# *Glucagon-like Peptide-1 Receptor Agonists as Novel Pharmacotherapies for Nicotine Dependence*

**ClinicalTrials.gov Number:**

**NCT03712098**

**Date: October 6, 2021**

# UNIVERSITY OF PENNSYLVANIA
# RESEARCH STUDY SUMMARY FOR POTENTIAL SUBJECTS

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| **Protocol Title:** | **Glucagon-like Peptide-1 Receptor Agonists as Novel Pharmacotherapies for Nicotine Dependence (IRB# 831835)** |
| **Short Title:** | **Daily Liraglutide for Nicotine Dependence** |
| **Principal Investigator:** | **Rebecca Ashare, Ph. D., Phone: 215-746-5789**<br>**Department of Psychiatry, University of Pennsylvania** |
| **Emergency Contact:** | **Anastassia Amaro, M.D., Phone: 267-240-2819**<br>**Perelman School of Medicine, University of Pennsylvania** |

You are being invited to participate in a research study. Your participation is voluntary and you should only participate if you completely understand what the study requires and the risks of participation. You should ask the study team any questions you have before agreeing to join the study. If you have any questions about your rights as a human research participant at any time before, during, or after participation, please contact the Institutional Review Board (IRB) at 215-898-2614 for assistance.

This research study is being conducted to test whether the medication liraglutide (Saxenda®) may help smokers quit smoking. Liraglutide is approved by the FDA for chronic weight management, not for smoking cessation, so its use in this study is investigational. Liraglutide comes in a pre-filled pen and is self-injected one time per day into the abdomen, thigh, or upper arm area. The needle used is very small – it is less than 1/4 of an inch long and as thin as two human hairs. A healthcare professional will show you how to use the study pen.

If you agree to join the study, you will be asked to self-inject the medication liraglutide, or a placebo, daily for the duration of the study. The placebo is an inactive substance and is designed to look like the study drug but contains no medication. During the study, you and the study team will not know whether you are taking the active study medication or the placebo. However, we can find out what you are taking in the case of a medical emergency. You will also receive eight sessions of smoking cessation counseling to assist you with quitting smoking.

After your initial Intake Visit, your participation in the study will last approximately 32 weeks (about 8 months). A schedule of study events can be found on the last page of the consent form.

Right now, it is not known if liraglutide will cause any change in your smoking behavior so there may be no direct benefit to you from participating in this research study. You may benefit from knowing that you are contributing to the advancement of treatments to help people quit smoking. Behavioral counseling may help you quit smoking.

The most common risks of study participation are potential side effects from the medication liraglutide. The most common side effects reported by participants taking liraglutide include nausea, vomiting, diarrhea, constipation, abdominal pain, indigestion, headache, dizziness, low blood sugar, fatigue, and increased lipase. You will be monitored for side effects throughout the study and for 4 weeks after you finish taking liraglutide or the placebo. The study may also involve unforeseen risks that have not yet been identified.

Please note that there are other factors to consider before agreeing to participate in this study, such as additional procedures, use of your personal information, and other possible risks. If you are interested in participating, a member of the study team will review the full study information with you. You are free to decline or stop participation at any time during or after the initial consenting process. If you do not wish to enroll in this study and still wish to seek assistance with quitting smoking, we can provide you information on other quit smoking studies at our center or other treatment programs located in the Philadelphia area.

# UNIVERSITY OF PENNSYLVANIA
# RESEARCH SUBJECT INFORMED CONSENT AND HIPAA AUTHORIZATION FORM

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**WHY AM I BEING ASKED TO VOLUNTEER?** You are being asked to take part in this 32-week research study because you are a smoker and have indicated that you are interested in quitting and potentially agreeable to using a medication. The medication is currently FDA-approved for chronic weight management, but not smoking cessation, which is why we are testing it in this study. All participants will receive smoking cessation counseling and either liraglutide 3.0 mg/day (Saxenda®) or a placebo. Your participation is voluntary which means you can choose whether or not you want to participate. Before you make this decision, you will need to know the purpose of the research study, the possible risks and benefits of being in the research study, and what you will have to do if you decide to participate. The research team is going to talk with you about these things today. Please ask them to explain anything you do not understand, including any language contained in this form.

