UNIVERSITY OF Cincinnati

**The Lindner Center of HOPE**
**CONSENT TO PARTICIPATE IN A RESEARCH STUDY**

**Study Title:**
A Randomized, Placebo-Controlled Study of Liraglutide 3mg daily (Saxenda®) in Obese or Overweight Patients with Stable Bipolar Disorder

**UC IRB Study #:** 2017-1579

**Sponsor Name:** Investigator Initiated Study with Support from Novo Nordisk

**Investigator Information:**

| Susan L. McElroy, M.D. | (513) 536-0700 | (513) 536-0700 |
|---|---|---|
| Principal Investigator Name | Telephone Number | 24 hr Emergency Contact |

Subject Name: _____ Date of Birth: _____/_____/____

**INTRODUCTION:**
A biomedical or health-related research study is performed to answer specific questions about a disease.

Before you agree to participate in this research study, it is important that you be told the purpose, procedures, benefits, risks, discomforts, and precautions of the research. You should also be told what alternative procedures are available to you if you do not participate in the research study. The informed consent document is a written summary of this information. Be sure to ask questions while you read this consent document and ask questions if there is anything that you do not understand.

Your participation in this research study is entirely voluntary.

You may choose either to take part or not to take part in this research study. If you decide to take part, you may decide to leave the study at any time. Leaving the study will not result in any penalty or loss of benefits to you.

The researcher and sponsor of this study do not promise that you will receive any benefits from this study.

**WHY IS THIS RESEARCH BEING DONE?**
The purpose of this research study is to explore if Liraglutide treatment will reduce body weight and improve metabolic health in obese or overweight patients with Stable Bipolar Disorder without worsening their psychiatric symptoms.

Liraglutide is approved in along with exercise and reducing caloric intake as a treatment option for chronic weight management in individuals with obesity.

Liraglutide is not approved in the treatment of bipolar disorder (BPD).

As many patients with BPD struggle with obesity, with this information we hope to be able to improve treatment and outcome in people with BPD and obesity.

**WHY HAVE YOU BEEN ASKED TO TAKE PART IN THIS RESEARCH STUDY?**

You are being asked to take part in this research study because you are 18 to 65 years of age, inclusive, you have been diagnosed with BPD, which is stable on a consistent medication schedule, and you are currently obese or overweight. You do not need to participate in this research study to be treated for BPD or to assist you with weight loss.

**HOW LONG WILL YOU BE IN THE RESEARCH STUDY?**

You will be in the research study for up to 45 weeks. The research study begins with a 2 to 4 week screening period, followed by a 40-week treatment period and concludes with a final follow up visit.

You may withdraw from the study at any time. If you decide to stop participating in the study, we encourage you to talk to the researcher and your regular doctor first so that stopping can be done safely. Another reason to tell your doctor that you are thinking about stopping is to discuss what follow-up care and testing could be most helpful to you.

The researcher may decide to take you off this research study at any time. The study doctor and the FDA have the right to stop the study or your participation in it at any time, with or without your consent, for any reason, including the following: if you have a side effect from the study drug; if you have unsatisfactory or insufficient response to the study drug; if you need a treatment not allowed in this study; if you do not keep appointments; if you do not take the study drug as instructed; pregnancy, or if the study is canceled by the FDA or the study doctor.

You may be contacted in the future by representatives of the University of Cincinnati who are interested in asking you survey questions about your participation in this research study. If you choose to participate in the survey, your responses will be used for quality assurance purposes only.

**WHO IS CONDUCTING THE RESEARCH STUDY?**

This study is Investigator Initiated and partially supported by Novo Nordisk. The study is conducted by Susan L. McElroy, MD, a researcher at the Lindner Center of HOPE, an affiliate of the University of Cincinnati. Medical supervision for the study is provided by Susan L. McElroy, MD.

Dr. McElroy has received payments from Novo Nordisk who manufactures and is supplying the study medication. This disclosure is made so that you can decide if this relationship will affect your willingness to participate in this study.

**HOW MANY PEOPLE WILL TAKE PART IN THE RESEARCH STUDY?**

Approximately 60 participants will take part in this study at the Lindner Center of HOPE. This study will be conducted only at Lindner Center of HOPE, Mason, Ohio.

UNIVERSITY OF Cincinnati

**WHAT IS INVOLVED IN THE RESEARCH STUDY?**

Before entering the study, all aspects of the study will be explained to you. After that, if you agree to participate you will be asked to sign this consent form.

