INFORMATION AND CONSENT FORM

Study Title: **A Phase 1/2, Multicenter, Open-label, Single-Dose, Dose-Ranging Study to Assess the Safety and Tolerability of SB-913, a rAAV2/6-based Gene Transfer in Subjects with Mucopolysaccharidosis II (MPS II)**

Study #: SB-913-1602

Sponsor: Sangamo Therapeutics, Inc.

Study Doctor: *Investigator Name*
Investigator Site name
Address

Telephone Number: *XXX*

For California subjects: Before you read this consent form, you should read and sign a copy of the California Experimental Subject's Bill of Rights. Ask the study staff for a copy of this document if you haven't already received one.

"You" refers to you or your child throughout this consent form.

The study doctor would like to know if you are interested in taking part in a research study.

If you have any questions or do not understand something in this form, you should ask the study doctor or study staff. You should also discuss your participation with anyone you choose to better understand this study and your options.

Participating in a research study is not the same as getting regular medical care. The purpose of regular medical care is to improve your health. The purpose of a research study is to gather information.

Your participation is voluntary which means you can choose whether you want to participate. If you choose not to participate, there will be no loss of benefits to which you are otherwise entitled. If you decide to participate, you will be asked to sign this form.

If you join this study, you will still need to see your regular doctor or specialist and continue care for your MPS II throughout the study.

WHY AM I BEING ASKED TO PARTICIPATE?

The study doctor and a company called Sangamo Therapeutics, Inc. ("Sangamo"), are studying MPS II (Mucopolysaccharidosis II or Hunter Syndrome) and are trying to find new ways to treat MPS II in males and females 5 years of age or older by using an investigational product called SB-913 (also known as the study drug). This investigational product (study drug) is not approved by any regulatory health agency (such as the U.S. Food and Drug Administration [FDA]).

You are being asked to take part in this study because you have MPS II.

WHAT IS THIS STUDY ABOUT?

This research is being done to study a new way to possibly treat MPS II. MPS II is a lysosomal storage disorder that results from mutations in the gene encoding an enzyme called iduronate-2-sulphatase (IDS).

The current therapy for MPS II is enzyme replacement therapy (ERT). The current ERT treatment consists in giving Elaprase® (a recombinant protein product) or equivalent. ERT has been shown to improve pulmonary function and exercise capacity. Limitations to ERT include the need for life-long treatment, development of neutralizing antibodies, its inability to reach the brain, and the inconvenience of weekly intravenous infusions.

This study will test to see if doctors can use a process called “gene therapy” to treat MPS II.

Genes are made of DNA and are present inside the nucleus of every cell in your body and they are responsible for determining things like hair color, eye color, and height, etc. A missing or broken gene can cause a disease like MPS II. When people have MPS II they are either missing the gene that makes IDS or the gene makes a version of IDS that doesn’t work. This missing or defective gene is what causes MPS II. MPS II is a genetic disorder in which people’s bodies are missing the IDS enzyme needed to properly break down different types of large sugar molecules called glycosaminoglycans (GAGs).

Gene therapy is an experimental technique that aims to replace the broken gene with a working copy. The gene will be delivered into your cells using a vector. A vector is actually a virus that has been modified to include the gene that makes IDS. It has also been changed so it cannot reproduce itself; therefore, the vector can deliver the gene into cells but it can no longer cause an infection. The virus used in this study is called adeno-associated virus (AAV). This type of virus is very good at entering cells.

This is the first study in which SB-913 will be given to humans. The main purpose of this research study is to see if receiving SB-913 is safe and doesn’t cause too many side effects. Also, the potential effect of SB-913 for improving your MPS II will be evaluated. This study will evaluate three treatment groups with low, mid and high doses of SB-913 as indicated in the following Table:

Group	Age Range	Total SB-913 Dose
1	≥18	5×10^{12} viral genomes/kg body weight
2	≥18	1×10^{13} viral genomes/kg body weight
3	≥18	5×10^{13} viral genomes/kg body weight
4	≥18	1.20×10^{14} viral genomes/kg body weight
5	12-17	5×10^{13} viral genomes/kg body weight
6	12-17	To Be Determined
7	5-11	To Be Determined
8	5-11	To Be Determined

A viral genome is the total of all of the DNA inside the vector and one kilogram (kg) is equal to 2.2 pounds. A number like 10^{12} means 1 followed by twelve zeros. Doctors and scientists use this kind of notation because it is short and easy to write. For example, group one subjects will receive 5,000,000,000,000 viral genomes for every 2.2 pounds of body weight.

Two participants will initially be enrolled and evaluated in each group. If there are no significant side effects observed, the next Group will be enrolled. If significant side effects are observed in one or both of the first 2 participants within a group, qualified medical and scientific professionals not participating in the study will assess whether additional participants should be enrolled within the group or if the next dose group should be reduced. Participants will only be enrolled into the same, or next dose group if it is considered safe to do so.

Up to a total of 32 people will enroll in this study at about 12 to 15 institutions.

HOW DOES SB-913 WORK?

SB-913 consists of 3 vectors, each carrying a gene. SB-913 will be given to you one time through a vein in your arm. SB-913 is made up of three AAV2/6 vectors and carries instructions to produce Zinc Finger Nucleases (ZFNs) that act like scissors to open your DNA in the liver and then place the new IDS gene into those selected liver cells. Think of the vector as a car and the gene as the passenger. The car (the vector) will drive the passenger (the IDS gene) where it needs to go (the liver cells) and drop it off there.

IS THERE ANYTHING ELSE I CAN DO FOR MY MPS II ILLNESS?

You do not have to be in this study to have treatment for your MPS II illness. Your other choices may include continuing your regular MPS II therapy or taking part in a different study. You should talk about whether you want to participate in this study with the study doctor or study staff, you may talk about your choices with your family's doctor or your regular MPS II doctor (if they are different from your study doctor).

WHO IS PAYING FOR THIS STUDY?

A company called Sangamo Therapeutics, Inc., ("Sangamo"), the sponsor of the study, is paying for this study. The sponsor will pay <Insert name of Hospital or clinic> to cover the costs to conduct the study and procedures not part of your standard medical care.

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HOW LONG WILL I BE IN THE STUDY?

If you agree to take part in this study, and the study doctor says you can be in the study, your participation may last about 39 months (just over 3 years).

After completing at least 12 months of follow up, you will be asked to participate in a separate long-term follow-up study to evaluate how you are for up to 10 years of total follow-up post SB-913 infusion to monitor potential long-term side effects. Based on the judgement of your study doctor and if agreed by Sponsor, you may be able to enroll in the long-term follow-up study before completing 12 months of follow-up. If you decided to enroll in the long-term follow-up, your study doctor will ask you to complete an end of study (EOS) visit.

You are encouraged to participate in the long-term follow-up study, but your participation in the long-term follow-up study is also voluntary. You don't have to be part of this long-term follow-up study if you don't want to.

WHAT WILL HAPPEN DURING THIS STUDY?

If you decide to be in this study, you must sign this form. If you have any questions or do not understand something, you should ask the study doctor or study staff before signing this form. Once these documents are signed, you will then enter the study's screening period to see if you meet all the requirements to join the study. If you agree to participate in this study it is strongly encouraged you refrain from consuming any alcohol or any medication that could have harmful effects on your liver health during the first year after you receive SB-913.

Screening Period: up to 3 months in duration.

Your medical history will be evaluated and the following exams, tests and procedures will be conducted over several screening visits. The study doctor or study staff will ask you about any medicines you are taking and about any medical issues you may be having. You may agree to only have screening blood tests done, to see if you pass those screening tests, prior to performing the rest of the exams, tests and procedures.