You do not have to make a decision about participating in this research study today; you can request a copy of this form to review at a later time, or share it with your family, friends, and/or doctor. Whatever you decide, there will be no loss of benefits to which you are otherwise entitled. If you do decide to participate, you will be asked to sign this form and will be given a copy for your records.

**WHAT IS LIRAGLUTIDE?** Liraglutide 3.0 mg (Saxenda®) is an injectable medicine that is approved by the U.S. Food and Drug Administration (FDA) for chronic weight management when combined with a reduced-calorie meal plan and physical activity. Liraglutide comes in a pre-filled pen and is self-injected one time per day into the abdomen, thigh, or upper arm area. The needle used is very small; it is less than 1/4 of an inch long and as thin as two human hairs. The research team can show you an example of what a liraglutide pen looks like.

Liraglutide belongs to a class of medications called glucagon-like peptide-1 (GLP-1) receptor agonists. Your body naturally produces glucagon-like peptide-1 (GLP-1), which helps regulate your appetite. Liraglutide works like GLP-1. When activated by liraglutide, the GLP-1 receptor stimulates the release of insulin into the bloodstream. Evidence shows that liraglutide may reduce appetite. We are interested in seeing if liraglutide can help prevent weight gain during a smoker's attempt to quit smoking and if this helps people stay smoke free. The present study aims to examine the effectiveness of liraglutide in helping people quit smoking compared to placebo. The placebo is an inactive substance and is designed to look like the study drug but contains no medication.

**WHAT IS THE PURPOSE OF THIS RESEARCH STUDY?** The main purpose of this research study is to examine whether the medication liraglutide (Saxenda®) may help smokers to quit smoking.

**HOW LONG WILL I BE IN THE STUDY? HOW MANY OTHER PEOPLE WILL BE IN THE STUDY?** A total of 40 participants will complete this study and each participant will be in the study for about 32 weeks (~8 months). The entire study (with all participants) will be completed in about 3 years.

**WHAT AM I BEING ASKED TO DO?** Your participation in this research study will first involve reviewing the study's informed consent/HIPAA authorization form, which provides a description of the study. If you are interested in participating after hearing the description and having your questions answered, you will be asked to sign this form

and then complete tasks to determine your eligibility for the study. These tasks make up the Intake session, and some may take place remotely. The intake session is necessary to make sure it is safe for you to participate in the study. If you are eligible to participate after the completion of these tasks, you will be asked to complete 15 additional sessions, including 8 smoking cessation counseling sessions, over approximately 8 months. Some of these sessions may be completed by phone, and as a result, some study materials may be mailed to you.

The smoking cessation counseling sessions are designed to enhance your awareness of the harmful effects of smoking, assist you in developing skills to quit smoking, emphasize the benefits of quitting, and help you avoid relapse. During the counseling sessions, you will speak with your counselor one-on-one for approximately 30 minutes at a time (up to an hour at your first session). Counselors are members of the research staff who have been trained to provide behavioral counseling that assists participants with developing strategies to help them quit smoking. All participants will take part in the same smoking cessation counseling program. You will still be allowed to participate in the study even if you are not successful in your attempt to quit smoking.

This study is divided into two study periods: a 5-week Pre-Quit period and a 6-month Monitoring period. Within each study period, you will take study medication or placebo, undergo brief physiological assessments, complete questionnaires, provide biological samples such as blood and urine, and have your glucose monitored. Study visits are described in more detail below. There is also a schedule of study events on the last page of this form.

**Intake Visit:** The purpose of this visit is to determine if you are eligible to participate in the study. This visit will last approximately 3 hours if conducted entirely in-person. Participants may be asked to complete some of the Intake procedures remotely. During this visit, you will:

- Provide a urine sample (at least 30ml [two tablespoons]) for drug and (if applicable) pregnancy tests. If you test positive for cocaine, methamphetamines, PCP, barbiturates, and/or ecstasy (MDMA), you may not be eligible to participate in this study. Results from this testing are used for research purposes only. They will not be shared with you and will not be placed in your electronic medical record. You will be informed of your eligibility status after testing, but specific results will not be shared. Your urine sample will be discarded after testing.
- **Female participants only:** If the result of your pregnancy test is positive, you will not be eligible to participate in this study.
- Provide a breath sample for a carbon monoxide (CO) assessment to confirm your smoking status. Carbon monoxide is a poisonous gas that comprises less than 1% of the air we breathe and is also produced through smoking a cigarette.
- Complete brief psychiatric assessments called the 'MINI' interview, 'C-SSRS', and 'CES-D' questionnaire. During these assessments, we will ask you about any current and past depressed mood symptoms as well as other psychiatric symptoms.
- Complete a medical history form with a member of the research team and provide information on medications you are currently taking or recently discontinued.
- Have your height, weight, blood pressure, and heart rate measured.
- Complete a brief physical examination led by a medical professional.
- Have your blood sugar measured via a finger prick and a handheld glucose monitor. You must have a blood glucose level ≥70 mg/dl in order to be eligible for the study.
- Provide a 12.5mL blood sample (less than 3 teaspoons) that will be used to confirm you do not have diabetes or any undiagnosed kidney or liver problems.
- Fill out questionnaires electronically or on paper. These questionnaires ask about your demographics, smoking history and behavior, and alcohol use and will take up to 45 minutes to complete.
- Complete a COVID-19 experience survey.
- Complete a computerized lab task by rating how appetizing you find a set of pictures of food.
- Schedule your study track and next in-person visit.
- Schedule the dates and times of your first three 24-hour dietary recalls, which will be completed prior to Laboratory Visit 1 (Week 1).

As you complete the tasks listed above, there is a chance you may not meet all of the study eligibility criteria. If this occurs, you will be deemed ineligible for the study. Study eligibility criteria have been established for data quality and/or safety purposes. If you successfully complete all of the Intake Visit tasks, you will be compensated $20 for your time, as well as $10 for transportation reimbursement, if you provided your own transportation. If you are deemed ineligible for any reason, we will compensate you $10 to cover your travel costs, or cover the cost of your RoundTrip service.

During your entire participation in this study, we ask that you:

- NOT use any forms of nicotine replacement therapy (e.g., nicotine gum, nicotine spray, cigars, e-cigarettes, any type of vaped nicotine, lozenge, etc.).
- NOT use any study prohibited medications or recreational drugs as listed above.
- Notify us if you are prescribed a new medication (prior to taking first dose if possible).
- NOT participate in any other quit smoking programs and/or quit smoking research studies while you are enrolled in this study.
- **Female participants only:** Notify us immediately if you become pregnant. If you become pregnant, you will NOT be able to continue in the study.
- Notify the research staff about any medical concerns and/or symptoms.
- Attend ALL study visits as scheduled.
- Follow ALL study instructions as directed.

**24-Hour Dietary Recalls (Prior to Weeks 1, 5, 18, and 32):** You will complete three 24-Hour Dietary Recall assessments at four separate time points (12 assessments in total) over the course of the study. During each 24-hour dietary recall, a member of the research team will contact you over the telephone during a predetermined time window to discuss your eating and drinking from the day before. If you are already scheduled for a study session on the day of a 24-hour dietary recall, your dietary recall assessment may be completed during that session. Each dietary recall assessment will take about 30 minutes.

**Randomization:** If eligible for the study, you will be randomly assigned to one of the two study groups: liraglutide 3.0 mg/day or placebo. You will not be able to choose the group that you prefer (if you have a preference) and you must be willing to participate in either of the two groups to be in the study. If you are not willing to participate in either of the two groups, then this research study may not be appropriate for you. The study team can provide additional resources to help you quit smoking.

Study Medication: Liraglutide (or placebo) will be prescribed at 0.6 mg per day for the first week, 1.2 mg per day for the second week, 1.8 mg per day for the third week, 2.4 mg per day for the fourth week, and then increased to 3.0 mg per day for the remainder of the study. Because some people need more time to adjust to the medication, you may be asked to remain on a lower dose of the study medication for a longer amount of time. This is a double-blind study so neither you nor the study staff will know whether you are taking liraglutide or placebo during the study. However, we can find out this information in the case of a medical emergency.

