Study Title: **CBDV vs Placebo in Children and Adults up to Age 30 With Prader-Willi Syndrome (PWS)**

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KEY INFORMATION FOR CANNABIDIVARIN (CBDV) VS. PLACEBO IN CHILDREN AND ADULTS UP TO AGE 30 WITH PRADER-WILLI SYNDROME (PWS)

We are asking you to choose whether or not to volunteer for a research study about using CBDV to treat irritability in children and adults up to age 30 with Prader Willi Syndrome (PWS). This page is designed to give you key information to help you decide whether to participate. We have included detailed information after this page. Ask the research team questions. If you have questions later, the contact information for the research investigator in charge of the study is below.

WHAT IS THE STUDY ABOUT AND HOW LONG WILL IT LAST?

By doing this study, we hope to learn if CBDV will help reduce irritability in 5-30 years old with PWS. Your participation in this research will last about 12 weeks with additional two weeks for screening and 2 weeks for follow-up, totaling up to 16 weeks.

The purpose of this research is to gather information on the safety and effectiveness of CBDV. CBDV is not approved by the U.S. Food and Drug Administration (FDA). This means that CBDV can only be used in research studies.

WHAT ARE KEY REASONS YOU MIGHT CHOOSE TO VOLUNTEER FOR THIS STUDY?

- Your child's behaviors may improve
- You will be reimbursed for your time ($50 for screening and $40 for each subsequent visit)
- Information collected from your participation may help people with PWS in the future
- Participation does not require you to change any of your current treatments

For a complete description of benefits, refer to the Consent Document below.

WHAT ARE KEY REASONS YOU MIGHT CHOOSE NOT TO VOLUNTEER FOR THIS STUDY?

- You may not receive the active drug (may be on placebo)
- *Your participation requires you to be evaluated every 2 weeks, with 2 in-person on-site visits and 7 remote visits, for a total of* up to 16 weeks.
- You will have to get some blood draws

For a complete description of risks, refer to the Consent Document below.

DO YOU HAVE TO TAKE PART IN THE STUDY?

If you decide to take part in the study, it should be because you really want to volunteer. You will not lose any services, benefits or rights or access to care you would normally have if you choose not to volunteer.

WHAT IF YOU HAVE QUESTIONS, SUGGESTIONS OR CONCERNS?

The person in charge of the study is Dr. Eric Hollander. If you have questions, suggestions, or concerns regarding this study or you want to withdraw from the study his/her contact information is:
Phone: 718-839-7516
Email: eholland@montefiore.org

If you have any questions, suggestions or concerns about your rights as a volunteer in this research, contact staff in the Einstein Institutional Review Board (IRB) between the business hours of 9am and 5pm EST, Monday-Friday at 718-430-2253 or irb@einstein.yu.edu

ALBERT EINSTEIN COLLEGE OF MEDICINE
MONTEFIORE MEDICAL CENTER

DOCUMENTATION OF INFORMED CONSENT AND HIPAA AUTHORIZATION

If you are a parent or legal guardian of a child who may take part in this study, permission from you and the assent (agreement) of your child may be required. When the word "you(r)" / "my" / "me" / "I" appears in this consent form, we mean the participant (you or your child); "we" means the research study doctors and research staff.

Introduction

You are being asked to participate in a research study called **CANNABIDIVARIN (CBDV) VS. PLACEBO IN CHILDREN AND ADULTS UP TO AGE 30 WITH PRADER-WILLI SYNDROME (PWS).** Your participation is voluntary -- it is up to you whether you would like to participate. It is fine to say "no" now or at any time after you have started the study. If you say "no," your decision will not affect any of your rights or benefits or your access to care.

The researcher in charge of this project is called the "Principal Investigator." His name is Dr. Eric Hollander. You can reach Dr. Hollander at:
Office Address: 1300 Morris Park Ave
Bronx NY, 10461
Telephone #: 718-839-7516
For questions about the research study, or if you believe you have an injury, contact the Principal Investigator or the IRB.

