Recordati Research and Development

LCI699

Protocol Title

An open-label, multi-center, roll-over study to assess long term safety in patients with endogenous Cushing's syndrome who have completed a prior Novartis-sponsored osilodrostat (LCI699) study and are judged by the investigator to benefit from continued treatment with osilodrostat

Global Model Informed Consent Form for Protocol No. CLCI699C2X01B

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CRO:	IQVIA

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Informed Consent Form Summary of Changes

You may have signed a previous version of the informed consent for this study; however, 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 patients who have been previously consented. It may not be applicable for new patients enrolled after the date the Summary of Changes has been approved.

If you have questions please ask the study doctor and/or staff assigned to the trial to answer them.

The following changes have been implemented throughout the document:

Section	**Brief description of the change and/or new text**
4	Sentence changed from: *"Osilodrostat has recently been approved in USA and European Union as Isturisa® for the treatment of Cushing's disease in adults"*. To: *"Osilodrostat has recently been approved in USA, European Union and Japan as Isturisa® for the treatment of Cushing's disease in adults"*.
5	Table 5-1: *Side effects* has been updated
10.4	Sentence changed from: *"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"*. To *"In those cases, the transfer will take place in the presence of the appropriate safeguards imposed by General Data Protection Regulation (GDPR) on the transfer of data outside the European Union"*.

1 Why have I been given this document to read?

You are being asked to give your voluntary consent to join in this research study to find out if the study treatment with osilodrostat is safe and can help others who have Endogenous Cushing Syndrome.

Please read this document carefully. It tells you about the study, including possible benefits and risks. This information is provided to you to help you make your decision on whether or not to join this study and is confidential. Do not share this information with anyone other than close family or friends or others who you need to help you make your decision.

If you have any questions about this information at any time, please ask the study doctor or study staff.

2 What is the purpose of this study?

This study is an extension of the previous study you participated in. The drug (osilodrostat) may still not be available in your country as it has been already approved as Isturisa® in USA and European Union only. The purpose of the study is to evaluate the clinical benefits and long-term safety data of osilodrostat and allow continued use of osilodrostat to patients who suffer from a chronic excess of a hormone called "cortisol". This is called "endogenous Cushing syndrome". The most common causes are: a tumor of a gland located in the brain (Cushing disease), outside the brain, or in the adrenal glands.
You should only take the study treatment as instructed and should not do anything else with it. 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.

You must always remember not to throw away your empty study drug containers. Instead keep them in a safe place and bring them back to the doctor's office at every visit and whenever your study doctor or nurse ask you to.

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 doctor.

In this study, you will receive osilodrostat. Your starting dose of osilodrostat will be the same as that given to you in the previous study. During this study, your study doctor may change the dose depending on how you tolerate and respond to osilodrostat. It is very important that you take the medicine given to you just as the doctor tells you to do. Do not miss any tablets. Tell the study staff about any medications you are taking during the study. This includes prescription drugs, over-the-counter medicines, vitamins, herbal treatments and alternative treatments.

Call your study doctor or study staff immediately if you have any unusual symptoms. Do not wait until your next visit to inform your study doctor of your symptoms. Your dose may need

to be changed. If necessary, you may also have to stop taking study drug temporarily and the side effect(s) will be closely monitored until resolution.

All study medication must be kept out of the reach of children.

This clinical study is sponsored (funded) by a company called Recordati and some of the study activities are managed on its behalf by the Contract Research Organization IQVIA.

3 What do I need to know if I join this study?

If you agree to join this study, the following table lists what will happen during the study. You will be given new information as it becomes available that may affect your willingness to stay in the study. You can then decide whether to continue with the study.