**Laboratory Visits (Weeks 1 and 5):** During the Pre-Quit period of the study, you will attend two in-person laboratory visits at our center. You may be asked to complete some of these procedures remotely to limit the amount of time spent at the center. You will be asked NOT to eat anything for at least one hour before these visits. During these visits, you will:

- Provide a urine sample (at least 30ml [two tablespoons]) for drug and (if applicable) pregnancy tests. If you test positive for cocaine, methamphetamines, PCP, barbiturates, and/or ecstasy (MDMA), you may not be able to continue in the study. Results from this testing are used for research purposes only. They will not be shared with you and will not be placed in your electronic medical record. You will be informed of your eligibility status after testing, but specific results will not be shared. Your urine sample will be discarded after testing.

- **Female participants only:** If the result of your pregnancy test is positive, you will not be able to continue in the study.
- Provide a breath sample for a carbon monoxide (CO) assessment.
- Review your current medications with a member of the research team and provide information on any new medications you may have started.
- Have your weight, blood pressure, and heart rate measured.
- Have your blood sugar measured via a finger prick and a handheld glucose monitor.
- Provide an 18.5mL blood sample (less than 4 teaspoons) that will be used to analyze exploratory cardiovascular risk markers.
- Fill out questionnaires, including a symptoms evaluation checklist, electronically via REDCap or on paper. These questionnaires will take up to 30 minutes to complete.
- Complete a series of food-related computer tasks (~30 minutes).

**Laboratory Visit 1 only:**

- Receive your first supply of study medication pens (liraglutide or placebo) and be trained by a medical professional on proper injection techniques. You will be given Instructions for Use with complete administration instructions and illustrations to refer to. You will also be trained on storing the study medication and returning used medication pens to our center. Additional study medication pens (liraglutide or placebo) will be given or mailed to you at Weeks 5, 7, 10, 12, 14, 18, 22, & 26.

**Laboratory Visit 2 only:**

- Confirm with study staff that you have been taking your study medication as prescribed (known as 'medication adherence') and return used medication pens.
- Attend your first smoking cessation counseling session (~1 hour) either in person or over the phone. This first counseling session will help prepare you for your upcoming target quit date, which will occur the following week (Week 6). Counseling sessions may be audio-taped to ensure that treatment is consistent for all participants. Audio recordings will be saved on password-protected computers and deleted at the end of the study.

**Pre-Quit Clinic Visits (Weeks 2, 3, and 4):** During the Pre-Quit period of the study, you will complete three sessions in between each lab session. These sessions will last approximately 30 minutes. During these visits, you will:

- **Female participants only:** Provide a urine sample for a pregnancy test. If the result of your pregnancy test is positive, you will not be able to continue in the study. Your urine sample will be discarded after testing. Pregnancy testing will not be completed if the session is conducted remotely.
- Provide a breath sample for a carbon monoxide (CO) assessment. CO will not be collected if the session is conducted remotely.
- Have your weight, blood pressure, and heart rate measured. These will not be completed if the session is conducted remotely.
- Review your current medications with a member of the research team and provide information on any new medications you may have started.
- Have your blood sugar measured via a finger prick and a handheld glucose monitor.
- Fill out questionnaires, including a symptoms evaluation checklist, electronically via REDCap or on paper. These questionnaires will take up to 10 minutes to complete.
- Confirm with study staff that you have been taking your study medication as prescribed and return used medication pens.

**Week 4 only:**

- Schedule the dates and times of your next three 24-hour dietary recalls, which will be completed prior to Laboratory Visit 2 (Week 5).

**Monitoring Clinic Visits (Weeks 6, 7, 8, 10, 12, 14, 18, 22, 26, and 32):** During the Monitoring period of the study, you will complete ten sessions. . Weeks 6-12, 18, and 26 visits will approximately one hour and Weeks 14, 22, and 32 visits will last approximately 30 minutes. During these visits, you will:

- **Female participants only:** Provide a urine sample for a pregnancy test. If the result of your pregnancy test is positive, you will not be able to continue in the study. Your urine sample will be discarded after testing. Pregnancy testing will not be completed if the session is conducted remotely.
- Provide a breath sample for a carbon monoxide (CO) assessment. If the session is not completed in-person, CO may be collected using the iCO Smokerlyzer. This is a personal carbon monoxide reader that you will connect to your phone and send results to the research team. You will be provided this device by the research team and instructed on how to use it.
- Have your weight, blood pressure, and heart rate measured. These will not be completed if the session is conducted remotely.
- Review your current medications with a member of the research team and provide information on any new medications you may have started.
- Have your blood sugar measured via a finger prick and a handheld glucose monitor.
- Fill out questionnaires, including a symptoms evaluation checklist, electronically via REDCap or on paper. These questionnaires will take up to 10 minutes to complete.
- Confirm with study staff that you have been taking your study medication as prescribed and return used medication pens.