The Institutional Review Board (IRB) of the Albert Einstein College of Medicine and Montefiore Medical Center has approved this research study. The IRB # is in the stamp in the upper right hand corner. If you have questions regarding your rights as a research subject you may contact the IRB office at 718-430-2253, by e-mail at irb@einstein.yu.edu, or by mail:

Einstein IRB
Albert Einstein College of Medicine
1300 Morris Park Ave., Belfer Bldg #1002
Bronx, New York 10461

Support for this research study is provided by the Foundation for Prader Willi Research and GW Pharmaceuticals

Why is this study being done?

There is an unmet need for treatments to treat a range of symptoms in Prader-Willi Syndrome (PWS). Irritability (often displayed through temper tantrums and rigid behaviors) is a key feature of PWS that significantly disrupts the daily functioning of individuals with PWS and their families. Research has shown CBDV has a good safety profile, good tolerability and efficacy in pediatric patients with epilepsy. This research trial is being completed to study the safety and efficacy of CBDV on irritability in individuals with age range from 5 to 30 years old diagnosed with PWS.

CBDV is not approved by the U.S. Food and Drug Administration (FDA). This means that CBDV can only be used in research studies.

Why am I being asked to participate?

You have been asked to take part in this research study because you/ your child is between the ages of 5 and 30 years and has been diagnosed with PWS.

How many people will take part in the research study?

You/ your child will be one of about 36 individuals who will be participating in this study. The study will be conducted at Montefiore Medical Center/Albert Einstein College of Medicine.

How long will I take part in this research?

It will take you about 16 weeks to complete this research study. During this time, we will ask you to make 2 study visits to Albert Einstein College of Medicine/ Montefiore Medical Center. (Baseline and Week 12)

In addition, we will ask you to complete 7 remote visits throughout the study duration as well. They will involve assessments performed over the phone, and 3 of the remote visits will include a blood draw at your local QUEST diagnostic center (Screening, Week 2, and Week 4).

What will happen if I participate in the study?

The **Screening Visit** will be performed remotely over the phone and takes about 4 hours. During this visit, we will collect some information to see if you/your child may be eligible to take part in this research study. The study doctor will review the results of these tests and procedures. If you aren't eligible, the study doctor will tell you why. At this visit we will:

- Review the Informed Consent and discuss Assent (if applicable)
- Ask you about your child's medical and psychiatric history
- Review your child's current medications and treatments.
- Give you some questionnaires to fill out about your child

If your child appears to be a good candidate for the study, we will schedule you for an appointment at your local Quest lab, where they will

- Draw a blood sample from you/ your child for screening safety labs
- Test your child's urine for drugs'
- For female participants who have reached menarche, a pregnancy test will be performed either by urine or blood. Pregnant women cannot take part in this research study.

If your lab results are within study parameter, we will contact you and schedule you for an in person visit.

Prior to your first in-person visit, we will send you an electronic device called Actigraphy in the mail. It tracks activity and sleep pattern. Please wear the device continuously for at least three days to allow adequate data capture before coming to the baseline visit.

If you are currently taking any medications, you can stay on them. However, you will need to be on the same dose of the medicine(s) for 4 weeks before you are assigned to the CBDV or placebo group.

The next visit, called the **baseline (or randomization) visit**, will be conducted on site at Montefiore/Einstein and take about 3 hours. At this visit, we will:

- Review you/ your child's current medications and treatments.
- Ask you about health problems since you/ your child's last visit.

- If your child is a female able to become pregnant, we will test her urine for pregnancy and collect a menstrual diary.
- Test your child's urine for certain drugs.
- Obtain blood samples for safety labs.
    - If your child has been unable to provide a urine sample (at this visit or the screening visit), drug testing will be done by blood.
- Give your child a physical exam, including height, weight, body composition and "vital signs" (blood pressure, temperature, heart and breathing rates)
- Perform an ECG with your child.
- Give your child a brief intelligence test (if able)
- Ask you to complete some questionnaires assessing your child's symptoms, dietary intake and family quality of life.

