UNIVERSITY OF CALIFORNIA, SAN FRANCISCO
CONSENT TO PARTICIPATE IN A RESEARCH STUDY

Study Title: A phase III, randomized, double blind, parallel group, placebo controlled, international, multicenter study to assess efficacy and safety of Cx601, adult allogeneic expanded adipose-derived stem cells (eASC), for the treatment of complex perianal fistula(s) in patients with Crohn's disease over a period of 24 weeks and a follow-up period up to 52 weeks. ADMIRE-CD II study.

Amendment 3 dated 28 Oct 2019

Protocol Number: Cx601-0303

Sponsor: TiGenix, S.A.U.

Research Project Director:	Sara Lewin M.D., Professor of Clinical Medicine UCSF, 1701 Divisadero Street, Suite 120, San Francisco, CA. Phone: 415-502-4444 e-mail: sara.lewin@ucsf.edu

Study Coordinator:	Jessica Lim, Phone: 415-885-3734 jessica.lim@ucsf.edu

This is a medical research study. Your study doctor, Sara Lewin, MD, or her associates from the Gastroenterology Faculty Practice at UCSF will explain this study to you.

Research studies include only people who choose to take part. Please take your time to make your decision about participating. You may discuss your decision with your family and friends and with your health care team. If you have any questions, you may ask your study doctor.

You are being asked to take part in this study because you have Crohn's disease (CD) and you have perianal fistulas.

TiGenix, S.A.U. is sponsoring this study. TiGenix, S.A.U. is paying the study doctor to perform this study.

Why is this study being done?

Cx601, a study drug, is under development by TiGenix, S.A.U. for the treatment of complex perianal fistulas in Crohn's disease patients. Complex fistulas can have several external openings and be associated with perianal abscess (a collection of blood and pus in your anus area), connection to the vagina or bladder, rectal stenosis (abnormal opening of the anal passage where it is too small or narrow)

-or proctitis (inflammation of the lining of the rectum). Cx601 is a solution containing human expanded adipose-derived stem cells (eASC) obtained from healthy donors. The study drug has shown the potential to aid the immune system in some non-clinical studies (research studies in which human subjects are not involved).
Additionally, to date, 2 clinical studies of study drug have been conducted in patients with fistulizing CD. One was completed in 24 patients with a single dose of 20 million cells or multiple doses, such as 20 million cells plus 40 million cells of eASC. In another recently finished clinical study, 212 patients were enrolled – about half of whom received a single dose of study drug of 120 million cells and about half received a placebo (a treatment that looks identical to the study drug but contains no active drug), both administered as a local injection in the fistula(s). The study drug has been demonstrated to be efficacious, safe and well tolerated at the dose of 120 million cells. Marketing approval was received from the European Medicines Agency in March 2018. Cx601 is considered an investigational drug in the U.S. as it is not yet approved by the U.S. Food and Drug Administration (FDA).

The purpose of this study is to confirm (1) how well the study drug works at a single dose of 120 million cells compared to a placebo; (2) how safe and tolerable the study drug is in patients with fistulizing CD.

How many people will take part in this study?

This study will involve about 554 patients and will be conducted at approximately 150 study centers in the United States of America (USA), Canada, the European Union (EU), and Israel. Approximately 10 subjects will be enrolled at UCSF.

Study location: All study procedures will be done at 1701 Divisadero Street, Ste. 120, San Francisco, CA 94115 and at 1600 Divisadero street, San Francisco, CA 94115.

What will happen if I take part in this research study?

In order to take part in the study, the study doctor will determine whether you are suitable to participate by means of a medical examination, blood tests, by checking your medical records, and by performing other tests.

To make the comparison between the study drug and the placebo as fair as possible, this study is “double blinded”. This means that neither you nor the study doctor will know whether you are receiving study drug or placebo. Which treatment you will be given will be decided randomly, like tossing a coin; this is also known as randomization, done purely by a computer. In this study, 50% of the patients will receive the study drug, while the other 50% of the patients receive the placebo.

Study Drug

You will receive a 24 mL injection (about 4.8 teaspoons) of study drug or placebo given locally to the fistula(s) by a surgeon trained specifically on study procedures while under anesthesia.

If necessary, the study doctor can find out which injections you were administered if there are any problems.

Study Visits

Please let the study doctor know if you are already receiving treatment for fistulizing CD. The study doctor will inform you whether you may continue taking this treatment during the study.

During the study, the following procedures will be done (listed in no particular order):

Informed consent: If you agree to take part, you will be asked to sign this form to record that you understand the study and agree to take part in it. No study-related procedures will be done before you sign this consent form.

Characteristics: You will be asked your date of birth, gender, and race (this information is needed for study analysis purposes and might be required by some regulatory authorities).

