INFORMED CONSENT FORM
AND
AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION

Sponsor / Study Title:	**University of Colorado Linda Crnic Institute for Down Syndrome/ "Mechanistic Investigation of Therapies for Down Syndrome Regression Disorder"**
Protocol Number:	**22-1992**
Principal Investigator: **(Study Investigator)**	**Joaquin Espinosa, Ph.D.**
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Address:	**University of Colorado Anschutz Medical Campus, Linda Crnic Institute** **12700 East 19th Ave.** **MS 8608** **Aurora, CO, 80045**

Key information about this study

You are being asked to take part in a research study. This section describes the key information that we believe most people need to decide whether to take part in this research. A member of the research team will describe this study to you and answer all of your questions. Later sections of this document will provide the details of the research.

If you are the parent or legal guardian of a child who may take part in this study, your permission will be needed. In this consent form the word 'you' refers to your child.

This form is for use in a research study that may involve participants who may or may not have the capacity to consent to take part in the study. When the participant cannot legally consent to take part, pronouns "you" and "your" should be read as referring to the participant rather than the person (legally authorized representative) who is signing this form for the participant. In cases where the participant's representative gives consent, the participant should be informed about the study to the extent possible given his/her understanding. During the course of the study, if the participant regains the capacity to consent, informed consent will be obtained from the participant, and the participant will be offered the ability to leave the study if desired.

What should I know about this research?

- Taking part in this research is voluntary. Whether you take part is up to you.
- If you don't want to take part, it won't be held against you.
- You can take part now and later drop out, and it won't be held against you.
- Please read the information below and ask questions about anything you don't understand before deciding whether to participate.
- Ask all the questions you want before you decide.

Why is this study being done?

This study plans to learn more about three therapeutic treatments for Down Syndrome Regression Disorder (DSRD). DSRD is a rare condition that can affect adolescents and adults with Down syndrome, resulting in the loss of language, adaptive skills, and social behaviors. Doctors do not know what causes DSRD. Currently, there is no standard treatment for DSRD.

This study will look at the safety and effectiveness of three different therapies to help understand regression and the effectiveness of different study treatment options:

- Lorazepam, a medication that is taken by mouth two to three times a day. This medication is often used to treat anxiety, psychiatric disease, and seizure disorders.
- Intravenous Immunoglobulin (IVIG), an infusion that is given by IV and works to modulate the immune system.
- Tofacitinib, an oral medication taken by mouth twice daily that works to suppress parts of the immune system.

The three therapies in this study have FDA approval to treat other conditions, but not DSRD. Thus, their use is considered investigational in this study. Study investigators have used each therapy to treat DSRD symptoms in individual people and other studies. Participants in this study will receive only one therapy, not all three.

Other people in this study

Up to 100 people with DSRD nationwide between the ages of 8 and 30 will participate in the study.

You are being asked to be in this study because you are a person with Down syndrome and have a possible or probable diagnosis of DSRD.

What happens to me if I agree to take part in this research?

- You must be able to present with a study partner or legal guardian at all study visits.
- A magnetic resonance imaging (MRI), electroencephalogram (EEG), and a lumbar puncture (LP) will be required to rule out other causes of regression and establish possible or probably DSRD.
    - A MRI is a scan that uses a magnetic field and pulses of radio wave energy to make pictures of organs and structures inside the body.
    - An EEG is a test that detects abnormalities in your brain waves, or in the electrical activity of your brain.
    - A LP (spinal tap) is performed in the lower back, in the lumbar region. During a lumbar puncture, a needle is inserted between two lumbar bones (vertebrae) to remove a sample of cerebrospinal fluid — the fluid that surrounds your brain and spinal cord to protect them from injury.