- Physical exam including vital signs, height and weight
- Assessment of any adverse events
- Blood and urine tests: Clinical laboratory tests, liver panel and urine GAG levels (samples on 3 separate days, at least 7 days apart)
- The study staff will record information about your ERT infusions
- Electrocardiogram (ECG) (to measure the electrical activity of your heart)
- Echocardiogram to create pictures of your heart
- Chest x-ray (to look at the image of the chest and internal organs like lung and heart)
- Liver magnetic resonance imaging (MRI), a type of imaging to take pictures of your liver and check for presence of any mass
- Blood samples will be taken to check the following:
    - The specific gene mutation you have that caused your MPS II*
    - If you have been exposed to viruses such as HIV, hepatitis and other infections
    - You cannot have active HIV and hepatitis infections in order for you to be in this study. Depending on state law, you may have to give consent before HIV and hepatitis testing can start. The HIV and hepatitis tests are confidential, and the study doctor or study staff will not share your results outside this study unless state law requires it. If required by state law, the study doctor or study staff may report positive test results to the local health department.
    - Immune response to AAV 2/6, which is the vector used in the study drug
    - α-fetoprotein level, a blood test to monitor for potential liver problems
    - If you have any variations in your DNA that could make the study drug ineffective*
    - Blood test to measure IDS and GAG levels in your blood

    *Saliva samples may be collected instead of blood for pediatric subjects.

- Pulmonary function test (test measurement of the lung volumes and of air moving in and out of the lungs by blowing into and breathing through a tube. (Will be done only if you are able)
- Blood pregnancy test (for females of childbearing potential only)
- Assessment of neurocognitive abilities, such as memory and learning tests (Will be done only if you are able)

Even if you have passed all of the screening tests, there is a possibility you will not be enrolled in the study. If you are enrolled and continue your participation, you will begin the following study periods described below.

The total amount of blood drawn at the screening visit is 51 mL (about 3.4 tablespoons) for adults. For pediatrics, the total amount of blood collected at Screening is approximately 43 mL (2.8 tablespoons).

SB-913 Infusion and Follow-up: 36 months in duration.

If you meet all entry criteria, you will be treated in one of the eight treatment groups, Group 1, 2, 3, 4, 5, 6, 7 or 8.

The group you are in will depend on when you are enrolled in the study and your age. The study doctor will tell you in which group you will be treated.

<u>Baseline Assessments Before the SB-913 infusion:</u>
Within approximately three weeks prior to the SB-913 infusion, the following will be completed:

- Physical exam including your heart rate, blood pressure, temperature, breathing rate, and weight
- Blood and urine tests: Clinical laboratory tests, liver panel and urine GAG levels
- Blood pregnancy test (for females of childbearing potential only)
- 6-minute walk test, a test to see how far you can walk in 6 minutes of time (will only be done if you are able)
- Assessment of any adverse events
- The study staff will record information about your ERT infusions
- Joint Range of Motion, a test to see how flexible your joints are (will only be done if you are able)
- Neurologic Cranial Nerve Exam and Muscle Strength Testing of Upper Extremities, a test to check the health of your nerves and muscles (will only be done if you are able)
- Electrocardiogram (ECG) to measure the electrical activity of your heart
- Pulmonary function test, measurement of the lung volumes and of air moving in and out of the lungs by blowing into and breathing through a tube. (will only be done if you are able)
- Collection of samples of plasma, saliva, urine, stool and semen* (males only) to test if you have any vectors in your body before the SB-913 infusion
    - For your convenience, you may have the option to collect stool and semen samples off-site. Please refer to your study site staff for instructions and supplies as applicable.
      *Collection of semen samples may be waived for pediatric subjects at the discretion of the Principal Investigator.
- Brain and cervical spine MRI, type of imaging to take pictures of your head and neck
- Assessment of neurocognitive abilities, such as memory and learning tests (will only be done if you are able)
- ACTH stimulation test, blood test for the body's steroid function
- Blood test to measure IDS and GAG levels in your blood

- Liver biopsy, a procedure to obtain a small sample of your liver for testing (unless contraindicated by study investigator). The liver biopsy will be used to check for GAG levels, to determine if the new IDS gene was placed into the DNA of the liver cells, and to look at the tissue under a microscope.
- Research samples to determine the effects on your immune system (will only be collected in adults)
- Collection of cerebral spinal fluid (CSF) by lumbar puncture (needle inserted in the lower spine) for cell count, total protein, glucose and biomarkers unless contraindicated by study doctor.

The total amount of blood drawn at this visit is 34 (about 2.3 tablespoons) for adults. For pediatrics, the total amount of blood collected at Baseline is approximately 19 mL (1.2 tablespoons).

If you are under enzyme replacement therapy (ERT), it should be withheld during the week of the administration of SB-913 to make sure baseline testing is accurate.

Two days before the SB-913 infusion you will start taking a medication called Prednisone, for about 20 weeks. Prednisone is a corticosteroid (also known as “cortisone,” “steroids,” “prednisone”) and has a potent anti-inflammatory effect. It is used to treat allergies and to decrease the body’s immune response. In this case it will be used to try to decrease the body’s response to AAV and reduce side effects such as liver inflammation, and elimination of the cells with the new gene.

Hospitalization for SB-913 infusion (Day 0 and Day 1):
The study doctor or study staff will ask you about any medicines you are taking and about any medical issues you may be having. You will receive the SB-913 infusion (Day 0) in the hospital and you will need to stay in the hospital for about 24 hours (one day) after the infusion. Before the infusion, you will have a physical exam, you will record information about your ERT infusions, you will have a urine pregnancy test (for females of childbearing potential only, and if >7 days from Baseline), and will be given Prednisone (as mentioned above). Your health status and vital signs will be monitored when you’re in the hospital. Weight will be taken once during Day 0 and once during Day 1.

In order to give you SB-913, the study staff will start an IV (place a needle into your vein). Depending on your weight and total dose, SB-913 will be given between 2-8 hours.

Day 1
Any changes to your health, including medications you are currently taking, will be evaluated and the following exams, tests and procedures will be completed.
- Physical exam
- Record your heart rate, blood pressure, temperature, breathing rate, weight.
- Blood draw and urine collection for routine laboratory tests including blood counts, liver and kidney function
- Collection of plasma sample 12 hours after the end of SB-913 infusion to test for how quickly the study drug leaves the body
- Administration of prednisone

The total amount of blood collected on day 1 is approximately 8 mL (about - 0.5 tablespoon).

You will be discharged from the hospital about 24 hours after the end of the infusion, if the doctor feels it is safe for you to go home.

Post SB-913 infusion follow-up and care:

After leaving the hospital you will then need to come to the study clinic every two weeks for 8 weeks to make sure that you are doing well medically. You will have twice weekly blood tests to check your liver function during the first 20 weeks after SB-913 infusion. If you are unable to come to the site frequently, some of these blood tests may be collected at your home using a home health service. Eventually the visits will be less frequent. After you have completed the full year of follow-up (Month 12) after the SB-913 infusion, you will need to come to the clinic for an additional 2 years for long-term follow-up: every 3 months (4 times a year).

Week 1 / Day 7 (+/- 1 day)
Any changes to your health, including medications you are currently taking, will be evaluated and the following exams, tests and procedures will be completed.

- Physical exam
- Vital signs: temperature, pulse and respiratory rate, blood pressure, and weight
- Assessment of any adverse events
- The study staff will record information about your ERT infusions
- Electrocardiogram (ECG) to measure the electrical activity of your heart
- Blood draw for liver functions tests.
- Collection of samples of plasma, saliva, urine, stool and semen* (if male) to test for how quickly the study drug leaves the body
  - For your convenience, you may have the option to collect stool and semen samples off-site. Please refer to your study site staff for instructions and supplies as applicable.
    *Collection of semen samples may be waived for pediatric subjects at the discretion of the Principal Investigator.
- Administration of prednisone

The total amount of blood drawn at this visit is approximately 14 mL (about 1 tablespoon).