Medical history: You will be asked about your disease history, other medical history including smoking history, transplantation(s), blood transfusion(s), and prior pregnancies, if applicable.

Eligibility discussion: You will be asked about your health and other potential co-existing health conditions.

Colonoscopy: You will undergo a colonoscopy (a kind of endoscopy that allows the doctor to see your whole colon, for which adequate digestive tube preparation is required including laxatives and enemas administration in advance of the procedure) if you haven't had one within 6 months prior to the Screening Visit. If you have had a colonoscopy within 6 months prior to the Screening Visit, but some of the requested information from it is not available, or the study doctor considers that you should have a colonoscopy based on your symptoms and or on some of the laboratory tests, you will also be requested to have the procedure. Anesthesia, sedation and possibly pain medication will be administered for this procedure

Well-being discussion: You will be asked about medicines you are currently taking and how you are feeling normal, unwell, or other than normal. You will also be asked if you have had any new health problems. At some visits, you will be asked about the symptoms related to fistulas such as daily stool frequency and daily abdominal pain.

Examination: The study doctor will examine you. Your height (only at screening) and weight will be measured.

Vital signs: Your blood pressure, heart rate, and body temperature will be measured.

Clinical evaluation of the fistula: The study doctor will examine the drainage at the external opening(s) by gently pressing with a finger; will check for anal pain, and for any suspicion of perianal abscess.

Fistula preparation: You will have a surgical procedure (named "curettage") in which a small amount of tissue will be removed by scraping or scooping and a "seton" will be placed (a seton is a thread that is inserted through the fistula tract, out of the anus and then tied in a knot outside. This allows the infection to drain and heal, without damaging your sphincter muscles). Anesthesia will be used for the curettage/seton placement.

After the surgery you will receive at least 7 days of antibiotic treatment to prevent infection

Study drug or placebo administration: First, you will undergo the procedure of "curettage" and"seton" removal (see above). Anesthesia will be used for seton removal with study/placebo

drug administration.. After that, a needle will be entered through your anus and 12 mL (about 2.4 teaspoons) of study drug or placebo will be injected into the tissue surrounding the internal opening(s) (communicating with digestive tube), making several small blebs (bubles). Then the needle will be entered through the external opening(s) (communicating with the exterior of the body), and a further 12 mL (about 2.4 teaspoons) of study drug or placebo will be injected superficially (on the surface) into the tissue walls along the length of the fistula tract(s) to be treated, making several small blebs (bubles). During the surgery and injection, a Sponsor representative who is specifically trained in the surgical procedure and treatment administration may be present to provide technical support to the study doctors and assess the quality and integrity of treatment administration procedure. You will be observed after this surgical procedure until a full recovery, and special attention will be paid to signs and symptoms of potential allergic reactions.

Magnetic resonance imaging (MRI): You will have a Magnetic Resonance Imaging (MRI) exam. For the MRI exam, you will lie down on a narrow bed that will then be placed in a tunnel that is 6 feet long by 22 inches wide and open at each end. You will need to lie there quietly for about one hour, during which time there will be a loud banging noise. You may feel warm during this procedure. It is a noninvasive diagnostic technique that uses a strong magnetic field and radio waves to produce computerized images of internal body tissues (no X-rays are used in this process). You will undergo a pelvic MRI to exam your fistulas including number of fistulas, anatomical location, and type. Contrast dye may be administered for this procedure. This will help give clearer images.

Routine blood sample:) Blood will be collected for routine laboratory tests, including hematology and biochemistry tests. If you are a woman of child-bearing potential, a blood pregnancy test will also be done at Screening Visit. If the pregnancy test is positive, you will not be allowed to take part in the study.

Extra blood sample: Blood will be collected to study how your body responds to the effect of the cells administered, by performing the following tests:

Immunological tests: This is called humoral responses. It includes the presence of antibodies against the donor cells and the type of human leukocyte antigen (HLA) being expressed. HLA proteins are a type of protein involved in the immune recognition and cell responses.

Cell responses: this is called cellular responses because we will study how the cells of your body act before and after treatment administration.

During the 8 study visits over your one-year participation in this trial, a total volume of approximately 266 mL of blood will be taken.

Urine pregnancy test: If you are a woman of child-bearing potential , you will be asked to give a urine sample for pregnancy test.