- Depending on your assigned treatment, you will take a study drug two or three times per day or receive 4 study infusions.
- You will complete several clinical and cognitive tests and assessments ("thinking tests") to assess your thinking and well-being with the clinical coordinators. These tests will be video recorded.
- Your study partner will complete online surveys about your daily activities, thinking and behaviors.
- You will receive blood draws at every visit by having a needle inserted into your vein.
- You will complete a diary every day to record medication administration and overall health.
- Study doctors will perform physical exams and review your medical record.

Detailed procedure information

Screening

1. The study investigator will review your medical history to confirm possible or probable DSRD. If you do not have all of the procedures that are needed to confirm possible or probable DSRD, the study investigator will order them or can consult with your local provider to ensure they are completed. If you recently have had some or all of the screening procedures completed, we will ask you to sign a Medical Records Release to access these records. You may have already given us this permission.
    - Procedures required to establish possible or probable DSRD may include diagnostic imaging, a group of blood tests, urine tests, cerebrospinal fluid (CSF) tests, EEG, MRI, and other testing as clinically indicated.
    - Procedures required to establish possible or probable DSRD are considered clinical procedures and will be billed to your insurance. These costs are not covered by the study.
        - If you are unable to obtain a lumbar puncture through your local provider, it may be performed as a research procedure and paid for by this study. You will be informed before the procedure takes place if it will be paid for by the study or billed to your insurance.
2. You will complete a screening appointment that includes blood work for safety and research labs, virology, tuberculosis, chest radiographs, electrocardiogram (ECG), and a serum pregnancy test for women of childbearing potential. Research labs will also be drawn.
        - An ECG traces the electrical activity of the heart.
        - Chest radiographs may be required as part of a tuberculosis screening.
3. You will be randomized into one of three study treatment groups: lorazepam, intravenous immunoglobulin (IVIG), or tofacitinib. Randomization assignments are final.

Baseline Appointment

1. You will be enrolled into the study and complete a Baseline appointment, which includes a physical exam and thinking tests.
2. You will receive your assigned study treatment.

Some participants, but not all, will join the Delayed Study Treatment Arm. They will complete two Baseline visits 12 weeks apart.

There is no treatment between these Baseline appointments. This helps us understand what DSRD looks like without therapy.

Subsequent Appointments

1. You will return for safety monitoring bloodwork at 2 weeks, 4 weeks, and 8 weeks. You will receive your assigned study treatment at 4 weeks and 8 weeks.
2. At 12 weeks, you will return for your endpoint visit which includes optional work-up procedures, safety monitoring, a physical exam, and doing the thinking tests.
3. You can return for three follow-up visits at 4 weeks, 6 months and 12 months after treatment ends, which will include bloodwork. These visits are optional. Longer study visits may be broken up over multiple days.

		Enrollment Period						Follow-up Period		
			Treatment Period							
	Screening Visit 1	Baseline Visit 2A[1]	Baseline Visit 2B	Week 2	Week 4	Week 8	Week 12 Endpoint	1 month Follow-up	6 month Follow-up	12 month Follow-up
Visit window (days)	*-1 day - 168 days*	*-84 days +/- 5 days*	*Day 0*	*Day 14 +/- 5 days*	*Day 28 +/- 5 days*	*Day 56 +/- 5 days*	*Day 84 +/- 5 days*	*Day 112 +/- 5 days*	*Day 266 +/- 14 days*	*Day 448 +/-14 days*
Consent	X									
Screening labs	X									
Randomization[2]	X									
DSRD workup[3]	X						X			
Health history	X	X	X	X	X	X	X	X	X	X
Safety monitoring	X	X	X	X	X	X	X	X[4]	X[4]	X[4]
Research blood draw	X	X	X	X	X	X	X	X[4]	X[4]	X[4]
Neurologic exam		X	X				X		X[4]	X[4]
IP dispense			X		X	X				
Clinical and cognitive endpoints		X	X				X			X

Figure 4. Schedule of Events.
[1] For the Delayed Treatment Group only.
[2] After eligibility criteria from Screening Visit are met.
[3] For procedures with abnormalities at Screening Visit or optional consent.
[4] Obtained for in-person visits only

How long will I be in this research?

