If appropriate for this study, a scanned copy of the signed consent form should be uploaded to the participant's Epic/EMR record.

Patient I.D. plate

# RESEARCH PARTICIPANT INFORMED CONSENT AND PRIVACY AUTHORIZATION FORM

**Protocol Title**: **Pilot Clinical Trial of Modified Atkins Diet for Kabuki Syndrome**

**Application No.:** **IRB00250195**

**Funded By:** **National Institute of Child Health and Human Development (NICHD) 1K23HD101646**

**Oryzon Genomics, Ltd.**

**Principal Investigator:** **Jacqueline Harris, MD, MS**
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You are being asked to join a research study. Participation in this study is voluntary. Even if you decide to join now, you can change your mind later.

The person being asked to be in this research study may not be able to give consent to be in this study. You are therefore being asked to give permission for this person to be in the study as his/her decision maker.

## 1. Research Summary (Key Information):

The information in this section is intended to be an introduction to the study only. Complete details of the study are listed in the sections below. If you are considering participation in the study, the entire document should be discussed with you before you make your final decision. You can ask questions about the study now and at any time in the future.

This study is being led by Jacqueline Harris at Kennedy Krieger Institute. The purpose of this research is to understand the effects the modified Atkins diet has on the cognitive and behavioral performance in people diagnosed with Kabuki Syndrome (KS). In other words, this study will help to determine how a person with Kabuki Syndrome may behave and process information differently after being on the Atkins diet. The study will last for a total of 12 weeks for each participant. We estimate that 15 participants with Kabuki Syndrome Type 1 who are 18 years of age and older will enroll in this study. Participants

must have clinically and genetically confirmed Kabuki Syndrome. Your participation will involve a total of two onsite study visits in Baltimore, Maryland. The first visit will last 2 days, and 12 weeks later, there will be a 1-day final visit.

Participants must comply with the modified Atkins diet, and caregivers will help keep a daily diet log over the course of 12 weeks. You may or may not benefit directly from this study. People who participate in this study may experience improvement in their cognition after the 12-week period of being on the modified Atkins diet, but this cannot be guaranteed. There are no significant costs for participating in this study. Participants will be responsible for any travel costs to Baltimore and for food during the diet period. The cognitive testing, behavioral testing and laboratory costs will be paid for by the research investigators.

The primary risks of this study are related to the modified Atkins diet. Possible risks on the diet include kidney stones, constipation, acidosis, diminished growth, weight loss, and high cholesterol blood levels. There will be weekly check-ins with participants to make sure they are following the diet as instructed and to address any negative side effects of the diet.

## 2. Why is this research being done?

This research is being done to better understand the effect the modified Atkins diet has on the cognitive and behavioral performance in people diagnosed with Kabuki Syndrome. This study is designed to establish a potential treatment through the modified Atkins diet for individuals with Kabuki Syndrome.

***Who can join this study?***

People with clinically definite and genetically confirmed Kabuki Syndrome Type 1 who are 18 years of age and older may join the study.

Participants will be unable to join in the study if they have been diagnosed with another genetic syndrome, a health problem that would make the modified Atkins diet harmful, or if they are unable to travel to Baltimore for the onsite visits, with the first and last visit separated by 12 weeks.

***How many people will be in this study?***

We plan to enroll 15 participants in this study.

## 3. What will happen if you join this study?

If you agree to be in this study, we will ask you to do the following things:

**Initial 2-day study visit in Baltimore, MD:**

**Day 1:**

- Complete exam for clinical diagnostic criteria (approximately 15 minutes)
- Complete Cognitive assessment (approximately 2 hours)
- Have standard blood labs drawn (including Complete Blood Count (CBC), Complete Metabolic Panel (CMP), lipids, urine analysis (UA), free and total carnitine, Vitamin D and selenium) – Please note these labs are a part of standard clinical care
- In addition we will draw blood for DNA methylation testing. Persons with Kabuki syndrome have a specific pattern on methylation testing. We will use this blood to establish a baseline. Later we will see if this changes with the diet. This gives us a clue whether there is any change in the dysfunctional KMT2D protein that is the cause of your Kabuki syndrome. We will also take this blood and expose it in the lab to drugs known to help mouse models with Kabuki syndrome to see if the pattern changes with these and compare that change with the change on diet.