Table 3-1 Study overview

	Details
Total number of subjects	About 180 subjects will join in this study.
Duration of the study and number of visits	If you join the study, you will be asked to come to the study doctor's office/clinic/study site every three months for a maximum period of 5 years. Each study visit should take about 1 hour. Your study doctor will need to confirm that you continue to benefit from treatment during these visits. If necessary, your study doctor may ask you to come more often if he/she thinks you need more frequent visits.
After signing the informed consent	The study doctor will discuss if there is any need for you to stop taking any of your current treatments before starting the study treatment. If you are eligible, you can start the treatment with osilodrostat as soon as you enter the study.
Study Treatment	**At the Baseline/Enrollment visit,** the study doctor will ask you about your health, your medical history and any medication you are taking. All the assessment as listed in the section "Assessments during the study" will be performed. If you meet the "entry criteria" of the study, you will receive sufficient study drug at the end of this visit for the period until the next 12-weeks (±2 weeks) follow-up visit. **During the study,** you will take study drug twice a day except if your disease worsens, you experience a side effect that you cannot tolerate, you leave the study, or the study is completed per protocol. You will return to your study doctor's office at regular intervals (every 12 weeks ±2 weeks) so that your condition can be monitored. You will receive sufficient re-supply of study medication at the end of the visit for the period until the next follow-up visit. The study doctor will assess whether you are still benefiting from treatment with osilodrostat. **Pay close attention to the dose of study drug on each pack, as you may receive more than one tablet strength at the same visit.** You will be asked to take the medication twice a day with liquids, with or without food. Study drug should be taken at approximately the same time each day, with about 12 hours between each dose administration. If vomiting occurs after you take your study drug, you should not take the study drug again before the next

	Details
	scheduled dose. Please do not miss any dose. You will be asked to return all unused/used study drug to the study site at every visit. Female patients of childbearing potential will be required to perform monthly home urine pregnancy tests during the study and during the 30 day safety follow up period. The urine pregnancy test will be provided. In case your urine pregnancy test is positive, you should inform your study doctor immediately, who will conduct an additional pregnancy test based on the analysis of your blood (5 ml, 1 teaspoon). If you decide to stop study medication on this study or leave the study, you should tell the study doctor or the study staff. They will ensure that proper procedures are followed and that a final visit (Safety Follow-up/End of Study visit) is made for your safety. **At End of Treatment visit**, your study doctor will ask you some health related questions. All the assessments as listed in the section "Assessments during the study" will be performed. At a **Safety Follow-up visit/End of Study visit** (30 days after stopping treatment) all the assessment as listed in the section "Assessments during the study" will be performed except Pituitary MRI scan.
Assessments during the study	The following safety assessments will be performed for the enrolled subjects in this study: **Physical Examination** Typically, the doctor will use tools to look in your eyes, ears, nose, and throat. They will listen to your heart and lungs. This exam also includes: touching, or "palpating," parts of your body (like your abdomen). This will be conducted at every visit (i.e. Baseline, week 12 and every 12 weeks (+/- 2 weeks) thereafter, End of Treatment and End of Study visits. **Body weight and blood pressure** Body weight (to the nearest 0.1 kilogram [kg] in indoor clothing, but without shoes) will be measured. Blood pressure will be measured at every visit (i.e. Baseline, week 12 and every 12 weeks (+/- 2 weeks) thereafter, End of Treatment and End of Study visits. **Laboratory evaluations** All laboratory evaluations will be performed using central laboratory: blood chemistry (Albumin, alkaline phosphatase, total bilirubin, calcium, creatinine, CK, g-GT, fasting plasma glucose, inorganic phosphorus, lipase, amylase, magnesium, potassium, total protein, AST, ALT, sodium, urea/BUN and uric acid, HbA1c), hematology (Hemoglobin, hematocrit, red blood cell count, white blood cell count with differential [monocytes, eosinophils, basophils, neutrophils, lymphocytes], and platelet count), testosterone, serum cortisol