**Weeks 6, 7, 8, 10, 12, 18, and 26 only:**

- Attend your Target Quit Date (Week 6) and Booster (Weeks 7, 8, 10, 12, 18, and 26) smoking cessation counseling sessions (~30 minutes).

**Weeks 7 and 32 only:**

- Based on your smoking behavior, you may be asked to provide a saliva sample that will be used to examine by-products of nicotine.

**Weeks 18 and 32 only:**

- Provide an 18.5mL blood sample (less than 4 teaspoons) that will be used to analyze exploratory cardiovascular risk markers.

**Weeks 14 and 26 only:**

Schedule the dates and times of your next three 24-hour dietary recalls, which will be completed before your next in-person visit.

**Final Check-in:** Four weeks after your last study visit, we will contact you by phone to ask about your smoking status and any delayed side effects you may have experienced. This call will take up to 15 minutes to complete.

**Visit Reminders:** For each of your scheduled study visits you will receive appointment reminders via phone call, email, or text message (depending on your preference). These reminders will occur 24 – 48 hours prior to your visits and will include important information for your visit.

**WHAT ARE THE POSSIBLE RISKS OR DISCOMFORTS?** The likelihood and severity of the potential risks to you are described below.

**Study Medication (liraglutide):** All drugs carry some risk of side effects. In order to prevent harm, you must inform the study team if you experience any side effects from the study medication. In several clinical trials that lasted at least one year, the following side effects were reported in greater than 5% of people taking liraglutide and more frequently than in people taking a placebo:

- Nausea
- Diarrhea
- Vomiting
- Indigestion
- Dizziness
- Low blood sugar (Hypoglycemia)
- Constipation
- Abdominal pain
- Headache
- Fatigue
- Increased lipase

Adverse reactions reported in greater than or equal to 2% of people taking liraglutide and more frequently than in people taking a placebo included:

- Bloating
- Belching
- Flatulence
- Dry mouth
- Insomnia
- Anxiety
- Gastroesophageal reflux disease (GERD)
- Injection site erythema (redness)
- Injection site reaction
- Asthenia (weakness)
- Gastroenteritis (stomach flu)
- Urinary tract infection

If you experience any severe side effects or related medical issues during your participation in the study, it is important that you contact research staff and/or the Study Physician (listed on page one) at the telephone number provided as soon as possible. The Study Physician's emergency contact information is also on the medication package that you will receive from us.

Thyroid C-Cell Tumors: Liraglutide causes both cancerous and non-cancerous thyroid C-cell tumors in mice and rats. The relevance of this finding to humans has not been determined. Individuals with a personal or family history of thyroid tumors are not eligible for this study. Tell your primary care provider (PCP) and the study staff if you get a lump or swelling in the neck, hoarseness, trouble swallowing, or shortness of breath as these may be symptoms of thyroid cancer.

Inflammation of the Pancreas: Inflammation of the pancreas (pancreatitis) has been observed in some patients taking liraglutide. Contact your PCP and the study staff if you experience severe pain in your stomach area (abdomen) that will not go away, with or without vomiting.

Gallbladder Problems: Gallbladder problems, including gallstones, have been reported in some patients taking liraglutide. Contact your PCP and study staff if you experience pain in your upper stomach (abdomen), fever, yellowing of your skin or eyes (jaundice), or clay-colored stools.

Increased Heart Rate: Liraglutide may increase your heart rate while you are at rest. During this study, your heart rate will be measured regularly to monitor any changes. Contact your PCP and study staff if you feel your heart racing or pounding in your chest and it lasts for several minutes.

Kidney Problems: Liraglutide may cause nausea, vomiting, or diarrhea leading to loss of fluids (dehydration). Dehydration may cause kidney failure which can lead to the need for dialysis. This can happen in people who have never had kidney problems before. Drinking plenty of fluids may reduce your chance of dehydration. Contact your PCP and study staff right away if you have nausea, vomiting, or diarrhea that does not go away, or if you cannot drink liquids by mouth.