At this visit, if you continue to meet all study criteria, we will assign you by chance (like a coin toss) to the CBDV group or the placebo group. You and the study doctor cannot choose your study group. You will have an equal chance of being assigned to the CBDV group or the placebo group.

This research study will compare CBDV to placebo. The placebo looks exactly like CBDV, but contains no medicine. During this study you may get the placebo instead of CBDV. Placebos are used in research studies to see if the results are due to the study drug or due to other reasons.

Visits at weeks 2, 4, 6, 8, 10, and 14 (follow-up visit) will take place remotely over zoom or the phone.

At these visits we will:

- Review any changes in your child's current treatments and medications.
- Assess for any side effect or adverse events.
- Assess suicidality with CSSRS.

At **weeks 2 and 4** we will also:

- Schedule the participant for a blood draw at your local QUEST Diagnostic for safety labs.
    - At week 4, if your child is a female able to become pregnant, we will test her urine or blood for pregnancy.

At **weeks 4 and 8**:

- We will email you some questionnaires to fill out and return.
- You will complete assessments and rating forms with our psychologist (remotely).
- You will complete a dietary diary
- If your child is female and has reached menarche, we will collect a menstrual diary
- Our pharmacy will FedEx to you a 1-month supply of treatment.
- We will email you a pre-paid FedEx label and FedEx envelop for you to return your used and unused bottles of treatment (from the previous month).

At **week 14** (follow-up visit):

- You will complete assessments and rating forms with our psychologist (remotely).

Visit 12 will be completed on-site and take about 3 hours. We will:

- Review any changes in your child's current treatments and medications.
- Ask you about side effects or health problems since your child's last visit.
- Check your child's vital signs, weight and body composition.
- Perform an ECG with your child.
- Perform a physical and neurological exam.
- Obtain blood samples for safety labs.
- If your child is a female able to become pregnant, we will test her urine or blood for pregnancy, and we will review her menstrual diary.
- Give you some questionnaires to fill out.
- You will complete assessments and rating forms with our psychologist.
- Review your actigraphy and dietary diary.
- Collect any unused study drug.

To obtain the blood sample, we will wipe the skin on your arm with alcohol to clean it. Then, we will insert a small needle into a vein. Three tubes of blood will be drawn at screening and your in-person visits, about 1.5 teaspoons. At some visits, we will require a lesser amount of blood to check for liver functions. Typically, only 1 tube will be drawn (0.5 tea-spoon).

A description of this clinical trial will be available on 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 study we will review your medical records and put the information we collect in our research records.

Will there be audio and/or video recording?

No

Genetic Testing

No. This study will not involve genetic research or genetic testing. **[**However, DNA extracted from **[specify, e.g., blood cells]** will be stored for future research studies

Genome Sequencing

Nearly every cell in the human body (from your skin to your blood to your saliva) contains a complete set of your DNA. This set of DNA, or operating instructions for everything from your hair color to your predisposition to disease, is known as your genome. Researchers will be mapping out your genome and then searching that genome for mutations (changes) or additions. These changes and additions can be inherited from your parents or can occur randomly.

You should not expect to receive genetic or other test results. We will not be conducting standard tests to evaluate your health. Researchers must study samples from many people over many years before they

know if the results have meaning. In the rare event that we discover something that may help you prevent or treat a serious illness, we may try to locate you and offer you the information.

Specimen Banking (Future Use and Storage)

For the samples draw on site here at Montefiore Medical Center, Albert Einstein College of Medicine, we will store your specimens and information about you in a "biobank", which is a library of information and specimens (tissue and blood) from many studies. These specimens and information can be linked to you. In the future, researchers can apply for permission to use the specimens and information for new studies to prevent, diagnose or treat disease, including genetic research. If you agree to the future use, some of your de-identified genetic and health information (not linked to you) may be placed into one or more scientific databases. These may include databases maintained by the federal government. Your specimens and information may be kept for a long time, perhaps longer than 50 years. You may remove your consent for future research at any time by contacting the Principal Investigator named on the first page of the consent or the IRB office at 718-430-2237. If you do, we will destroy remaining specimens and information but if these were already shared with other researchers, we cannot get them back.