	Details
	as clinically indicated, urine free cortisol (two 24-hour urine specimens collected) plasma ACTH, 11-deoxycortisol and 11 deoxycorticosterone. You will be asked to collect the urine samples before each visit and bring to the study site. These urine samples should preferably be collected over consecutive days with the last sample being taken the day just before the visit. You have to bring the urine samples to the site at the visit. All laboratory evaluations will be performed at Baseline, week 12 and every 12 weeks (+/- 2 weeks) thereafter, and at End of Treatment and End of Study visits. Only 11-deoxycortisol, 11 deoxycorticosterone, testosterone, blood chemistry and hematology will be analyzed at Baseline, week 24 and every 24 weeks (+/- 2 weeks) thereafter, and at End of Treatment and End of Study visits. **Electrocardiogram (ECG)** Twelve-lead safety ECGs are collected at the study site using ECG equipment available at the sites. ECG procedure is as follows: electrodes are placed on the skin of the chest and connected in a specific order to a machine that, when turned on, measures electrical activity all over the heart. ECG will be collected at Baseline, week 24 and every 24 weeks (+/- 2 weeks) thereafter, End of Treatment and End of Study visits. **Magnetic Resonance Imaging (MRI)** Pituitary MRI scanning with gadolinium enhancement will be performed using the local site facility, to monitor any change in size. If you cannot have intravenous contrast (eg due to allergy or kidney problems), a non-contrast MRI scan may be performed. If MRI cannot be performed at all then a computer tomography (CT) (with i.v. contrast if not contraindicated) may be performed. MRI uses a magnetic field and radio waves to create detailed images of the organs and tissues within your body. Pituitary MRI scanning will be performed at Baseline, week 48 and every 48 weeks thereafter and End of Treatment visits. **Pregnancy and assessments of fertility** If you are a female and of child-bearing potential you will be tested to see if you are pregnant with a urine pregnancy test. In case it is positive, a serum pregnancy test will be required and 5 ml (1 teaspoon) of blood will be taken. Urine pregnancy test will be performed monthly at home and at Baseline, week 12 and every 12 weeks (+/- 2 weeks) thereafter, End of Treatment and End of Study visits.
Sample collection	Blood and urine will be collected for the laboratory evaluations. Approximately 1 to 2.5 tablespoons (up to 32 ml) will be taken for routine blood safety tests. The minimum required urine volume per sample will be 5 ml (1 teaspoon). Your biological samples will be coded with a unique number and stored under Recordati' control for a maximum of 15 years.
Access to study treatment after study completion	Study completion is defined as when the last subject finishes their Study Completion visit, and any repeat assessments associated with this visit have been documented and followed-up appropriately by the study doctor, or in the event of an early study termination decision, the date of that decision.

	Details
	All treated subjects should have a safety follow-up visit conducted 30 days after last administration of study treatment.

After the study is completed and all data examined, a summary of the study results will be shared with your study doctor. The study doctor and/or representatives may share these results with you.

After the study is completed, a summary of the study results will be publically available at www.ClinicalTrials.gov, and/or at the European Clinical Trials Database (EudraCT, www.eudract.ema.europa.eu/).

3.1 Can I decide to *stop* my participation in the study?

You are free to stop your participation in this study at any time. If you want to stop participation in the study, you should notify the study doctor *(in writing or in any other form required locally)*. This could mean:

1. Stopping study treatments and continuing visits. If you decide to stop study treatments you will be asked to return to the study center as soon as possible to have a physical check-up
2. Or, stopping study treatments and all future visits. Your study doctor or staff may ask you to do regular phone calls until the end of the study.

The information already collected during the study including your samples (defined as Personal Data in this consent) will still be used together with the data collected from other patients in the study according to this informed consent and local laws.
In addition to stopping participation in the study, you could decide to withdraw your consent as explained in Section 3.2. If you decide to stop study treatment and/or other study-related activities you should tell the study doctor or study staff. They will make sure that proper procedures are followed.

3.2 Can I withdraw my consent to collect and use my Personal Data?

You may decide to withdraw your consent from this study. You should inform your study doctor at any time in writing, *(or in any other form required locally)*. This means that you want to stop full participation in the study and any further collection of your Personal Data.

You can discuss your ongoing medical care with the study doctor, and return to your regular medical care.

Recordati will continue to keep and use your collected study information (including any data resulting from the analysis of your samples until your time of withdrawal) according to local laws. This is done to guarantee the study results can be verified, to determine the effects of the study treatment, and to ensure complete study documentation.

You also have the right to request that your samples be destroyed (or returned at any time) *(only add if mandated by local laws and regulations).*

ALWAYS USE THE FOLLOWING TEXT FOR TRIALS IN EU. FOR ROW COUNTRIES ALSO USE THIS LANGUAGE, UNLESS SPECIFIC COUNTRY LAWS REQUIRE MORE MANDATORY CUSTOMIZATIONS.