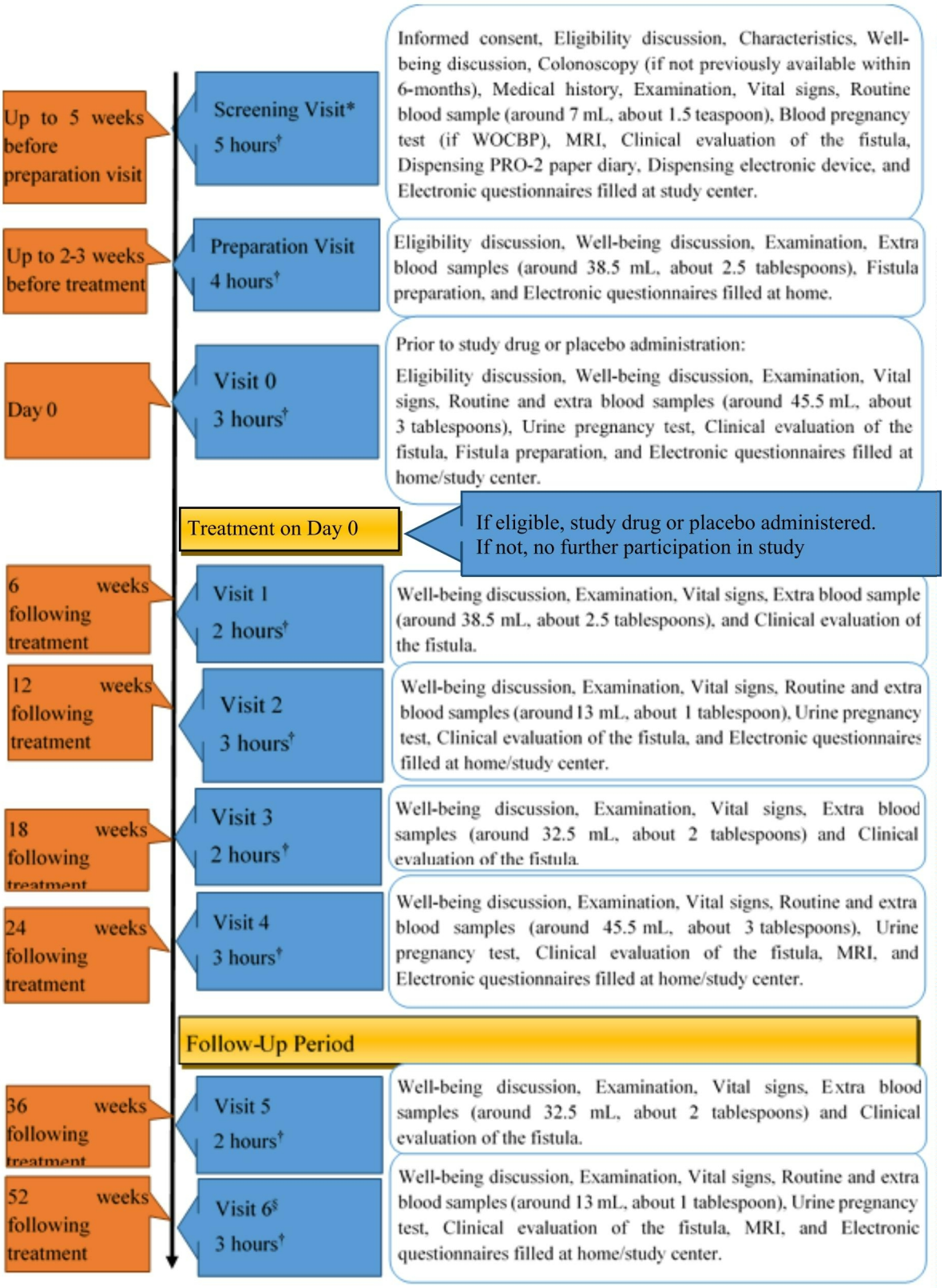
Paper questionnaire: Patient reported outcome (**PRO-2).** A paper diary will be dispensed to you at the Screening visit only, to collect some information during the following 7 days, about diarrhea and abdominal pain. You will also be dispensed this diary for the subsequent study visits, in order to collect some information during the 7 days prior to each visit, about diarrhea and abdominal pain.

Electronic questionnaires (electronic patient-reported outcomes, ePROs): An electronic device will be dispensed to you at the Screening Visit and you will need to answer some questions about your disease and quality of life; such information should be recorded as instructed by the study doctor.

Electronic questionnaires at home: You will be asked to complete some questionnaires starting 2 weeks **before** these visits. The questionnaires should be completed everyday using the device at home.

Electronic questionnaires at study center: You will be asked to complete some questionnaires using the device during the visit at the study center.

This diagram shows when the visits will take place and what procedures will be done at each visit.



* The Screening Visit may be split between a couple of days if not all the assessments can be completed at one visit.

†: The times given are estimations.

§: Visit 6 is also the end of the study visit.

Unscheduled Phone-call Follow-up:

At any time from Week 6 to Week 36 after treatment or as needed, you will receive unscheduled phone calls for well-being discussions and review of questionnaires if the study doctor believes that this is needed to ensure your safety.

