CONSENT TO PARTICIPATE IN A CLINICAL RESEARCH STUDY

Title of Study:	**A Multicenter, Open-label Study of SI-6603 in Patients with Lumbar Disc Herniation (Phase III)**
Protocol Number:	**6603/1132**
Sponsor:	**Seikagaku Corporation**
Principal Investigator: (Study Doctor)	**Scott Adelman, M.D., FABPMR, FABNEM**
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1. WHY HAVE I BEEN GIVEN THIS FORM?

You are being invited to take part in a clinical research study of an investigational new drug to treat patients with a lumbar disc herniation (a rupture or protrusion of the disc between the bones of the spine). Clinical research studies are voluntary and include only those who wish to participate. "Investigational new drug" means a drug that has not been approved as a marketed product (i.e., available to be prescribed or sold) by any regulatory authorities including the US Food and Drug Administration. This clinical research study is being sponsored by the Seikagaku Corporation (hereafter referred to as the Sponsor), and the name of this investigational new drug is SI-6603 (containing the active ingredient condoliase), called the study drug.

Before you decide if you want to participate in this study, it is important for you to understand why the research is being done, how your information will be used, what the study will involve, and the possible benefits, risks and discomforts. Please take time to read the following information carefully. Some terms may be unfamiliar to you. If there is anything you do not understand or if you would like more information, please ask the study doctor or study staff. You may also discuss the study with family members, friends, and your own doctor if you wish. If you decide that you want to take part in this study, you will be asked to sign and date the consent statement at the end of this informed consent form (you will be a given a copy of this to take home with you). No study procedures will be done until you have read and signed this form. You will be free to withdraw from the study at any time without having to give any reason. A decision not to take part in this study, or to withdraw at any time, will not affect your health care.

You are being considered for participation in this study because you have been diagnosed with a lumbar disc herniation (also called a herniated disc). Lumbar vertebrae are located in the lower back area and make up part of the spinal column. An intervertebral disc is located between each of the lumbar vertebrae and serves as a "shock absorber" and

support for the back. The disc consists of 2 parts: a firm outer layer and a soft central area. A "lumbar disc herniation" occurs when the soft central portion swells or sticks out of the normal disc area and may press or push on a spinal nerve that is close to the vertebrae. The pressure or pushing on the spinal nerve can result in symptoms such as lower back pain, leg pain, and numbness.

2. WHAT IS THE BACKGROUND AND PURPOSE OF THE STUDY?

The purpose of this study is to evaluate the efficacy (how well the study drug works) and safety (whether there are side effects) of SI-6603 (study drug) in subjects with a lumbar disc herniation by following them for 13 weeks after the administration of a single dose of SI-6603 into the intervertebral disc (the space between the bones of the spine).

SI-6603 is a possible drug for chemonucleolysis. Chemonucleolysis is a method in which the soft central portion of the herniated lumbar intervertebral disc is chemically degraded (broken down) or dissolved by directly injecting a drug into the area. As a result, the disc herniation can be reduced and lower back pain, leg pain, and/or numbness may be improved. This is how SI-6603 works. SI-6603 contains condoliase, a bacterial enzyme that degrades (breaks down) the major part of the soft central portion of the disc.

3. WHAT IS THE STUDY ABOUT?

This is a study of the efficacy (how well the study drug works) and safety (whether there are side effects) of SI-6603 (study drug) in subjects with a lumbar disc herniation. Subjects with a lumbar disc herniation who agree to be in this study and are of age between 30 to 70 years at the time of signing the informed consent will receive an injection of SI-6603 into the herniated disc.

This study is "open label," which means that both you and the study doctor will know what study treatment you are receiving.

Approximately 1,000 subjects will take part in this study at about 60 sites in the United States and European Union.

You will come to the study center for a total of 5 visits over up to 17 weeks (about 4 months). Before you receive study treatment, you will participate in a "screening period," when the study doctor will find out if you are eligible to enter the study. If you are eligible for the study, you will receive the study drug injection.