The study treatment will last up to 12 weeks. There are three optional follow-up visits: 4 weeks, 6 months, and 12 months after study treatment ends, for a total of 16, 38, and/or 64 weeks, respectively, so that the study team can collect data on long-term outcomes. In-person follow-up visits will be dependent on funding availability.

A select number of participants will be included in the Delayed Study Treatment Arm and will be in the study for 24 weeks, plus the optional follow-up visits 4 weeks, 6 months, and 12 months later, for a total of 28, 50, and/or 76 weeks.

What are the possible discomforts or risks? Could being in the research hurt me?

The most common risks or discomforts that you may expect from taking part in the research are:

- Fatigue (tiredness)
- Feeling drowsy or unsteady
- Headache
- Nausea
- Bruises from blood draws
- There is a small risk that people outside of the research team will see your research information. We will do all that we can to protect your information, but it cannot be guaranteed.

Please see the risks section below for a complete list of expected risks.

Procedure Risks

You may experience discomfort with some of the study procedures.

- There is the potential for bruising and minor pain typically associated with a blood draw.
- You may experience minor anxiety, fatigue, or frustration during assessments of cognition and quality of life. Some of the questions may be uncomfortable to answer.
- Lumbar punctures are a low-risk procedure to look at markers in cerebrospinal fluid. Risks of this procedure include local bleeding (at the site of needle insertion), local pain (at the site of needle insertion), local infection (at the site of needle insertion), pain and discomfort, or nerve irritation. The most common side effect of this procedure is a headache, which usually goes away with rest, increased fluid intake, caffeine, and over the counter medicine.

  Rarely, a prolonged headache related to cerebrospinal fluid leak can occur. This is treated with a blood patch. A blood patch takes a small amount of blood from your arm, like a normal blood draw, which is then injected at the lumbar puncture site. This makes the headache go away at once. In extraordinarily rare circumstances, permanent neurologic injury could occur due to traumatic insertion into a spinal nerve, the spinal cord, or by compression associated with epidural/subdural hematoma (bleeding around the brain) formation. We make sure that our medical staff are highly trained.
- There are no significant risks associated with the use of magnetic resonance imaging (MRI), but you might feel claustrophobic and hear loud noises. There is a big risk if you have any metal in your body, although dental fillings are ok. We will ask you about your health history to make sure you are safe.
- Electrocardiogram (ECG): Skin irritation is rare but could occur during an ECG from the electrodes or gel that is used.
- There may be risks that have not been thought of. You will be made aware of any new risks that may affect your safety.

Study Treatment Risks

All treatments have some risk. You will receive one of the three study treatments below, but not all of them. There may be risks in addition to those listed below.

Lorazepam (Ativan™)

Lorazepam is an FDA-approved medication from a class of drugs known as benzodiazepines that is commonly used to treat anxiety, psychiatric disease, and epilepsy (seizure disorders).

Common, moderate side effects may include:

- Sedation or drowsiness
- Dizziness
- Weakness or unsteadiness

Less common, moderate side effects include:

- Fatigue (tiredness)
- Memory impairment
- Eye function/visual disturbance (including diplopia and blurred vision)
- Dysarthria (difficulty forming or speaking words)/slurred speech
- Headache
- Emotionally unstable
- Worsening of psychiatric disease (unmasking of psychiatric symptoms due to treatment of catatonia)
- Respiratory changes, including worsening sleep apnea
- Gastrointestinal symptoms, including nausea, change in appetite, constipation, change in liver enzyme levels
- A syndrome called ***SIADH*** which can cause cramping, nausea, and vomiting. In severe cases, causing excess urination
- Low blood sodium or a low blood platelet count
- Inconsistent reactions may occur, including anxiety, excitation, agitation, aggression, sleep disturbances, and hallucinations

Rare but severe side effects may include:

