Electrophysiological Markers for Interventions in Phelan-McDermid Syndrome and Idiopathic Autism

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STUDY INFORMATION:

Study Title: Electrophysiological Markers for Interventions in Phelan-McDermid Syndrome and Idiopathic Autism

Study site(s): Icahn School of Medicine at Mount Sinai

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SUMMARY OF THIS RESEARCH STUDY:

This document explains a research study you might be interested in allowing your child to join. Participation in the study is voluntary. You can agree to allow your child to join or not. Your decision will not limit your child's ability to receive care at Mount Sinai. You should only agree for your child to take part if you understand the study and if all of your questions about the research study are answered. If you allow your child to join the study, the research team must share any new information with you that may change your mind about your child taking part.

The purpose of this research study is to better understand the use of recombinant human growth hormone (rhGH) treatment in Autism Spectrum Disorder (ASD) and in Phelan-McDermid Syndrome (PMS; a genetic disorder caused by changes within the SHANK3 gene). rhGH is an injection under the skin that contains recombinant human growth hormone. rhGH is approved by the FDA under the brand name Zomacton for the treatment of children with short stature due to primary growth hormone deficiency, among several other indications. It is being used off-label in the current study and is not FDA approved for use in ASD or PMS. This study will also evaluate the use of electrophysiological markers (measures of brain activity) as measures of treatment response.

If you choose to allow your child to take part, your child will be asked to participate in two phases that are both 3 months long with a one month washout period between for a total of 7-8 months.

For the first 12 weeks (3 months) of the study, your child will be put into one of two groups. This is called being "randomized," and it means that your child will be put into a group by chance, like flipping a coin. Half of the individuals in this study will be in the group that takes the active study drug (recombinant

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human growth hormone), and half will be in the other group that takes a placebo. Neither you, your child, nor the Lead Researcher will know which group your child will be in. This information could be obtained in an emergency, however. A placebo looks just like the active study drug but contains no real medicine.

After the first 12 weeks (Phase 1), there will be a 4 week wash-out before Phase 2, which is another 12 weeks. During Phase 2, your child will be placed into the other group, either taking the active study drug or the placebo. This is called a "crossover design."

During each of the two treatment phases, your child will attend a baseline visit where the study drug will first be administered, and then 10 follow-up assessments. Follow-up assessments will occur at Week 2, Week 4, Week 8, and Week 12 in each treatment phase (rhGH or placebo). Assessments will include safety monitoring, physical exams, electrophysiology, interviews, and blood collection.

There is not cost or payment to you for taking part in this research study.

The researchers will ask your permission to have private information and study data stored for as long as deemed necessary by the research team.

If you choose to allow your child to take part, the main risks to your child are headaches, muscle pain, extremity stiffness, and swelling of arms and legs due to retaining water in body. Because rhGH is administered subcutaneously, there is also a risk of pain and irritation at the injection site.

It is important to know that your child may not get any benefit from taking part in this research. Others may not benefit either. However, your child may benefit from taking part in this research. Some possible benefits may be that your child's condition may get better over the course of treatment. We hope that the information gained from this study will help doctors learn more about the use of rhGH in children with ASD and PMS. Seaver Autism Center investigators will not be able to provide rhGH treatment after the trial is complete.

If you are interested in learning more about this study, please continue to read below.

STUDY PARTICIPATION:

Your child may qualify to take part in this research study because they are between ages 2 to 12 and has a diagnosis of ASD or PMS.

Your child's participation in this research study is expected to last 8 months with approximately 11 assessments. Your child will have three months of treatment with rhGH and three months of placebo, in random order, separated by a four week wash-out period.

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The number of people expected to take part in this research study is 45.

Funds for conducting this research are provided by the National Institutes of Health (NIH) grant number R01 NS105845 and New York Community Trust. Pfizer is the manufacturer of growth hormone and has provided the study drug for this research.

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 your child. At most, the Web site will include a summary of the results. You can search this Web site at any time.

This research study will be fully explained to you by a member of the study team. Feel free to ask all the questions you want before you make a decision about whether or not to participate. Any new information that develops during this research study that might make you change your mind about participating will be given to you promptly.

DESCRIPTION OF WHAT IS INVOLVED:

If you agree to permit your child's participation in this research study, the following information describes what may be involved.

Your child will participate in two treatment phases, each 12 weeks long. During one treatment phase, your child will receive active study drug (rhGH), and during another treatment phase, your child will receive placebo. The order of treatment phases will be random, like flipping a coin, and neither you, your child, nor the Lead Researcher will know which group your child will be in. Therefore, your child will receive active drug for 12 weeks and placebo for 12 weeks. There will be a 4 week wash-out period between each of the two phases.

During each of the two phases, there will be a baseline visit where the study drug will first be administered, and then 10 follow-up assessments. Follow-up assessments will occur at Week 2, Week 4, Week 8, and Week 12 in each treatment phase (rhGH or placebo).

You will be asked to administer rhGH/placebo by injection at home once daily. You will be trained in these methods and you will have scheduled phone calls and appointments where dose and tolerability will be discussed.