There may be reasons you are not allowed to take part in this study. Some of these reasons are:

- If you are pregnant or wish to become pregnant during the study, or are breast-feeding.
- If you have 2 or more herniated lumbar discs.
- If you have specific types of lumbar disc herniation with separated parts (free fragments) of the herniated disc.
- If you are unable to receive a magnetic resonance image (MRI); an imaging procedure that uses radio waves and a magnetic field to take pictures of the inside of your body but which does not involve radiation).

- If you recently had lumbar surgery resulting in less than complete improvement in symptoms.
- If you have received SI-6603 at any time.
- If you have severe or progressive neurological disorders.
- If you have spinal deformities or spinal canal stenosis or any clinically significant disorder of the lumbar spine other than disc herniation.
- If you have cancer or a past history of cancer within 5 years prior to the time of informed consent.
- If you have participated in another clinical study within the past 4 months, or are expected to participate in another study during the period of this study.
- If you have any medical conditions or diseases that could affect your safety or the study results. These and other reasons you may not be allowed to take part in this study will be discussed with you.
- If you are receiving compensation according to the Workers' Compensation Act or are involved in personal injury legal process due to a lumbar-related injury.

4. DO I HAVE TO TAKE PART?

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, including medical treatment and care you are entitled to receive. If you decide to participate, you may change your mind and decide to withdraw from the study at any time and for any reason. Your reasons for withdrawing will be asked by the study doctor for collecting any safety information. However, you are not required to explain your reasons for withdrawing if you do not wish to do so. If you withdraw, you will not suffer any penalty or loss of benefits regarding your future 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 (for example, an Institutional Review Board/Institutional Ethics Committee (IRB) that review study safety and ethics to ensure that subjects' rights are not violated) at any time without your consent, after the reason(s) for doing so (for example, 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 subjects 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 detailed in Section "WHAT WILL HAPPEN TO ME DURING THE STUDY" and information about you will be collected as detailed in Section "WILL MY INFORMATION BE KEPT CONFIDENTIAL".

5. WHAT WILL HAPPEN TO ME DURING THE STUDY?

5.1. Study Drug

You will be given a single 1 mL intervertebral (between the vertebrae) injection containing 1.25 units of SI-6603 (study drug).

5.2. Tests and Procedures

If you decide to take part in this study and after you have signed the consent form, you will have tests and examinations done to be sure that you qualify for the study. Throughout the study you will have various tests and examinations and will be asked questions about your pain level of leg and lower back, how your back or leg trouble affects your ability to manage in everyday life, recent medications, lumbar surgeries, injuries, and illnesses.

You will have physical examinations, and your vital signs (body temperature, blood pressure, heart and respiration rate) will be recorded. You will also have neurological examinations that will include a test to determine if your leg and lower back pain is caused by a herniated disc, tests to assess sensation and muscle strength, and a test to evaluate specific nerve function.

Blood samples will be taken for laboratory tests. The laboratory tests will include standard tests of your general health, a human immunodeficiency virus (HIV) test, and a test to measure the presence and amount of SI-6603 antibodies in your blood to help determine how your body is responding to SI-6603. If you are a woman who may be able to have children, you will be given a blood and urine pregnancy test.

During the screening period, Visit 4 (Week 6), Visit 5 (Week 13), and if you withdraw (or are withdrawn) from the study, you will be asked to have an X-ray and an MRI to record any changes in your herniated disc.

5.3. Study Visits

Screening (Visit 1):

- If you decide to take part in this study, you will be asked to sign the consent statement.
- To find out if you qualify to be in this study, you will be asked about your demographic (e. g. year of birth, gender, smoking history), your medical history, what medications you have taken during the last 6 weeks, what treatments you have had during the last 6 weeks, and if you have had any lumbar surgeries in the past.
- A physical examination (including vital signs), neurological examination, and pain assessment will be completed.
- You will be asked to have an X-ray and an MRI. (In some circumstances, repeat X-ray and/or MRI examinations may be required.)
- Blood samples will be taken including a blood pregnancy test if you are a woman who may be able to have children. About 15 to 20 mL (3 to 4 teaspoons) of blood will be collected during this visit. Some of your blood will be tested for HIV. The study doctor may be required by law to report the result of this test to the local health authority.