Your samples that have not yet been analyzed at the time of your withdrawal will no longer be used, unless permitted by local laws. They will be stored according to applicable legal requirements.

(USE THE FOLLOWING TEXT FOR TRIALS IN THE US or JAPAN)

Otherwise, your samples that have not yet been analyzed at the time of your withdrawal may still be used for further testing/analysis in accordance with the terms of the protocol and of this informed consent form.

3.3 Are there any reasons that my study treatment or participation may be stopped early?

The study doctor may remove you from this study for any justified reason and will discuss your options.

Examples why you may have to stop some or all study-related activities, including study treatment are:

1. You need treatment that is not allowed in this study
2. You do not follow instructions
3. You become pregnant. (If you or your partner becomes pregnant, an additional ICF for pregnancy follow-up will be required)
4. You experience side effects from the study treatments that you find unacceptable
5. The study doctor thinks keeping you in the study might be harmful and is not in your best interest
6. Recordati decides to stop this study
7. Your current therapy becomes locally available and reimbursed in this indication.

3.4 Who owns the data and results created during the study?

Recordati will own all data and results created during this study.

3.5 Can my samples be used after the study? (Health Authority requests)

Health Authorities may request more testing on your samples in order to generate more study data. In such a case, Recordati will perform the requested testing.

4 What are the possible benefits if I join this study?

The study drug may help to manage signs and symptoms of Cushing’s disease but taking part in this research study may not benefit you directly, but we may learn new things that could help other patients with the same condition.

You will receive medical care during the study. Osilodrostat has recently been approved in USA, European Union and Japan as Isturisa® for the treatment of Cushing's disease in adults. Information from this study may help you and/or other people with Cushing's disease.
If new scientific developments occur during the course of the study that may relate to your willingness to continue participation, information regarding these developments will be provided to you so that you can make the decision whether or not you wish to continue study participation.

5 What are the possible risks if I join this study?

Risks are possible side effects from the study treatment and from tests done during the study. **You should tell the study doctor if you have any unusual complaints, behaviors, or side effects, or had other doctor visits or hospitalizations outside of the study.**
The most common side effects include such events as fatigue/asthenia (weakness), nausea, vomiting, headache, oedema (swelling) and adrenal insufficiency (low cortisol levels). In some patients, these symptoms may be caused by lowering of the cortisol level. Such symptoms could happen even if the cortisol level is normal - this is called steroid withdrawal. In other cases, the symptoms are because the cortisol level is too low (below normal) - this is called hypocortisolism or adrenal insufficiency. If your doctor thinks you have adrenal insufficiency, you may be told to take a lower dose or stop taking the study medication for a short time until the symptoms improve. Your doctor may also give other medications such as hydrocortisone, which can help with these symptoms.
In some women, hirsutism (hair growth in a pattern like men, such as on the face) and acne has been seen. The most common changes on blood testing were low potassium and increases in some hormones.
Animal studies show that when very high doses of osilodrostat were used (many times higher than would be used in humans) changes in the conduction of electrical activity in the heart, called QT interval prolongation on the ECG (ECG; a tracing of electrical activity in the heart) were seen, and in one case there was a temporary irregular heartbeat. Increase (prolongation) in the QT interval may lead to an irregular heartbeat which in rare instances can develop into a sudden, life-threatening condition. Although the risk is small, these findings suggest a risk for prolonged QT interval and associated risk for irregular heart rate in patients with Cushing's disease treated with osilodrostat. For safety reasons, you will have monitoring of your heart rhythm during this study. ECGs (tracings of the heart rhythm) will be done each time you attend your study visit.

There have been cases of neutropenia observed with osilodrostat treatment. Neutropenia is an abnormally low concentration of neutrophils (a type of white blood cells) in the blood. Neutrophils serve as the primary defense against infections. Patients with neutropenia may be more susceptible to infections. A Complete Blood Count (CBC) will be regularly performed during the study to detect any changes of your white blood cells.

Your study doctor is aware of these potential side effects, as well as methods for treating them, and will discuss the risks with you before you begin taking study medication. If you expect to

undergo surgery or have any new illness, you should inform your study doctor so that appropriate measures can be taken.