Study participation will occur at the Seaver Autism Center and the Clinical Research Unit (CRU) at Mount Sinai. Due to COVID-19, specific assessments will be completed remotely via phone call, video conferencing, RedCap forms, or paper forms when appropriate.

Because this research study involves the use of rhGH, a note must be included in your child's electronic medical record that your child is taking part in the research. This way, anyone involved in your child's

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medical care will know that your child is a study participant, and they can work to avoid any problems or negative outcomes that could arise if they do not know.

Baseline Assessments (Phase 1 & Phase 2) – approximately 2-3 days of testing

- *Physical and Neurological Exam*
- *Medical and Psychiatric History – will include a diagnostic interview as well as measurement of height, weight, and head circumference*
- *Bone X-ray of the hand and wrist – to ensure your child's growth plates are not closed.*
- *Electrocardiography (EKG) – uses non-invasive electrodes taped to the skin on the chest to measure electrical activity of the heart and record the rate and regularity of heartbeats, as well as provide information about the size and position of the heart chambers and whether there is any damage to the heart.*
- *Pregnancy Test (if applicable)*
- *Laboratory Safety measures (through blood draw): 30 mL (approximately 2 tablespoons) of blood will be drawn.*
- *Side effect monitoring*
- *Autism Diagnostic Observation Schedule-2 (ADOS-2) – is a semi-structured play interview that allows the study team to confirm an ASD diagnosis and to quantify symptoms.*
- *Autism Diagnostic Interview-Revised (ADI-R) – is a diagnostic interview about early development in social, communication, and behavior domains.*
- *Intelligence assessment*
- *Vineland Adaptive Behavior Scales-III (Vineland-III) – is an interview about your child's daily functioning.*
- *Aberrant Behavior Checklist (ABC) – is a rating scale used to monitor an array of behavioral features among participants with intellectual disabilities. It takes 15-30 minutes.*
- *Clinical Global Impressions (CGI) Rating Scales – is commonly used to measure symptoms severity and global improvement in treatment studies of participants with developmental disorders. The Severity Scale (CGI-S) is a 7-point scale that requires the clinical to rate the severity of illness at the time of assessment. The Improvement Scale (CGI-I) is a 7-point scale that requires the clinician to assess how much the illness has improved or worsened relative to baseline.*

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- *Caregiver Strain Index (CSI) Questionnaire – is a 21-item questionnaire to assess burden experienced by caregivers and was developed for use in families with children and adolescents with emotional and behavioral disorders.*
- *Children's Sleep Habits Questionnaire (CSHQ) – is a 22-item questionnaire to assess your child's sleep habits and difficulty with sleep.*
- *Sensory Profile – is a parent report instrument that is used to assess various aspects of sensory integration theory. It consists of three scales with correlated subscales. The three primary scales include: Sensory Processing, Modulation, and Behavioral and Emotional Responses.*
- Repetitive Behavior Scales-Revised (RBS-R) is a 42-item rating scale that is completed by a parent of caregiver. It reports on the severity of repetitive behaviors.
- *Caregiver Top 3 Concerns Visual Analogue Scale (VAS) – is a parent/caregiver's explanation of three signs/symptoms causing concern, as well as a rating of severity of those signs/symptoms.*
- *MacArthur-Bates Communication Developmental Inventory (MCDI) – is a parent/caregiver report used to assess the child's expressive vocabulary.*
- *Electroencephalography (EEG) – is a noninvasive recording of your child's brain activity in which they will be asked to wear a spongy cap. While we are recording brain activity, they may be asked to view images on a computer screen, listen to sounds, and/or respond to tasks.*
- *Visual Evoked Potential (VEP) – is a noninvasive technique to evaluate the functional integrity of visual pathways in the brain from the retina to the visual cortex via the optic nerve/optic radiations. Your child will have three electrodes placed on his or her head, and will then need to watch moving patterns on a computer screen for approximately 15 minutes.*
- *Sensory Assessment for Neurodevelopmental Disorders (SAND) – is a sensory observation in which your child is presented with different sensory toys and a corresponding caregiver interview to assess visual, tactile, and auditory sensory reactivity.*

***Week 2 Assessments (Phase 1 & Phase 2)** – approximately 30 minutes of remote testing*

- *Side effect monitoring*

***Week 4 and Week 8 Assessments (Phase 1 & Phase 2)** – approximately one half day of testing*

- *Side effect monitoring*
- *ABC*
- *CGI*

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- *Caregiver Strain Index*
- *CSHQ*
- *Sensory Profile*
- *VAS*
- *EEG/VEP*
- *RBS-R*

Week 12 Assessments (Phase 1 & Phase 2) *– approximately 2-3 days of testing*

- *Physical and Neurological Exam (including height, weight, vital signs, head circumference)*
- *Medical and Psychiatric History*
- *Bone X-ray for bone age*
- *Laboratory Safety measures (through blood draw): 30 mL (approximately 2 tablespoons) of blood will be drawn.*
- *Side effect monitoring*
- *IQ assessment*
- *Vineland*
- *ABC*
- *CGI*
- *Caregiver Strain Index*
- *CSHQ*
- *Sensory Profile*
- *VAS*
- *RBS-R*
- *MCDI*
- *EEG/VEP*
- *SAND*

Please note that participants will be able to use concomitant medications provided they are safe to use with rhGH and provided they are on a stable regimen for at least three months prior to study initiation.