This Screening Visit (Visit 1) will take about 3 up to 5 hours.

If you are considered to be eligible to take part in the study, the next visit will take place within 28 days after this visit.

Study Treatment Administration Day 0 (Visit 2):

If you do not meet all of the requirements to be in the study, you will be withdrawn from the study.

- You will be asked if you have had any illness, injury, or lumbar surgery since your last visit and if there have been any changes in the medications you take.
- A physical examination (including vital signs), pain assessment and disability survey will be completed.
- A blood sample will be taken to measure any SI-6603 antibodies. About 3 mL (½ teaspoon) of blood will be collected during this visit. (Antibodies are protein molecules your body makes to destroy materials it detects and perceives as not part of itself.)
- If you are a woman who may be able to have children, you will be asked to give a urine sample for a pregnancy test. If your pregnancy test is positive, you will be withdrawn from the study.
- You will receive an intervertebral injection of the study drug. You will have to wait at least 4 hours after receiving the study drug before you leave the study site.
    - Before starting the injection, an intravenous catheter (a small, plastic tube inserted into a vein) will be placed in your arm as part of the safety procedures in case you need medication to treat a reaction.
    - During the injection of the study drug, an X-ray will be taken to confirm the needle is in the correct place.
    - During the resting period after the injection, your vital signs and general health status will be monitored.

This visit will take about 7 hours.

During the next 13 weeks, you will come to the study site for 3 visits:

Week 1 (Visit 3):

- You will be asked if you have had any illness, injury, or lumbar surgery since your last visit and if there have been any changes in the medications you take.
- A neurological examination, pain assessment and disability survey will be completed.
- Your vital signs will be recorded.
- Blood samples will be taken for general tests. About 15 to 20 mL (3 to 4 teaspoons) of blood will be collected during this visit.

This visit will take about 2 to 3 hours.

Week 6 (Visit 4):

- You will be asked if you have had any illness, injury, or lumbar surgery since your last visit and if there have been any changes in the medications you take.
- A neurological examination, pain assessment and disability survey will be completed.
- Your vital signs will be recorded.
- You will be asked to have an X-ray and an MRI. (In some circumstances, repeat MRI and/or X-ray examinations may be required.)
- Blood samples will be taken for general tests. About 15 to 20 mL (3 to 4 teaspoons) of blood will be collected during this visit.

This visit will take about 3 to 5 hours.

Week 13 (Visit 5):

- You will be asked if you have had any illness, injury, or lumbar surgery since your last visit and if there have been any changes in the medications you take.
- A neurological examination, pain assessment and disability survey will be completed.
- Your vital signs will be recorded.
- You will be asked to have an X-ray and an MRI. (In some circumstances, repeat MRI and/or X-ray examinations may be required.)
- Blood samples will be taken for general tests and to measure any SI-6603 antibodies. About 20 to 23 mL (4 to 4½ teaspoons) of blood will be collected during this visit.

This visit will take about 3 to 5 hours.

Withdrawal from the study (Discontinuation Visit):

If you withdraw voluntarily or are withdrawn involuntarily from the study, you will be asked to have a Discontinuation Visit that will include:

- You will be asked if you have had any illness, injury, or lumbar surgery since your last visit and if there have been any changes in the medications you take.
- A neurological examination, pain assessment and disability survey will be completed.
- Your vital signs will be recorded.
- You will be asked to have an X-ray and an MRI. (In some circumstances, repeat X-ray and/or MRI examinations may be required.)
- Blood samples will be taken for general tests and to measure any SI-6603 antibodies. About 20 to 23 mL (4 to 4½ teaspoons) of blood will be collected during this visit.
- You will be asked if you have had any lumbar surgery until 13 weeks after administration even if you withdrew from the study.

This visit will take about 3 hours.