Problems or side effects that are not currently known could also occur. You will be given any new information as it becomes available that can help you choose to continue in the study. Should you experience any possible side effects, or other health problems, you should report them to your Study Doctor.

If you experience any of these serious side effects, **tell your doctor immediately.**

- Report **if you experience more than one** of the following: nausea, vomiting, fatigue, abdominal pain, loss of appetite, and dizziness, as these may be symptoms suggestive of very low cortisol level, known as adrenal insufficiency.
- Heart problem or a heart rhythm problem, such as an irregular heartbeat could be a sign of QT prolongation.

Other possible side effects

Other side effects include the following listed below. **If these side effects become severe, please tell your doctor.**

Table 5-1 Side effects

Very common: *may affect more than 1 in 10 people*	• fast heartbeat (tachycardia) • very low cortisol levels (adrenal insufficiency) • nausea • vomiting • tiredness (fatigue) • swelling of the legs, ankles or other signs of fluid retention (oedema) • increased level of a hormone called corticotrophin in the blood (increased ACTH) • increased level of testosterone in the blood • abnormal results of liver function test • decreased appetite • pain in joint (arthralgia) • muscular pain (myalgia) • headache • dizziness • low blood pressure (hypotension)

Common: *may affect up to 1 in every 10 people*	• diarrhoea • abdominal pain • feeling of general discomfort, illness (malaise) • abnormal electrical signal in the heart (electrocardiogram QT prolongation) • low level of potassium in the blood (hypokalaemia) • fainting (syncope) • acne • excessive facial and/or body hair growth (hirsutism) • rash

As part of this study, you will have a sample of your blood collected. The risks of collecting blood may include fainting, pain, and/or bruising. Rarely, there may be a small blood clot or infection at the site of the needle puncture or central line.

The blood pressure cuff may also cause discomfort or bruising to the upper arm. Physical examinations and electrocardiograms (ECGs) are routine procedures in clinical practice and present practically no risk for you.

In rare instances, a nurse, study doctor, or laboratory technician, may be exposed to your blood, tissue or body fluids by needle stick, cut, or damaged skin. If this happens, it may be necessary to test your sample for *certain viral infections including* Hepatitis B and C and HIV and, if possible, will be done on a sample already available. This will make it possible for that person to receive appropriate monitoring and treatment as needed. The study doctor will provide results of your tests and advise on the next steps. Confidentiality of the results of your tests will be respected at all times.

Imaging risks:

You may not have an MRI done if you have metal in your body, for example, some hip replacements, hearing aids, pacemakers, bullets, or jewelry that cannot be removed. You should inform the technologist or physician if you have any metal in your body. During the MRI exam, you may feel some heat and hear banging noises but have no reason to worry. Some people may have a 'closed in' (claustrophobic) feeling while inside the machine. The injection may make you sick to your stomach or have pain, warmth, swelling, bruising, a small blood clot or infection at the injection site. Rarely, you may get a rash or other signs of allergy from the injection or get a rare disease where some of your body parts get scarred. If you have a history of kidney problems you must inform the technologist or physician as you may not be able to receive an injection during the MRI exam. **You should inform the physician or technologist if you are pregnant, or suspect to be, as this exam may cause harm to unborn babies.** Your physician or technologist can explain the procedure and risks in greater detail and clarify any concerns or questions.

If you are not able to have the MRI exam as advised by your Study Doctor you will do instead a CT scan. You will receive radiation when CT is done. The radiation received during one CT exam is the same as 2 - 10 years of normal radiation received in everyday life, depending on

the body parts included. Although repeated radiation exposure may damage your body tissues and slightly increase your chances of having cancer, you should not expect an increased risk from the imaging being done for this study. Some people may have a 'closed in' (claustrophobic) feeling while inside the machine. The injection may make you sick to your stomach, pass-out, or have pain, warmth, swelling, bruising, a small blood clot or infection at the injection site. You may get a rash or other signs of allergy from the injection. You should inform the physician or technologist if you have any history of allergies, for example, to seafood or medications, asthma, high blood sugar (or diabetes), heart problems, kidney problems, or thyroid problems, as all of these may increase your chances of having problems with the CT injection. **You should inform the physician or technologist if you are pregnant, or suspect to be, as this exam may cause harm to unborn babies.** Your physician or technologist can explain the procedure and risks in greater detail and clarify any concerns or questions.