Randomization

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During one treatment phase, your child will receive active study drug (rhGH), and during another treatment phase, your child will receive placebo. No one, not you, or anyone from your medical team or from the research team will be able to choose what group your child is assigned to. It will be by chance, like flipping a coin. Your child will have an equal chance of being in the study group that gets study drug in the first phase and the study group that gets the study drug in the second phase. Neither you nor the Lead Researcher or your child's doctor will know which study group your child is in. If there is an emergency, they can get this information.

Pregnancy

If your child can possibly get pregnant, a urine test for pregnancy will be done before your child begins the study.

Your child cannot be included in the study if they are or become pregnant, as the study drug could harm the fetus. Your child also should not be in the study if they are producing milk to feed a child as the study drug could harm your child's baby.

Unless your child is sexually abstinent (not having genital sex) the recommended methods of birth control are:

- The consistent use of an approved hormonal birth control (pill/patches, rings),
- An intrauterine device (IUD),
- Contraceptive injection (Depo-Provera),
- Double barrier methods (Diaphragm with spermicidal gel or condoms with contraceptive foam),
- Sexual abstinence (no sexual intercourse) or
- Sterilization.

All birth control methods (other than abstinence and sterilization) are only effective if your child uses them properly, starts them at least one month before they begin the research study, and continues using them throughout the research study and for one month after the research study ends. If you are unsure whether the method of birth control your child uses is approved to use while your child is in this study, you should ask the Lead Researcher before your child begins the study. If your child or your child's partner becomes pregnant, or may be pregnant, at any time during the study, you must tell a person from the research team immediately. The team may stop the study drug and refer your child/your child's partner to an obstetrician/gynecologist for follow-up.

Should your child/your child's partner become pregnant, whether or not your child/your child's partner has the baby, the people funding and overseeing the research may ask for information on the

pregnancy, even if your child is no longer part of the study. Additional written consent will be obtained to share this information if that happens.

Semen/Sperm:

Drugs can be found in semen and alter sperm. Since your child is taking part in a study using experimental drugs or treatments, it is recommended that 1) your child use a condom, 2) your child does not get a partner pregnant or expose them to semen, and 3) your child does not donate semen. These recommendations apply both while your child is taking the study drug, and for 3 months after your child stops taking the study drug. This is because levels of the study drug may be present in the sperm and/or semen even after your child stops taking the study drug. Your child is encouraged to tell female partner(s) and/or their doctor(s) that they are participating in this clinical trial.

Future Contact:

The researchers may wish to use your personal contact information to contact you in the future. Do you give the researchers permission to **contact you** in the future to request the collection of additional information about your child, discuss how your child's private information, study data and/or samples might be used, or discuss possible participation in another research study?

Please initial your choice: Yes_____ No_____

If "Yes", please indicate your preferred method of contact: (initial all that apply)

[ ] Email [ ] Phone [ ] Letter [ ] Text

USE OF YOUR DATA:

The researchers would like your permission to keep your child's personal information (such as, name, address, date of birth, social security number), study data and/or samples (blood, tissue, urine, saliva, or any other body matter) to use or share in future studies. Your child can still be part of the study if you do not allow us to use or share them. Please select Yes or No to each of the questions below. To decline all future uses/sharing please select 'No' each time.

You should also know that it is possible that products may someday be developed with the help of your information, and there are no plans to share any profits from such products with you or your child.

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(1) Will you allow the researchers to store your child's data to use in future research studies?

Please initial your choice: Yes_____ No_____

If you select No, please stop here and move to the next section, **'Your Responsibilities If You Take Part in This Research**' section below."

If yes, please continue to the next question and tell us how your child's personal information, study data and/or samples may be used in future research studies.

(2) Do you give the researchers permission to keep your child's data indefinitely, so they could use it in future studies that are **directly related** to the purpose of the current study?
Please initial your choice: Yes_____ No_____

(3) Do you give the researchers permission to keep your child's data indefinitely, so they could use it for future studies that are **not related** to the purpose of the current study (for example a different area of research)?

Please initial your choice: Yes_____ No_____

(3.1) From time to time, researchers outside of medicine and related sciences would like to use your child's data and/or samples. This might be in the fields such as anthropology, human origins, mapping human migration patterns. Do you give permission for researchers **outside the field of medicine** to use your child's data and/or samples?

Please initial your choice: Yes_____ No_____

a. If the future research in a different area can be done without having to know that the data and/or samples came from your child personally, that will be done.
b. If the future research in a different area requires that it is known specifically who the data and/or samples came from, then one of the following will be done:
   I. If you allowed the researchers to contact you in the future, they may be able to contact you to explain why your child's data and/or samples is needed and what will be done with it. Your permission will be asked to use your child's data and/or samples in that research project.
   II. If you do not give permission to be contacted in the future, or if it is found that contacting you is not practical (for example, because you have moved), your child's data and/or samples may still

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be used. The Institutional Review Board (IRB) will be asked for permission to use the data and/or samples linked to your child's identity. The IRB can give permission for researchers to use and share identifiable health information without contacting you, but only if it determines that sharing the data and/or samples will not be more than minimal risk to your child or your child's privacy. The IRB is a committee of doctors and scientists and nonscientists, including people not associated with this hospital or medical school, whose job it is to protect people who participate in research.