Unscheduled visits or tests:

If your study doctor believes that you should have additional visit(s) or test(s) for your safety, for example, in the event of a new symptom or side effect or if a blood test needs to be recollected in order to evaluate the safety profile of the study drug, you may be asked to come for additional visit(s) or test(s). If necessary, additional tests related to such a safety concern may be ordered at no additional cost to you.

6. 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 attend all the study visits.
- Do not begin any new medication or change the dosage of a medication you take now without consulting with the study doctor first. It is important that you tell the medical staff about any other medication you are taking before and during the study. This includes if you take over-the-counter drugs (including oral medications, adhesive skin patch, and ointments).
- Certain procedures, for example, lumbar operation and nucleotomy [a surgical procedure to remove the prolapsed (out of place) tissue of the herniated disk] and therapies, for example, chemonucleolysis or intradiscal (into the disc) electrothermal (heat from electricity) therapy for treatment of back and leg pain are not permitted from the time that you agree to take part in the study until you finish the study. Discography (procedure that involves injecting a substance, for example, steroids, into the disc to help diagnose back problems) is not also allowed from the time that you agree to take part in the study until you finish the study. The study doctor or study staff will discuss this with you.
- It is important that you practice effective contraception (birth control) during the study as you have been instructed by the study doctor or staff. Contact the study doctor if you (or your partner) become pregnant during the study.
- You should report any side effects to the study doctor. This includes any signs or symptoms that are not normal for your daily routines even if the signs or symptoms disappear before contacting the study doctor or study staff.

7. WHAT ARE THE POSSIBLE RISKS?

As with all research studies, the study drug and study procedures may involve unknown risks. Any medication can have temporary and permanent side effects and can cause unforeseen adverse reactions. SI-6603 may not control your discomfort related to the herniated lumbar disc.

7.1. Risks Related to Study Procedures

Blood Tests:

Blood samples will be taken from a vein in your arm during the study. Taking a blood sample may cause some temporary discomfort, bleeding, or bruising, and there is a possibility of infection. Other risks, although rare, include dizziness and fainting. The maximum amount of blood that will be taken at any 1 visit of the study is about 15 to 23 mL (about 3 to 4½ teaspoons). The total amount of blood that will be taken over the entire study is about 86 mL (about 6 tablespoons).

X-ray and MRI:

An X-ray machine sends radiation through your body and records the image on a computer or on film. X-rays are painless, but you will need to stay still when you are having the X-ray, since motion can cause the image to be blurry. You may also be asked to briefly hold your breath when the image is being taken. You must not have an X-ray if you think you could be pregnant.

An MRI is painless and does not expose you to radiation; it is an imaging procedure that uses radio waves and a magnetic field to take pictures of the inside of your body. During the MRI scan, you will need to remain still until the pictures have been taken. 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 a MRI scan. Also, if you have a pacemaker you should not have a MRI scan. Each MRI scan will take less than 1 hour.

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, after you have been lying down for 5 minutes. You may experience mild discomfort in your arm while the cuff is inflated.

IV catheter (Study treatment administration day only):

An intravenous (IV) catheter (a small tube) will be inserted in a vein in your arm before you receive study treatment. You may have temporary discomfort, bleeding, or bruising, and/or get an infection at the insertion site.

7.2. Risk Related to Study Treatment

It is important that you understand the possible risks of the study treatment.

Risk Related to SI-6603:

You may develop antibodies against condoliase (SI-6603, the study drug) in your body. If the antibody develops in your body, an allergic reaction such as hypersensitivity that could include:

- rash,
- itching,
- hives,

- fast heart rate,
- problems breathing, and/or swelling of your face or throat

may possibly occur if you receive another injection of SI-6603 in the future. Therefore, special blood tests to detect the presence or absence of antibodies will be conducted during this study.