Weeks 2, 4, 6, and 8 (+/- 2 days)
You will need to come to the study clinic at weeks 2, 4, 6, and 8 after the infusion. Any changes to your health, including medications you are currently taking, will be evaluated and the following exams, tests and procedures will be completed.

- Physical exam
- Vital signs including heart rate, blood pressure, temperature, breathing rate, and weight
- Assessment of any adverse events
- The study staff will record information about your ERT infusions
- Urine pregnancy test (for females of childbearing potential only) (Weeks 4 & 8 only)
- Blood draw and urine collection for routine lab assessments including: blood counts, and kidney functions
- Blood draws for Liver function testing (2x per week)
- Urine collection to measure GAG levels in your urine
- Blood test to measure circulating α-fetoprotein level; a blood test to monitor for potential liver problems (Weeks 4 and 8 only)

- Collection of plasma, saliva, urine, stool and semen* to test how quickly the study drug leaves the body (Weeks 2, 4, and 8 only)
    - Samples of blood, urine, saliva, stool, and semen will be collected during the first few visits, and the collection of each specimen type will stop when three consecutive samples of each specimen have been negative for the presence of the viral vectors. For your convenience, you may have the option to collect stool and semen samples off-site. Please refer to your study site staff for instructions and supplies as applicable.
      *Collection of semen samples may be waived for pediatric subjects at the discretion of the Principal Investigator.
- Blood test to measure IDS and GAG levels in your blood
- Blood test to measure your immune response (Will only be collected in adults at Week 4)
- Administration of prednisone

The total amount of blood drawn at all of these visits is approximately 102 mL (about 6.9 tablespoons) for adults. For pediatrics, the total amount of blood collected during Week 2-8 is approximately 90 mL (6.1 tablespoons).

<u>Weeks 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52 (+/- 1 week)</u>
Any changes to your health, including medications you are currently taking, will be evaluated and the following exams, tests and procedures will be completed.

- Physical exam (Weeks 12, 16, 20, 24, 36, and 48 only)
- Vital signs including heart rate, blood pressure, temperature, breathing rate, and weight. (Weeks 12, 16, 20, 24, 36, and 48 only) Height collected at week 48 only
- Assessment of any adverse events
- The study staff will record information about your ERT infusions
- Joint range of motion (Weeks 24 and 48 only. Will only be done if you are able)
- Neurologic cranial nerve exam and muscle strength testing of the upper extremities including shoulder, elbow and hands (Weeks 24 and 48 only. Will only be done if you are able.)
- Electrocardiogram (ECG) to measure the electrical activity of your heart (Weeks 24 and 48 only)
- Echocardiogram to examine heart function (Week 48 only)
- Urine pregnancy test (for females of childbearing potential only; at Weeks 12, 16, 20, 24, 36, and 48 only or until 3 consecutive plasma samples are negative for AAV2/6)
- Blood draw and urine collection for routine lab assessments including blood counts, and kidney functions (Weeks 12, 16, 20, 24, 36, and 48 only)
- Blood test to determine liver function twice a week from weeks 12 - 20 (see above); then at Weeks 24, 28, 32, 36, 40, 44, 48 and 52.
- Urine collection to measure GAG levels in your urine
- Blood test to measure circulating α fetoprotein level, a blood test to monitor for potential liver problems (Weeks 12, 24 and 48 only)

- Collection of plasma, saliva, urine, stools and semen* (if male) to test for how quickly the study drug leaves the body (unless three previous consecutive samples of each specimen have been negative) at Weeks 12, 16, 20, 24, 36, and 48 only
    - For your convenience, you may have the option to collect stool and semen samples off-site. Please refer to your study site staff for instructions and supplies as applicable.
      *Collection of semen samples may be waived for pediatric subjects at the discretion of the Principal Investigator.
- Six-minute walk test (Weeks 24, and 48 only. Will only be done if you are able.)
- Pulmonary Function Tests (PFTs) to determine lung function (Weeks 24 and 48 only. Will only be done if you are able)
- Assessment of neurocognitive abilities, such as memory and learning tests (Weeks 24 and 48 only. Will only be done if you are able)
- MRI of liver (Weeks 24 & 48 only)
- MRI of brain and cervical spine (Week 48 only)
- Blood test to determine ACTH stimulation (cosyntropin) test (Week 20 only or at the end of prednisone taper)
- Blood test to measure IDS and GAG levels in your blood (Weeks 12, 16, 20, 24, 36, and 48 only)
- Liver biopsy unless contraindicated by study doctor (Week 24 and 48 only)
- Lumbar puncture to collect Cerebrospinal fluid (CSF) unless contraindicated by study doctor (Weeks 24 and 48 only)
- Blood test to measure your immune response (Weeks 12, 24, 36, and 48 only. Will only be collected in adults.)
- Administration of prednisone through Week 20 or per instruction

Weeks 28, 32, 40, 44 and 52 may be conducted off-site.

The total amount of blood drawn during weeks 12 through 52 is approximately 236 mL of blood (about 16 tablespoons) for adults. For pediatrics, the total amount of blood collected during weeks 12 through 52 is approximately 170 mL (12 tablespoons).

<u>Months 15, 18, 21, 24, 27, 30, 33 and 36/EOS Visit Following SB-913 Infusion (+/- 1 month)</u>

You will be evaluated every 3 months in year 2 and year 3 after SB-913 infusion. An End of Study (EOS) visit will be conducted at Month 36. At the EOS visit you will be asked to participate in the Long Term Follow-up Study. You will be asked to review and sign a separate Informed consent prior to participating in the Long Term Follow-up Study.

Any changes to your health, including medications you are currently taking, will be evaluated and the following exams, tests and procedures will be completed.

- Physical examination
- Vital signs including heart rate, blood pressure, temperature, breathing rate (height collected at months 24 and 36 only)
- Assessment of any adverse events
- The study staff will record information about your ERT infusions
- Joint range of motion at Months 18, 24, 30, and 36/EOS only (Will only be done if you are able)

- Neurologic cranial nerve exam and muscle strength testing of the upper extremities including shoulder, elbow and hands (Months 18, 24, 30, and 36/EOS only. Will only be done if you are able)
- Electrocardiogram (ECG) to measure the electrical activity of your heart (Months 18, 24, 30, and 36/EOS only)
- Echocardiogram to examine heart function (Months 24 and 36/EOS only)
- Blood draw and urine collection for routine lab assessments including blood counts, liver and kidney functions
- Urine collection to measure GAG levels in your urine
- Blood draw to measure circulating α fetoprotein level (Months 18, 24, 30, and 36/EOS only)
- Pulmonary Function Tests (PFTs) to assess lung function (Months 18, 24, 30, and 36/EOS only. Will only be done if you are able.)
- Six-minute walk test (6MWT) (Months 18, 24, 30, and 36/EOS only. Will only be done if you are able)
- Assessment of neurocognitive abilities, such as memory and learning tests (Months 18, 24, 30 and 36/EOS only. Will only be done if you are able.)
- MRI of liver (Months 18, 24, 30 and 36/EOS only)
- MRI of brain and cervical spine (Months 24 and 36/EOS only)
- Blood test to measure IDS and GAG levels in your blood
- Blood test to determine your immune response (Months 18 and 24 only. Will only be collected in adults.)

The total amount of blood drawn during months 15 through 36 is approximately 152 mL of blood (about 11 tablespoons) for adults. For pediatrics, the total amount of blood collected during months 15 through 36 is approximately 136 mL (9.2 tablespoons).

ERT Withdrawal Visit (any time after week 12)

If you are willing and it's been at least 12 weeks after your last administration of SB-913 you may be able to withdrawal from ERT infusions. To participate in ERT withdrawal you must be medically stable and agree to increased safety monitoring and lab testing until your ERT Withdrawal Follow-Up visit.. Your study doctor can decide at any time to restart the ERT if needed.

The ERT Withdrawal visit may occur at a regular scheduled visit or it can be scheduled as a separate visit.