(4) Do you give permission to have your child's data and/or samples given **to other researchers,** including those at Mount Sinai, other medical or scientific institutions and for-profit companies, for use in research within the limits you have chosen above?

Please initial your choice: Yes_____ No_____

(5) Do you give permission to have portions of your child's data deposited in large public databases (repositories) for use in research with the limits you may have chosen above? Please read the paragraphs below which explains repositories, then initial your choice:

Please initial your choice: Yes_____ No_____

To do more powerful research, it is helpful for researchers to share data and/or samples from the people they study. They do this by putting data and/or samples into a repository. A repository is where something is stored safely for a specified period of time. Data and/or samples from one study may be stored in a repository along with data and/or samples from other studies. Sample repositories are commonly called biobanks, while data repositories are commonly called databases. Researchers can then use the data and/or samples from multiple studies to learn even more about health and disease. If you agree to allow your child to take part in this study, some of your child's genetic and health information might be placed into one or more scientific databases, but they will not share your child's direct identifiers (for example, name, address, date of birth). These databases are maintained by either Icahn School of Medicine at Mount Sinai, another institution, the federal government, or private companies. Any researcher who wants to do a study using data and/or samples from the repository must apply for permission. There are different ways of reviewing such requests. Researchers with an approved study may be able to see and use your child's data, along with that from many other people. Researchers may use your child's samples for genetic sequencing and other experimental testing. Researchers will always have a duty to protect your child's privacy and to keep your child's information confidential, but there are always risks associated with data and/or sample collection and sharing. They are described in more detail in the Risks section.

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National Database for Autism Research (NDAR) Data-Sharing

With your consent, this study will collect and provide research data and related findings to the National Database for Autism Research (NDAR). NDAR is a biomedical informatics system and data repository created by the National Institutes of Health—part of the U.S. Department of Health and Human Services (DHHS), an agency of the U.S. Government—to assist biomedical researchers working to develop a better understanding of autism and/or to develop more effective methods to diagnose, treat and prevent autism spectrum disorders. Data entered into NDAR will be kept confidential, but may be accessed and used broadly by approved users for research and other activities as authorized by and consistent with law. Data provided to NDAR as part of your child's participation in this research study will be de-identified using a Global Unique Identifier, a computer-generated ID, which cannot be linked back to your child's identity—for example, your child's name will be separated from the data. However, since this institution and others submitting data to NDAR will still retain individually identifying information related to the data provided, the NIH has issued a legislatively authorized "Certificate of Confidentiality" to help NDAR and participating institutions avoid being forced (for example, by court order) to disclose information that may identify you as an NDAR participant in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings.

You should understand that we, the investigators, are also permitted to make voluntary disclosures with respect to information that is submitted to NDAR, but do not plan to do so except in the event of severe threats to public health or safety. If, as part of your child's participation in this research study itself, we learn about serious harm to your child, or someone else, we would take steps to prevent that harm including notifying appropriate authorities like the police or child welfare.

If you consent to sharing your data with NDAR, you may at any time request that your child's data be removed from NDAR, but you must do so in writing to the Lead Researcher at the address on the first page. If you do not to consent to sharing your child's data with NDAR, you will still be eligible to participate in this study.

(6) I consent to sharing my child's data with NDAR:

Please initial your choice: Yes_____ No_____

Whether or not you have allowed us to share your child's data and/or samples with NDAR, the researchers at Mount Sinai will keep data and/or samples collected about your child during this research study to use in future research studies consistent with the wishes you expressed above.

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Further, upon reaching the legal age of 18, your child will gain autonomy over their data. The researchers will make their best effort to contact your child using the caregiver contact information provided during the initial visit. This will enable researchers to provide the opportunity for your child to re-consent to the use and sharing of their data, both at Mount Sinai and in aforementioned data repositories. It is emphasized that researchers will make every effort to contact and re-consent your child, though this process may be made difficult by circumstances beyond our control (for example: outdated contact information, study protocol closed or personnel no longer at the institution). If after 3 attempts (e.g., e-mail, phone, mail) we are unable to reach you or your child, we will retain your child's data with the same access or restrictions designated in this consent. Retained data will be anonymized, and identifiers will be destroyed if no consent is obtained. Because we are recruiting children between 2 and 12 years of age, most children's participation will be completed many years before they reach the legal age of 18. We want you to anticipate that we will contact you again in the future.