Withdrawal Visit:

If you withdraw voluntarily or are withdrawn involuntarily, you will be asked to undergo the tests and examinations described above for Visit 6 except for the electronic questionnaires at the study center. Some tests may be repeated until the results are acceptable. If you withdraw or are withdrawn before Week 24, the blood collected from you will be 45.5 mL (3 tablespoons) at this visit. Some tests will not be performed if they have been done within about 1 to 3 weeks prior to your withdrawal.

Blood Tests and Urine Pregnancy Test

Blood samples will be collected for laboratory and central laboratory tests at all visits.

Laboratory tests: The tests will include standard tests of your general health. If you are a woman of child-bearing potential , there will also be a blood pregnancy test at the Screening Visit.

Central laboratory tests: Blood sample will be collected to test how your body responds to the study drug. These extra blood samples will be processed in a central laboratory.

Central laboratories:

Safety evaluation: Eurofins Lancaster.

Cell responses: Hospital Ramón y Cajal (Spain).

Immunological tests: FIRALIS SAS (France).

Urine samples will be collected at Visit 0, 2, 4, and 6 for pregnancy tests.

All your test results are confidential and will be disclosed only as required by law.

The urine samples will be destroyed immediately after the laboratory tests are completed.

The following samples will be stored at Millennium, its agents or its affiliated companies including TiGenix for up to 15 years from when the study results are reported or the maximum period permitted under applicable law or until consent is withdrawn. This includes blood samples for white blood cell (peripheral blood mononuclear cells; PBMCs), immunological tests. These samples will be labeled with a code, without your name, and will not include information that can identify you directly.

The information obtained from these samples may be used by TiGenix, its agents and its affiliated companies for research related to investigation and development of the study drug, Cx601, and understand the diseases it may help. For example, the information may be used:

- To develop a better understanding of how people's genetic makeup affects the safety and effectiveness of Cx601.
- To help develop new ways to monitor and treat peri-anal fistula and other disorders.
- To help determine how Cx601 works in the body.
- To generate information needed for research and development of Cx601 and diagnostic tests related to diseases or conditions that Cx601 might treat.

WHAT WILL I HAVE TO DO DURING THE STUDY?

First, you will be asked to sign this consent form if you agree to be included in this study. If you take part in this study, you should follow the study procedures and you must attend all the study visits. You should report any side effects to the study doctor.

You must use the electronic device to record symptoms as instructed by the study doctor and take it back to study center as requested.

If you are a woman of child-bearing potential, you must use effective contraception (as explained by the study doctor) during the entire study (15 months). An adequate method of contraception is defined as complete, non-periodic sexual abstinence, (not having heterosexual intercourse during the entire study duration), single-barrier method, adequate hormonal contraception (to have started at least 7 days prior to Screening Visit), or an intra-uterine device (to have been in place for at least 2 months prior to Screening Visit).

If you are a man, you and/or your female sexual partner must use effective contraception (as explained by the study doctor and described above) during the entire study (15 months); vasectomy is considered as an effective contraception method.

Also please:

- Notify the study doctor if you are unable, in any way, to follow the study procedures.
- Answer all study questions (including medical history) honestly, disclose all medications that you are currently taking, and report any side effects.

How long will I be in the study?

You will be in the study for approximately 15 months.
There will be a minimum of 9 visits during the study, including an approximately 5-week Screening Period, a preparation visit (to prepare the fistula for the administration of the treatment), a treatment administration visit (you will receive single dose of study drug or placebo injection once on "Day 0") followed by regularly visits at the study center as scheduled up to 24 weeks when primary assessment of the treatment efficacy will be made and a subsequent Follow-up period up to 52 weeks. Your participation in this study will take about 30 hours of your time.

Can I stop being in the study?

It is up to you to decide whether or not to take part in this study. You are free to refuse to participate. Even if you refuse to participate in this study, you will not be disadvantaged in any

way; you will continue to receive medical treatment and care you are otherwise entitled to. If you decide to participate, you may change your mind and decide to withdraw from the study at any time and for any reason. You are not required to explain your reasons for withdrawing. If you withdraw, you will not suffer any penalty or loss of benefits regarding your future medical care.

The study doctor can withdraw you from the study at any time if he or she feels it is in your best interest or if you cannot comply with study requirements.

In addition, your participation in the study may be stopped by the Sponsor or by the regulatory authorities or by an independent ethics committee (e.g., an Institutional Review Board [IRB]); these committees review study safety and ethics to ensure that patients' rights and safety are not violated) at any time without your consent, after the reason(s) for doing so (e.g., your own safety, study drug safety, Sponsor decision) have been explained to you, and after you have been given advice about continued care for your condition, if this is appropriate. Also, the Sponsor has the right to stop the study for medical or business reasons. If this happens, all patients participating in the study will be withdrawn.