Side effects that may be related to **SI-6603** include:

- infection of lymph nodes,
- itching,
- rash,
- warm skin,
- blister,
- toxic skin eruption,
- back pain,
- a decrease in neutrophils (a type of white blood cell),
- increased C-reactive protein (protein produced by the liver in response to inflammation),
- increased triglycerides (a type of fat found in your blood),
- decreased white blood cell counts,
- increased alanine aminotransferase (ALT; an enzyme found in the liver),
- increased aspartate aminotransferase (AST; an enzyme found in various parts of the body),
- increased blood bilirubin (a substance produced when the liver breaks down old red blood cells),
- an increase in eosinophils (a type of white blood cells) count,
- a decrease in platelets (cells that are found in the blood and help the blood to clot),
- Lasegue's test (straight leg raise test) positive,
- abnormal nuclear MRI (changes in the bone marrow adjacent to vertebral end plates of the spine),
- abnormal spinal X-ray (decrease of disc height).

In subjects who had abnormal nuclear MRI and spinal X-ray reported, no subjects exhibited any clinical symptoms posing safety concerns during our past studies. In addition, the changes seen in spinal X-ray (decrease of disc height) were equal to or milder than those seen in patients who had a lumbar discectomy (surgical removal of part of the problem disc in the lower back). However, the clinical significances remain unclear and the long-term risks are not fully known.

Your study doctor will discuss these possible side effects with you.

Risk Related to Injection to Lumbar Disc:

As a result of the intervertebral injection, you may have temporary discomfort including:

- temporary increased back or leg pain due to increased disc volume,
- bleeding,
- vascular damage (a blood vessel was injured),
- bruising,
- vagal reaction (a slow heart rate or possible fainting),

- nerve damage,
- disc damage,
- pain at the injection site and/or get an infection at the injection site.

Risks of Local Anesthetic: If you receive a local anesthetic as part of your study injection, you may experience the following side effects:

- Low blood pressure
- Heart rhythm disturbances
- Confusion
- Seizures

7.3. Pregnancy and Contraception

If you are or become pregnant, or if your partner becomes pregnant, there may be unknown risks to the baby.

Females:

If you are a woman who may be able to have children, you will be given a pregnancy test at screening, and if the result is positive, you will not be able to be in the study. Women who may be able to have children must be using reliable contraception, and must continue to use reliable contraception until Week 13.

If you become pregnant or think you 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. You must not be breast-feeding an infant during the study.

Males:

If you are a sexually-active man, you must be willing to use adequate contraceptive measures until Week 13 of the study. If your female partner becomes pregnant before the end of Week 13, the study doctor will ask to follow up and document the course of the pregnancy and its outcome.

Adequate methods of birth control include the following:

- Hormonal contraception (female subjects) or use of at least one acceptable double-barrier method

  Acceptable double-barrier methods include the following:
  - diaphragm plus a spermicidal agent
  - condoms (male or female) plus a spermicidal agent
- Vasectomy, intrauterine device (IUD), and/or exclusive sexual partner for whom one of the above acceptable methods applies

The study doctor will discuss methods of birth control with you if needed.

8. WHAT ARE THE POSSIBLE BENEFITS?

We hope that SI-6603 (the study drug) will help the discomfort associated with lumbar disc herniation. However, you may not get any direct benefit from taking part in this

study. You will be given close attention from the study staff during the time you are involved in the study. You may receive information about your health from physical examinations and medical tests done in this study.

This study is expected to benefit the Sponsor by providing information about how well SI-6603 is tolerated and how well SI-6603 relieves the symptoms of a herniated lumbar disc.

If the results of this study are favorable along with other studies, and lead to approval by the regulatory authorities of SI-6603 for use in humans, there may be benefits for patients in the future. These benefits may include reduced leg pain, which is the major complaint of patients with lumbar disc herniation and may also include reduced back pain.

9. ARE THERE ALTERNATIVE TREATMENTS?

You do not have to be in this study to get treatment for your lumbar disc herniation. Lumbar disc herniations are usually treated with conservative or surgical treatments. Conservative therapy includes a variety of different treatments including: rest, bed-rest, drug therapy (for example, nonsteroidal anti-inflammatory drugs, steroids, and muscle relaxants), a back brace (corset), traction therapy, thermotherapy, epidural block (a numbing medicine given by injection into the epidural space of the spine), nerve root block (the nerve that is being compressed is blocked by local anesthetic), and physical therapy. Conservative therapy usually improves the lower back pain, leg pain, and numbness, but surgical therapy may be required if your symptoms are not improved.