You will be "randomized" to receive either the investigational medication (Liraglutide 3 milligrams per day by an under the skin injection) or placebo (injection with no active medication). Randomization means that you are put into a group completely by chance. It is like flipping a coin.

Neither you nor the researcher conducting this study will know or choose what group you will be in. You will have an equal chance of being placed in any group. However, in the event of an emergency, if deemed necessary, or if you wish to, the researcher will be able to find out which treatment you are receiving.

**PROCEDURES DURING THE STUDY**

The following evaluations will be performed during the study:

**Pretreatment Period Screening Visit:**

If you agree to be in this study and sign this informed consent, you will first be evaluated to see if you qualify for the study. The Screening period will be a minimum of 3 days and maximum of 28 days.

- You will be asked to give some background information about your general medical history, your psychiatric history, medications you have taken in the past and those that you are currently taking.
- You will have your vital signs (blood pressure, heart rate, etc.) taken.
- You will have your height, weight, and body mass index (BMI) measured.
- You will be given a physical examination.
- You will have routine blood and urine tests done, including urine drug screen.
- You will have an electrocardiogram (ECG), which is a record of electrical activities of the heart.
- You will be interviewed to measure your psychiatric symptoms.

If your study doctor feels that your laboratory tests or other medical examinations show that you may not be healthy enough to participate in the study, you will not be able to continue further.

There may be certain medications that you are currently taking that you must discontinue using in order to be entered into the study. If this applies to you, your study doctor will discuss the medication discontinuation with you.

**Baseline Visit (Visit 0):**

If after the screening process you meet all the eligibility criteria, and still consent to take part in the study, you will be seen by your study doctor for the baseline visit. At this visit the following will occur:

- Review of Inclusion/Exclusion Criteria for study participation.
- You will have your vital signs taken.
- You will have your body mass index (BMI), weight, and waist measured.

- You will be asked questions to measure your psychiatric and eating disorder symptoms.
- You will be asked about the medications that you are currently taking.
- In females, urine pregnancy test will be performed

If your study doctor feels that your laboratory tests or other medical examinations show that you may not be healthy enough to participate in the study, you will not be able to continue further.

If you meet the eligibility criteria, a counseling session for reducing diet and increasing physical activity will be conducted. The first injection of study medication will be done at the end of this visit with guidance from the research team.

**Treatment Phase Visits**

You will return to the study clinic once a week during the first four weeks (Visits 1, 2, 3, 4): every other week for the next twelve weeks (Visits 5 through 10) and then every 4 weeks for the remaining 24 weeks (Visits 11-16).

During the Treatment phase the following will occur:

- You will have your vital signs taken.
- You will have your height, weight, BMI and waist measured.
- You will be asked questions to measure your psychiatric and eating disorder symptoms.
- You will be asked about any side effects or illnesses that you may be experiencing from any medication you are currently taking.
- You will be asked if you are taking any other medications.

Laboratory tests, ECG, and urinalysis will be repeated at Visits 6, 10, and 16. Urine pregnancy tests will be performed at every visit (Visits 0-16/ET).

You will be offered nutritional and lifestyle modification counseling at Visit 0, Visit 4, Visit 6, Visit 8, and Visits 10-15.

You will be asked to bring your used and unused study medication and packaging to every visit.

Study medication or placebo will be supplied in identical, pre-filled, multi-dose pens that can deliver the following doses under the skin: 0.6mg, 1.2mg, 1.8mg, 2.4mg, and 3mg. At the beginning of the Treatment period, the dosage of liraglutide or placebo will be 0.6 mg/day. Study drug dosage will be increased to 1.2mg/day on day 7 (Visit 1). In the following 3 weeks, the dose will be increased to 1.8mg/day (day 14, Visit 2), 2.4mg/day (day 21, Visit 3), and then to the target dose of 3mg/day (day 28, Visit 4), respectively. The study medication dose (3 mg/day) or placebo will remain unchanged during the final 36 weeks of the Blinded Treatment Phase.

You will receive thorough instruction of how to use the pens and will have opportunity to practice on a dummy and ask questions if needed.

**Study Discontinuation Visit**
Previous studies have shown that there is no need to decrease liraglutide dosage over time; it can just be stopped without side effects. If you withdraw from the study before completing, or if you complete the study, the following assessments will be conducted at the final treatment evaluation:

- You will have your vital signs taken and a physical examination will be performed.
- You will have your height, weight, BMI and waist measured.
- An ECG and blood draw will be performed.
- You will be asked questions to measure your psychiatric and eating disorder symptoms.
- You will be asked if you are taking any other medications.