(7) Do you give permission for your child to be videotaped while completing the study assessments? The video is only being made so that the person rating the assessment can go back and look it over again, to make sure that everything was scored correctly and reliably. Please mark below if you accept for your child to be videotaped. Videotaping is optional and videos will be recorded into an encrypted video storage account to which only the research staff will have access. You have the right to request that the recording be erased at any time. (Please initial your choice):

Yes _____ No _____

Study drug will need to be picked up at the research site approximately every 14 days during the duration of each treatment phase. If you are unable to pick up the study drug, it may be shipped to your residence, and a signature will be required upon receipt. The research staff will track drug shipments and ensure that the research medication has been delivered properly and no temperature excursions have occurred. You must wait for the research team's review of temperature monitoring and subsequent approval prior to using the medication. Accordingly, it will be necessary for the research team to release your personal information (i.e., name, address, contact information) to the courier.

(8) I consent to sharing my personal information with the courier (Please initial your choice):

Yes _____ No _____

YOUR RESPONSIBILITIES IF YOU TAKE PART IN THIS RESEARCH:

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If you decide to allow your child to take part in this research study you/your child will be responsible for the following things: maintaining your child's existing medications, diets, and therapies at current doses/regimens for the duration of the study, attending regular study visits, and administering study medications (by subcutaneous injection) as directed.

COSTS OR PAYMENTS THAT MAY RESULT FROM PARTICIPATION:

You and your child will not be paid for participating in this research study. Being in this research study will not cost you anything extra. Researchers will not pay you or your child for your travel or the time it will take for your child to be in the study.

POSSIBLE BENEFITS:

It is important to know that your child may not get any benefit from taking part in this research. Others may not benefit either. However, possible benefits may be that your child's condition may get better over the course of treatment. Any improvements would likely be short-lived and not persist after treatment ends. We hope that the information gained from this study will help doctors learn more about the use of and treatment with rhGH in children with ASD and PMS. Seaver Autism Center investigators will not be able to provide rhGH treatment after the trial is complete.

POSSIBLE RISKS AND DISCOMFORTS:

Relatively common (>10%) side effects of recombinant human growth hormone (rhGH) include: headaches, muscle pain, extremity stiffness, and swelling of arms and legs due to retaining water in body. Some less common (1-10%) side effects include: bruising, lumps under the skin, gynecomastia (enlarged breast tissue in males), progression of previously present curvature of the spine, resistance to insulin hormone and low thyroid hormone levels. Rare (<1%) side effects include: allergic reaction (such as hives, itching, breathing difficulty, swelling of face/lips), slipped capital femoral epiphysis (a fracture through the growing part of the bone at the hip), benign intracranial hypertension (increased pressure in the brain with headaches and blurring of sight), and pancreatitis (inflammation of the pancreas). Cancer has been found to be associated with long-term treatment with rhGH only in children with a previous history of cancers or with certain syndromes or genetic conditions which are predisposed to cancers.

In addition to these risks, this research may cause harm in ways that are not known.

Because rhGH is administered subcutaneously (under the skin), there is risk of pain and irritation at the injection site. There is also risk of inflammation and increased growth of skin fat cells at the injection

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site. It is recommended to alternate injection sites (upper arm, thigh, buttock or abdomen) with each injection to reduce these risks.

rhGH may also have significant effects on growth. However, growth improvement is not the goal of therapy in this study. Moreover, the rate of growth in participants who have an exuberant response is unwanted. Height, weight, body mass index (BMI) and head circumference will be collected throughout the study.

This research study includes exposure to radiation from X-rays. This radiation exposure is for research purposes, and is in addition to any radiation needed for your medical care. X-rays can damage the genetic material (DNA) in cells. At low doses, cells usually can repair this damage.

Risk from radiation is believed to be related to the total lifetime exposure. For each research study we calculate an "effective dose" to estimate the effects or harm of the radiation on your organs. This quantity will help predict the effect of radiation on tissue. You should think about your own history of radiation exposure from tests (like x-rays or CT scans) in deciding about the radiation usage in this study. If you have questions about the total amount of radiation exposure you will be receiving, you should ask your doctor.

To put your estimated effective dose in perspective, the radiation that you will get for this research study will be 2 mSv (mSv, or milliSieverts, are units representing radiation exposure). This will be less than the average person in the United States receives each year (6.2 mSv) from natural sources (sun, outer space, air, food, and soil) and medical procedures. Based on these calculations, the risk from the radiation exposure in this research study is very small.

An additional risk related to participation is the blood draw procedure. The risks of a blood draw include: pain, bruising, and the remote possibility of infection at the place where the needle goes in, which is reduced by sterile techniques and trained personnel. Some people feel dizzy or may faint during or after a blood draw. We will ask you whether your child has had a history of this in order to reduce possibility of it happening again.

Blood sampling may be uncomfortable for your child and will be kept to a minimum in order to reduce stress of the procedure on your child. The procedures for reducing risk during blood drawing include the assistance of parents in the blood draw procedure, the use of a special lounge chair that will help the child/children relax during the procedure, the use of a numbing cream, if needed, and the use of individuals trained in drawing blood.

This drug may harm a pregnancy or fetus. If your child is pregnant or becomes pregnant, this research may hurt your child's baby or your child's pregnancy in ways that are unknown. The unknown risks could be minor or major (death) for the pregnancy. Your child should not become pregnant or get

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someone pregnant while taking part in this study. Please read the acceptable methods of birth control found under the Description of What Is Involved section of this document.