If you withdraw (or are withdrawn) from the study, you will be asked to go through study withdrawal procedures.

What side effects or risks can I expect from being in the study?

There is limited information about the risk of the study drug from clinical studies so far. The dose of study drug chosen for this study is considered safe based on the available animal data and data from previous clinical studies. At present, 146 patients have been treated with the study drug.

Any drug can have temporary and permanent side effects and can cause unforeseen adverse reactions. The study drug may not control your fistulas. Your health care team may give you medicines to help lessen side effects. Many side effects go away soon after you stop taking the Cx601. In some cases, side effects can be serious, long lasting, or may never go away. There also is a risk of death.

You should talk to your study doctor about any side effects you experience while taking part in the study.

Risks and side effects related to the Cx601 include those which are:

Likely

- Anal (perianal) abscess (collection of pus in the anus or around the anus)
- Proctalgia (pain in the anal/perianal region)
- Fistula (anal)
- Infected fistula

Other potential risks of study drug may include:

The study drug, as explained, is a solution that contains human expanded adipose-derived stem cells. In theory, there are some potential risks associated to any type of stem cell, so that, they are detailed for study drug, too: the possibility of tumor formation, or abnormal tissue formation at the site of administration (ectopic tissue) or undesired local or general immune responses, or infective agents transmissions. None of these potential risks have appeared in the previous patients treated with study drug.

Most of the reactions detailed appeared in a similar proportion among the patients that were treated with placebo in other clinical studies.

*** Please tell the staff immediately if you do experience any "new symptoms " while participating in this clinical study, even if minor. ***

Blood samples: Blood samples will be collected from a vein in your arm during the study. The taking of a blood sample may cause some discomfort, bruising, bleeding, nerve damage, arterial puncture, and laceration, and there is a potential for infection. Other risks, although rare, include dizziness and fainting. The maximum amount of blood that will be collected on any day of the study is about 45.5 mL (about 3 tablespoons). The total amount of blood that will be collected over the entire study, over the 57-week period, is about 266 mL (about half of what you would give as a blood donor).

MRI: An MRI scan is painless and will not expose you to X-ray radiation. Before the scan, contrast medium may be injected into one of your veins; this is like a dye and will spread through your body and will help give clearer images. You may experience a serious allergic reaction to the MRI contrast agent. When the MRI contrast agent containing gadolinium is injected, it is common to have a cool sensation in the area of the injection, nausea (uncommon), and allergic reaction (rare). Gadolinium is a metal that can remain in the body, including in the brain, bones, skin, and other parts of the body for a long time (from months to years). In rare cases, some people with kidney disease who receive gadolinium are at risk of developing a disease that causes fibrosis (the formation of too much connective tissue in the skin and internal organs) which very rarely can cause death. It is not known if gadolinium retention causes other health effects. Studies in patients with normal kidneys showed no found harmful effects. Your doctor will check how well your kidneys are working before you have an MRI.

Some people may feel frightened by the cramped space inside the machine or by the loud, repeated sounds the machine makes. The greatest risk of having an MRI is the chance of metal objects flying through the air toward the magnet and hitting you. To reduce this risk, all people giving and getting the MRI scan will be asked to remove all metal from their clothing and all metal objects from their pockets. Please inform the study doctor if you have metal in your body from an operation, since you may not be able to have an MRI scan. Also, if you have a pacemaker you should not have an MRI scan.

Blood pressure and heart rate: An inflatable cuff will be placed on your arm and a machine will measure your blood pressure and heart rate. You may experience mild discomfort such as pressure and squeeze in your arm while the cuff is inflated.

Colonoscopy: Colonoscopy is a test to examine the lining of your large intestine. Before these procedures, you will need to take bowel cleansing agents to empty your large intestine. This is important to obtain a clear view and an accurate result from the procedures. You may experience cramping, bloating, nausea, and vomiting or other risks due to the bowel cleansing procedure like dehydration and changes in your electrolytes, which can be dangerous if you have kidney or heart disease or other health problems. The examination uses an endoscope, which is a flexible tube about the thickness of your little finger, with a camera and light at one end. They are conducted by inserting an endoscope through your anus. Most procedures are done without any problem but you may also experience pain, fever, leakage of liquid accompanied by gas. Other side effects include a tear in the colon or rectum wall and infection. The study doctor will explain the test to you to ensure that you understand the test and any other potential complications that may occur. A health care professional might place an intravenous (IV) needle in a vein in your arm to give you sedatives, anesthesia, or pain medicine so you can relax during the procedure. The health care staff will also monitor your vital signs and keep you as comfortable as possible.

General anesthesia and sedation: General anesthesia/sedation is overall very safe; most people, even those with significant health conditions, are able to undergo general anesthesia itself without serious problems. Older adults, or those with serious medical problems, particularly those undergoing more extensive procedures, may be at increased risk of postoperative confusion, pneumonia, or even stroke and heart attack.