You can choose not to participate in the biobank and still be part of the main study and this will not affect your treatment at this facility**.**

INITIAL ONE (1) OF THE FOLLOWING OPTIONS

_____ I consent to have my specimens and information about me used for future research studies.
_____ I do NOT consent to have my specimens and information about me used for future research studies. Information about me will be kept as long as required by regulations and institutional policy, but will not be used for future studies.

INITIAL YOUR CHOICE BELOW

_____ I consent to be contacted in the future to learn about:
_____ New research protocols that I may wish to join.
_____ General information about research findings.
_____ I do not want to be contacted at all.

Will I be paid for being in this research study?

You will receive a total of $370 for 9 study time points ($50 at screening and $40 for each subsequent time points). If you choose to withdraw from the study before all visits are completed, you will be paid only for the visits you completed.

Some researchers may develop tests, treatments or products that are worth money. You will not receive payment of any kind for your specimens and information or for any tests, treatments, products or other things of value that may result from the research.

Will it cost me anything to participate in this study?

There will be no cost to you to participate in the study.

Taking part in this study will not involve added costs to you. All study drugs will be given free of charge by the sponsor, company or the drug makers. You and/or your insurance company will have to pay for any costs that are part of your regular medical care.

What will happen if I am injured because I took part in this study?

Taking part in this research study may result in injury or harm to you. In the event of an injury resulting from your participation in this study, you should seek appropriate medical care and inform the study doctor. In the event of an emergency you should go to an emergency room.
If you are injured or harmed as a result of participating in the study and receive medical care through the Montefiore Medical Center, a Montefiore doctor, or any other health provider, you will be sent a bill for whatever medical care you receive. All or part of your bill may be paid by your health insurance.

Albert Einstein College of Medicine and Montefiore Medical Center are not offering to provide you the drug/device after the termination of the study or to pay you for pain, worry, lost income, the cost of your medical care or non-medical care costs that might occur as a result of your taking part in this study. However, you do not waive any of your legal rights in signing this form.

Immediately report any discomforts, problems or injuries you experience during the course of your participation in the study to Dr. Eric Hollander at (718) 839-7516.

What else do I have to do?

- aware of and about all medications you are taking including "over-the-counter" remedies and nutritional supplements or herbs.
- You must take your study drug as instructed, returning any unused study drug (including any empty bottles), at every visit.
- If you do not feel well at any time, call your doctor or the research study doctor immediately.
- ***Drugs may cause a reaction that, if not treated promptly, could be life-threatening. It is important that you report all symptoms, reactions and other complaints to the research study doctor.***
- If you think you have become pregnant, contact your research study doctor immediately.
- If any other doctor recommends that you take any medicine, please inform him/her that you are taking part in a research study. You should give the other doctor the research study doctor's name and phone number.
- You may carry out all your normal daily activities.

Confidentiality

The researchers and study staff follow federal and state laws to protect your privacy. This part of the consent form tells you what information about you may be used and shared in the research described in this form. You do not have to sign this form but, if you do not, you may not participate in the research.

The health information that we may use or disclose for the research described in this form includes information from your entire medical record, such as your name, phone number, email, medical diagnoses, dates, test results, social security number, medical record numbers, etc.

Your information and research records will be kept confidential. Your study information will be kept as long as they are useful for the research described in this form.
The only people who can see your research records are:

- Researchers and other individuals who work with the researchers
- Organizations and institutions involved in this research, including those that fund the research, if applicable
- Groups that review research such as central reviewers, Institutional Review Boards, the Office for Human Research Protections, the US Food and Drug Administration, data coordinating centers, and domestic and foreign agencies that regulate research.

The purposes of these uses and disclosures are to (1) conduct the study and (2) make sure the study is being done correctly. The information covered under this form may no longer be protected by federal privacy laws (such as HIPAA) once disclosed, and those persons who receive your health information may share your information with others without your additional permission. All of these groups have been asked to keep your information confidential.