**Day 2:**

- Complete IQ and adaptive testing (approximately 2 hours)
- Complete Neurobehavioral questionnaires (approximately 45 minutes)
- Complete Cognitive assessment (approximately 2 hours)
- Review the modified Atkins diet (referred to as "MAD") with the nutritionist (approximately 2 hours)

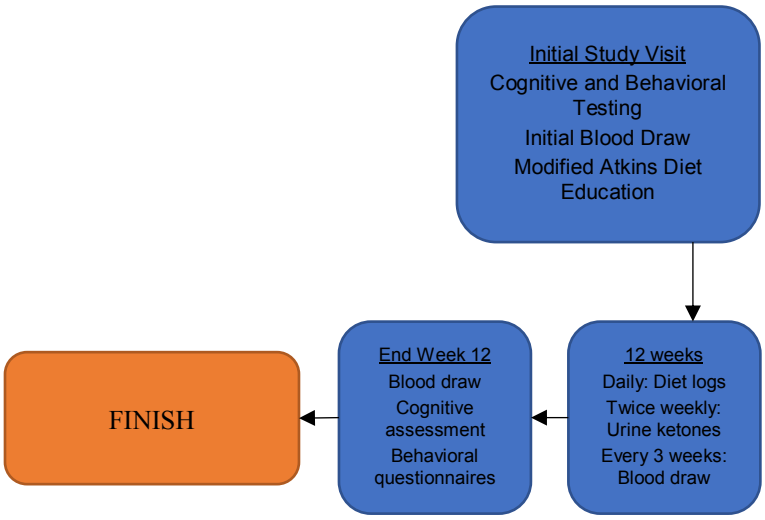
**Over the following 12 weeks after the initial visit:**

- Download free Carb Manager application onto your smartphone and complete diet logs daily
  - Use of the app is optional. You can opt to just type your diet logs and email them to the study team.
- Twice weekly: Use urine ketone strips that are provided to document urine ketones levels in diet log
- Every 3 weeks: Have blood drawn from your local laboratory facility and sent back to Baltimore every 3 weeks to measure Beta-hydroxybutyrate (BHB) levels and DNA methylation blood signatures. BHB is a ketone body that measures if your body is doing what we want it to do on the diet.
- At 6 weeks: Send a urine specimen back with the blood samples for metabolic testing

**Final study visit in Baltimore, MD:**

- Have standard blood labs drawn (including CBC, CMP, lipids, Urine analysis, free and total carnitine, Vitamin D, selenium) – Please note these labs are a part of standard clinical care. We will also measure BHB and DNA methylation and urine metabolic testing.
- Complete cognitive assessment (2 hours)
- Complete Neurobehavioral questionnaires (45 minutes)

**Figure 1: Study Flow**




**Will research test results be shared with you?**

This study involves research tests that we do not expect to be useful for your clinical care. We will not share these results with you.

**How long will you be in the study?**
Participants will be expected to participate in this study for 12 weeks.

## 4. What happens to data and biospecimens that are collected in the study?

If you join this study, your data and biospecimens will be used to answer the research question and your data will be used to publish the findings of this study. Biospecimens may include any of the following: blood, tissue, saliva, urine, bone marrow, cells, etc. Most biospecimens contain DNA, which is the genetic code for each person.

You will not own the data and/or biospecimens collected from you as part of this research study. If researchers use them to create a new product or idea, including those that may have commercial value, you will not benefit financially from those efforts.

Johns Hopkins/Kennedy Krieger Institute researchers and their collaborators may use the data/biospecimens collected in this study for future research purposes and may share some of the data/biospecimens with others.