Clinical evaluation of the fistula: You may feel slight discomfort, pain from the affected region during the examination.

Fistula preparation: This type of surgery depends on where your fistula is. If the fistula is deep or complex, there may be an increased risk of damage to your anal sphincter muscles which are important for bowel control and continence. In most cases, surgery does not involve cutting a significant section of these muscles, so bowel continence is not at risk. However, you should be aware that any damage to the sphincter muscles can lead to a change in your ability to control wind or stools. It is not always possible before surgery to tell whether your fistula runs through your sphincter muscles. Therefore, if your fistula runs through these muscles, rather than cutting them, your surgeon will put a stitch in your fistula, called a ‘seton’. Your surgeon may lay open the part of your fistula that does not involve the sphincter muscles, and then insert a seton for the section that lies within the sphincter muscles. Therefore, you may end up with both a wound and a seton. Your surgeon will discuss this with you in more detail during your consultation.

Injection in the local fistulas: For most people, needle punctures for injections do not cause any harm. However, discomfort, bleeding, bruising, or pain at the injection side might occur. Since there is a potential risk of allergic reactions, you will be observed after the administration of the treatment until a full recovery. Special attention will be paid to signs and symptoms of potential allergic reactions.

Randomization risks: You will be assigned to a treatment program by chance, and the treatment you receive may prove to be less effective or to have more side effects than the other study treatment(s) or other available treatments.

Placebo risks: If you are in the group that receives placebo, your condition will go without the active (study) treatment for 52 weeks.

Blood drawing (venipuncture) risks: Drawing blood may cause temporary discomfort from the needle stick, bruising, infection, and fainting.
Reproductive risks: If you are or become pregnant, or if your partner becomes pregnant, there may be unknown risks to the baby. If you are a woman of child-bearing potential , you will be given a pregnancy test at screening, and if the result is positive, you will not be able to take part in the study. If you are a sexually-active man or woman, you must use an accepted form of birth control throughout the study (until Visit 6). The study doctor will discuss methods of birth control with you if needed. If you become pregnant or think you may be pregnant during the study or within 30 days of the last study visit, please contact the study doctor's office **immediately**. You may be asked to withdraw from the study. As the effects on the study drug on a breastfed child are not known at this time, breastfeeding women cannot enroll in the study and you must not be breast-feeding an infant during the study. If you are a male who is sexually active, you must inform your partner(s), if they are able to have children, that the effects of the investigational product on sperm are unknown. If you are a man and your female partner becomes pregnant or thinks she may be pregnant during the study, contact the study doctor's office **immediately.**

The study doctor must follow up and document the course and the outcome of all pregnancies, even if you withdraw from the study or if the study has finished. If you or your partner becomes pregnant during the study or within 30 days after the last study visit, the study doctor or his/her staff will ask to contact you/your partner and your/your partner's physician for information about the pregnancy and the child until 3 months after the birth.

Unknown Risks: The experimental treatments may have side effects that no one knows about yet. The researchers will let you know if they learn anything that might make you change your mind about participating in the study.

For more information about risks and side effects, ask your study doctor.

Are there benefits to taking part in the study?

Taking part in this study you may or may not receive direct benefit. A possible benefit is improvement in your disease or condition. The knowledge gained from your taking part may help other patients with the same disease in the future.

This study is expected to benefit the Sponsor by providing information about the treatment of fistulizing Crohn's Disease with the study drug.

If the results of this study are favorable and, along with additional studies, lead to approval by the regulatory authorities of the study drug for use in humans, there may be benefits for patients in the future. These benefits may include better control of their fistulizing Crohn's Disease.

What other choices do I have if I do not take part in this study?

Your other choices may include:

- Getting treatment or care for your condition without being in a study. Other treatments may include antibiotics, immunomodulators, biologicals, surgical, and seton placement.
- Taking part in another study.
- Getting no treatment.

Please talk to your doctor about your choices before deciding if you will take part in this study.

How will information about me be kept confidential? Processing of my personal data

Personal Data. Data Controller
The controller of your personal data, including information regarding your physical and mental health, date of birth (day, month and year), your sex, and your race, as well as information generated as a result of your participation in the study (hereinafter, "**Personal Data**") is TiGenix S.A.U., with registered office at Calle Marconi 1, Parque Tecnológico de Madrid, Tres Cantos, 28760 Madrid, Spain ("**Sponsor**") being the Sponsor of the study. However, Sponsor will only receive your Personal Data after having undergone a pseudonymization, the process of replacing the data that identifies a person with an artificial identifier or a code.

