Thank you for attending FPWR’s webinar on the Clinical Trials for PWS. The slides from the presentation are available at <http://fpwr.org/research-webinars>.

We weren’t able to get to several questions; please see responses below.

**QUESTION GROUP #1 – HOW DO I FIND WHAT CLINICAL TRIALS ARE AVAILABLE?**

***Q: Several questions focused on how to stay informed about clinical trials as they became available, and the best way to get specific information on the clinical trials. Another concern was that the clinicaltrials.gov site can be overwhelming. Is there any way to help explain what clinical trials are recruiting participants?***

The clinicaltrials.gov website is extensive and can take some time to learn to navigate, so FPWR has revamped its webpage: <http://fpwr.org/participants-needed-pws-studies> to provide a list of clinical trials that are actively recruiting participants. We will update this site whenever a new PWS trail opens. Weblinks are provided for each study, linking directly to the study on the clinicaltrials.gov site. Once there, you might want to first scroll down to “Eligibility” and see if your child is the correct age and meets the other criteria to be included. Continue scrolling for “Contacts and Locations”. Here you will find the information for the contact person. We encourage you contact that person – they will be knowledgeable about the trial and will be able to get all of your questions answered. You are not obligated to participate in any way.

The <http://fpwr.org/participants-needed-pws-studies> page also lists other types of research studies that are seeking participants with PWS, studies not listed on clinicaltrials.gov (generally surveys and/or non-drug research). We encourage you to think about participating in those studies as well.

There are a number of additional ways to stay informed of opportunities.

1. Sign up for FPWR mailings at fpwr.org. We will announce new clinical trails as they open.
2. Join the FPWR Yahoo! group to get in touch with other PWS families like yours. [Click here](http://health.groups.yahoo.com/group/FPWR/" \t "_blank) to find our group on yahoo and request to join the group.
3. Become a fan of the FPWR Facebook page **[Click here to visit our page!](https://www.facebook.com/pages/The-Foundation-for-Prader-Willi-Research/78626677947?fref=ts" \t "_blank)** , and join the FPWR Facebook group.
4. Sign up to for notifications about the Global PWS Registry and participate once it goes live. In the registry, you will be given the option of allowing researchers to contact you about trial opportunities. To sign up, email Jessica: [Jessica.Bohonowych@fpwr.org](mailto:Jessica.Bohonowych@fpwr.org)

The ClinicalTrials.gov site remains the most comprehensive site for information about clinical trials around the world. We suggest you search with just the term ‘prader-willi’ to get the most relevant studies, specifically for people with PWS.

**QUESTION GROUP #2 – WHO IS ELIGIBLE TO PARTICIPATE?**

***Q: Why is the availability of participation restricted by age? Might not the drug be more effective at one age over another?***

***Q: if a participant of phase 2 was successful will they automatically be asked to phase 3?***

***Q: When looking at the number of subjects for each phase of the clinical trials - are a new set of subjects needed for each stage, or can it be the same subjects for each phase?***

***Q: Can you participate in more than one trial?***

***Q: Would a person have to have genetic confirmation of PWS to be in a study?***

***Q: Do they look at the child and what PWS characteristics affect them the most to know if they are a good candidate for a trial?***

***Q: If a child has an Intellectual Disability and has difficulty communicating, are they always excluded from trials?***

***Q: Many of our kids are not technically obese because their diets are so heavily restricted. Does this create an obstacle when recruiting patients for a new research study?***

***Q: Can families from other countries participate in clinical trials?***

Once you have identified what clinical trial opportunities are available, the next step is to see if you meet the general inclusion/exclusion criteria (“Eligibility”). This information can be found on the clinicaltrials.gov page for each individual trial and may include such things as: age, BMI, medication use, chronic illnesses, type of PWS, etc. These criteria are very carefully designed with the intention of maximizing benefit and minimizing risk, and are scientifically based upon the pre-clinical and early clinical data. So, for example, if a drug is being evaluated for effectiveness in weight loss, it’s likely the participants will need to have a BMI in the “obese” range, so that the effect of the drug can be readily measured. Other drugs may not have weight loss as a primary measure, and thus may allow lean or modestly overweight participants. Most trials do require a genetic confirmation of PWS, but will vary in terms of level of cognitive function or communication required. Participants are not able to be enrolled in more than one trial at a time. This would make it too difficult to tease out the benefits and or risks/side effects of each drug. However, it is possible to complete a trial and to then participate in another, later trial. This is often addressed in the inclusion/exclusion criteria wherein there may be a requirement to have not participated in any other trials over a certain time frame, e.g. the past 6 months. Each trial, even if with the same drug, is completely independent with regards to seeking participants. Inclusion/exclusion criteria can change through phases of trials, based upon previous results and/or the goals of the current study. There are usually no limitations on where you live, as long as you are able to make the required travel/visits/stays.

