data will be stored for the period requested by local regulations after the end of the study.

A description of this study will be available in registries in countries where the study is conducted, and will not include information that can directly identify you. For example, a description of this clinical study will be available on ClinicalTrials.gov.

A summary of the results may also be published at conferences or in journals. If the results of the study are presented to the public, you will not be named. Some authorities may ask that Recordati disclose study data for transparency reasons. However, the data shared will not identify you.

Who can see my Personal Data?

Your Personal Data will be kept secure and will only be available to the people listed below:

- The study doctor and study staff,
- Recordati, companies of Recordati's group, Recordati study/research staff (e.g., monitors, auditors, and authorized agents such as contract research organizations (CROs),
- In the future a new company acquiring or licensing rights from Recordati or part of its business,
- Review boards checking ethics of the study,
- Health Authorities or other authorities, as applicable,
- Other third parties (which may include third parties in other jurisdictions) *(Be as specific as possible)*.

However, these people must keep the Personal Data confidential. They may be located in Switzerland, in countries of the European Economic Area (EEA), or other countries like the United States. The data protection laws in these countries may not be as strict as in your own country. In those cases, the transfer will take place in the presence of the appropriate safeguards imposed by GDPR on the transfer of data outside the European Union (such as, for example, the adoption of standard contractual clauses, pursuant to articles 46 and following of the GDPR).

Your specific rights about your Personal Data

You have the right to review your Personal Data. However, during the study, access to the Personal Data may be limited to protect the integrity of the study. You may have access to your Personal Data at the end of the study.

You should ask the study doctor if you have any questions about the collection and use of information. You should also inform him/her if you wish to exercise your rights about this information; such as if you decide to have some Personal Data corrected or to withdraw consent *(add additional contact information as required by local law).*

You can at any time contact *(enter contact details of the Data Privacy Officer at the site or of other responsible person)* or the Recordati Data Protection Officer at GroupDPO@recordati.com if you have any questions about this Informed Consent Form or the collection, processing, or use of your Personal Data as described above. You are also entitled by law to lodge complaints in front of the relevant data privacy authority.

What are Anonymized Data and who can use them?

Recordati may anonymize your Personal Data, which means that your Personal Data cannot be traced back to identify you. Therefore, it is no longer considered Personal Data. This Anonymized Data may be shared by Recordati with external parties, which include health authorities and authorized external researchers to help predict how people might respond to a treatment in a future, unrelated study, or to learn more about this or other diseases.

Contacts

If you have questions about the research, please contact: *(insert name and the phone number; usually the investigator and/or study nurse/study coordinator)*.

Role	Name	Telephone Number
Principal Investigator		
Study Nurse/ Coordinator		

If you have questions related to your rights as a research subject, please contact: *(insert name of the IRB/IEC and the phone number (ICH q))*.

Role	Name	Telephone Number
IRB/EC		

In the event of a research-related injury, please contact *(insert name and phone number (ICH q) (EIC 7))*.

Role	Name	Telephone Number
Principal Investigator		

Sample signature page (using HIPPA approved wording, for US)

Protocol number and version: CSOM230B2412, Version 05.07 dated 02-Nov-2021

Protocol title: An open label, multi-center pasireotide roll-over protocol for patients who have completed a previous Novartis-sponsored pasireotide study and are judged by the investigator to benefit from continued pasireotide treatment

I have read this document/had its contents explained to me. I understand the purpose of this study and what will happen to me in this study. I do freely give my consent to join in this study, as described to me in this document. I understand that I will receive a copy of this document as signed below.

By signing this consent form, I authorize the use, access, and sharing of my personal medical information as described in the section "Confidentiality and Authorization approval to collect, use, and disclose Personal Medical Information and Biological samples". This consent is valid unless and until I revoke it.

type/print name		
Patient	Signature	Date
type/print name		
Witness (if patient gives oral, not signed consent)	Signature	Date
type/print name		
Legal representative (legally authorized to act as personal representative to sign for [name of patient])	Signature	Date
type/print name		
Investigator	Signature	Date
type/print name		
Name of presenter (who presented/explained the document)	Signature	Date

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type/print name		
Patient	Signature	Date
type/print name		
Legal guardian (if patient is a minor)	Signature	Date
type/print name		
Witness (if patient gives oral, not signed consent)	Signature	Date
type/print name		
Investigator	Signature	Date
type/print name		
Name of presenter (who presented/explained the document)	Signature	Date

type/print name		
Patient or Legal representative (legally authorized to act as personal representative to sign for [name of patient])	Signature	Date
type/print name		
Name of presenter (who presented/explained the document)	Signature	Date