Some information from your medical records will be collected and used for this study. If you do not have a UCSF medical record, one will be created for you. Your signed consent form and some of your research tests will be added to your UCSF medical record, which is the UCSF' responsibility. Therefore, people involved with your future care and insurance may become aware of your participation and of any information added to your medical record as a result of your participation. Study tests that are performed by research labs, and information gathered directly from you by the researchers will be part of your research records but will not be added to your medical record.

Legal basis for the processing of your Personal Data
The legal basis for processing your Personal Data is the consent you provide by signing this Consent Form. This means that once you have voluntarily decided to participate in the study, you are expressly consenting to the use of your Personal Data in accordance with the Health Insurance Portability and Accountability Act (HIPAA), Regulation (EU) 679/2016, of the European Parliament and the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and the free movement of personal data (GDPR) and the terms and conditions set out in this document.

You can only participate in the study if you authorize the use and disclosure of the information as described above. If you decide not to sign this consent form, you will not be enrolled in the study. If you sign this consent form and decide later to withdraw your consent, you will not be permitted to continue your participation in the study.

You can withdraw your consent at any time by giving written notice to your study doctor, informing him or her that you are revoking your consent to use and disclose your health information. In the event you decide to withdraw from the study no further Personal Data will be collected from you. Nevertheless, the withdrawal of your consent does not have retroactive effect, which means that the information generated prior to withdrawal of your consent and which was lawfully obtained, will continue to be used for the purposes of the study. Additionally, new data may be collected if required by law, such as data related to adverse events or in the interest of public health. In case you wish to cease to participate in the study, please contact your study doctor.

Purpose for processing of Personal Data
The collected Personal Data will be used and processed for the purposes of this study, which is the confirmation of the safety and efficacy of the study drug, such that it can be commercialized in the future. Additionally, the data obtained in this clinical trial as well as the results of analyses of any medical sample taken, may be used for scientific research related to the medical treatment you will receive, taking into account the safeguards and requirements established by law. Additionally, your personal information may be given out if required by law.

Security measures adopted for protecting the confidentiality of your Personal Data

Before you enroll in the study, a special code will be assigned to you. Only the study doctor and study team at your hospital will have access to the key that can link your code with your identifying information. The key is stored in a confidential and secure manner. The key will never be given to the Sponsor. As a consequence, all information generated during your participation in the study is referred to by using this code, without identifying you directly.

Who may access your Personal Data and to whom it may be communicated

Authorized representatives from the following organizations may review your data for the purpose of monitoring or managing the conduct of this study:

- The study doctor, who directs the study at the hospital, as well as his/her study team and collaborators.
- Representatives of the Sponsor TiGenix, S.A.U., including monitors and auditors which have been appointed by Sponsor in order to check whether the study is being performed correctly.
- Affiliates of sponsor related to the management and execution of the study.
- Service providers related to the performance of the study, such as laboratories for analysing tests, samples and results; courier services; medical experts for assessing study results; randomization service providers for the blinding of the study; providers of imaging services.

- The Clinical Research Organization ("**CRO**"), who executes the study on behalf of the Sponsor, performing amongst others monitoring and pharmacovigilance activities.
- Representatives of the University of California.
- Representatives of the Food and Drug Administration (FDA) or other competent regulatory or governmental Authorities for clinical trials and public health.
- The insurance company with whom Sponsor has subscribed an insurance policy to cover the risks associated with the study.

You should know that once information is disclosed under this consent form to someone who is not a health care provider, the information is no longer protected by United States of America federal law. The Sponsor and those working with the Sponsor on this study will only use and disclose your information as described in this consent form.

Dissemination of study related information

The Sponsor may wish to use the information generated by your participation in the study other than for the management of the clinical trial (such as for scientific publications or presentations at conferences). However, these disseminations will never identify you personally, as they will only include aggregate and general results from the study.
Please be aware that MRI and other images collected during this study will be saved to a computer program and sent in a secure way to third parties working with the Sponsor for analysis. After analysis, the images collected during this study will be archived by the Sponsor for possible future reference or additional analysis.
Please note that within the limits imposed by technology and the law, every effort will be made to maintain the privacy of your information. Images will be maintained in a secure location with limited access. A unique participant number that is assigned to you will identify the recorded images, so none of your personal identifying information will be saved in the computer program or with any archived images. Your name or other personal identifying information will not be used in records or publications. Only authorized personnel of the third parties will have access to these recordings unless otherwise permitted by law.