- Thinking of suicide/attempting suicide
    - If you are having suicidal thoughts or feel in crisis, call the study investigator at the telephone number listed on the first page of this form. You can also call or text the National Suicide & Crisis Lifeline at 9-8-8 or 1-800-273-TALK (8255). The Lifeline numbers are answered 24 hours a day every day of the year by a skilled, trained counselor. You can also present to a healthcare provider, your local emergency room, or call 9-1-1 to be connected to local emergency services.
- Seizure if medications are abruptly discontinued
- Abuse or addiction when not properly administered

As with all CNS-depressant drugs, anyone receiving lorazepam should be warned not to operate dangerous machinery or motor vehicles and that their tolerance for alcohol and other CNS depressants will be lowered.

Intravenous immunoglobulin (IVIG, Gammagard 10%™)

IVIG is given as an infusion at baseline and then the following day, then once at 4 weeks, and once at 8 weeks. Each infusion takes between 150 - 240 minutes and requires an hour observation after treatment. You can watch videos, walk around, talk with your family, and use the restroom during the treatment.

Common, mild side effects may include:

- Headache
- Fatigue (tiredness)

Common, moderate side effects may include:

- Nausea/vomiting
- Diarrhea
- Migraine
- Dizziness
- Cough
- Rash
- Joint and muscle pain
- Swelling of the limbs

Rare but severe side effects may include:

- Swelling of lining of brain and spinal cord
- A blood clot in the lung
- Allergic reaction

In addition, extravasation is a risk with any infusion. Extravasation is the unintentional leakage of fluid or medication into the surrounding tissues. It can cause discomfort and, in some cases, tissue injury with certain medications. Common symptoms of extravasation may include pain, swelling, and inflammation. If extravasation occurs, the clinic team will follow internal protocols and ensure that the event is assessed by the Study Doctor.

Tofacitinib (Xeljanz™)

Tofacitinib is a member of a class of drugs, called JAK inhibitors, that modulate the immune system and are being studied for their ability to treat a wide variety of immune conditions. tofacitinib is FDA-approved for psoriatic arthritis, rheumatoid arthritis, ulcerative colitis, and polyarticular course juvenile idiopathic arthritis, but not for DSRD. As such, the use of tofacitinib in this study is considered investigational.

Less common, moderate side effects may include:

- Infections, such as upper respiratory tract infections, nasopharyngitis (common cold), and urinary tract infections
- Diarrhea
- Headache
- Hypertension (high blood pressure)

Rare, mild side effects may include:

- Abnormal blood chemistry or cell counts
- Rash
- Nausea

Rare, but severe side effects may include:

- Serious infections, such as pneumonia, cellulitis, and herpes zoster (shingles)
- Development of a tear in your stomach or intestines

- Development of blood clots in your legs or lungs
- Development of cancer

In 2021, the Food and Drug Administration (FDA) issued a warning about the safety of tofacitinib. The warning was in response to a study comparing tofacitinib to a related drug, called Humira. The study was performed in typical individuals ages 50 years and older with rheumatoid arthritis (RA), who were also taking methotrexate and who had risk factors for cardiovascular disease. The study found an increased risk of serious heart events, cancer, blood clots, and death in people taking tofacitinib compared to Humira over approximately four years. More specifically, the tofacitinib group had higher rates of cardiovascular events (3.4% vs. 2.5%) and cancer (4.2% vs. 2.9%).

Because of these findings, this study excludes participants who are over 50 years old, who are taking methotrexate, or who have recent history of blood clot disorders or cancer. In addition, the study team will also monitor your heart function.

If you become pregnant, Tofacitinib may involve risks to the embryo or fetus which are currently unclear. Therefore, we would ask you to immediately stop taking your study drug and you would be removed from the study.