Because science constantly advances, we do not yet know what future use of research data or biospecimens may include. This future research may be unrelated to the current study and may include outside collaborators.

Sharing data and/or biospecimens is part of research and may increase what we can learn from this study. Often, data/biospecimen sharing is required as a condition of funding or for publishing study results. It also is needed to allow other researchers to validate study findings and to come up with new ideas. Your data and/or biospecimens may be shared with researchers at Johns Hopkins and other institutions, for-profit companies, sponsors, government agencies, and other research partners. Your data and/or biospecimens may also be put in government or other databases/repositories.

We (Johns Hopkins/ Kennedy Krieger Institute) will do our best to protect and maintain your data/biospecimens in a safe way. One of the ways we protect data/biospecimens is by limiting the uses of the information and the type of information that is shared, especially your personal information. This may occur through data/specimen sharing agreements and review by oversight groups within Johns Hopkins.

If data/biospecimens are used or shared with types of information that may be likely to identify, you such as your name, address or medical record number, further institutional review and approval would be required. In these cases, Johns Hopkins will review whether additional consent from you is required. Generally, if your data/biospecimens are used/shared without any personal identifiers or with information that is less likely to identify you (such as the date of a procedure), further review and approval is not needed.

Data/biospecimen sharing could change over time, and may continue after the study ends.

The use and sharing of your data and biospecimens is required for participation in this research study. If you are not comfortable with the use and sharing of your data/biospecimens in future research without further consent, you should not participate in this study.

## 5. What are the risks or discomforts of the study?

**Modified Atkins diet**

- The main risk of this study is related to the modified Atkins diet. Possible risks while on the diet include the following:
  - Kidney stones, constipation, acidosis, diminished growth, weight loss, and high blood cholesterol levels.
  - There will be weekly check-ins with participants to make sure they are following the diet. Participants will also have their follow-up labs monitored closely to address any of the possible effects listed above.
- Patients may show feelings of unhappiness as being on the modified Atkins diet is more restricted than their typical diet.

**Neurological examination and Neuropsychological testing**

- A neurological examination is part of a routine physical examination and involves no more than minimal risk to the participants.
- Minimal risks of the neuropsychological testing include anxiety and discomfort from the long amount of time of the test. If significant anxiety or discomfort occurs, participants will be able to take breaks during the testing periods. You do not have to answer any question you do not want to answer.

**Travel to Baltimore**

Participants may incur a financial fee by having to travel to Baltimore on two occasions separated by a period of 12 weeks.

**Blood Draw**

Taking blood may cause discomfort, bleeding, or bruising where the needle enters the body. In rare cases, it may result in fainting. There is a small risk of infection.

**Identifiable private information**

There is the risk that information about you may become known to people outside this study.

## 6. Are there risks related to pregnancy?

There is no known increased risk during pregnancy. If the participant is pregnant or becomes pregnant during the course of the study, please notify the research team. It is unknown whether this research may hurt an embryo or fetus.

## 7. Are there benefits to being in the study?

You may or may not benefit from being in this study. There is a possibility that participants may experience improvement in their cognition after the 12-week study period while on the modified Atkins diet, but this cannot be guaranteed. If you take part in the study, you may help others in the future.

## 8. What are your options if you do not want to be in the study?

You do not have to join the study. If you do not join, your care at Johns Hopkins and Kennedy Krieger Institute will not be affected.

## 9. Will it cost you anything to be in this study?

Participants will not be responsible for taking on significant costs as part of this study. The neurobehavioral testing and laboratory costs will be covered by the research investigators. Participants will be responsible for their own travel costs to Baltimore. Participants will also be responsible for the cost of their own food during the diet period.

## 10. Will you be paid if you join this study?

No, participants will not receive any payment as part of this study.

## 11. Can you leave the study early?

- You can agree to be in the study now and change your mind later.
- If you wish to stop, please tell us right away.
- Leaving this study early will not stop you from getting regular medical care.