Group Risks - Although your child's name will not be given to researchers, basic information such as your child's race, ethnic group, and sex may be shared. This information helps researchers learn whether the factors that lead to health problems are the same in different groups of people. It is possible that such findings could one day help people of the same race, ethnic group, or sex as your child. However, they could also be used to support harmful stereotypes or discrimination.

Privacy Risks - Your child's name and other information that could directly identify your child (such as an address, date of birth, or social security number) will never be placed into an external database. However, because your child's genetic information is unique to your child, there is a small chance that someone could trace it back to your child. The risk of this happening is very small, but may grow in the future. Since the database contains genetic information, a break in security may also pose a potential risk to blood relatives as well as your child. For example, it could be used to make it harder for your child (or a relative) to get or keep a job or insurance. If your child's private information was misused, it is possible your child would experience other harms, such as stress, anxiety, stigmatization, or embarrassment from revealing information about your family relationships, ethnic heritage, or health conditions.

There always exists the potential for loss of private information; however, there are procedures in place to minimize this risk. Please note that this also includes sharing data with the National Database for Autism Research (NDAR).

OTHER OPTIONS TO CONSIDER:

You may decide not to allow your child to take part in this research study. If you decide not to allow your child to take part, this will not affect the clinical care your child receives at Mount Sinai. The choice is totally up to you.

Instead of being in this research study, the choices may include: behavioral interventions, speech therapy, physical therapy, and occupational therapy.

There is accumulating evidence of the effectiveness of behavioral interventions, speech therapy, physical therapy, and occupational therapy in improving the behavior, speech, and motor skills in developmental disabilities. There are not physical risks of these interventions although it is possible that they will not be effective.

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New findings that might affect willingness to participate in this study will be communicated to you throughout the study.

IN CASE OF INJURY DURING THIS RESEARCH STUDY

If your child is injured or made sick from taking part in this research study, medical care will be provided. Generally, this medical care will be billed to you and/or your child's health care insurance in the ordinary manner and you will be responsible for all treatment costs not covered by your child's insurance, including deductibles, co-payments and coinsurance. This does not prevent you from seeking payment for injury related to malpractice or negligence. Contact the investigator for more information. In the event of injury, contact Dr. Kolevzon at 212-659-9134 (office) or 347-752-7324 (cell).

ENDING PARTICIPATION IN THE RESEARCH STUDY:

You may stop your child's participation in this study at any time. No matter what you choose, your child's care and benefits through Mount Sinai will not be negatively impacted.

If you decide to stop being in the research study, please contact the Lead Researcher or the research staff.

You may also withdraw your permission for the use and disclosure of any of your child's protected information for research, but you must do so in writing to the Lead Researcher at the address on the first page. Even if you withdraw your authorization, the Lead Researcher for the research study may still use the information that was already collected if that information is necessary to complete the research study. Your child's health information may still be used or shared after you withdraw your authorization if your child has an adverse event (a bad effect) from participating in the research study.

If you decide you don't want your child's data to be used for research anymore, you can contact the researcher and ask to have your child's data withdrawn or labeled so that it will not to be used in additional projects or shared. If your child's data has already been shared with researchers, those researchers will be asked to stop using them. However, if any data has already been shared without your child's identity or a linking code, it won't be possible to retrieve it. Data that has already been used will not be affected by your decision. If your child's data has already been deposited in an external repository, the study team will request that your child's data be removed.

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If you stop your child from being in the research study, the research team may not remove information they have already placed in the study database, and may continue to use that data as part of this study. The research team may ask you whether they can continue to collect information from your child's medical record.

Withdrawal without your consent: The Lead Researcher, the funder or Mount Sinai may stop your child's involvement in this research study at any time without your permission. This may be because the research study is being stopped, the instructions of the research team have not been followed, the Lead Researcher believes it is in your child's best interest, or for any other reason. If data has been stored as part of the research study, it too can be destroyed without your permission.

CONTACT INFORMATION:

If you have any questions, concerns, or complaints at any time about this research, or you think the research has harmed your child, please contact the office of the research team and/or the Lead Researcher at phone number 212-659-9134 or 347-752-7324.

If your child experiences an emergency during your participation in this research, call 347-752-7324 or call 911 or go to the emergency room. Let the emergency room staff know that your child is in a research study so they can contact the Lead Researcher if needed.

DISCLOSURE OF FINANCIAL INTERESTS:

Researchers sometimes get paid for consulting or doing work for companies that produce drugs, biologics or medical devices. If you have questions regarding industry relationships, you are encouraged to talk to the Lead Researcher or visit our website at http://icahn.mssm.edu/ where Mount Sinai publicly discloses the industry relationships of our faculty.

Dr. Paige Siper (a Co-Investigator in this study) is the inventor of the Sensory Assessment for Neurodevelopmental Disorders, one of the tools used in this study to quantify sensory reactivity symptoms. This intellectual property is licensed to Stoelting Co.

If you have questions regarding paid relationships that your physician/researcher may have with industry, we encourage you to talk with him or her, or check for industry relationships posted on individual faculty pages on our website at http://icahn.mssm.edu/.