Allergic Reaction Risk

As with taking any drug, there is a risk of allergic reaction. If you have a very serious allergic reaction, you may be at risk of death. Some symptoms of allergic reactions are:

- Rash
- Wheezing and difficulty breathing
- Dizziness and fainting
- Swelling around the mouth, throat or eyes
- A fast pulse
- Sweating

Please seek treatment immediately and tell the study investigator and research staff if you have any of these symptoms.

Unforeseen Risks

There is a risk of potential loss of privacy, although the study team will do everything they can to mitigate this risk, it cannot be guaranteed.

Since the use of the study treatments in this study is investigational, there may be other risks that are unknown. Additionally, there may be unknown risks to a pregnancy, embryo, or fetus if you or your female partner become pregnant.

What are the possible benefits of the study? Will being in this research benefit me?

This study is designed to compare the effects of three potential treatment options for DSRD. Your DSRD symptoms might get better with your randomly assigned study treatment. However, there is no guarantee that your health will improve if you join this study.

Participation in this study will also benefit the greater society. Knowledge that the researchers gain from this study could also help to accelerate research on autoimmunity, inflammation, skin conditions, and neurological conditions in all people, not just in people with Down syndrome.

Are there alternative treatments? What other choices do I have besides taking part in this research?

Instead of being in this study, you may choose to get clinical care through another doctor or through one of the study investigators. There are alternative treatments for DSRD, which you should discuss with your study investigator before enrolling in this study, if you have not already done so.

Make sure you understand all of your choices before you decide to take part in this study. You may leave this study and still have other treatment choices available to you.

Who is paying for this study?

The National Institutes of Health (NIH) Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) is sponsoring this research.

Will I be paid for being in the study?

You will be paid to participate in this study. You will be paid $25 for each blood draw completed for research purposes, up to $175. You will be paid following each completed visit. If you do not complete the study, for any reason, you will be paid for each study visit you do complete.

If you have any questions regarding your compensation for participation, please contact the research staff.

It is important to know that payments for participation in a study is taxable income.

Travel and lodging assistance is available for those more than one hour travel to a study site [maximum]. You will be reimbursed approximately 1 month after you submit your travel receipts to the research staff or arrangements may be made on your behalf. Travel reimbursements are not subject to IRS regulations and will not be reported as income.

Will I have to pay for anything?

The screening procedures in this study are the same tests that would be requested by your doctor for clinical treatment. Thus, they will be billed to your insurance. You may be responsible for co-pay amounts to your insurance. You or your insurance company may be billed for any standard medical care given during this research study.

Research assessments, such as research blood draws, Visit 6 EEG, Visit 6 lumbar puncture, and/or Visit 6 MRI will be provided by the study at no cost to you. Tests and procedures that are done only for the study will **not** be billed to you or your insurance company.

Will I receive any compensation for a research related injury?

If you are hurt or injured during this study, we will arrange to get you medical care if you have an injury that is caused by this research. However, you or your insurance company will have to pay for that care.

By signing this document, you will not lose any of your legal rights or release anyone involved in the research from responsibility for mistakes.

Is my participation voluntary?

Taking part in this study is voluntary. You have the right to choose not to take part in this study. If you choose to take part, you have the right to stop at any time. If you refuse or decide to withdraw later, you will not lose any benefits or rights to which you are entitled and without any effect on

your future medical care. However, please note that the FDA requires that any information collected up to the point of your withdrawal cannot be removed from the study.

Can I be removed from this study?

The study investigator may decide to stop your participation without your permission if the study investigator thinks that being in the study may cause you harm, or for any other reason.

If you leave the study for any reason, the study investigator may ask you to have some end-of-study tests for your safety.

What else should I know about this research?

Other information that may be important for you to consider so you can decide whether to take part in this research is the amount of time this study will take, as well as travel time to and from the study site.

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.

As part of this research, you may be required to use one or more of the following: a phone or web app/ site, an electronic study diary (eDiary), or a device that tracks information about you. While using these, information about you may be collected and shared with the researchers or people outside of the study. This data might include personal health information, location, call logs, text message history, web browsing history, or social media use. A complete description of the data collection and sharing for an app, eDiary, or device can commonly be found in the Terms of Use, End User License Agreement, or Privacy Policy associated with the device. If you would like to read these documents, request a copy or instructions about how to access this information from the study investigator.