If you leave the study early, Kennedy Krieger Institute may use or share your health information that has already been collected if the information is needed for this study or any follow-up activities.

You can go back to your regular diet after the study ends or if you choose to end the study early.

## 12. Why might we take you out of the study early?

You may be taken out of the study if:

- Staying in the study would be harmful.
- You cannot tolerate and/or adhere to the diet during the 12 weeks by your own self report and diet logs.
- You fail to follow instructions.
- The study is cancelled.
- There may be other reasons to take you out of the study that we do not know at this time.

If you are taken out of the study early, Kennedy Krieger Institute may use or give out your health information that it has already collected if the information is needed for this study or any follow-up activities.

## 13. How will your privacy be maintained and how will the confidentiality of your data be protected?

### HIPAA Authorization for Disclosure of Protected Health Information

**What information is being collected, used, or shared?**

To do this research, we will need to collect, use, and share your private health information. By signing this document, you agree that your health care providers (including both Kennedy Krieger Institute and others) may release your private health information to us, and that we may use any and all of your information that the study team believes it needs to conduct the study. Your private information may include things learned from the procedures described in this consent form, as well as information from your medical record (which may include information such as HIV status, drug, alcohol or STD treatment, genetic test results, or mental health treatment).

**Who will see, use or share the information?**
The people who may request, receive, or use your private health information include the researchers and their staff who may be a part of Johns Hopkins Health System, Johns Hopkins University or the Johns Hopkins Applied Physics Laboratory. Additionally, we may share your information with other people at Kennedy Krieger Institute, for example if needed for your clinical care or study oversight. To improve coordination of your research and clinical care, some information about the study you join will be included in your electronic medical record.

By signing this form, you give permission to the research team to share your information with others outside of Kennedy Krieger Institute. This may include the sponsor of the study and its agents or contractors, outside providers, study safety monitors, government agencies, other sites in the study, data managers and other agents and contractors used by the study team.

We try to make sure that everyone who sees your information keeps it confidential, but we cannot guarantee that your information will not be shared with others. If your information is disclosed by your health care providers or the research team to others, federal and state confidentiality laws may no longer protect it.

**Do you have to sign this Authorization?**
You do not have to sign this Authorization, but if you do not, you may not join the study.

**How long will your information be used or shared?**
Your Authorization for the collection, use, and sharing of your information does not expire. Additionally, you agree that your information may be used for similar or related future research studies.

**What if you change your mind?**
You may change your mind and cancel this Authorization at any time. If you cancel, you must contact the Principal Investigator in writing to let them know by using the contact information provided in this consent form. Your cancellation will not affect information already collected in the study, or information that has already been shared with others before you cancelled your authorization.

**How will your information be protected?**
Any physical data forms will be kept in a locked office in a locked cabinet to which only the research investigator has the key. The linking document with patient identifiers and study ID numbers will be kept on a password-protected computer in the locked office, within a password-protected file. This file will be kept separate from all data files including imaging data and testing results. These files will be deidentified and marked with a study identifier only and stored on a secure server.

Therefore, instead of using information that identifies you, there will be other labels assigned to your file. Blood and urine specimens returned to Baltimore will only have a study ID number on them and no other patient identifiers.

The risk of loss of security of private information from use of the CarbManager application is minimal. You will not enter your name or date of birth. You will enter a username (which will be your subject ID for this study), sex, and year of birth. However sex and year of birth can be left out. Other than that you will just enter daily diet logs. You then have the ability to generate weekly reports through the app that will be saved as a pdf to your device which you then will email to the study team. Use of the app is optional for participants and you can opt to just type your diet logs and email them.

## 14. What is a Certificate of Confidentiality?

Your study information is protected by a Certificate of Confidentiality. This Certificate allows us, in some cases, to refuse to give out your information even if requested using legal means.
It does not protect information that we have to report by law, such as child abuse or some infectious diseases. The Certificate does not prevent us from disclosing your information if we learn of possible harm to yourself or others, or if you need medical help.