There are a number of different surgical procedures used to treat lumbar disc herniations that you can discuss with your study doctor. Typically discectomy, percutaneous (performed through the skin) nucleotomy, percutaneous laser disc decompression, and microendoscopic discectomy are known as surgical options for lumbar disc herniation that remove a portion of the disc that has herniated and reduce pressure of the nerve that is being compressed. These alternative procedures also carry risks and your study doctor can explain those risks to you.

Chemonucleolysis may be the last resort for conservative treatment. As explained earlier, this is a method in which the central portion of the herniated lumbar intervertebral disc is chemically degraded (broken down) or dissolved by directly injecting a drug into the area. As a result, the herniated disc can be reduced and lower back pain, leg pain, and/or numbness associated with the disc herniation may be improved. SI-6603 is a potential drug for chemonucleolysis.

Other experimental treatments may also be available. Your study doctor can discuss your treatment options with you.

10. WILL I INCUR ANY EXPENSES OR RECEIVE ANY PAYMENTS?

Some treatments that you are given in this study may be part of routine treatment for your lumbar disc herniation. The cost of these routine treatments will be billed to your insurance company. You will not be charged for treatments that you are given in this study beyond what is covered by your health insurance. You may have some expenses from being in the study, such as bus fare or parking fees when you visit the study center.

You will be reimbursed for these expenses at a rate of $100 for Screening (Visit 1), Week 6 (Visit 4), and Week 13 (Visit 5). You will receive $75 for the Study Treatment Administration Day (Visit 2), Week 1 (Visit 3), and Unscheduled Visits. You will be reimbursed following each completed visit or at the end of your participation in the research study, whichever you prefer.

The Sponsor is paying the study doctor and/or the study site for their work in this study.

11. WHAT IF I AM INJURED DURING THE STUDY?

If you have an injury or illness because of your participation in this research study, you will be given any medical treatment that is necessary to help you recover from the injury or illness. If such study-related treatment is required, the sponsor will pay your copayment and/or any treatment costs not covered by your health care benefit. However, these will not apply if the injury results from your own fault or intention.

The Sponsor has insurance to cover study-related injuries.

To pay these medical expenses, the sponsor will need to know some information about you like your name, date of birth, and social security number or Medicare Health Insurance Claim Number. This is because the sponsor has to check to see if you receive Medicare and if you do, report the payment it makes to Medicare.

If you experience any unexpected symptoms or injury, and if emergency medical treatment is required, get medical care right away and please report it immediately to the study doctor or the study staff at the telephone number listed on the first page of this form.

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

12. WHAT WILL HAPPEN IF THERE IS ANY NEW INFORMATION?

If any new information about the study drug becomes available which may influence your decision to continue in the study, you will be told in a timely manner.

13. WILL INFORMATION ABOUT ME BE KEPT CONFIDENTIAL?

By signing this form you consent to the study doctor and his or her staff collecting and using your personal data for the study. This includes: your initials and/or your date of birth (day, month and year), your sex, your ethnic origin and information on your physical or mental health or condition.

The information shared with the Sponsor is protected by the use of a code, which is a number specifically assigned to you. The study doctor is in control of the code needed to connect your data to you.

All medical records and research materials that identify you by name will be held confidential (confidential data) unless required to be disclosed by law. However the study doctor, the Sponsor and its representatives, the study monitor (who checks how the study is going and makes sure that the information is being collected properly) and, under

certain circumstances, the regulatory authorities such as the US Food and Drug Administration (FDA) and ethics committees will be able to inspect confidential data that identify you by name.

Please note that if you test positive for HIV, the results will be reported to health agencies, as required by state and/or federal law.

All personal data from this study will be treated in accordance with national and local data protection laws.