The following assessments and procedures will be performed:

- Review and record concomitant medications
- Physical exam
- Record your heart rate, blood pressure, temperature, breathing rate, weight
- Assessment of any adverse events or change in the condition of your health
- The study staff will record information about your ERT infusions
- Blood draw and urine collection for routine lab assessments including blood counts, and kidney functions
- Blood test to determine liver function
- Urine collection to measure GAG levels in your urine
- Blood test to measure IDS and GAG levels in your blood
- Lung function testing. This test is done by blowing in and out of a tube to measure how much air moves in and out of your lungs. (Will only be done if you are able)

- 6 Minute Walk Test. (Will only be done if you are able)

If a separate ERT Withdrawal visit is done, the amount of blood drawn is approximately 16 mL (1.1 tablespoons).

ERT Withdrawal Monitoring Visits (ERT Withdrawal Weeks 1, 2, 3, 4, 6, 8, 10, and 12)

ERT Withdrawal Monitoring visits will take place on a weekly basis for the first 4 weeks, and on a biweekly basis for the last 8 weeks following the ERT Withdrawal visit until the ERT Withdrawal Follow-up visit. The ERT Monitoring visits may occur at a regular scheduled visit or it can be scheduled as a separate visit. ERT Monitoring visits may be conducted off-site.

The following assessments and procedures will be performed:

- Review and record concomitant medications
- Assessment of any adverse events or change in the condition of your health
- The study staff will record information about your ERT infusions
- Blood test to determine liver function
- Urine collection to measure GAG levels in your urine
  Blood test to measure IDS and GAG levels in your blood

At each ERT Withdrawal Monitoring visit, the amount of blood drawn is approximately 12 mL (0.81 tablespoon).

ERT Withdrawal Follow-Up Visit

The ERT Withdrawal Follow-up visit will can occur at any time up to 12 weeks after the ERT Withdrawal visit at the discretion of the study doctor. After completion of the ERT Withdrawal Follow-Up, ERT does not need to be restarted.

The following assessments and procedures will be performed:

- Review and record concomitant medications
- Physical exam
- Record your heart rate, blood pressure, temperature, breathing rate, weight
- Assessment of any adverse events or change in the condition of your health
- The study staff will record information about your ERT infusions
- Blood draw and urine collection for routine lab assessments including blood counts, and kidney functions Blood test to determine liver function
- Urine collection to measure GAG levels in your urine
- Blood test to measure IDS activity and GAG levels in your blood
- Lung function testing. This test is done by blowing in and out of a tube to measure how much air moves in and out of your lungs. (Will only be done if you are able)
- 6 Minute Walk Test. (Will only be done if you are able)

At the ERT Withdrawal Follow-Up visit, the amount of blood drawn is approximately 16 mL (1.1 tablespoons).

Early Termination Visit (ETV)

If you are discontinued from the study early or are withdrawn from the study, or if you decide to leave the study, you will be asked to return to the clinic for an Early Termination Visit (ETV).

- Any changes to your health, including medications you are currently taking, will be evaluated and the following exams, tests and procedures will be completed.
- Physical examination
- Vital signs
- Assessment of any adverse events
- The study staff will record information about your ERT infusions
- Joint range of motion (will only be done if you are able)
- Neurologic cranial nerve exam and muscle strength testing of the upper extremities including shoulder, elbow and hands (will only be done if you are able)
- Electrocardiogram (ECG) to measure the electrical activity of your heart
- Echocardiogram to examine heart function
- Blood draw and urine collection for routine lab assessments, including blood counts and liver and kidney function tests
- Urine collection to measure GAG levels in your urine
- Blood test to measure IDS and GAG levels in your blood
- Blood draw to measure circulating α fetoprotein level
- Pulmonary Function Tests (PFTs) to determine lung function (will only be done if you are able)
- Six-minute walk test (will only be done if you are able)
- Assessment of neurocognitive abilities, such as memory and learning tests (will be done only if you are able)
- MRI of liver
- MRI of brain and cervical spine

During an early termination visit approximately 20 mL of blood (about 1.4 tablespoons) will be collected.

The study staff will explain the tests performed during the visits after infusion. See the table below for additional information about what happens at these visits.

Study Period	Visit Type
Screening (approximately 3 months)	Clinic visit(s)
Baseline	Clinic visit
Hospitalization Day 0 – Day 1	SB-913 infusion and monitoring
Week 1 / Day 7	Clinic visit
Weeks 2, 4, 6, 8	Bi-weekly clinic visits Twice a week liver tests
Weeks 12, 16, 20, 24, 28*, 32*, 36, 40*, 44*, 48 and 52* (Month 12)	Monthly clinic visits Twice a week liver tests through Week 20
Months 15, 18, 21, 24, 27, 30, 33, and 36/EOS (2nd and 3rd year)	Clinic visits every 3 months
ERT Withdrawal, if applicable	Clinic visit at least 12 weeks post SB-913 administration; may be combined with another scheduled visit
ERT Withdrawal Monitoring*, if applicable	Weekly clinic visits for first 4 weeks and biweekly for last 8 weeks until ERT Withdrawal Follow-Up
ERT Withdrawal Follow-Up, if applicable	Clinic visit up to 12 weeks after ERT Withdrawal; may be combined with another scheduled visit
End of Study (EOS)	Clinic visit if transitioning to long-term follow-up study; can happen any time after Week 52, but before the next scheduled study visit

* These visits may be conducted at home with the home health care service.

Not all the same study procedures are performed during each visit.

While you are in the study, you must:

- Follow the instructions you are given.
- Come to the study center for visits with the study doctor or study staff.
- Tell the study doctor or study staff about any changes in your health or the way you feel.
- Tell the study doctor or study staff if you want to stop being in the study at any time.
- See your regular doctor for your MPS II care.

After the study is over, you should talk to the study doctor and your regular doctor about your future treatment for MPS II.

Biological Samples

Your samples will not be labelled with your name or other directly identifying information. Your samples will have a code (subject number) instead. The list that matches the code with your name and information will be stored separately from your samples. Samples for IDS activity in your blood and cells, immune response to AAV 2/6, variations in your DNA that could make the study drug ineffective, the specific gene mutation you have that caused your MPS II, urine

GAGs, liver biopsy, cerebrospinal fluid, and to test how quickly the study drug leaves the body will be tested in the US. Each sample will be labelled only with the fully anonymized participant ID and may also have the visit identification name.

What else should I know about the study procedures?

You may have to sign a separate consent form before you have some of the procedures listed above.

Your regular medical care might include some of the study tests and procedures. The study doctor or study staff member can answer any questions you may have about which tests and procedures are not part of your regular medical care.

Ask the study doctor or study staff for the estimated recovery time of your participation in this study.

In order for researchers to learn more about your MPS II status and the effects of SB-913, the study doctor may request an autopsy be performed upon your death no matter when this occurs and what the cause. An autopsy would involve an exam and tests to determine the cause of death and may help researchers learn more about the effects of SB-913. In this situation, legal authorization of consent to perform an autopsy would be requested from your family or next of kin; therefore, we encourage you to talk to them of your wishes in advance. You and your family will not be responsible for the costs of the autopsy performed at the request of the Sponsor. You should inform your family that this request is important and may have benefit to future Mucopolysaccharidosis research.

WILL BEING IN THIS STUDY HELP ME?

You should not expect to receive any benefit from this study. This study is being done to see if the investigational product, SB-913 is safe and tolerable. SB-913 may help your MPS II, but there is no guarantee that being in this study will help you. Your MPS II might not get better or may even get worse while you are in this study. Information from this study might help researchers to come up with new tests or medications to help others in the future. If the study shows this study drug helps you and other people in the study, we hope to be able to treat more people with MPS II in the future.

ARE THERE RISKS TO ME IF I AM IN THIS STUDY?

