PATH for PWS™
Paving the way for Advances in Treatments & Health for PWS

Informed Consent Form

Sponsors' Information:	Zafgen, Inc. 175 Portland St, 4th Floor Boston, MA 02114 USA Phone: +1 (617) 622-4003 Foundation for Prader-Willi Research (FPWR) 340 S Lemon Ave, Suite 3620 Walnut, CA 91789 USA Phone: +1 (888) 322-5487
Protocol Title:	Non-Interventional, Observational, Natural History Study of Serious Medical Events in Prader-Willi Syndrome
Branded Title:	PATH for PWS Study: Paving the way for Advances in Treatments & Health for PWS
Protocol Number:	ZAF-PWS-001
Protocol Version:	Version 1.0
Protocol Date:	11 June 2018
Principal Investigator:	Theresa Strong, PhD Director of Research Programs Foundation for Prader-Willi Research
Sub-Investigators:	Shawn McCandless, MD Section Head, Genetics and Metabolism University of Colorado Jennifer Miller, MD Associate Professor Department of Pediatrics University of Florida
Site(s) of Investigation:	There are no sites of investigation as all information will be collected using a web interface.
Study Staff Contact:	Global PWS Registry 5455 Wilshire Blvd, Suite 2020 Los Angeles, CA 90036 info@pwsregistry.org phone: +1 (888) 322-5487 ext 702
Emergency Contact:	In the case of an emergency, study participants are to call their local emergency number.

UNDERSTANDING THE TERMS USED IN THIS CONSENT FORM

In this consent form, **"study participant"** refers to the person diagnosed with Prader-Willi syndrome (PWS). Study participants over the age of 18 who understand the consent form and legally provide their own consent are eligible to join this study on their own.

If the study participant is a minor or is unable to provide consent, the consent of the study participant's legally authorized representative is required for participation. **"You"** refers to the study participant's legally authorized representative, who may be a family member or guardian who is legally responsible for the care and health of the study participant. As the authorized representative for the study participant, we encourage you to discuss the study with the study participant to the extent compatible with their understanding.

This is an **"observational research study,"** meaning individuals are observed and certain outcomes are measured over a period of time. This study is also **"non-interventional,"** meaning no treatment is given as part of the study.

The "**sponsors"** of this study are Zafgen, Inc. and the Foundation for Prader-Willi Research (FPWR). Sponsors are responsible for managing and financing the study. Zafgen, Inc. is a biopharmaceutical company that is developing an investigational therapy for patients with Prader-Willi syndrome (PWS). FPWR is a non-profit organization that is working to eliminate the challenges of PWS through the advancement of research and therapeutic development.

The PATH for PWS Study is a **"substudy"** of the Global PWS Registry. A substudy collects additional information from some of the study participants enrolled in the main study to investigate additional research questions. To participate in this study, you and the study participant must also participate in the Global PWS Registry, which is an international registry for patients with PWS that is funded by FPWR and hosted by the National Organization of Rare Disorders (NORD). A **"registry"** collects and stores patient medical information, family history, and other relevant information that may be used by researchers to better understand a disease or medical disorder. The same Investigators and staff members from FPWR who conduct the Global PWS Registry will also conduct this study and are being paid by Zafgen to conduct this study. These individuals will collectively be referred to as **"study staff."**

THE INFORMED CONSENT PROCESS

The study participant is being invited to participate in this observational research study sponsored by Zafgen Inc. and FPWR.

Before you decide if the study participant should participate, you need to understand the purpose of the study, the possible risks and benefits, and what would be expected of you. This process is called Informed Consent.

This informed consent form will explain to you the purpose and procedures of the study, describe possible risks that the study participant may experience, and describe possible benefits, if any, from participating.

This form also describes how the study participant's medical information will be used and disclosed in the study and seeks your authorization for that use and disclosure. This form will also include information about any compensation you may receive for participation and contact information if you have any questions about the study or the rights of study participants.

Please read this form carefully as it will help you be fully informed and aware of what participation in this study will include. If you have additional questions after reading this consent, please contact the study staff using the information listed on page 1 and ask as many questions about the study as you would like. If there are any words or information that you do not understand, the study staff will explain them to you.

If you agree the study participant should participate in this study, you must sign this consent form before starting the study. Study participation is voluntary and you/study participant have the right to stop study participation at any time.