While the Terms of Use, End User License Agreement, or Privacy Policy may include statements limiting your rights if you are harmed as a result of your use of the app, eDiary, or device in this study, you do not release the investigator, sponsor, institution, or agents for responsibilities from mistakes. You also do not waive any of your rights as a research participant.

Whom to contact about this study

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns or complaints about the study such as:

- Whom 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 research participant;
- Eligibility to participate in the study;
- The study investigator ‘s or study site’s decision to withdraw you from participation;
- Results of tests and/or procedures;

Please contact the study investigator at the telephone number listed on the first page of this consent document.

If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in this research study.

An institutional review board (IRB) is an independent committee established to help protect the rights of research participants. If you have any questions about your rights as a research participant, contact:

- By **mail**:

  Study Subject Adviser
  Advarra IRB
  6100 Merriweather Dr., Suite 600
  Columbia, MD 21044

- or call **toll free**: 877-992-4724
- or by **email**: adviser@advarra.com

Please reference the following number when contacting the Study Subject Adviser: Pro00067387.

Who will see my research information?

The University of Colorado Denver (UCD) and its affiliated hospital(s) have rules to protect information about you. Federal and state laws including the Health Insurance Portability and Accountability Act (HIPAA) also protect your privacy. This part of the consent form tells you what information about you may be collected in this study and who might see or use it.

The institutions involved in this study include:

- University of Colorado Denver
- Children's Hospital Colorado (Children's Colorado)

Children's Colorado shares a medical record system with the Barbara Davis Center and PedsConnect; therefore, it is also possible that your information could be viewed by healthcare professionals at these organizations.

It is possible that in the future de-identified genetic information could be sent to a national database (for example, dbGAP).

We cannot do this study without your permission to see, use and give out your information. You do not have to give us this permission. If you do not, then you may not join this study.

We will see, use and disclose your information only as described in this form. We will do everything we can to maintain the confidentiality of your personal information, but confidentiality cannot be guaranteed.

The use and disclosure of your information has no time limit. You can cancel your permission to use and disclose your information at any time by writing to the study's Principal Investigator (PI), at the name and address listed below. If you do cancel your permission to use and disclose your information, your part in this study will end and no further information about you will be collected. Your cancellation would not affect information already collected in this study.

Joaquin Espinosa, Ph.D.
(303) 724-7389
Linda Crnic Institute for Down Syndrome
12700 E. 19th Ave. MS 8608
Aurora CO 80045

If you agree to be in this study, you will receive a signed and dated copy of this consent form for your records.

Both the research records that identify you and the consent form signed by you may be looked at by others who have a legal right to see that information, such as:

- Federal offices such as the Food and Drug Administration (FDA) and the Office of Human Research Protections (OHRP) that protect research participants like you.

- People at the Colorado Multiple Institutional Review Board (COMIRB).
- Advarra Institutional Review Board (IRB) that is responsible for overseeing this research.
- The study investigator and the rest of the research team.
- Core labs who perform paid services in conjunction with the study.
- Officials at the institution where the research is conducted and officials at other institutions involved in this study who are in charge of making sure that we follow all of the rules for research.
- Research collaborators or external companies that perform analyses related to the study goals who may receive samples with a Study ID and/or limited data sets.

Your information may be used and disclosed, to do the research, to study the results, and to make sure that the research was done right.

We might talk about this research study at meetings. We might also print the results of this research study in relevant journals. But we will always keep the names of the research participants, like you, private.

You have the right to request access to your personal health information from the study investigator. To ensure proper evaluation of test results, your access to these study results may not be allowed until after the study is completed.