**Final (Follow-Up) Visit Evaluation (Visit 17):**
You will be asked to come to the clinic one week after you stop injecting the medication or placebo. The following assessments will be conducted at the follow-up study visit:

- You will have your vital signs taken and your weight measured; urine pregnancy test will be performed in women.
- You will be asked questions to measure your psychiatric and eating disorder symptoms.
- You will be asked if you are taking any other medications and if you experienced any side effect after the dosing was terminated.

## WHAT ARE THE RISKS AND DISCOMFORTS OF THE RESEARCH STUDY?

All drugs have the potential to cause some side effects. As with any drug, whether it is an established and marketed drug or one still being tested in clinical studies, there may be unknown side effects.

There may be unknown or unforeseen risks associated with study participation.

**Side Effects of Liraglutide 3.0 mg sc injection:**
As with any medicine, side effects are possible with liraglutide 3.0 mg sc injection; however, not everyone who takes the drug will experience side effects.

Risks of Taking Liraglutide 3.0 mg sc injection

Possible serious adverse reactions of liraglutide 3.0 mg sc injection include:

- Acute Pancreatitis- occurring in less than 1 in 100 people treated with liraglutide
- Acute Gallbladder Disease – occurring in 1 in 100 people treated with liraglutide
- Suicidal Behavior and Ideation- occurring in less than 1 in 100 people treated with liraglutide
- Heart Rate Increase- occurring in less than 1 in 100 people treated with liraglutide
- Risk for Hypoglycemia (very low blood pressure) with Concomitant Use of Anti-Diabetic Therapy - occurring in less than 1 in 100 people treated with liraglutide
- Hypersensitivity Reactions- occurring in less than 1 in 100 people treated with liraglutide
- Renal Impairment

- Risk of Thyroid C-Cell Tumors – described in animal studies

Most common adverse reactions, reported in greater than or equal to in 5 out of 100 people include:

- nausea
- low blood sugar
- diarrhea
- constipation
- vomiting
- headache
- decreased appetite
- stomach discomfort
- fatigue
- dizziness
- abdominal pain
- increased liver enzymes

**Other risks**

Blood draw risks
You may feel faint; have pain and/or bruising at the site where the blood is drawn. An infection at the site where the blood is drawn is possible. During the study your blood will be drawn by either a catheter (a small plastic tube) or a needle. If the catheter does not work well, you will need to have several needle sticks to obtain the necessary blood samples.

Electrocardiogram (ECG) risks
You may experience mild irritation, slight redness and itching at the site on your skin where the electrodes for the ECG measures are placed. The electrodes may hurt when being removed from your skin.

## WHAT ARE THE REPRODUCTION RISKS?

The possible risks to an embryo or fetus of liraglutide 3.0 mg sc injection are unknown. Pregnant or lactating women, or women not using adequate birth control, will not be allowed in the study.

Because there might be unknown risks to an unborn child if you become pregnant during the study, you must not participate in this study if you are pregnant, plan to become pregnant during the research study period, or are breast-feeding a child. A serum pregnancy test will be done to confirm that you are not pregnant before you take part in this study. Additionally, you will be asked to provide a urine sample at each visit to test for pregnancy. You must use the following approved methods of birth control during the study: intrauterine device (IUD), barrier protection (condom, sponge etc), a contraceptive implantation system (depo-provera), oral contraceptive pills, Nuva Ring, Implanon, a surgically sterile partner, or abstinence.

Pregnancy will be a reason to stop study treatment. If you become pregnant during the study, you will be discontinued from study participation for safety reasons. With your permission, your pregnancy will be followed to term by the study team by telephone calls once every trimester (a total of 3 phone calls) and one follow up call 3 months after the baby is born or your medical provider will be contacted to collect documentation of your pregnancy.

Because the drug in this research study can affect an unborn baby, you should not become pregnant or father a baby (cause a pregnancy) while in this research study. You should not nurse your baby while on this research study. You will notify the researcher immediately if you become pregnant or suspect you have caused a pregnancy. You should discuss birth control options with your researcher.

**ARE THERE BENEFITS TO TAKING PART IN THE RESEARCH STUDY?**

If you agree to take part in this research study, there may or may not be a direct medical benefit to you. We hope the information learned from this research study will benefit other patients with BPD disorder in the future. Potential benefits to you may include more frequent than usual medical exams.