***Q: Are there any studies recruiting infants?***

A study in France is evaluating oxytocin in newly diagnosed infants with PWS was recently completed. There are other, preclinical studies ongoing, developing new therapies that may be applicable to infants/babies, and which may transition to clinical trials in the near future (1-2 years). We will post about these as soon as they are ready to recruit participants.

**QUESTION GROUP #3 – HOW DO I DECIDE IF I WANT TO PARTICIPATE? (QUESTIONS FOR THE STUDY COORDINATOR AND PRINCIPAL INVESTIGATOR)**

If your family meets the inclusion/exclusion criteria for a trial, or is fortunate to be eligible for more than one trial, you will want to start gathering information on the trial(s) and asking a lot of questions. It is important to understand that seeking information is no way a commitment to participate. It is an opportunity to learn about the study and find the facts you need to make the best decision for your family. In addition, you are able to withdraw from any study at any time. Your points of contact during this process will be the study coordinator and principal investigator (PI) for each individual trial. These individuals are the expert on that trial and their contact information will be available on the clinicaltrials.gov page for that trial. It is important to get to know and be comfortable with the investigators of a study, to develop a relationship of trust where you know all of your questions and concerns are fully addressed. Some of the types of questions that should be directed to the **study coordinator** include:

***Q: How many trips to the facility are you expected to make during the study period, and when? Is there flexibility in the schedule?***

**Q: *How long will the trial last?***

**Q*: How much of drug trials are conducted at the universities and how much in the participant's home? Can blood be drawn at the person's local lab? Could my child's ped act as a medium on behalf?***

***Q: What if my son lives at Latham Centers?***

A: Trial lengths, number of visits, and length of visits vary greatly depending on the Phase and goals. Many of the ongoing and upcoming trials are shorter term with all visits taking place within ~3 months. In general, all samples are collected and clinical exams given at the study site. Those living in group or residential housing are generally still eligible to participate in clinical trials as long as they are able to travel to study sites for the required visits. Sometimes health care personnel will come to participants where they live.

***Q: When an individual is interested in participating in a clinical trial, at what point do they find out whether or not there will be financial assistance for the family - travel expenses, etc***

Information regarding financial assistance and/or reimbursements will be available prior to agreeing to participate in a trial. Usually, the study coordinator will go over those details with you early on, as they review the study schedule.

***Q: How long is the wait period after you apply, to find out if you are selected for the trial?***

A; Investigators are eager to find qualified participants for their trials. Once you have gathered the necessary information, had your questions answered, and have decided to participate, you will generally begin the informed consent process. There may be a short delay if the study has several participants enrolling at once, as the visits will need to be staggered.

***Additional questions for the study coordinator or principal investigator include:***

***Q: When researching clinical trials, where could we find adverse events reported?***

A: The PI and study coordinator receive all information on adverse events and potential side effects from the drug company and will review it with you during the informed consent process to make sure you know about any potential risk. This information includes toxicity data from animal studies that the FDA requires prior to the drug entering clinical studies, as well as data from all previous human studies. Please note that ALL side effects/safety issues are reported to the FDA and PIs, no matter how benign (e.g. delay in time to fall asleep is a known side effect for Beloranib, but may not be any problem for those with PWS). During the course of the study, if a new potential side effect or adverse event occurs, the investigator/study coordinator should also be able to inform you of that. Thus, it is important to have a strong relationship of trust with the investigator/study coordinator and to feel comfortable that they have best interest of the participants in mind.

***Q: Will being in a drug trial have any effect on regular health insurance coverage? (if a trial drug causes some kind of medical issue will regular insurance still cover the issue?)***

A: Most drug trials have a clause in the informed consent documents that states that any medical problems/complications caused by the study medication will be paid for by the sponsor of the study. However, it is up to the PI of the study to determine if the complication is due directly to the drug or not. So, it should not have any effect on health insurance coverage

***Q: Do any of the current studies address cognitive deficits vs. the more dominant issues of appetite & behavior?***

A: Most of current trials are focused on body composition/appetite and social function including anxiety, temper, mood, and autistic behaviors. A study of BDNF levels in PWS is evaluating cognitive function; the study coordinator can provide more specific information. <http://clinicaltrials.gov/ct2/show/NCT01517048?term=prader&recr=Open&rank=13>

Treating cognitive deficits is a relatively new area for therapeutic development, primarily because it was previously felt that intellectual deficits couldn’t be modified by drugs. However, it’s become quite clear that cognitive function might be improved with drugs, and this is most notable in the field of Down syndrome (DS) research, where clinical trials of drugs to improve cognition and memory are underway. Basic research in DS has provided a solid basis for the development of drugs to specifically improve cognition for this population. To date, our understanding of the underlying basis of cognitive difficulties in PWS is much less well understood. Nevertheless, this is an area of investigation that is likely to receive attention moving forward (particularly if the DS studies turn out well).