To maintain the integrity of this research study, you generally will not have access to your research-related personal health information. If it is necessary for your care, your research-related health information will be provided to you or your physician.

Are there any times you would not keep my data confidential?
If you give us information that suggests that your child or any other child is being abused, we are required by law to report that information to the Administration for Children's Services (ACS). Reporting this information may put you, your family, or others who are involved at risk of questioning and legal action by the authorities.

What about the results of pregnancy tests for minors (under age 18)?

Under New York law minors (under age 18) who understand the risks and benefits of available treatments can consent to and obtain sexual and reproductive health care without parental involvement or knowledge. New York State law protects the confidentiality of minors regarding such care. When a minor independently consents to sexual and reproductive health care, the health care provider may not disclose information about it to parents or any other third party without the minor's permission, or unless otherwise required or permitted by law.

We will not tell your parents about the results of your pregnancy test unless you give us permission to tell them.

Are there any risks to me?
A risk of taking part in this study is the possibility of a loss of confidentiality or privacy. Loss of privacy means having your personal information shared with someone who is not on the study team and was not supposed to see or know about your information. The study team plans to protect your privacy – see the Confidentiality section above for details.

Questionnaires
You may feel uncomfortable answering questions about you/your children's stress and behavior. You can choose not to answer questions that make you feel uncomfortable.

Blood Draw
Rarely, the vein where we inserted the needle will become sore or red. Sometimes, a temporary harmless "black and blue" may develop. Very rarely, fainting may occur.

Risks of Taking CBDV
To date, 282 people (adult patients and healthy adult volunteers) have taken GWP42006 as a research participant in a GW-sponsored clinical trial. The side effects reported by people who have taken GWP42006 were generally mild to moderate in severity.

In a GW-sponsored trial which looked at convulsions in a type of epilepsy, the following common side effects were reported:

Very common side effects (affected more than 1 person in every 10)

- Diarrhea
- Feeling sleepy.

Common side effects (affected 3 or more people in every 100)

- Feeling nauseous.
- Headache.
- Feeling dizzy.
- Stomach-ache/pain.
- Changes in blood tests that look at how the liver works.
- Changes in anticonvulsant drug levels in the blood.
- Low sodium levels in blood.
- Anemia (low iron levels in blood).
- Back pain.
- Feeling itchy
- Rash.
- Convulsions (only in people who have had convulsions before).

There may be other risks of CBDV that are currently unknown. If you are concerned, please contact your child's trial physician.

As GWP42006 may affect the results of some blood tests, if your child needs a blood test please tell the tester that he/she is taking cannabidivarin as part of a clinical trial

Risks to Women Who Are or May Become Pregnant

The effect of CBDV on an embryo or fetus (developing baby still in the womb), or on a breastfeeding infant, is unknown and may be harmful. Because of these unknown risks, women cannot take part in this study if they are:

- Pregnant
- Trying to become pregnant
- Breastfeeding or sharing breast milk

If you are sexually active and able to become pregnant, you must agree to use one of the birth control methods listed below. You must use birth control for the duration of the study**.**
Acceptable birth control methods for use in this study are:

- Hormonal methods, such as birth control pills, patches, injections, vaginal ring, or
- implants
- Barrier methods (such as a condom or diaphragm) used with a spermicide (a foam,
- cream, or gel that kills sperm)
- Intrauterine device (IUD)
- Abstinence (no sex)

If you miss a period, or think you might be pregnant during the study, you must tell the study doctor immediately. If you become pregnant, you must stop taking the study drug

Taking Study Drug with Other Medications
For your safety during this study, call your study doctor BEFORE you take any:

- New medications prescribed by your doctor
- Other medications sold over-the-counter without a prescription
- Dietary or herbal supplements

Allergic Reaction to Study Drug
Any drug can cause an allergic reaction which could be mild or more serious and can even result in death. Common symptoms of an allergic reaction are rash, itching, skin problems, swelling of the face and throat, or trouble breathing. If you are having trouble breathing, call 911immediately.

New Findings
If we learn any significant new findings during the study that might influence your decision to participate, we will contact you and explain them.