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MAINTAINING CONFIDENTIALITY – HIPAA AUTHORIZATION:

As part of this study, some of your child's private and/or protected health information will be obtained, used, and shared with your permission. There is a Federal Health Insurance Portability and Accountability Act (HIPAA) that makes sure this is done correctly and safely.

What is protected health information (PHI)?
PHI is the combination of two things:

1. PHI contains information that identifies your child. It will be used to contact you and link your child to their health information, like name, date of birth, medical record number, and address.
2. PHI also contains health information, including information about your child's mental and physical health from your child's visits to doctors or hospitals, or from study visits.

Every time your child visits a hospital or their doctor, PHI is created and recorded in your child's medical record by their healthcare providers. In the same way, the PHI created as part of this study will be linked to who your child is and your child's medical information.

What PHI is collected and used in this research study, and might also be shared with others? As part of this research project, the research team at the hospital(s) involved in the research will collect your child's name, address, telephone number, medical history, (includes current and past medications or therapies, illnesses, conditions or symptoms, family medical history, allergies, etc.). The researchers will also review previous genetic results.

The researchers will also get information from your child's medical record which may come from Mount Sinai Hospital or, with your signed permission, your private doctor.

During the study, the researchers will gather information by:

- Taking a medical and psychiatric history (includes current and past medications or therapies, illnesses, conditions or symptoms, family medical history, allergies, etc.)
- Completing the tests, procedures, questionnaires and interviews explained in the description section of this consent
- Reviewing genetic tests
- Videotaped assessments
- Blood will be drawn for safety assessment

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- You and your child will meet with the study psychiatrist and a trained member of the research staff. The psychiatrist and/or research staff will ask you to fill out rating forms and answer questions about your child's condition.

Why is your child's PHI being used?
Researchers need the information that identifies your child so they can contact you during the study. They need your child's health information and the results of any tests and procedures being collected as part of this study to answer the questions posed in the study. The purpose of the study is discussed earlier in this consent form. Before researchers analyze the data, they remove any information that would let others know who your child is or that your child took part in the study. If researchers publish or present study results at scientific meetings, lectures, or other events, their presentations would not include any information that would let others know who your child is, unless you give separate permission to do so.

The Lead Researcher may also use and share the results of these tests and procedures with other healthcare providers at Mount Sinai who are involved in your child's care or treatment. The research team and other authorized members of The Mount Sinai Health System ("Mount Sinai") workforce may use and share your child's information to ensure that the research meets legal, institutional or accreditation requirements. For example:

1. The Mount Sinai Program for the Protection of Human Subjects is responsible for overseeing research on human participants and may need to see your child's information.
2. If you receive any payments for taking part in this study, the Mount Sinai Finance Department may need your child's name, address, social security number, payment amount, and related information for tax reporting purposes.

- I*f the research team uncovers abuse, neglect, or reportable diseases, this information may be disclosed to appropriate authorities.*

Who, outside Mount Sinai, might receive your child's PHI?
As part of the study, the Lead Researcher, study team and others in the Mount Sinai workforce may disclose your child's protected health information, including the results of the research study tests and procedures, to the following people or organizations: (It is possible that there may be changes to the list during this research study; you may request an up-to-date list at any time by contacting the Lead Researcher.)

- The sponsoring government agency and/or their representative who need to confirm the accuracy of the results submitted to the government or the use of government funds: The National Institute of Health (NIH)

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- The United States Department of Health and Human Services and the Office of Human Research Protection.
- Pfizer – the manufacturer of the study drug.

In almost all disclosures outside of Mount Sinai, your child will not be identified by name, social security number, address, telephone number, or any other direct personal identifier. Some records and information disclosed may be identified with a unique code number. The Lead Researcher will ensure that the key to the code will be kept in a locked file or will be securely stored electronically. The code will not be used to link the information back to your child without your permission, unless the Institutional Review Board (IRB) allows it after determining that there would be minimal risk to your privacy. The Certificate of Confidentiality obtained from the Department of Health and Human Services will not be used to prevent disclosure to local authorities of child abuse and neglect, or harm to self or others. It is possible that a sponsor or their representatives, a data coordinating office, a contract research organization, may come to inspect your child's records. Even if those records are identifiable when inspected, the information leaving the institution will be stripped of direct identifiers. Additionally, *OHRP, as well as the Food and Drug Administration (FDA) will be granted direct access to your child's medical records for verification of the research procedures and data. OHRP and FDA are authorized to remove information with identifiers if necessary to complete their task. By signing this document, you are authorizing this access.* The results of this research may be published. However, your child's name and other identifying information will be kept confidential.

In the event of a serious adverse event, we will ask your permission to share your child's protected health information with Pfizer, the manufacturer of the study drug. A serious adverse event is defined as any undesirable experience with the study drug that results in death, life threatening complications, disability or permanent damage, or hospitalization.

<u>For how long will Mount Sinai be able to use or disclose your child's PHI?</u> Your authorization for use of your child's protected health information for this specific study does not expire.

<u>Will you be able to access your records?</u>
During your participation in this study, you will have access to your child's medical record and any study information that is part of that record. The investigator is not required to release to you research information that is not part of your child's medical record.