***Q: What type of trials are these? In other words, if we commit to travel and expenses, would we see benefits even if we get a placebo?***

A: It is important to note that a clinical trial is a scientific experiment. Basically, there is a scientific reason/rationale for why the drug will work, but the only way to know if it is going to work is to conduct the trial. The best way to demonstrate a true effect of the drug is to compare it to a placebo, in fact, in most cases, the FDA will only approve a drug if it has been studied in a blinded, placebo-controlled clinical trial. This is the most rigorous study design and is the least likely to give false results, and therefore the most widely used to gain FDA approval. Drug companies and PIs do recognize that it may be frustrating to participate in a clinical study and never receive the drug. Sometimes, an ‘open label extension” is included in the study design, which allows everyone at the end of the study choose whether or not they would like to receive the drug. This part of the study is not blinded and the data gathered is not as robust as the blinded, placebo-controlled portion of the trial, but it can be beneficial for the company to get more data, and beneficial for individual participants to see if the drug seems to have an effect on them.

**QUESTION GROUP #4 – WHAT HAPPENS AFTER THE TRIAL IS OVER?**

***Q: If a drug is working well and the clinical trial ends, is the drug no longer available to the patient?***

A: In general, once a clinical trial is completed, participants will not have access to the drug again until they are able to enroll in another trial, or the drug is approved and comes to market. Until a drug approved, the only way to gain access to it is through a clinical trial. It is important to remember that the clinical trial process is at the core, a careful scientific experiment. All data must be collected, compiled, and analyzed in order to determine how to proceed.

***Q: What is an average timeline from the time a drug is finally approved by FDA until it is available to the general population?***

A: Once approved by the FDA, a drug is available to the public as soon as the company can manufacture, market, and distribute, typically do so within ~ 6 months.

***Q: Can the public access the clinical trials website to see the results of trials, or is access restricted to researchers/doctors?***

A: The clinical trails website is open to the public.

**QUESTION GROUP #5 – IF I CAN’T PARTICIPATE, HOW CAN I HELP OTHERS DO SO?**

***Q: If a group of parents would like to participate in a trial, however there are no trials going on in their area, how can we petition or request a trial in our area?***

A: Selecting the right study sites is critical for the success of the trial. The doctor(s) leading the study have to have the appropriate scientific and clinical expertise, and the institution(s) need to have the necessary facilities, equipment, laboratories, clinics, and support staff. Unfortunately, it is very difficult to petition a trial to a specific area. Later phase studies (Phase III) do tend to have more sites than a Phase I or II study. Also, for company-supported studies, the travel costs to an approved study site are often reimbursed, and steps can be taken to minimize travel as much as possible.

***Q: Is it possible for a donation to be made for a specific drug study for participant travel expenses, rather than donating to FPWR or PWSA(USA)?***

If you are interested in making a donation directly for a specific study, it’s probably best to contact the study coordinator and/or the study sponsor (found on the clinicaltrials.gov site).

***Q: What else can we do to help if our child is too young to be in a trial?***

Please consider joining the PWS Global Registry (email [Jessica.Bohonowych@fpwr.org](mailto:Jessica.Bohonowych@fpwr.org)); and continue to learn about the clinical trial process. Moral support for trial participants is great, too!

**QUESTION GROUP #5 – WHAT IS THE STATUS OF OXYTOCIN? BELORANIB? GENE THERAPY?**

***Q: What happened to the oxytocin study in Austrailia?***

***Q: Is oxytocin showing to have benefits only when given at a young age- similar to growth hormone?***

***Q: Just wondering how far it would be before oxytocin would get approved for PWS?***

A: The study in Australia did not find any significant changes with oxytocin treatment within the dose, time-frame, age of participants, and endpoints of the study. As mentioned in the webinar, the upcoming oxytocin related trials vary in age group, dosing regimen, and endpoints in hopes of identifying subsets of the PWS population for whom oxytocin therapy will be beneficial. If and when oxytocin is accepted as a standard therapy for PWS will depend in part upon the results of upcoming trials. Currently, oxytocin is only FDA approved for the induction of labor. The intranasal form of oxytocin is only available by prescription from a physician and insurance will not cover the costs because it is not FDA-approved to be given as a nasal spray. If the studies show that oxytocin is beneficial for PWS, then the sponsoring company will try to get orphan drug approval for intransasal oxytocin so that insurance will have to cover the costs.