All investigational products and drugs carry a risk of side effects. Ask the study doctor or study staff if you have questions about the signs or symptoms of any side-effects you read about in this consent form. Below is a list of the risks that the investigators think are possible with this study

RISKS OF SB-913

This is the first time SB-913 is being given to humans. Unexpected and severe risks are possible in research studies using genetic materials not previously tested in humans. Side effects of SB-913 are not fully known, and you may or may not have any of the following:

Possible Side Effects:

- Based on what has been seen in people who have received SB-913 so far, you might experience:
    - Reddening of the skin including the face and/or neck
    - Cold sweat
    - Dizziness
    - Weakness or fatigue
    - Itching

    These side effects were mild, temporary, and resolved without treatment.

- Allergic reaction
    - This may include rash, difficulty breathing, wheezing, drop in blood pressure (making you feel dizzy or lightheaded), fainting, a feeling of dread, wheezing, swelling of the mouth, throat or eyes, fast pulse, sweating and inability to breathe without assistance. This may be severe and could result in death. The study doctor and nurses will be watching you closely in case this happens.

- General Infusion Risks: You will receive SB-913 intravenously, which means you will receive it directly into your vein. This may cause any of the following side effects, some of which could be very serious and other side effects may occur:
    - Injection site reaction - Because SB-913 is given in your vein by a needle, bruising, swelling, black and blue marks at the injection site;
    - Irritation and damage to your vein
    - Damage to the skin or tissue around the injection site - your skin near the vein could become warm, swell, hurt, or get red and infection at the site could occur
    - Increase or decrease in electrolyte levels (the amount of certain salts and other chemicals in your blood), causing health problems
    - A blood clot or an air bubble could form, which could block a blood vessel in another part of your body

- Risks Associated with Immune Response
    - Your immune system may react to the infusion of SB-913 by making small molecules, called antibodies, and affecting your normal immune function. Antibodies can develop when a person is given an injection of a substance that the body does not recognize.
    - If your body makes antibodies against SB-913, the treatment might not work.
        - Once you receive SB-913, you cannot receive it again due to your immune response to the study drug.

A strong immune response could attack the liver cells that received SB-913 and are producing IDS, which could stop or reduce the production of IDS and may damage your liver.

- You will be closely monitored for any potential liver damage during the study. If this occurs, you may need to take additional doses of prednisone.

Unlikely Side Effects:

- Worsening of your MPS II if you develop an antibody that destroys infused iduronate-2-sulphatase (idursulfase or Elaprase).
- You may be less likely to respond to similar gene therapy trials in the future because you may develop an immune response to the components used in gene therapy (kind of like an allergy).

Very Unlikely Side Effects:

- Potential Risk of Cancer
  - SB-913 is intended to make a permanent change in the DNA of your cells to allow your liver to produce IDS. There is a potential risk that genetic changes to your cells may increase your likelihood of having cancer (such as liver cancer). While this complication is expected to be very rare, it can be a serious potential complication of the treatment. No evidence of cancer was found in animal studies.
- Potential Risk on Albumin Production
  - Another potential risk is the effect on albumin synthesis. Albumin is the most abundant protein in the blood and is produced in the liver. The IDS gene insertion is targeted to a specific area of the albumin gene, however, only a small percentage (< 1%) of cells are expected to have the albumin gene modified. Therefore, SB-913 is unlikely to have severe side effects on albumin production.
- Potential Risk of Unintended Off-Target Cutting
  - Other tests of SB-913 show that it might also target another gene that has been linked to reproduction (having children), tumor suppression, DNA damage repair and a type of muscular dystrophy (Facioscapulohumeral muscular dystrophy, FSHD, a condition causing muscular weakness). Since the chance that SB-913 affects other genes is very low and primarily targets the liver, these risks are considered small.
  - This is why the study doctor will monitor your muscle strength during the study. Low level targeting of other genes did not cause any side effects in animal studies.

Please tell the study doctor if you have any side effects or any other problems with your health or the way you feel during the study, whether or not you think they are related to SB-913 or the study procedures.

You should ask the study doctor about the risks of using medication you receive to help treat or prevent side effects, such as Tylenol or Benadryl.

It is possible that receiving SB-913 with your regular medications or supplements may change how SB-913, your regular medications, or your regular supplements work. It is very important you tell the study doctor about all medications or supplements you are taking during the study.

Reproductive Risks of SB-913:

It is not known whether SB-913 causes side effects to pregnant women, to an unborn child, or to children of nursing women.

If you are past puberty and become sexually active during the study, you and your partner must agree to use a barrier method of contraception (e.g., male condom) until at least three semen samples in a row after the SB-913 infusion are negative for AAV2/6. If you are male you must also refrain from sperm donation during this period. The consequence of the presence of the vector in the semen is unknown, but it could result in birth defects, fatal death, or abnormal health in the offspring.

If you are female you also must agree to use a highly effective method of contraception (e.g., hormonal contraception, IUD) until at least three blood samples in a row after your SB-913 infusion are negative for AAV2/6.

The Investigator will discuss these methods of contraception with you and will let you know when it is safe to stop the methods of birth control. You or your partner should not become pregnant during this study.

If you think you or your partner is pregnant during the study, you should tell the study doctor immediately. The study doctor may ask for information about the pregnancy and the birth of the baby. The study doctor may share this information with the sponsor, and U.S. Food and Drug Administration (FDA).

OTHER RISKS ASSOCIATED WITH THE STUDY

Possible Side Effects of Prednisone (corticosteroids):

Prednisone is a corticosteroid (also known as “cortisone,” “steroids,”), when used in high doses for long term treatment (usually longer than three months), may be associated with the development of side effects, some of which can be serious. In this study, high doses of prednisone are planned to be given only for a short period and reduced gradually over 20 weeks. The side effects of prednisone may include the following:

COMMON, SOME MAY BE SERIOUS In 100 people receiving Prednisone, more than 20 and up to 100 may have:
• High blood pressure which may cause headaches, dizziness, blurred vision • Pain in belly • Loss of bone tissue • Mood swings • In children and adolescents: decreased height • Swelling of the body, tiredness, bruising • Increased appetite and weight gain in the belly, face, back and shoulders • Difficulty sleeping • Skin changes, acne

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Prednisone, from 4 to 20 may have:
• Blood clot which may cause swelling, pain, shortness of breath • Infection • Kidney stones • Diabetes • Glaucoma • Cloudiness of the eye, visual disturbances, blurred vision • A tear or a hole in the bowels which may cause belly pain or that may require surgery • Heartburn • Damage to the bone which may cause joint pain and loss of motion • Numbness and tingling of the arms, legs and upper body • Muscle weakness • Non-healing wound

RARE, AND SERIOUS In 100 people receiving Prednisone, 3 or fewer may have:
• Bleeding from sores in the stomach • Broken bones

Risks of Temporary Suspension of Enzyme Replacement Therapy (ERT) and Withdrawal of ERT:

If you are receiving ERT, you may continue receiving it during the study except during the week after you receive the study drug unless you undergo ERT withdrawal. During the study, the timing of your ERT and enzyme testing for the study needs to be coordinated by the study staff to make sure that the tests are performed at the right time. The risks of temporary suspension of ERT in this study are thought to be minimal.

Risks associated with ERT withdrawal

In this study, you may have the option to have medically-supervised discontinuation of weekly ERT infusions. If it has been at least 12 weeks since your SB-913 infusion and you are doing well medically, the study doctor will discuss with you if it is appropriate to withdraw ERT. If you withdraw ERT, you will be closely monitored for side effects and have frequent blood and urine testing to determine how you are doing.

There is a risk that symptoms of your MPS II disease, such as tiredness, weakness, or joint pain may worsen when ERT is withdrawn. If you experience worsening symptoms or if SB-913 is determined to not be effective, you or your study doctor can decide to restart your weekly ERT infusions at any time. It is expected that any side effects from withdrawal of ERT for a short period (about 2 to 3 months) will be temporary and should improve when ERT is restarted, but this is not known for longer periods of ERT withdrawal. ERT withdrawal is completely optional, and you do not have to withdraw ERT to participate in the trial.