Retention of Personal Data

Sponsor will retain the information generated during the clinical trial for 30 years after completion of the study in order to be able to comply with its legal obligations as Sponsor, after which the authorization to use or disclose the information as described in this document expires, unless your consent is obtained or the information is anonymized.
Anonymized information collected during the clinical trial may be kept for longer. This anonymized information may be added to research databases and used in the future by the Sponsor and other companies and people working for or with the Sponsor to develop a better understanding of the safety and effectiveness of the study drug, study other therapies for patients, develop a better understanding of diseases included in the study, and improve the efficiency, design and methods of future studies. In addition, the Sponsor is committed to responsible sharing of clinical data with the goal of advancing medical science and improving patient care. Independent researchers may be permitted to use anonymized data collected from subjects during the study to conduct additional scientific research, which may be unrelated to the study drug or

your disease. The anonymized data kept in research databases or provided to external researchers will not include information that identifies you.

Exercising your rights relating to your Personal Data

You may exercise the rights attributed to you in accordance with HIPAA as well as the GDPR.

Therefore, you have the right to access your Personal Data, as well as to request the rectification of incorrect data, or the erasure of the same if, amongst others the data is no longer necessary for the purposes for which they were collected. You also have the right to object to the processing of your data; the right to restrict the processing of your personal information, as well as the right to portability of your data to another controller.

You may exercise your rights by contacting your study doctor, whose contact details may be found below.

You agree that, while the study is still in progress, you may not be given access to health information about you that is related to the study. This may include, for example, information about whether you are receiving study drug or placebo, or any other information that is "blinded" (that is, kept secret during the study to prevent bias). While a request for access to health information can be denied, the study doctor and staff will consider whether it is medically appropriate under the circumstances to allow access. Your agreement that you may be denied access to your study-related health information during the study will not be used to deny you access to that information after the study is completed at all locations and study results are analyzed.

The Sponsor has a Data Protection Officer ("DPO"), whose contact details are dpo@tigenix.com. The DPO can assist you regarding any doubts or questions you may have concerning your Personal Data. Without prejudice to the foregoing, you may file a complaint with the data protection authority of Spain, being the country of establishment of the Sponsor, in particular when you are not satisfied with the response concerning your rights.

Are there any costs to me for taking part in this study?

Two types of procedures will be done during this study. Some are part of your standard medical care and others are only for research. You or your insurer will be billed for the standard medical care. You will be responsible for your co-pays, deductibles, and any other charges that your insurer will not pay. There is a possibility that your insurer may not cover all standard medical care costs if you are receiving medical services out of network. Any procedures done only for research will not be charged to you or your insurer.

The study drug will be provided by the Sponsor and will not be billed to you or your insurance company. Any visits, procedures or tests that are required solely for this study protocol and would not be done as part of your routine care, will not be billed to you or your insurance company. You and/or your insurance company will be billed for the costs of routine tests and procedures (tests and procedures you would receive even if you were not participating in this study) in the usual

manner. You will be responsible for any co-payments, co-insurance and deductibles that are standard for your insurance coverage.

Will I be paid for taking part in this study?

You will be paid $66 per visit. The total sum you can receive for completing all visits in the study is $594.
You will be paid by check. You should receive the check six to eight weeks after your visit You must give the researchers your address and Social Security Number so the check can be processed.

What happens if I am injured because I took part in this study?

It is important that you tell your study doctor, Sara Lewin, if you feel that you have been injured because of taking part in this study. You can tell the doctor in person or call her at (415)-502-4444.

Treatment and Compensation for Injury: If you are injured as a result of being in this study, the University of California will provide necessary medical treatment. The costs of the treatment may be billed to you or your insurer just like any other medical costs, or covered by the University of California or the study sponsor TiGenix, S.A.U., depending on a number of factors. The University and the study sponsor do not normally provide any other form of compensation for injury. For further information about this, you may call the office of the Institutional Review Board at 415- 476-1814.

What are my rights if I take part in this study?

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your medical care. You can still get your medical care from our institution.

We will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

Who can answer my questions about the study?

You can talk to your study doctor about any questions, concerns, or complaints you have about this study. Contact your study doctor, Sara Lewin, MD, at **415-502- 4444**. If you wish to ask questions about the study or your rights as a research participant to someone other than the researchers or if you wish to voice any problems or concerns you may have about the study, please call the office of the Institutional Review Board at 415-476-1814.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.
Information about this study will also be put on other websites, including http://www.TakedaClinicalTrials.com, but you will not be personally identified on any of these websites.

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CONSENT

You have been given copies of this consent form and the Experimental Subject's Bill of Rights to keep.
You agree that your Personal Data, including data relating to your physical or mental health or condition, and ethnic origin, may be used as described in this consent form. You will be asked to sign a separate form authorizing access, use, creation, or disclosure of health information about you as required by HIPAA.

PARTICIPATION IN RESEARCH IS VOLUNTARY. You have the right to decline to participate or to withdraw at any point in this study without penalty or loss of benefits to which you are otherwise entitled.

If you wish to participate in this study, you should sign below.

Date	Participant's Signature for Consent
Date	Person Obtaining Consent
Date	Witness – Only required if the participant is a non-English speaker