**WHAT OTHER CHOICES FOR CARE ARE THERE?**

You do not need to participate in this study to have your BPD and obesity treated. There are various medications and psychological treatment available for the treatment of BPD and obesity. If you choose not to participate or withdraw from the study your study doctor will discuss different alternative treatment options with you.

**WHAT IS THE CLINICAL TRIALS REGISTRY?**

A description of this clinical trial will be available on www.clinicaltrials.gov, as required by U.S. Law. ClinicalTrials.gov is a registry and results database of publicly and privately supported clinical studies of human participants conducted around the world.

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.

**AVAILABILITY OF INFORMATION**

You will receive a copy of this signed consent form for your records.

You will be told about any new information from this or other studies that may affect your health, welfare, or willingness to stay in this study.

**WHAT ARE YOUR COSTS TO BE IN THIS STUDY?**

All study drugs, study visits, and study-related procedures will be provided at no cost to you for the duration of your participation in this study.

**WILL YOU BE PAID TO PARTICIPATE IN THIS RESEARCH STUDY?**

Reasonable and necessary expenses in connection with the study, such as travel and parking, will be reimbursed $50.00 dollars in cash at the end of each completed study visit. If you receive compensation for being a part of this research study, you may be asked to complete a W-9 tax form to

report the compensation to the Internal Revenue Service. The amount you receive will count as income and may affect your income taxes. Your social security number will be required to complete the W-9 tax form.

**WHAT COMPENSATION IS AVAILABLE IN CASE OF INJURY?**

In the event that you become ill or injured from participating in this research study, emergency medical care will be provided to you. Lindner Center of HOPE will decide on a case-by-case basis whether to reimburse you for your out of pocket health care expenses. No other compensation is available.

**WHAT ARE YOUR RIGHTS AS A PARTICIPANT?**

You may choose either to take part or not to take part in this research study. If you decide to take part, you may decide to leave the study at any time. Leaving the study will not result in any penalty or loss of benefits to you. The investigators will tell you about new information that may affect your health, welfare, or willingness to stay in this study.

If you have questions about the study, you will have a chance to talk to one of the study staff or your regular doctor. Do not sign this form unless you have had the chance to ask questions and have received satisfactory answers.

Nothing in this consent form waives any legal rights you may have nor does it release the investigator, the sponsor, the institution, or its agents from liability for negligence.

**HOW WILL INFORMATION ABOUT YOU BE KEPT PRIVATE AND CONFIDENTIAL?**

Every effort will be made to maintain the confidentiality of your medical and research records related to this study. Agents of the United States Food and Drug Administration (FDA) if the study involves articles regulated by this agency, the University of Cincinnati, the sponsoring company, the Institutional Review Board (IRB), and other regulatory authority(ies) will be granted direct access to your original medical and research records for verification of clinical trial (research study) procedures or study data without violating your confidentiality, to the extent permitted by the applicable laws and regulations. By signing this consent form, you or your legally authorized representatives are authorizing such access. The data from the study may be published; however, you will not be identified by name. Your identity will remain confidential unless disclosure is required by law.

**WHO DO YOU CALL IF YOU HAVE QUESTIONS OR PROBLEMS?**

If you have any questions, concerns or complaints and/or suggestions about this research study or to report a research-related injury, please contact the researcher Susan McElroy, MD at 513-536-0700 or 24-hour emergency number 513-536-0700.

Please call the University of Cincinnati Medical Institutional Review Board at 513-558-5259 (Monday – Friday 8 am to 5 pm) if you:

- Think the research has hurt you.
- Have general questions about giving consent or your rights as a research participant in this research study.

- Have questions, concerns, or complaints and/or suggestions about the research.
- Cannot reach the research team or you want to talk to someone else.

To report complaints or concerns to an independent agency in an anonymous and confidential manner, please call the Research Compliance Hotline at 1-800-889-1547.

UNIVERSITY OF Cincinnati

## Authorization to Use and Disclose Health Information

A federal regulation known as the Privacy Rule gives you certain rights concerning the privacy of your health information. Researchers covered by this regulation are required to get your authorization (permission) to use and disclose (share with others) any health information that could identify you. You should have received a Notice of Privacy Practices when you received health care services here. If not, let us know and a copy will be given to you.

If you sign this informed consent form, you are giving permission for the use and disclosure of your health information for purposes of this research study. You do not have to give this permission. Your health care outside of the study, payment for your health care, and your health care benefits will not be affected if you choose not to sign this form. However, if you do not sign this form, you will not be able to participate in the study.