PURPOSE OF THE STUDY

The primary purpose of this study is to study the type and frequency of serious medical events in the PWS population. Serious medical events are those that result in death, are life-threatening, require hospitalization or an emergency room visit, or are medically significant. Medically significant events may include psychosis, significant self-injury, extreme aggression, suicidal thoughts, seizures, pneumonia, major infections, extreme food consumption in short amount of time, and severe edema (swelling due to excess fluid). The frequency of blood clots, prescription medications use, the complexity of PWS, hyperphagia behavior patterns, hyperphagia management strategies, and food-related behavior in the PWS population will also be studied. Hyperphagia means the intense, constant hunger that often occurs in individuals with PWS. Data from the study will be used to help advance the understanding and treatment of PWS as described in the "Potential Benefits from Study Participation" section.

DESCRIPTION OF THE STUDY AND PROCEDURES INVOLVED

Approximately 500 people with PWS who are at least 5 years old, live in the United States, Canada, or Australia, and who are enrolled or are willing to enroll in the Global PWS Registry will participate in this study. (Refer to the consent form for the Global PWS Registry for more information about that study.) This study is anticipated to be active for approximately 4 years. You will be asked to enter information into surveys specific to this study and specific to the Global PWS Registry using the internet, into an online database at study entry and every 6 months. The information entered into the surveys will be combined into one database and analyzed together.

The types of data that you will be asked to enter into the database for use in this study includes, but are not limited to:

Survey Name	Description of Survey	Data Entry Schedule
Consent for the PATH for PWS Study	The consent is this form, which will to help you be fully informed and aware of what participation in the study will include.	Must be completed before enrolling into the study
Getting Started	Asks for you to provide information to personalize your surveys such as your preferred unit of measure and the age and sex of the study participant.	Study entry
Contact Information	Asks for you to provide the study participant's contact information and residence, and your contact information.	Study entry
Participant Demographics	Includes questions about the study participant's weight, height, race, and ethnicity.	Study entry

Survey Name	Description of Survey	Data Entry Schedule
Diagnosis	Includes questions about the study participant's genetic testing, diagnosis details, and symptoms of PWS.	Study entry
Research Trials	Includes questions about the study participant's current participation in other clinical trials or research related to PWS.	Study entry and should be updated if the information changes during the study
General Medical History	Includes questions about the study participant's birth defects, normal body temperature, presence of hernias, medical care, cancer diagnoses, and if the participant has passed away.	Study entry
Thrombosis Risk History	Includes questions about the study participant's history of blood clots and related risk factors.	Study entry
Psychological and Mental Health	Includes questions about the study participant's mental health conditions and psychiatric hospitalizations.	Study entry
Neurological History	Includes questions about neurological problems, tests, hospitalizations, and surgeries and visits to neurologists.	Study entry
Vision History	Includes questions about eye/vision problems, visits to ophthalmologists or optometrists, and eye surgeries.	Study entry
Thrombotic and Serious Medical Events	Includes questions about the study participant's serious medical events, blood clotting events, and related prescription medications.	Study entry and as soon as possible after the event but at least every 6 months
Hyperphagia / Food Behavior Questionnaires and Caregiver Information	The Hyperphagia Questionnaire Clinical Trials (HQ-CT) is a 9-item questionnaire designed to measure the frequency and severity of the study participants' behaviors you observe that are associated with hyperphagia. The Food Behavior Survey is an 8-item questionnaire that assesses the study participant's food-related behavior. Caregiver information includes questions about the study participant's living environment and any significant life changes. Also asks for you to provide the study participant's height and weight.	Study entry and every 6 months
Food Safety Zone Questionnaire	A 30-item questionnaire that assesses the various strategies you may use to manage the study participant's hyperphagia.	Study entry and every 6 months
PWS Profile	A 58-item questionnaire that provides a clinical picture of the complexity of PWS by assessing the frequency and severity of 5 areas: compulsive behavior and hoarding, anxiety and depression, disordered thoughts and perceptions, and externalizing behaviors and aggression.	Study entry and every 6 months
Medications	Includes questions about the name, dose, frequency, start/stop dates of medications that were used to treat a blood clot or a serious medical event.	Only if a blood clot or serious medical event occurs

The surveys required at study entry are expected to take approximately 2 to 3 hours overall to complete. Although you should complete these surveys as soon as possible after entering the study, they do not need to be completed all at once. You can save partially completed surveys online and come back later to complete and submit the surveys. The surveys given every 6 months are expected to take approximately 1 to 2 hours overall to complete. The time it takes to complete the surveys may depend on the amount of information, medical history, or serious medical events that a study participant has.

The study staff may contact you via phone or email to clarify any data entries and may enter data into the database on your behalf based on information you provide. You will also be contacted approximately every 6 months to remind you to complete the required surveys. The study staff may also ask you to upload the study participant's medical records and blood work or test results related to blood clots or serious medical events into the database.

Because this is an observational study, no study drug will be provided and no visits to a doctor or clinic are required.