By signing this consent form, you grant permission for medical information about you obtained during this study (your study data) to be made available to authorized representatives of the regulatory authorities and other government agencies. You also grant permission for your study data to be made available to the Sponsor, the study monitor, other study personnel, and ethics committees. The Sponsor may transfer your study data to countries outside of the United States for the purposes described in this document. Please be aware that the laws in such countries may not provide the same level of data protection as in the United States and may not stop your study data from being shared with others. The study doctor, the regulatory authorities, and the Sponsor may keep the study data indefinitely.

In addition, the Sponsor will use your collected samples for assay(s) development of determination of SI-6603 antibodies for the future. The samples will be destroyed upon completion of the assay development. You may request that your samples be destroyed at a later date by contacting the study doctor at the telephone number listed on the first page of this form. All data collected from your samples before that time will be retained by the Sponsor.

You have the right to request information about your study data held by the study doctor and the Sponsor. You also have the right to request that any inaccuracies in such data be corrected. If you wish to make a request, then please contact the study doctor (either in writing or verbally), who can help you contact the Sponsor if necessary.

Your consent for the use of your study data as described above does not have an expiration date. If you withdraw your consent for participating in this study, your study data and samples that were collected before you withdrew your consent may still be used as described above. Once you have withdrawn your consent for participating in the study, no further data will be collected about you for the purposes of this study unless you agree otherwise, for example, you agree to have further tests and examinations. If you do agree to have further data collected after you have withdrawn your consent, these study data may also be used as described above.

The results of this study may be published in a medical journal and shown at medical meetings. You will not be identified (by name or any other means, for example, a photo) in any of these publications.

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.

Please see the separate supplementary form for authorization to use and disclose medical information. The supplementary form is prepared in accordance with the Health Insurance Portability and Accountability Act (HIPAA).

14. GETTING ANSWERS TO YOUR QUESTIONS OR CONCERNS ABOUT THE STUDY

You can ask questions about this consent form or the study (before you decide to start the study, at any time during the study, or after completion of the study). Questions may include:

- Who to contact in the case of a research-related injury or illness;
- Payment or compensation for being in the study, if any;
- Your responsibilities as a study subject;
- Eligibility to participate in the research;
- The study doctor's or study site's decision to exclude you from participation;
- Results of tests and/or procedures;
- Other questions, concerns, or complaints.

Contact the study doctor or study staff listed on the first page of this form with any questions, concerns or complaints.

15. GETTING ANSWERS TO YOUR QUESTIONS ABOUT YOUR RIGHTS AS A RESEARCH SUBJECT

This study has been reviewed by an Institutional Review Board (IRB). This Committee reviewed this study to help ensure that your rights and welfare are protected and that this study is carried out in an ethical manner.

For questions about your rights as a research subject, contact:

- By mail:
  Study Subject Adviser
  Chesapeake IRB
  6940 Columbia Gateway Drive, Suite 110
  Columbia, MD 21046
- or call **toll free**: 877-992-4724
- or by **email**: adviser@chesapeakeirb.com

Please reference the following number when contacting the Study Subject Adviser: Pro00013033.

16. CONSENT STATEMENT OF SUBJECT

I have received verbal information on the above study and have read the attached written information. I have been given the chance to discuss the study and ask questions.

I voluntarily consent to participate in this study, including all assessments, lifestyle restrictions, contraception requirements, and taking of blood samples.

I understand that I am free to withdraw at any time. I understand that I if I choose to not participate or to withdraw, my current medical care will not be affected by this decision.

I agree that my primary physician may be informed of my participation in this study.

I consent to having my family doctor or primary health care provider notified by the study site of my participation in this study and/or any significant findings related to my health (please check yes or no).

1. ❒Yes (If yes, please complete the information below)
2. ❒No

Name and Address of Family Doctor or primary health care provider:	Name: Address:
Telephone and Fax Number:	Tel:

I agree that my personal data, including data relating to my physical or mental health or condition, and ethnic origin, may be used as described in this consent form.

I understand that I will receive and may keep a copy of this signed and dated consent form.