The investigator (or research staff acting on behalf of the investigator) will use your information for the research outlined in this consent form. They will also make *all or some* of the following health information about you collected in this study available:

- Study team personnel at other study sites
- Your provider, if you give us written permission
- The INCLUDE Data Coordinating Center, where de-identified data for all NIH-funded Down syndrome projects must be deposited, after this study concludes.
- External companies who perform services in conjunction with the study objectives.

Information about you that will be collected in this study:

- Name and Demographic Information (age, sex, ethnicity, address, phone number, etc.
- Portions of your previous and current Medical Records that are relevant to this study, including but not limited to diagnosis(es), history and physical, laboratory or tissue studies, radiology studies, procedure results, immunizations.
- Research visit and research test records.
- Psychological and mental health tests.
- Tissue samples and the data with the samples.

What will happen to my recorded information?

In this study we will be recording cognitive testing. We will use video and audio recordings. We will keep this information secure and private. We will store it for 50 years. At the end of that time, we will destroy it.

What happens to data, tissue, blood and specimens that are collected in this study?

Scientists at the study site and the hospitals involved in this study work to find the causes and cures of disease. The data, tissue, blood and specimens collected from you during this study are important to this study and to future research. If you join this study:

- Samples will be transferred to the Linda Crnic Institute for Down Syndrome at the University of Colorado.
- The data, tissue, blood, or other specimens given by you to the investigators for this research no longer belong to you.
- Both the investigators and any sponsor of this research may study your data, tissue, blood, or other specimens collected from you.
- If data, tissue, blood, or other specimens are in a form that identifies you, researchers involved in this study may use them for future research only with your consent or Institutional Review Board (IRB) approval.
- Any product or idea created by the researchers working on this study will not belong to you.
- There is no plan for you to receive any financial benefit from the creation, use or sale of such a product or idea.
- Researchers can look closely at large amounts of your genetic information by sequencing, or “reading”, every letter in your DNA (your genome). Reading a person’s entire genetic code is called whole genome sequencing. The research might include whole genome sequencing (for example, sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen).

HIPAA Authorization for optional additional study procedures (if applicable)

In this form, you are given the option to agree to additional, optional research procedures. You must also give us your permission, under HIPAA rules, to use and disclose the information collected from these optional procedures, as described above.

If you decline to give us permission to use and disclose your information, you cannot take part in these optional procedures, but you can still participate in the main study.

Please **initial** one of the following options:

_____ I give permission for my information, from the optional procedures, to be used and disclosed as described in this section.

_____ I **do not** give permission for my information for any optional procedures to be used and disclosed; I understand that I will not participate in any optional procedures.

Statement of authorization

I have read this form and its contents were explained. My questions have been answered. I voluntarily agree to allow research staff to collect, use and share my health data as specified in this form. I will receive a signed and dated copy of this form for my records. I am not giving up any of my legal rights by signing this form.

Child Participant's Printed Name:

Printed Name of Parent/Legal Guardian (if subject is under AOM)

Signature of Parent/Legal Guardian (if subject is under AOM) **Date**

Adult Participant's Printed Name*

*If the above-named participant is unable to provide direct authorization for the use and disclosure of their personal health information, then a legally authorized representative must sign this form on their behalf. Therefore, by signing and dating this form, I give my authorization for the use and disclosure of the participants personal health information.

Legally Authorized Representative's Printed Name

Legally Authorized Representative's Relationship to Participant:

Legally Authorized Representative's Signature **Date**

Certificate of Confidentiality

A Certificate of Confidentiality has been obtained from the National Institutes of Health for this study to help ensure your privacy. This Certificate means that the researchers cannot be forced to disclose information that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative or other proceedings. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research participants.

The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of federally funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law of, for instance, child abuse or neglect, harm to self or others, and communicable diseases.

The Certificate of Confidentiality will not be used to prevent disclosure for any purpose you have consented to in this informed consent document.

Future Contact

There may be studies in the future that you may be eligible to take part in. Can we contact you in the future about these studies?