Risks Associated with Collecting your Blood:

Occasionally there are risks associated with collecting your blood such as pain, bruising, swelling, black and blue marks, dizziness, fainting and/or infection at the site. You may also experience a decrease in hemoglobin and hematocrit (red blood cell number, called (anemia) from having blood drawn frequently. The total amount of blood that could be drawn because you are in this study is 559 mL (about 38 tablespoons).

Risks Associated with Liver Biopsy

Liver Biopsy is generally a safe procedure, but it requires a needle or catheter (tube) to enter the body. There is a small risk of bleeding or infection after having this procedure, which may require an operation to stop the bleeding or medicine to stop infection. In rare cases, taking liver tissue this way may injure an organ next to the liver. Even though you will receive some numbing medicine, you may experience pain during or right after the procedure. You could also have an allergic reaction to the numbing medicine, but this is rare. In very rare cases, it can be fatal.

The liver biopsy will be done using ultrasound to guide the needle. Ultrasound pictures allow the doctor to see the outline of all of your internal organs. An Ultrasound also allows the doctor to see where the large blood vessels are in the liver so they can be avoided.

Risks Associated with Lumbar Puncture (LP) and Collection of Cerebrospinal Fluid (CSF):

Lumbar puncture is generally a safe procedure, but it requires CSF to be collected by inserting a needle into the spinal canal low in the back. Medicine will be used to numb your back while the needle is being inserted. The LP may also be done while you are under general anesthesia. Lumbar punctures may cause a mild to severe headache which may last for several days. Other risks with the lumbar puncture include pain at the site where the needle entered the spinal canal, meningitis (an infection of the nervous system), bleeding, spinal fluid leakage, nerve damage and paralysis. It is also possible that an attempt to collect fluid will not yield any fluid. To decrease the risk of headache with lumbar punctures, you will be encouraged to lie flat in a bed for about two hours after the procedure is done. You may feel lower back pain or tenderness after the procedure, and the pain might spread down the back of your legs.

Risks Associated with General Anesthesia

You will be asked to sign a separate consent form for anesthesia every time it is used for liver biopsy or lumbar puncture. General anesthesia is a combination of medicines that a person inhales (breathes) through a mask, a breathing tube, or receives through a needle in a vein. These medicines make a person unable to move or feel pain. General anesthesia affects the whole body, including the brain, heart, and lungs, and increase a person's risk of side effects, most of which are minor and can be easily managed. You will be under close supervision from the time general anesthesia is given until you are fully awake.

Serious side effects of anesthesia are uncommon but include breathing problems, swallowing problems, an irregular heartbeat, increases or decreases in blood pressure, difficulty putting in or taking out a breathing tube, rapid changes in body temperature, allergic reactions, heart attack or stroke, a reaction to a medicine used in the anesthesia, or very rarely, spinal cord injury, or death from these complications.

Risk of Magnetic Resonance Imaging (MRI)
MRI uses high powered magnets to generate a picture of the inside of the body. There are no known harmful side-effects associated with temporary exposure to the strong magnetic field used by MRI scanners. However, MRI can be uncomfortable or frightening for some people. You cannot move while you are having an MRI so if you are uncomfortable with small spaces or don't think you can lie still please let the study doctor know right away. The presence of metal in your body may be a safety hazard or affect a portion of the MRI image. Before receiving an MRI, tell the doctor or technologist if you have any metal or electronic devices in your body.

Risk of X-Rays
You will need to have one chest x-ray at the beginning of the study to verify that you do not have any medical problems or infections, such as pneumonia, that would prevent the infusion of SB-913.

X-rays involve exposure to radiation. This radiation exposure is not necessary for your medical care and is for research purposes only. This exposure involves minimal risk and is necessary to obtain the research information desired.

Risk of Electrocardiograms (ECG)
ECGs measure the electrical activity of the heart. Sticky pads and wires will be attached to the chest. These sticky pads may cause a temporary skin reaction or skin irritation. In addition, these pads may cause some discomfort when they are removed, similar to the pulling sensation associated with the removal of a Band-Aid.

Risks of Genetic Testing
In order to be in this study, the study doctor will need to know which mutation you have that caused your MPS II. Mutations are the errors in the gene that cause disease. If you have had mutation analysis in the past we do not need to do it again but will need the results of the test you had. If you have not had mutation analysis, we will need to do it.

Mutation analysis involves a process called genetic testing.

There are risks associated with research involving genetic or related testing. Such risks could include the possibility of reduced access to or retention of benefits or entitlements (e.g. insurance, educational opportunities, employment, etc.); stigmatization; psychological distress in response to information; or detection of biological relationships within a family.

A Federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans and most employers to discriminate against you based on your child's genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

All health insurance companies, group health plans and employers with 15 or more employees must follow this law.

Be aware that this Federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. In addition, this Federal law may not protect you against genetic discrimination on the basis of a genetic disease or disorder that is already obviously visible, apparent or manifest.

It is possible that you could have problems and side effects of SB-913 that nobody knows about yet, which include your MPS II getting worse or even death.

Confidentiality Risks and others

There is a risk of loss of confidentiality of your information. You will read more about the protection of your information later in this form. Please ask the study doctor or study staff if you would like to know more about how your information will be protected while you are in this study.

You may not be able to have future gene therapy or participate in vaccine trials as a result of your participation in this study.

COULD I HAVE ANY OTHER PROBLEMS WITH MY HEALTH IF I AM IN THIS STUDY?

It is possible that you could have problems and side effects of SB-913 that nobody knows about yet, which include your MPS II getting worse or even death.

WILL I RECEIVE ANY NEW INFORMATION DURING THE STUDY?

Yes, if the study doctor or study staff learns any new information that might change your mind about continuing in the study, the study doctor or study staff will tell you about it.

WILL IT COST ANYTHING TO BE IN THIS STUDY?

You and/or your health-care payer/insurer will not be billed for costs for the following:

- SB-913
- The costs of the study doctor or study staff giving you SB-913
- Medication you may take as part of the study to help treat or prevent side effects
- Study visits
- Procedures and tests that are described in this form unless they are part of your Standard of Care.

You and/or your health-care payer/insurer will be billed for costs for the following:

- Costs of your regular medical care not part of this study

You and/or your health-care payer/insurer may be billed for costs for the following:

- Costs of diagnosing and treating a condition or injury.

You can ask the study doctor or study staff to find out more about costs.

WHAT IF I GET HURT OR SICK WHILE I AM IN THIS STUDY?

In the event that this research activity results in an injury, treatment will be available, including first aid, emergency treatment and follow-up care as needed. The sponsor of the study has some funds available to pay for care for injuries resulting directly from being in this study. If you think that you have suffered a research related injury, let the study physicians know right away.

The sponsor does not plan to pay for an injury or illness that happens if you did not follow the directions of the study doctor or study staff. To ask questions about this, talk to the study doctor or study staff.

Be aware that your health plan might not cover the costs of study-related injuries or illnesses. Medical treatment will be available if you need it. If you have an illness or injury during this research study that is not directly related to your participation in this study, you and/or your insurance will be responsible for the cost of the medical care of that illness or injury. Sangamo Therapeutics, Inc. does not routinely provide other compensation. To ask questions about any of this, talk to the study doctor or study staff.

You do not give up any of your legal rights by signing this form.

WILL I RECEIVE PAYMENT?

No, you will not be paid for being in this study. The study sponsor will cover all costs associated with travel including: airfare, bus or cab fare, local transportation, and hotel. The sponsor will provide a per diem to cover the cost of food and miscellaneous items.

DO I HAVE TO BE IN THIS STUDY?