Unknown Risks
We have described all the risks we know. However, because this is research, there a possibility that you will have a reaction that we do not know about yet and is not expected. If we learn about other risks, we will let you know what they are so that you can decide whether or not you want to continue to be in the study.

Are there possible benefits to me?
You may or may not receive personal, direct benefit from taking part in this study. The possible benefits of taking part in this study include**:**

- Direct benefits of participating in the study include:
  - Families will receive feedback on the results of the cognitive and behavioral testing, which may be used to help guide educational and support services for the subject.
- Possible benefits of participating in the study include:
  - Improvement in the symptoms of irritability
- Indirect benefits of participating in the study include:
  - Information learned from this study may, in the future, benefit other people with PWS

What choices do I have other than participating in this study?

You can refuse to participate in the study. You can talk to your doctor about using current treatments for PWS, including Growth Hormone therapy, pharmaceuticals and treatments/therapies for other symptoms. If you decide not to participate, the medical care providers at this facility will still give you all of the standard care and treatment that is appropriate for you.

Are there any consequences to me if I decide to stop participating in this study?

No. If you decide to take part, you are free to stop participating at any time without giving a reason. However, some of the information may have already been entered into the study and that will not be removed. The researchers may continue to use and share the information they have already collected.

To revoke (take back) your consent and authorization, you must contact the Principal Investigator in writing at the address on page 1 of this form. However, you may first call or speak to the Principal Investigator and he will stop collecting new information about you. If you take back your consent and authorization, you will not be allowed to continue to participate in this research study.

If you decide to stop taking part in the study for any reason, we will ask you to make a final study visit. You will need to return all unused study drug and your study drug diary at this visit. The final study visit will take about 3 hours. At this visit, we will:

- Review you/ your child's current medications and treatments
- Ask you about side effects or health problems since you/ your child's last visit
- If your child is a female able to become pregnant, we will test her urine for pregnancy.
- Collect menstrual diary (if applicable)
- Collect height, weight, and "vital signs" (blood pressure, temperature, heart and breathing rates)
- Give you some questionnaires to fill out about your child
- You will also meet with a staff member to complete some assessments
- Draw a blood sample from you/ your child for standard safety labs
- ECG
- Physical and Neuro exam

Can the study end my participation early?

We will not let you participate in the study any more if

- You fail to follow instructions given to you by the research study doctor.
- New information about important medical risks and benefits becomes available.
- You become pregnant.
- For health reasons you need to begin taking medications that are not able to be used while participating in the study.
- You develop medical problems that affect your participation in the study.
- You have a negative reaction to the study treatment or worsening of symptoms.
- Administrative reasons.
- If the investigator or study sponsor stops the study earlier than expected

CONSENT TO PARTICIPATE

I have read the consent form and I understand that it is up to me whether or not my child will participate in a research study. I have had the opportunity to ask questions and have had them answered to my (my child's) satisfaction. I know enough about the purpose, methods, risks and benefits of the research study to decide that I want to take part in it. I authorize the use and disclosure of my child's health information to the parties listed in the authorization section of this consent for the purposes described. I understand that I am not waiving any of my legal rights by signing this informed consent document. I will be given a signed copy of this consent form.

Please initial one selection below:

_____My child appears to understand the research to the best of his or her ability and has agreed to participate.

_____My child is not capable of understanding the information in the assent form.

Parent/Legal Guardian:

_____
Printed Name of Parent/ Legal Guardian

_____
Relation to Subject Subject Name (Printed)

CONSENT TO PARTICIPATE (Parental Permission)

I have read the consent form and I understand that it is up to me whether or not I participate. I know enough about the purpose, methods, risks and benefits of the research study to decide that I want to take part in it. I understand that I am not waiving any of my legal rights by signing this informed consent document. I will be given a signed copy of this consent form.

Printed name of participant	Signature of participant (not applicable for participants under age 13)	Date	Tim
Printed Name of Parent or Guardian (when applicable)	Signature		Time
Printed Name of Person Conducting the Consent Process	Signature	Date	Time