6 What do I need to know about birth control and pregnancy?

Women who are pregnant or nursing (breastfeeding) a child cannot participate in this study. 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 study.

Studies in pregnant animals have shown that the medication you are required to take in this study can potentially harm an unborn or nursing baby.

The risks to an unborn human fetus or a nursing child from the medications you are required to take in this study are not presently 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 respects your cultural and religious situation. Examples of highly effective birth control methods are:

- Total abstinence, 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 bilateral removal of ovaries (woman's reproductive system that stores and releases eggs for fertilization and produces female sex hormones), or tubal ligation (getting your "tubes tied") at least six weeks prior to starting the 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).

If you become pregnant or suspect being pregnant during study treatment or within 1 week after completing study treatment, you must inform the Study Doctor immediately, and you have to stop ongoing study treatment 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.

7 What are my responsibilities and are there any costs for me if I agree to join this study?

If you agree to join this study, you have the following responsibilities:

Table 7-1 Responsibilities related to study appointments/visits, study treatment, and costs

Study appointments/visits and procedures	• Follow the instructions given by the study doctor and staff • Attend all of the study appointments. If you have to miss an appointment, you must reschedule with the study doctor or staff • Complete and return required study documents such as surveys, or diaries, as instructed.
Study treatment	It is very important to; • take the study treatment as you have been instructed • ensure that the study treatment is stored in a safe place You may discuss with a doctor or health care professional (who is not directly involved in the study) any health issues or your medical problems related to the study treatment or disclose information related to the study treatment. You should tell your doctor or health care professional that the Recordati treatment, and any information relating to it, is Recordati' property and is confidential. **Other treatments you may be taking:** You must tell the study doctor about any treatments you are currently taking or may take during the course of the study (e.g. prescription, vitamins, over the counter, herbal supplements etc.) some of these may need to be stopped/reduced. **Returning study treatment after stopping study treatment:** When the study ends or if you decide to stop study treatment early, return all of extra osilodrostat and empty pill bottles as instructed.
Costs	You will not have to pay for your study treatment(s) or any of the tests and procedures done for study purposes.

8 What other choices are available if I choose not to join this study?

You do not need to participate in this study to receive treatment for your condition. Treatment alternatives for Cushing's disease depend on your disease history and on locally available therapy. They may include surgical removal of the pituitary tumor (where feasible),

radiotherapy and, other locally available medications (depending on your country, this may include drugs called metyrapone and ketoconazole), other experimental therapies (in a clinical trial), or in very rare and severe cases, a removal of the adrenal glands. These alternatives may be discussed with your study doctor about their potential benefits and risks.

Participation in this study is not a substitute for your usual medical care by your regular doctor or specialist. You are strongly encouraged to ask the study doctor or a member of the study staff if you have questions about study treatment or any other possible therapies.

During your participation in this study, you may not participate in any other clinical study.

9 What if I become injured because of participation in this study?

If you are injured as a result of this study, please contact the study doctor immediately *(investigator's name and contact information)*; he/she will arrange treatment.

Recordati will cover the reasonable costs of treatment for study-related injuries beyond what is reimbursed by your health insurance under the following conditions and in accordance with local laws:

- If you received medical care and followed instructions,
- If the injury is related to the study treatment or to study procedures (not usual medical care), and if such procedures are properly performed,
- If the injury is not the result of the natural course of any disease existing before proper administration of the study treatment.

(*Remove for US*) If you become injured as a result of the clinical study, Recordati has taken out an insurance policy for this purpose.

By signing this consent, you do not give up any legal rights.

10 What will happen to my Personal Data?

10.1 What is Personal Data?

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

If you have a primary doctor, the study doctor may let him/her know that you are participating in this clinical trial. If you do not want your primary doctor to be informed, please discuss this with your study doctor.

Your study doctor may collect more information from your other doctors.

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 Via Civitali 1, 20148 Milan (Italy), will receive some of 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
- Biological samples.