Your participation in this study is voluntary. You can decide not to be in the study and you can change your mind about being in the study at any time. There will be no penalty to you, and you won't lose any benefits you are otherwise entitled to. If you want to stop being in the study, tell the study doctor or study staff.

The study doctor or study staff or sponsor can remove you from the study at any time, even if you want to stay in the study. Even if you have passed all of the screening tests, there is a possibility that you will not be enrolled in the study.

This could happen if:

- The study doctor, study staff, or sponsor believes it is best for you not to participate or to stop being in the study.
- You do not follow directions about the study.
- The U.S. Food and Drug Administration or the study sponsor (Sangamo Therapeutics, Inc.) stops the study for any reason.

If you stop being in the study early, the study doctor or study staff may ask you some questions about being in the study. The study doctor or study staff may ask you to participate in some procedures or tests to help you leave the study safely and/or to collect more information for the study. If you leave the study, the study doctor and study staff will still be able to use your information that they have already collected.

If you change your mind about being in the study later, be aware that your blood, urine and other samples collected may or may not be withdrawn from the research, depending on the sponsor's policies.

HOW WILL MY INFORMATION BE KEPT CONFIDENTIAL?

Your confidentiality will be protected as required by law and according to any policies the study center or sponsor may have. Be aware that your study records (which include your medical records, your signed consent form, and other information) will be shared and copied as needed for the study. Those data and study records will be handled confidentially in accordance with applicable national legislation regulating privacy and data protection. The medical data collected from you during your participation in the study will be documented. All data will be pseudo-anonymized, meaning that all reference to the data will be done by using only a patient number and not your name. Your initials and date of birth may also be collected. Such data will be made available and transferred to the Sponsor and/or its representatives without disclosing your name and contact details for the purposes of scientific evaluation and will be used by Sponsor to support the development, registration and marketing of the study drug in your country and abroad. The pseudo-anonymized data may also be transferred to authorities in relation to the registration of the study drug. If results of the study are published or will be presented at meetings, it will not include any personal data by which you could be identified.

To verify that the study is being conducted correctly authorized representatives of the Sponsor (Sangamo Therapeutics, Inc.), the Contract Research Organization used by the Sponsor (CTI Clinical Trial & Consulting Services, the Institutional Review Boards and representatives of regulatory authorities in your county and from abroad may inspect the study records held by your study doctor. The purpose of such inspections is to verify that the study is being conducted correctly. Your name and contact information will be protected.

If you choose to use the home health service for collection of liver function blood samples your name, phone number, and address will be provided to the home health service so that they can contact you to arrange for blood sample collection. Your information will also be shared with a travel and reimbursement vendor in order to arrange for any travel to study visits and reimbursement during the study. Your information will be kept confidential per applicable laws and will only be used by the home health service and travel and reimbursement vendor for this purpose. If you would like to know how the sponsor will protect the privacy of your records, ask the study doctor or study staff how to get this information.

The data collected during the study may be transferred to countries where the laws about the protection of personal data may not be as strict as in the United States, but all the parties involved in this process have a duty to protect your identity and to use the data for legitimate healthcare and scientific purposes only.

If you wish to withdraw your authorization to use or disclose data, you must notify your study doctor in writing.

The FDA, the sponsor and IRB may look at your study and medical records. Please note that the study doctor or study staff may also share personal information about you if required by law (for example, if the study doctor or study staff suspects that you are going to harm someone or yourself). If you have questions about this, please ask the study doctor.

If you would like to know how the sponsor will protect the privacy of your records, ask the study doctor or study staff how to get this information.

The study doctor or study staff or sponsor may use some facts or information derived from your participation in this study in books, magazines, journals, and scientific meetings. If this happens, no one will use your name or other information that could be used to identify you.

If you consent to take part in this study, certain personal and medical data about you will be collected by the study doctor and recorded in the study records.

A Federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

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.

The study doctor and study staff will make efforts to provide protection from the media in an effort to protect your privacy. The study doctor and study staff will not give away your identity to news reporters at any time.

Use of Leftover Biological Samples for Future Research

Researchers may use leftover material from already collected biological samples that will be obtained from you during the study for other types of investigations in the future. These research tests may be developed during the time you are on study or, in some cases, years later. These tests may provide additional information that will be helpful in understanding your disease or response to the study drug, but it is unlikely that these studies will have a direct benefit for you. These studies may benefit patients in the future.

In addition, samples obtained from you may be used to establish products that could be patented or licensed. Financial compensation will not be provided to you should this occur.

Samples will be stored by the study sponsor indefinitely. Researchers from the sponsor of this study will have access to these samples or specimens. These specimens may be used to conduct new studies regarding your disease or regarding your response to the study drug you received.

You will not be given results of these additional research studies. Study data from stored specimens will not be placed in your medical record.

You have the right to withdraw your sample from additional research studies providing samples are available by contacting the study doctor.

Your samples will not have your name on them. Your samples will have a code on them. The code will link your samples to information about the test results. Some people who work for the sponsor will be able to find your name from the code on your sample.

Your confidentiality will be protected as required by law and according to any policies the study center or sponsor may have. Be aware that your study records (which include your medical records, your signed consent form, and other information) will be shared and copied as needed for the study. For example, the FDA may look at your records.

Who do you contact if you have questions about the study?

In the event of an emergency, dial 911 immediately.

If you require emergency care, be sure to tell the emergency care provider about your participation in this study. Contact the study doctor or study staff < insert study doctor name and phone # > as soon as possible.

You can ask questions about the study at any time. You can call the study doctor or study staff at any time if you have any concerns or complaints. You should call the study doctor or study staff at the phone number listed above if you have questions about the study procedures, study costs (if any), study payment (if any), or if you get hurt or sick during the study.

For questions about your rights as a research participant while taking part in this research study, you may contact your study doctor or the following person(s): <insert IRB or site ombudsman contact info>.

WHO WILL USE AND SHARE INFORMATION ABOUT MY BEING IN THIS STUDY?

This section explains who will use and share your private health information if you agree to be in this study. If you do not sign this form, you cannot be in the study.

During the study, the study doctor and study staff will use, collect, and share health information about you (your "records"). Your records may include any information about you that the study doctor needs to do the study and other identifying information about you, such as your name, address, phone number, or social security number. Your records will include:

- medical records
- medical history
- physical exams
- laboratory test results, including those for MPS II, HIV, Hepatitis B and C.
- medical images and reports
- mental health diagnosis or treatment
- interviews and/or questionnaires
- information from other procedures you have as part of the study

If you sign this form:

- You allow the study doctor and study staff to use your records to carry out this study.
- You allow the study doctor to share your records with the sponsor, Sangamo Therapeutics, Inc.; people who work with or for the sponsor, such as CTI Clinical Trial & Consulting Services; and other researchers involved in this study. These people will use your records to review the study, to check the safety and results of the study, and to seek government approval for SB-913. When the study doctor sends your records to

these people, your records will not have your name on them. They will have a code that links them to you. However, the sponsor can find out your name if necessary.

- You allow the study doctor or sponsor to use some facts about your being in this study in books, magazines, journals, and scientific meetings. If this happens, no one will use your name or other information that could be used to identify you.
- You allow the study doctor to share all of your records and this signed authorization form with government agencies, including the Department of Health and Human Services (DHHS), the U.S. Food and Drug Administration (FDA), and other government agencies in the United States and other countries. The study doctor may also share your records with regulatory agencies, like Institutional Review Board (IRB). These agencies may use your records to check the study information, how researchers are doing the study, subject safety, and the results of the study.
- You allow the study doctor to share your records with your health care payer to resolve your claim if you are hurt because of being in this study. If this happens, the study doctor or the sponsor may share your records with their insurance carriers to resolve your insurance claim, and the study doctor may also request medical records from your other health care providers to learn more about your condition.