Note that autism studies have been going on for at least 5 years, and there is still not enough definitive data to prove that insurance should cover the cost for children with autism, so it could be many years before it would be approved for PWS.

***Q: So for the oxytocin trials we would have to go to Winthrop (in NY) weekly?***

A: The Ferring/Carbetocin trial has study sites at Winthrop and Vanderbilt Universities. For specific information regarding visit requirements, please contact the study coordinator(s) at [elizabeth.roof@vanderbilt.edu](mailto:elizabeth.roof@vanderbilt.edu) or [DK0-Disclosure@ferring.com](mailto:DK0-Disclosure@ferring.com). More information can also be found at [http://fpwr.org/participants-needed-pws-studies](http://fpwr.org/participants-needed-pws-studies" \t "_blank) and at <http://clinicaltrials.gov/ct2/show/NCT01968187?term=prader&rank=19>

***Q: Do you know when the NYC study (for oxytocin) will begin recruiting patients? And what facility it will be done at?***

A: An additional study will be opening at Montefiore Medical Center, Albert Einstein College of Medicine under the direction of Dr. Eric Hollander. This study is not yet open, but should start in 2014. It will be open to children and adolescents, 5-18. We will notify everyone when the study opens.

***Q: If we are interested in joining an Oxytocin study for the 5+ year olds, when will that information be available and where should we look for it?***

There are 2 trails we know of that are for 5+ years old, the trial through the Rare Disease Network (<http://clinicaltrials.gov/ct2/show/NCT02013258>) and the trial through Dr. Hollander (see above). We expect both trials will start in 2014, and will advertise those when the start recruiting.

***Q: Was the Beloranib study a phase I? Will Beloranib have an additional study to a younger age population?***

A: The Beloranib study recently completed in PWS was a Phase II trial. Details can be found in the press release from Zafgen. <http://www.zafgen.com/zafgen/newsroom/news-details?ID=efeac3b2-5885-6f14-8089-ff0000fc4595>. The next step will likely be a Phase III in adolescents/adults. Typically, a company would then seek approval from the FDA to use the drug adolescents/adults, where they have the most data, and where they are likely to see greatest effect. Once approved, the company may want to develop a program to study the drug in children.

***Q: What research is being done at the gene level to better understand PWS? Could  gene therapy one day be developed to eliminate PWS in an individual?***

A: There is a lot of work ongoing to better understand PWS at the gene level, and FPWR has been pleased to support many studies in this area, as well as fund the development of some of the ‘tools’ needed to support this work. At this time, the work is mainly ‘discovery’ and ‘preclinical’ stages. While gene therapy strategies provide excellent approaches to figuring out what might be ‘work’ in PWS, the current gene therapy technology is not good enough to be used in our kids - regulating where/when/ and how much of the therapeutic gene is expressed is challenging, and the risks would outweigh the benefit at this point. Nonetheless, this area continues to develop very rapidly, and some of the newer technology may prove more specific. At the very least, these approaches will help point the way to identifying the best pathways for drug development.

***Q: What is the process to be added to the global PWS registry?***

***Q: When your child is included in the Global PWS Registry will you automatically be contacted about clinical trials for which your child is likely eligible (based on age, etc.) or is the onus on you to check the site regularly?***

Please email [Jessica.Bohonowych@fpwr.org](mailto:Jessica.Bohonowych@fpwr.org) to be added to the mailing list for the registry. Once registered, companies/universities seeking participants will be able to send you a notice (if you choose) that your child is potentially eligible for a clinical study. You will then have the option of contacting the study coordinator. We will be working to make sure you get information about all trials that are recruiting, but it’s also a good idea to check our ‘participants wanted’ website and the clinicaltrials.gov site periodically.

Thank you again for your participation, and please let us know if you have any additional questions or if you’d like to see particular issues addressed. Our goals through this process are to educate, share information, and share resources so that you can find answers to your questions about specific trial opportunities. Many factors play into the decision of whether to participate in the clinical trial, and if so, in which trial to participate. Participating in a trial is a very personal decision and you shouldn’t feel pressure to participate in any particular trials, nor do we advocate certain trials over others. We do want to empower you to learn about the process and opportunities, seek answers to your questions, and once armed with the knowledge, make decisions that best fit your family. We also welcome your thoughts on barriers to clinical trial participation and how best to address/mitigate those.