Depression or Thoughts of Suicide: Individuals who are at risk for suicide attempts or those with active suicidal thoughts should not take liraglutide. This is why study staff will ask you questions about these issues during your Intake Visit. Your mood will be monitored throughout this study. You should pay attention to any mental changes, especially sudden changes, in your mood, behaviors, thoughts, or feelings. Contact your PCP and study staff right away if you have any mental changes that are new, worse, or worry you.

Potential Drug Interactions: Liraglutide delays stomach emptying and can affect medicines that need to pass through the stomach quickly. Taking liraglutide may impact the absorption of some oral medications and how they work. Contact your PCP and study staff if you feel delays in stomach emptying, such as feeling uncomfortably full after little food is eaten.

Unforeseen Risks: People may have allergic reactions to medications. A severe allergic reaction could be life-threatening. Examples of an allergic reaction include rash, difficulty breathing, wheezing, sudden drop in blood

pressure, fast pulse, sweating, and swelling around the mouth, throat, or eyes. There may be other risks associated with liraglutide that have not been identified. If additional risks are identified during the study, the study team will inform you.

Reproductive Risks (Females Only): The use of liraglutide may pose risks to pregnancy and an unborn child. Therefore, you should not become pregnant while you are in the study. If you are able to become pregnant, you will be required to follow a study-approved method of birth control while participating in the study. Adequate birth control in this study is the use of double barrier methods (condom with spermicide or diaphragm with spermicide), stable hormonal contraception (such as oral contraceptive pills, Depo-Provera injection or the contraceptive patch), intrauterine device (IUD), abstinence, or tubal ligation.

Liraglutide may also have unknown risks for breast-fed babies. Therefore, you should not breastfeed while you are in the study.

Although pregnancy testing will be performed during the study, it is possible that the results could be wrong. If you do become pregnant while in this study, you will be asked to immediately notify the study team, discontinue the study drug/placebo, and consult an obstetrician or maternal-fetal specialist. If you become pregnant, we will find out if you were taking the study drug or placebo. The Study Physician or Nurse Practitioner will remain in contact with you to learn the outcome of your pregnancy. If you were taking the study drug, the Study Physician or Nurse Practitioner will confirm that you are consulting with an obstetrician or a maternal-fetal specialist, record any complications, and obtain information regarding the overall health of you and the baby. The Study Physician will share this information with the University of Pennsylvania Institutional Review Board and with Novo Nordisk, the company that manufactures liraglutide.

**Subcutaneous Injection:** Risks of subcutaneous injection of the study medication or placebo include pain or discomfort, bruising at the puncture site, swelling, feeling faint or lightheaded, and (rarely) infection.

**Withdrawal:** Many people who smoke cigarettes have symptoms of withdrawal when they stop smoking. These symptoms can occur almost immediately and last for about 7-10 days. These symptoms can include: sadness and mood changes, insomnia, anxiety, constipation, decreased heart rate, muscle pain, irritability, craving for nicotine, headaches, anger, difficulty concentrating, restlessness and nervousness, and appetite change and weight gain. These symptoms are usually low risk. The study staff know how to identify these symptoms and inform you about them. Although nicotine replacement therapy may help reduce withdrawal symptoms, we ask that you do not use any nicotine-containing products (other than your cigarettes) for the duration of the study.

**Psychological Distress:** You may experience emotional distress during assessments from discussing feelings and attitudes about smoking and/or from learning about the risks of smoking. This happens rarely and, in almost all cases, does not last long and is of low intensity. The research staff that work with you know how to help you if you have any concerns.

**Blood Draws:** Blood draws may result in bruising and/or slight bleeding at the needle site or may cause you to feel faint. All of these side effects are rare. Blood will be drawn by a trained professional to reduce the risk of these discomforts.