<u>Do you need to give the researchers permission to obtain, use or share your child's PHI?</u>
NO! If you decide not to let the research team obtain, use or share your child's PHI, you should not sign this form, and your child will not be allowed to participate in the research study. <u>If you do not sign, it will</u>

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not affect your child's treatment, payment, or enrollment in any health plans or affect your child's eligibility for benefits.

Can you change your mind?
If you withdraw your permission for your child to be in the study, please contact the Lead Researcher or the research staff.

The research team may ask you whether they can continue to collect information from your child's medical record. You will also have to decide if you wish to limit the continued use of the information collected during the study. Under US privacy laws you may also withdraw your permission for the researchers to use and share any of your child's protected information for research, but you must do so in writing to the Lead Researcher at the address on the first page.

Even if you withdraw your permission, the Lead Researcher may still use the information that was already collected, but only to complete this research study. Your child's health information may still be used or shared after you withdraw your authorization if you have an adverse event (a bad effect) from taking part in the research study.

It is important for you to understand that once information is disclosed to others outside Mount Sinai, the information may be re-disclosed and will no longer be covered by the federal privacy protection regulations. However, where possible, Mount Sinai has entered into agreements with those who will receive your child's information to continue to protect your confidentiality.

If researchers are reviewing your child's medical records or asking questions about your child's medical history or conditions, it is possible that they may learn information related to your child's HIV status. If that is the case, the following information concerns you. If researchers are not reviewing your child's medical records or asking questions about your child's medical history or conditions, then you may ignore the following section.

Notice Concerning HIV-Related Information
If you are authorizing the release of your child's HIV-related information, you should be aware that the recipient(s) is (are) prohibited from re-disclosing any HIV-related information without your authorization unless permitted to do so under federal or state law. You also have a right to request a list of people who may receive or use your child's HIV-related information without authorization. If you or your child experiences discrimination because of the release or disclosure of HIV-related information, you may contact the New York State Division of Human Rights at (888) 392-3644 or the New York City Commission on Human Rights at (212) 306-5070. These agencies are responsible for protecting your child's rights.

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Rev 11.11.2022

Effective Date: 3/26/2024
End Date:3/25/2025

Certificate of Confidentiality: To further protect your child's privacy, the researchers have obtained a Certificate of Confidentiality from the Department of Health and Human Services. This is intended to ensure that your child's identity as a participant in this research study will not have to be disclosed as a result from a subpoena, for the purpose of identifying your child in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings other than to the FDA or OHRP as identified above.

The research staff will not share any of your child's personal information, study data and/or samples with anyone who is not a member of the research team, including any family members or friends, other than those identified above. However, you should know that if it is learned that your child or someone else is threatened with serious harm, such as a child or an elderly person being abused, the research team may notify the appropriate authorities if necessary to protect your child or others. A Certificate of Confidentiality does not prevent you, your child or a member of your family from voluntarily releasing information about your child or their involvement in this research. This means that you, your child and your family must also actively protect your child's privacy. If an insurer or employer learns about your child's research participation, and you agree that they can have your child's research information, then the researchers may not use the Certificate of Confidentiality to keep this information from them.

How the Institutional Review Board (IRB) can help you:

This research has been reviewed and approved by an Institutional Review Board (IRB). You may reach a representative of the Mount Sinai Program for Protection of Human Subjects at telephone number (212) 824-8200 during regular work hours (Monday-Friday, 9am-5pm, excluding holidays) for any of the reasons listed below. This office will direct your call to the right person within the Mount Sinai Health System:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You are not comfortable talking to the research team.
- You have questions about your child's rights as a research participant.
- You want to get information or provide input about this research.

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ADULT PARTICIPANT:
Your signature below documents your permission for the child named below to take part in this research study and to the use and disclosure of this child's protected health information. A signed and dated copy will be given to you.

Printed Name of Child: _____

_____	_____	_____	_____
Signature of Parent/Guardian	Printed Name of Parent/Guardian	Date	Time

❑ Parent
❑ Guardian (May provide permission only if legally authorized to consent to the child's general medical care.)

_____	_____	_____	_____
Signature of second Parent/Guardian	Printed Name of second Parent/Guardian	Date	Time

Note on Second Parent: *If the IRB determined both parents must give permission unless an exception below applies, and if documented permission of the second parent of this child is not obtained, indicate the reason: (select one)*

❑ *Second parent is deceased*
❑ *Second parent is unknown*
❑ *Second parent is incompetent*
❑ *Second parent is not reasonably available*
❑ *Only one parent has legal responsibility for the care and custody of the child*

PERSON EXPLAINING STUDY AND OBTAINING CONSENT:

_____	_____	_____	_____
Signature of Consent Delegate	Printed Name of Consent Delegate	Date	Time

WITNESS SECTION:
My signature below documents that the information in the consent document and any other written information was accurately explained to, and apparently understood by, the parent(s)/guardian(s), and that permission was freely given by the parent(s)/guardian(s).

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Signature of Witness	Printed Name of Witness	Date	Time

Assent

- ❑ Obtained
- ❑ Not obtained because the capability of the child is so limited that the child cannot reasonably be consulted.

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