**Who Will Use and Disclose My Health Information?** The study doctor and research staff (the study team) may use your health information to conduct, review, and determine the results of the study. The study team may also use your information to prepare reports or publications about the study. However, your name will not appear in any report or publication without your permission.

**What Health Information will be Used and Disclosed?** The study team will record your medical history, the treatment you receive, and the results of examinations and tests done during the study on study forms. The study team will send the completed study forms to the study sponsor. Representatives from the groups identified below may need to look at your medical records to make sure that the information on the study forms is correct or that the study was conducted properly. Your medical records may include other health information about you and may include documents that directly identify you. Reviews like that will take place at the study center or where the medical records are stored and can take place after the study is over.

**Who Will Receive My Health Information?** Your study information or medical records (as described above) or both may be shared with the following people or groups:

- The study sponsor or its representatives, including companies it hires to provide study-related services
- Researchers who are conducting this study at other study centers
- UC Institutional Review Board and any other committees responsible for overseeing the research
- Staff of the UC Human Research Protection Program
- LCOH employees providing service or care to you
- Federal and State agencies, such as the U.S. Food and Drug Administration
- (FDA), Department of Health and Human Services (DHHS), the National Institutes of Health (NIH), and other US and non-US government bodies that oversee or review research

**Will My Information be Protected by the Privacy Rule After it is Disclosed to Others?**
LCOH is required by the Privacy Rule to protect your health information. After your information is shared with others, such as the study sponsor, it may no longer be protected by the Privacy Rule. The people who receive this information could use it in ways not discussed in this form and could disclose it to others. The sponsor will use and disclose your information only for research or regulatory purposes or to prepare research publications. In addition to using it for this study, the sponsor may reanalyze the study data at a later date or combine your information with information from other studies for research purposes not directly related to this study. The goal of any such research would be to learn more about drugs, devices or diseases or to help design better studies in the future. When using your information in these ways, the sponsor may share it with regulatory authorities, other researchers, its business partners, or companies it hires to provide research-related services.

**What Happens if I Leave the Study Early?** If you stop participating in the study early for any reason, the study team will tell the sponsor why. If the study team asks you to come to any more study visits and you agree, the study team will send the sponsor information from those visits as well. All information collected about you may continue to be used and disclosed.

**Will My Authorization Ever Expire?** This Authorization does not have an expiration date. The study team may need to correct or provide missing information about you even after your study participation is over and a review of your medical records may also take place after the study is over.

**May I Take Back My Authorization?** You have the right to take back (revoke) your Authorization at any time by writing to the person in charge of this research study whose information is listed on the front of this form. If you revoke your Authorization, the study team will not collect any new health information about you. However, they can continue to use and disclose any already-collected information if that is necessary for the reliability of the study. The sponsor can also still keep and use any information that it has already received. If you revoke your Authorization, you can no longer continue to participate in the study.

**May I Look At My Study Information?** You have a right to see and make copies of your medical records. However, to ensure the reliability of the study, you will need to wait to see your study records until the study is completed.

UNIVERSITY OF Cincinnati

**UC IRB Study #: 2017-1579** **Sponsor Name:** Investigator Initiated Study with Support from Novo Nordisk

**Investigator Information:**

| | | |
|---|---|---|
| Susan McElroy, M.D. | (513) 536-0700 | (513) 536-0700 |
| Principal Investigator Name | Telephone Number | 24 hr Emergency Contact |

**SIGNATURES**

I have read or someone has read to me, this Informed Consent Document which describes the purpose and nature of this research. I have had time to review this information and have been encouraged to ask questions. If I do not participate or if I discontinue my participation, I will not lose any benefits or any legal rights. My participation in this research is completely voluntary. I have received (or will receive) a copy of this signed and dated form for my records and future reference. I have been given the information about the use and disclosure of my health information for this research study.

I give my consent to participate.

Participant Date

*PERSON OBTAINING CONSENT*

I have read this form to the participant and/or the subject has read this form. An explanation of the research was given and questions from the subject were solicited and answered to the subject's satisfaction. In my judgment, the subject has demonstrated comprehension of the information.

Signature and Title of Person Obtaining Consent and Identification of Role in the Study Date

Please indicate below whether you want us to notify your primary care physician or your specialist of your participation in this study.

_____ I **want** the researcher to inform my primary care physician/specialist of my participation in this study.

_____ I **do not want** the researcher to inform my primary care physician/specialist of my participation in this study.

_____ I do not have a primary care physician/specialist.

_____ The researcher is my primary care physician/specialist.**

Participant Date