The Sponsor 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. The Sponsor has contracted a Clinical Research Organization IQVIA for the data processing activities for the purpose of this study.

10.2 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 treatment 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 treatment.

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 treatment. 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 technologies 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 allow such access to your Personal Data including your original medical records.

Your coded medical images (for example X-ray, MRI, CT, ultrasound, etc.) will be studied. They may also be used to develop new ways to look at this type of information.

(USE THE FOLLOWING TEXT FOR TRIALS IN THE US)

The individuals mentioned in bullets 2 and 3 of the Section ‘Who Can see my Personal Data’ (Section 10.4) may use your Personal Data, including any of your remaining coded biological samples, for additional medical and/or scientific research outside of the current study purpose and objectives.

10.3 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 (such as the Contract Research Organization IQVIA) may operate these systems. Your Personal Data at the investigational site 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.

10.4 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' 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 General Data Protection Regulation (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).

10.5 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*) 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.

10.6 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.

11 Where can I receive more information?

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

Role	Name	Telephone Number
Principal Investigator		
Study Nurse/ Coordinator		

If you have questions related to your rights, please contact: *(insert name of the IRB/EC and the phone number)*.

Role	Name	Telephone Number
IRB/EC		

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

Role	Name	Telephone Number
Principal Investigator		

12 Signature pages

Use for US Sites: Please use/modify the following signature page with the currently approved HIPAA wording for the signature page.

Use for non-US sites: Use/modify the following signature page; add or delete signature lines according to local laws

Protocol number and version: *CLCI699C2X01B*, Version *02* dated *06-May-2020*

Protocol title: *An open-label, multi-center, roll-over study to assess long term safety in patients with endogenous Cushing's syndrome who have completed a prior Novartis-sponsored osilodrostat (LCI699) study and are judged by the investigator to benefit from continued treatment with osilodrostat*

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

By signing this consent form, I authorize the use, access, and sharing of my Personal Data as described in this document.

This consent is valid unless and until I revoke it.

type/print name		
Subject name	Signature	Date

(The execution by witness must be authorized under local laws. The witness cannot be a healthcare professional in charge of the subject. A copy of their ID must be obtained and archived with the executed consent form. Please check with local legal regulations)

type/print name		
Witness (If subject gives oral consent but cannot sign the consent form)	Signature	Date

(The execution by a legal representative, when the subject cannot provide consent, must be governed by local laws. Please check with local legal about local requirements)

type/print name		
Legal representative (if required) (Legally authorized to act as personal representative to sign for (name of subject))	Signature	Date

type/print name		
Investigator	Signature	Date

type/print name		
Name of presenter (Who presented/explained the document)	Signature	Date

13 Optional Consent for additional research using your Personal Data

During or after the study, Recordati may want to use your Personal Data for additional research projects. Personal Data includes your year of birth, gender, a special code that identifies you, study information, as explained in the section 'What will happen to my Personal Data?'

Wherever permitted by law or requested by the authorities, this additional research may include studies to get more information on Cushing's Disease. It may be used to design or improve methods for analyzing, comparing, or combining your study data with data from subjects given other treatments. It may involve new approaches or biological markers of Cushing's Disease and other aspects of the disease. Researchers may study the benefits and risks effects of osilodrostat and compare the data from osilodrostat with other treatments. This will allow Recordati and other researchers to better understand Cushing's Disease, how osilodrostat works and to be able to find the best way to treat patients with Cushing's Disease or other diseases in the same therapeutic area.

The information under the 'What will happen to my Personal Data?' section is applicable to this optional consent.

You will not own any data and discoveries generated from the additional research studies. The data will not become part of your medical record.

If you choose to give consent for additional research, you can change your mind at any time. If you decide you no longer want Recordati to use your Personal Data for additional research this is possible. You can continue to be in the main study. Please notify the study doctor if this is the case.

By signing below, I agree to the use of my Personal Data for additional research as described above.

This consent is valid unless and until I revoke it

type/print name		
Subject Name	Signature	Date
type/print name		
Legal representative name (legally authorized to act as personal representative to sign for)	Signature	Date

type/print name		
Name of presenter (who presented/explained the document)	Signature	Date