Disclosures that you consent to in this document are not protected. This includes putting research data in the medical record or sharing research data for this study or future research. Disclosures that you make yourself are also not protected.

## 15. What treatment costs will be paid if you are injured in this study?

Kennedy Krieger Institute does not have a program to pay you if you are hurt or have other bad results from being in the study.

However, medical care at Johns Hopkins and Kennedy Krieger Institute is open to you as it is to all sick or injured people.

The costs for any treatment or hospital care you receive as the result of a study-related injury that are not covered by a health insurer will be billed to you.

By signing this form, you will not give up any rights you have to seek compensation for injury.

## 16. What other things should you know about this research study?

During the study, we will tell you if we learn any new information that might affect whether you wish to continue to participate.

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. If you would like to review the information for this study, or a summary of the results, ask the study team doctor for the ClinicalTrials.gov study registration number.

During this study, you will not have access to certain medical information and test results collected for study purposes. If an emergency occurs while you are in the study, medical information needed for your treatment can be made available to your study doctor and other physicians who treat you. When the study is completed, all the information in your medical record will be available to you.

**What is the Institutional Review Board (IRB) and how does it protect you?**
This study has been reviewed by an Institutional Review Board (IRB), a group of people that reviews human research studies. The IRB can help you if you have questions about your rights as a research participant or if you have other questions, concerns or complaints about this research study. You may contact the IRB at 410-502-2092 or jhmeirb@jhmi.edu.

**What should you do if you have questions about the study, or are injured or ill as a result of being in this study?**
Call the principal investigator, Jacqueline Harris at 667-205-4295. If you wish, you may contact the principal investigator by letter. The address is on page one of this consent form. If you cannot reach the principal investigator or wish to talk to someone else, call the IRB office at 410-502-2092.

If you have an urgent medical problem or think you are injured or ill because of this study, call 911 or go to your local emergency department. You should also call Jacqueline Harris at 667-205-4295 during regular office hours and at 937-681-0492 after hours and on weekends.

## 17. Optional Study Components:

This part of the consent form is about optional component(s) of the study that you can choose to take part in or not. You can still take part in the main study even if you say "no" to this/these optional component(s).

**Future Contact**

We would like your permission for our research team to contact you in the future. Please note that your decision below does not prevent other researchers at Kennedy Krieger Institute from contacting you about other research.

**Please sign and date your choice below:**

**YES** ☐ _____ _____
Signature of Participant Date

**NO** ☐ _____ _____
Signature of Participant Date

## 18. What does your signature on this consent form mean?

Your signature on this form means that you have reviewed the information in this form, you have had a chance to ask questions, and you agree to join the study. You will not give up any legal rights by signing this consent form.

## WE WILL GIVE YOU A COPY OF THIS SIGNED AND DATED CONSENT FORM

| Signature of Participant | (Print Name) | Date/Time |
|---|---|---|

| Signature of Person Obtaining Consent | (Print Name) | Date/Time |
|---|---|---|

| Signature of Legally Authorized Representative (LAR)<br>**FOR ADULTS UNABLE TO CONSENT** | (Print Name) | Date/Time |
|---|---|---|

| Relationship of LAR to Participant<br>(Indicate why the LAR is authorized to act as a surrogate health care decision-maker under state or applicable local law) | Date/Time |
|---|---|

**NOTE: A COPY OF THE SIGNED, DATED CONSENT FORM MUST BE KEPT BY THE PRINCIPAL INVESTIGATOR AND A COPY MUST BE GIVEN TO THE PARTICIPANT. IF APPROPRIATE FOR THIS STUDY, A SCANNED COPY OF THE SIGNED CONSENT FORM SHOULD BE UPLOADED TO THE PARTICIPANT'S EPIC/EMR RECORD (UNLESS NO MEDICAL RECORD EXISTS OR WILL BE CREATED).**