POSSIBLE RISKS

There are no physical risks to you or the study participant for allowing the study participant's data to be stored and used in this study.

There is an unlikely risk of breach of confidentiality, meaning that someone could get unauthorized access to the information collected about you or the study participant from this study. There are laws against the misuse of confidential information, but they may not give full protection. Strict security safeguards are in place to reduce the chance of misuse or unplanned release of information. If there is a breach in this study's computer system, you will be notified.

POTENTIAL BENEFITS FROM STUDY PARTICIPATION

There is no treatment being provided so there is no direct benefit to the study participant from participating in this study.

Data from this study will be used to help advance the understanding and treatment of PWS by:

- Increasing the understanding of the full range of PWS characteristics
- Identifying trends that generate new insights into PWS, and identifying areas for additional study
- Guiding the development of standards of care
- Expediting the completion of PWS clinical trials
- Accelerating solutions for PWS

VOLUNTARY PARTICIPATION AND HOW TO REVOKE YOUR AUTHORIZATION

Participating in this study is voluntary. Refusing to participate will involve no penalty or loss of benefits to which you/the study participant are otherwise entitled (such as health care outside the study, the payment for health care, and health care benefits).

If the study participant does participate, you are free to change your mind at any time, on behalf of the study participant, but the information collected before you changed your mind may still be used to complete the research that has already started.

You may revoke your authorization regarding the use of the study participant's health information at any time by sending a written notice using the study staff contact information listed on page 1 of this consent form.

STOPPING THE STUDY UNEXPECTEDLY

This study may be stopped unexpectedly for a variety of reasons, including decisions made in the commercial interests of the Sponsors or by local regulatory/health authorities.

In addition, the study doctor or the Sponsors can stop your participation at any time without your consent for any reason including:

- If it is discovered that you do not meet the study requirements
- For administrative reasons including if sufficient number of participants have been enrolled

The study staff will notify you if the study is stopped and inform you of all remaining study requirements.

ALTERNATIVES TO BEING IN THE STUDY

The alternative is for the study participant not to be in the study.

CONFIDENTIALITY AND USE AND DISCLOSURE OF PERSONAL HEALTH INFORMATION

This section explains who will use and share the study participant's health information if you agree for the study participant to be in this study. You must authorize this use and sharing of this information by signing this form or the study participant cannot be in the study.

All of the study participant's information from the Global PWS Registry (including data from surveys described in the table on pages 3 and 4) will be added to the database for this study. The information provided concerning the study participant will be de-identified before being shared beyond the study staff. De-identified means that all the personal identifiers have been removed, including the study participant's name, address, and all other information that identifies the study participant or the study participant's family. Except as set forth in this consent, only the study staff will have access to identifying information, such as names and addresses, that can directly identify you or the study participant. Please refer to the consent form from the Global PWS Registry for more information about how identifiable information is protected.

When the results of this research are published or discussed in conferences, unless your specific consent is obtained, any personal information that could identify you or the study participant will be removed or coded to ensure that, by current scientific standards and known methods, no one will be able to identify you from the information we share. Despite these measures, we cannot guarantee anonymity of your or the study participant's personal data.

A description of this study will be available on https://www.ClinicalTrials.gov, as required by United States law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

Representatives from the National Institutes of Health, United States Food and Drug Administration, NORD, Hummingbird Institutional Review Board (IRB), or other authorized parties may inspect study records during auditing procedures to be sure that this study is being protected according to regulations and policies.

Information that is disclosed pursuant to this authorization may be redisclosed by the recipient, in which case the information may no longer be covered by the federal privacy protection regulations.

Your authorization for use of the study participant personal health information for this specific study does not expire.

You may withdraw your permission for the use and disclosure of any of the study participant's personal information for research, but you must do so in writing to the study staff using the address or email on page 1. Even if you withdraw your permission, the study staff may still use the study participant's personal information that was already collected if that information is necessary to complete the study.

You will be given a copy of this consent/authorization form describing the study participant's confidentiality and privacy rights for this study.

For persons living outside the United States who choose to share information about themselves (or about a person for whom they serve as a legally authorized representative), the same protections for privacy and confidentiality are offered as in the United States. By signing this consent, you acknowledge that you are disclosing information that would otherwise be private. Privacy laws in your country may have different protections than those provided in the United States.

GETTING ANSWERS TO YOUR QUESTIONS ABOUT THE STUDY

You can ask questions about this form or the study at any time. You may have questions about this study or payment during the study. You may have other questions. You should contact the study staff using the contact information listed on page 1 with any questions or concerns.