By signing and dating this consent form, I have not waived any of the legal rights that I would have if I were not a participant in a medical research study.

		AM/PM	
Signature of Subject	Date (mm/dd/yyyy)	Time	Printed Name of Subject

17. STATEMENT OF PERSON CONDUCTING INFORMED CONSENT DISCUSSION

I, the undersigned, certify that to the best of my knowledge, the subject signing this consent form had the study fully and carefully explained including the nature, risks, and benefits of participation in this research study as described in this informed consent document.

		AM/PM	
Signature of Investigator (or other Person Obtaining Consent)	Date (mm/dd/yyyy)	Time	Printed Name of Person Obtaining Consent

HEALTH INSURANCE PORTABILITY AND ACCOUNTABILITY ACT (HIPAA) RESEARCH AUTHORIZATION

AUTHORIZATION TO USE & DISCLOSE MEDICAL INFORMATION

As part of this study, medical information about you will be collected and analyzed. This medical information will include (but is not limited to) your date of birth, gender, medical history (that is, data from your medical records such as past or present health conditions and medications, and the results of procedures and test you undergo during the study and had before the study), laboratory test results, physical exam data and data collected from the procedures described in your informed consent form for this study.

Under federal law, your medical information cannot be used or disclosed by your study doctor for research purposes unless you sign this authorization. By signing this document, you authorize the study doctor and staff to use this information in conducting the study, and to provide access to or copies of this information to Seikagaku Corporation, PAREXEL (contract research organization conducting the study on Seikagaku Corporation's behalf), Eurofins Global Laboratory (central laboratory), and other organizations working with Seikagaku Corporation to monitor the progress of the study or analyze the study data. Access to this information is necessary for Seikagaku to check that the study is being done correctly, and to collect and analyze data about the safety and effectiveness of the study drug.

In addition, this information may also be disclosed to the Food and Drug Administration or similar, foreign, regulatory authorities, for the purpose of attaining regulatory approval. The information may also be disclosed to the Chesapeake IRB (institutional review board). The purpose of this board is to ensure that a subject's safety and rights are protected.

This authorization to use or disclose the information as described above is not time-limited (that is, will not automatically expire). In California and any other state that requires an expiration date, the Authorization will expire 50 years after you sign this authorization document.

You agree that, while the study is still in progress, you may not be given access to medical 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 medical information can be denied, the study doctor and staff will not automatically deny a request, but will consider whether it's medically appropriate under the circumstances to allow access. Your agreement that you may be denied access to your study-related medical 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.

You may decide not to sign this authorization, or you may revoke (withdraw) this authorization at any time. You can do this by giving written notice to your study doctor, informing him or her that you are revoking your authorization to use and disclose your medical information. The contact information for your study doctor is provided below.

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 authorization form, you will not be enrolled in the study. If you sign this authorization and decide later to withdraw this authorization, you will be not be permitted to continue your participation in the study. Information collected up to the time that you end this authorization may continue to be used and disclosed as described above, but only as necessary to protect the integrity of the research study.

You should know that, once information is disclosed under this authorization to someone who is not a health care provider, the information is no longer protected by federal law. The Sponsor and those working with the Sponsor on this study (such as PAREXEL) will only use and disclose your information as described in this Authorization. If reports or articles are written about the study, you will not be identified by name in them.

You will be given a copy of this authorization after you have signed and dated it.

WHO TO CONTACT IF YOU HAVE ANY QUESTIONS:

If at any time before, during or after the study, you have any questions about the use or disclosure of your study-related information, or if you wish to withdraw your authorization to use or disclose your medical information, you should contact the study doctor or study staff at the telephone number listed on the first page of this document.

STUDY SUBJECT'S STATEMENT OF CONSENT:

I confirm that I have read the statements in the HIPAA Authorization for this study. I confirm that the information has been explained to me. I agree to participate in this study, with the understanding that I am authorizing the use and disclosure of the information as described above.

I understand that I will receive a signed and dated copy of this Authorization for my records.

Signature of Subject	Date (mm/dd/yyyy)	Printed Name of Subject