There are national and state laws that make the study doctor protect the privacy of your records. However, you do not have a guarantee of absolute privacy because of the need to share your information. After the study doctor shares your records with the sponsor and others, the laws may no longer protect the privacy of your records. The sponsor or others may share your records with other people who do not have to protect the privacy of your records. If all information that does or can identify you is removed from your records, the remaining information will no longer be subject to this authorization and may be used or shared for other purposes.

No publication or public presentation about the research described in this consent will reveal your identity without permission from you.

You might have the right to see and copy your health records related to this research. You might not be able to see or copy some of your records until after all subjects finish the study. If it is necessary for your care, your records will be provided to you or your regular doctor.

You can cancel this authorization to use and share your records at any time. If you want to cancel your authorization, you must write a letter to the study doctor at the address listed on page 1 of this form. If you cancel your authorization, you will not be able to continue in the study.

Even if you cancel your authorization and leave the study early, the study doctor and study staff will still be able to use and share your records that they have already collected as described above.

This authorization to use and share your records expires in 50 years.

You will receive a signed copy of this form.

Permission for use of Leftover Biological Samples for Future Research:

Check only one of the boxes below to indicate whether you will allow your leftover biological samples to be used for future research. You can change your mind at any time and withdraw this permission.

☐ Yes, I give the study center my permission to use my leftover biological samples for future research

☐ No, I DO NOT give the study center my permission to use my leftover biological samples for future research

_____ _____

Signature of Subject Date

CONSENT

I have read this form, and I have been able to ask questions about this study. The study doctor or study staff has talked with me about this study. They have answered all my questions. I voluntarily agree to be in this study. I agree to allow the use and sharing of my study-related records as described above.

By signing this form, I have not given up any of my legal rights as a research subject. I will get a signed copy of this consent form for my records.

_____
Printed Name of Study Subject

_____ _____
Signature of Study Subject Date

I attest that the subject named above had enough time to consider this information, had an opportunity to ask questions, and voluntarily agreed to be in this study.

_____ _____
Printed Name of Legally Authorized Representative (if different that subject)

Relation to subject:
☐ Parent ☐ Legal Guardian

_____ _____
Signature of Legally Authorized Representative (if different than subject)

Date

_____
Printed Name of Person Explaining Consent

_____ _____
Signature of Person Explaining Consent Date

I attest that I or my representative discussed this study with the subject named above.

_____
Signature of Principal Investigator or Sub-Investigator

CTI CLINICAL TRIAL & CONSULTING
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Informed Consent Review for Required Elements (non-EU)

(REVISED COMMON RULE COMPLIANT – ENACTED 21JAN2019)

PROTOCOL NUMBER:	SB-913-1602	PROTOCOL VERSION/DATE:	7.0 dated 12Dec2019
☐ MASTER ICF	Adult ICF	MASTER ICF VERSION/DATE:	7.0 dated 18Dec2019
☒ SITE ICF		IRB APPROVAL DATE:	
REVIEWED BY:	D. Splichal	REVIEW DATE:	18Dec2019

REVISED COMMON RULE ELEMENTS (If Yes, complete the following section)		**COMMENTS**
Key information is included at the beginning of the ICF	☐Yes ☒No	
Information included on why a person might or might not want to participate	☐Yes ☒No	
Statement on future use of identifiable private information and identifiable biospecimens (for studies that collect identifiable private information or identifiable biospecimens)	☐Yes ☒No	
Statement that the subjects biospecimens (even if de-identified) may be used for commercial profit and whether the subject will or will not share the commercial profit.	☐Yes ☒No	
Statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions	☐Yes ☒No	
Statement about genome sequencing (if applicable). For research involving biospecimens, whether the research will (if known) or might include whole genome sequencing.	☐Yes ☒No	

Informed Consent Review for Required Elements (non-EU)

ESSENTIAL ELEMENTS OF INFORMED CONSENT		COMMENTS
A statement that the trial involves research	☒Yes ☐No	
The purpose of the trial is explained	☒Yes ☐No	
The trial treatment(s) and the probability of random assignment to each treatment	☒Yes ☐No	
The expected duration of the subjects participation in the trial	☒Yes ☐No	
The approximate number of subjects involved in the trial	☒Yes ☐No	
The trial procedures to be followed, including all invasive procedures	☒Yes ☐No	
The aspects of the trial that are experimental	☒Yes ☐No	
The subjects responsibilities	☐Yes ☒No	
The reasonably foreseeable risks or inconveniences to the subject and, when applicable, to an embryo, fetus, or nursing infant	☒Yes ☐No	
A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable	☒Yes ☐No	
The alternative procedure(s) or course(s) of treatment that may be available to the subject, and their important potential benefits and risks.	☒Yes ☐No	
The reasonably expected benefits. When there is no intended clinical benefit to the subject, the subject should be made aware of this.	☒Yes ☐No	
That the subject or the subject's legally authorized representative will be informed in a timely manner if information	☒Yes ☐No	

Informed Consent Review for Required Elements (non-EU)

ESSENTIAL ELEMENTS OF INFORMED CONSENT		COMMENTS
becomes available that may be relevant to the subject's willingness to continue participation in the trial.		
For research involving more than minimum risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information can be obtained.	☒Yes ☐No	
The anticipated prorated payment, if any, to the subject for participating in the trial.	☒Yes ☐No	
The anticipated expenses, if any, to the subject for participating in the trial.	☒Yes ☐No	
That the subject's participation in the trial is voluntary and that the subject may refuse to participate or withdraw from the trial, at any time, without penalty or loss of benefits to which the subject is otherwise entitled.	☒Yes ☐No	
That the monitor(s), the auditor(s), the IRB/ICE, and the regulatory authority(ies) will be granted direct access to the subject's original medical records for verification of the clinical trial procedures and/or data, without violating the confidentiality of the subject, to the extent permitted by the applicable laws and regulations and that, by signing a written informed consent form, the subject of the subject's legally acceptable representative is authorizing such access.	☒Yes ☐No	
The records identifying the subject will be kept confidential and, to the extent permitted by the applicable laws and/or regulations, will not be made publicly available. If the results of the trial are published, the subject's identity will remain confidential.	☒Yes ☐No	
The person(s) to contact for further information regarding the trial, the rights of trial subjects, and whom to contact in the event of a research related injury.	☒Yes ☐No	
The foreseeable circumstances and/or reasons under which the subject's participation in the trial may be terminated by the investigator without regard to the subject's consent.	☒Yes ☐No	

Informed Consent Review for Required Elements (non-EU)

ESSENTIAL ELEMENTS OF INFORMED CONSENT		COMMENTS
The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject	☒Yes ☐No	
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	☒Yes ☐No	
Signature block contains lines for the subject's signature/date and any other required signatures (legally authorized representative (LAR), witness, etc.)	☒Yes ☐No	

DOES THE ICF CONTAIN HIPAA LANGUAGE? (If Yes, complete the following section)		COMMENTS
Description of Protected Health Information (PHI) to be collected and disclosed	☐Yes ☒No	
Specific ID of the persons/groups authorized to use the subject's PHI	☐Yes ☒No	
Description of the purpose of the disclosure of the subject's PHI.	☐Yes ☒No	
An expiration date or statement that there is no expiration date for the disclosure of research data and PHI.	☐Yes ☒No	
A statement of the subject's right to revoke the use of their PHI and that it must be done in writing to the PI.	☐Yes ☒No	
A statement of the possibility of the re-disclosure of PHI by the recipient and that the PHI will no longer be protected by the Privacy Rule (HIPAA) in the event of re-disclosure.	☐Yes ☒No	

Informed Consent Review for Required Elements (non-EU)

DOES THE STUDY INVOLVE GENETIC RESEARCH? (If Yes, complete the following section)		COMMENTS
If the study involves genetic research, a statement describing the Genetic Information Nondiscrimination Act (GINA) is recommended. The following language is suggested: A Federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways: • Health insurance companies and group health plans may not request your genetic information that we get from this research2 • Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums. • Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.	☒Yes ☐No	