This research has been reviewed by an IRB for the purpose of protecting your and the study participant's rights. An IRB is a group of people who are responsible for protecting the rights and welfare of people who participate in studies. For questions about your rights as a participant in this study or to discuss other study related concerns or complaints with someone who is not part of the study staff, you may contact Hummingbird IRB, One Broadway, 14th Floor, Cambridge, MA, 02142 USA at 1-855-447-2123 (toll free). Review and approval of this study by Hummingbird IRB is not an endorsement of the study or its outcome.

Do not sign this form unless you have had a chance to ask questions and have received satisfactory answers to all of your questions. Please call the IRB with your questions and concerns about rights as a participant.

COSTS OF PARTICIPATING IN THE STUDY

There will be no cost for participating in the study.

COMPENSATION FOR PARTICIPATING IN THE STUDY

For your time and effort related to your participation in this study, you will receive a $100 e-gift card (to Amazon.com) for completing the required surveys at study entry and a $50 e-gift card (to Amazon.com) for completing the required surveys every 6 months as outlined in the table on pages 3 and 4 of this consent form. If you have any questions regarding your compensation for

participation, please contact the study staff number using the information listed on page 1 of this consent form.

Because this study will evaluate the health and challenges of a large number of participants with PWS over a number of years, some study participants may experience a serious medical event during this time, including death. In the unfortunate event that the study participant passes away, you may be asked to consent to an autopsy at no cost to you to help researchers better understand the cause of death and to learn more about PWS. If the study participant passes away during the study, please contact the study staff number right away using the information listed on page 1 of this consent form.

YOUR ROLE IN THE STUDY

While the study participant is in the study, you must:

- Complete the surveys described in the table on pages 3 and 4 using the data entry schedule provided
- Measure the participant's body weight (ideally on the same scale) and height every 6 months
- Keep your contact information current (address, email, and phone number).

STATEMENT OF THE PERSON SIGNING THE CONSENT

I have read and understand the information provided above describing this study. If appropriate, I have discussed the study with the study participant to the extent compatible with his/her understanding. My questions have been satisfactorily answered and I have signed this form as indication of my desire to allow the study participant to participate in this study. I understand that I will receive an electronic copy of this consent/authorization form.

I authorize the release of the study participant's information to the parties identified in this consent, including the sponsors, the Food and Drug Administration (or other Regulatory Agencies) and Hummingbird IRB. By signing this consent form, I have not given up any of the legal rights that I or the study participant would otherwise have as a participant in an observational study.

[electronic signature field]

If appropriate, select the category that best describes the study participant's legally authorized representative who signed above, select all that apply:

☐ Court-appointed guardian

☐ Durable power of attorney

☐ Health care proxy

☐ Family member / next of kin (describe relationship below):

Relationship to study participant: _____

CHECK all that apply (Yes or No)

You must select "yes" and provide required information for all bullets below to participate in this study.

- I confirm that the study participant has been diagnosed with PWS. Yes _____ No _____
- The study participant is: Male_____ Female _____
- I confirm that the study participant is at least 5 years of age. Yes _____ No _____
- The study participant's birthday is: Date_____ Month _____ Year_____
- I confirm the study participant lives in the United States, Canada, or Australia. Yes _____ No _____
- I give permission on behalf of the study participant to provide research data for this study only for the purposes described above. Yes _____ No _____
- I give permission on behalf of the study participant to provide research data from the Global Prader-Willi Syndrome Registry as described above to be used for this study. Yes _____ No _____
- I give permission to being contacted by the study staff to clarify any data entries, to receiving reminders approximately every 6 months to complete timely entry of new data and to allowing the study staff to enter data on my behalf. Yes _____ No _____

Experimental Research Subjects Bill of Rights

California law, under Health & Safety Code Section 24172, requires that any person asked to take part as a study participant in research involving a medical experiment, or any person asked to consent to such participation on behalf of another, is entitled to receive the following list of rights written in a language in which the person is fluent. The list includes the right to:

1. Be informed of the nature and purpose of the experiment.
2. Be given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be utilized.
3. Be given a description of any attendant discomforts and risks reasonably to be expected from the experiment.
4. Be given an explanation of any benefits to the subject reasonably to be expected from the experiment, if applicable.
5. Be given a disclosure of any appropriate alternative procedures, drugs, or devices that might be advantageous to the subject, and their relative risks and benefits.
6. Be informed of the avenues of medical treatment, if any, available to the subject after the experiment if complications should arise.
7. Be given an opportunity to ask any questions concerning the experiment or the procedures involved.
8. Be instructed that consent to participate in the medical experiment may be withdrawn at any time and the subject may discontinue participation in the medical experiment without prejudice.
9. Be given a copy of the signed and dated written consent form.
10. Be given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element of force, fraud, deceit, duress, coercion, or undue influence on the study participant's decision.