Please **initial** one of the following options:

_____ **Yes,** you may contact me about future studies

_____ **No,** you may not contact me about future studies

Optional biospecimen (sample) storage

Do you agree that the samples (blood, genetic samples, CSF) collected from you during this study may be stored and used for future research?

Please **initial** one of the following options:

_____ **Yes, I agree** that my samples may be stored and used for future research

_____ **I do NOT agree** that my samples may be stored and used for future research

Optional consent for incidental findings

This study is not designed to give individual results back to the participant. In very rare instances, we may find results about your health that we feel are important for you and your doctor to know. We may require that these results are returned to you through a medical doctor or genetic counselor whom you choose. This requires us to break the study ID linker that protects your privacy.

Please **initial** one of the following options:

_____ **Yes,** I give my permission to be contacted with results which the study investigator feels is important for me to know.

_____ **No,** I do not give my permission to be contacted with results which the study investigator feels are important for me to know.

Optional consent for research MRI at end of study

You will require an MRI as part of screening purposes before you begin this study. If there are changes seen in this first MRI, the study investigators would like to compare it to a follow-up MRI after the study treatment. This MRI at the end of the study is optional and costs will be covered by the research study. We anticipate about 30% of participants will be asked to complete a research MRI at the end of the study.

Please **initial** one of the following options:

_____ **Yes,** I would like to participate in a research MRI at the end of the study.

_____ **No,** I would not like to participate in a research MRI at the end of the study.

Optional consent for research lumbar puncture at end of study

You will require a lumbar puncture as part of screening purposes before you begin this study. If the results from this test show changes, the study investigators would like to compare it to a follow-up lumbar puncture after the study treatment. This lumbar puncture at the end of the study is optional and costs will be covered by the research study. We anticipate about 20% of participants will be asked to complete a research lumbar puncture at the end of the study.

Please **initial** one of the following options:

_____ **Yes,** I would like to participate in a research lumbar puncture at the end of the study.

_____ **No,** I would not like to participate in a research lumbar puncture at the end of the study.

Optional consent for follow up research visits

You may complete follow up research visits 4 weeks, 6 months and 12 months after the treatment period ends. These visits can be completed with phone or online questionnaires, or in-person as study finds allow. These visits are optional and you can change your mind at any time.

Please **initial** one of the following options:

_____ **Yes,** I would like to participate in follow-up visits after the treatment period.

_____ **No,** I would not like to participate in follow-up visits after the treatment period.

Agreement to be in this study and use my data

I have read this paper about the study or it was read to me. I understand the possible risks and benefits of this study. I choose to be in this study. I will get a signed and dated copy of this consent form.

Permission to enroll

I have been told about the study. I know what is expected of me. I was allowed to ask questions. I had all my questions answered. I give permission to enroll in this study.

Child Participant's Printed Name: _____

STATEMENT OF PARENTAL / LEGAL GUARDIAN PERMISSION

I have read and understand the information in this informed consent document. I have had an opportunity to ask questions and all of my questions have been answered to my satisfaction. I voluntarily agree for my child to participate in this study until I decide otherwise. I do not give up any of my or my child's legal rights by signing this consent document. I will receive a copy of this signed consent document.

_____ _____

Signature of Parent/Legal Guardian (if subject is under AOM) **Date**

_____

Printed Name of Parent/Legal Guardian (if subject is under AOM)

_____

Adult Participant's Printed Name*

*If the above-named participant is unable to provide direct consent for study participation, then a legally authorized representative must sign this form on their behalf. Assent for the adult participant should try to be obtained as well. Therefore, by signing and dating this form, I give my consent for his/her participation in this research study.

_____

Legally Authorized Representative's Printed Name:

_____

Legally Authorized Representative's Relationship to Participant:

_____ _____

Legally Authorized Representative's Signature **Date**

_____

Printed Name of Person Obtaining Consent

_____ _____

Signature of Person Obtaining Consent **Date**