**Email Communications:** Throughout this study you may get appointment reminders via email or choose to ask questions related to the study via email. Email is not a secure method of communication. Email messages travel across the Internet passing through multiple computers before reaching their final destination. It is not possible to know whether an email you send will be viewed along the way. Additionally, if sent messages are not deleted, an email provider may have a folder of everything that is sent. If someone gets access to an email account (for example, a family member), they could see old messages. There are many other ways in which emails are not secure—these are only selected examples. For these reasons we ask that you only use email communication for

routine matters and never for personal or confidential messages or questions. If you have questions or concerns that are personal in nature, we suggest you contact the study staff via phone.

**Loss of Confidentiality:** As this study involves the use of your identifiable, personal information, there is a chance that a loss of confidentiality could occur. The researchers have procedures in place to lessen the possibility of this happening (see "Who can see or use my information? How will my personal information be protected?" below).

**WHAT IF NEW INFORMATION BECOMES AVAILABLE ABOUT THE PROGRAM?** During the course of this study, we may find more information that could be important to you and your health. When feasible, we will notify you as soon as possible if such information becomes available. For example, we would contact you immediately if new information became available about the study medication that might cause you to change your mind about being in the program.

**WHAT ARE THE POSSIBLE BENEFITS OF THE PROGRAM?** It is not known if the study medication (liraglutide) will cause any change in smoking behavior. Participants who enroll in this study may benefit from the knowledge that they are contributing to the advancement of treatments to help people quit smoking. All participants will receive smoking cessation counseling which may help you make a successful quit attempt.

**WHAT OTHER CHOICES DO I HAVE IF I DO NOT PARTICIPATE?** The alternative to participation is to decide not to enroll in this study. If you do not wish to enroll in this study and still wish to seek assistance with quitting smoking, we can provide you information on other quit smoking studies at our center or other treatment programs located in the Philadelphia area.

**WILL I BE PAID IN THIS PROGRAM?** To reimburse you for the time and effort needed for completing assessments, you may earn up to $610, which includes $10 for travel-related expenses at each in-person visit and $5 for each dietary recall. In place of $10/session to cover travel expenses, you may elect to use a round-trip car ride service (such as Lyft) which will be arranged and paid for in full by the research study. If you choose to use the ride service, you will not receive $10 for your travel reimbursement and your total visit compensation will be up to $365. You will receive a reminder call 24-48 hours prior to your study visit to confirm your ride.

The "task completion" compensation will depend on you arriving on time for scheduled visits. If you do not follow the study instructions, some or all of the task completion compensation may be withheld. If you are withdrawn from the study by the investigator during a study visit, you will only be compensated $10 to cover your travel costs, unless you have elected to use the ride service.

The GreenPhire ClinCard will be the primary form of payment for this study. The ClinCard is a reloadable, pre-paid card for the purposes of compensation. Compensation will be loaded onto the ClinCard within 24 hours of completed visits. Staff may ask you to provide a Social Security Number, or complete a W-9 for this purpose, after determining eligibility so that a ClinCard can be assigned. Since this form will contain your Social Security number, it will be kept in a separate location from your study chart, stored in a locked filing cabinet in the locked office of our business administrator, and used for tax purposes only. It will be shredded when all tax documents are submitted to the IRS. Additionally, the University of Pennsylvania is required to report to the IRS any cumulative payments for participation in research studies that exceed a total of $600 in a calendar year. ClinCards may be mailed to subjects following the eligibility determination for the study.

You may receive a $100 bonus for completing the study. You may also receive a $10 bonus for each person successfully referred to the study once your participation has ended, for a maximum of two referrals.

The study payment schedule is as follows:

| Compensation Schedule | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Week** | **Study Visit** | **Task Completion** | **Travel[1]** | | **Dietary Recalls** | **Bonus** | **Total** |
| | Intake | $20 | $10 | | | | $30 |
| **1** | Lab Visit 1 | $35 | $10 | | $15 | | $60 |
| **2** | Pre-Quit Clinic Visit | $15 | $10 | | | | $25 |
| **3** | Pre-Quit Clinic Visit | $15 | $10 | | | | $25 |
| **4** | Pre-Quit Clinic Visit | $15 | $10 | | | | $25 |
| **5** | Lab Visit 2 | $35 | $10 | | $15 | | $60 |
| **6** | Monitoring Clinic Visit | $15 | $10 | | | | $25 |
| **7** | Monitoring Clinic Visit | $15 | $10 | | | | $25 |
| **8** | Monitoring Clinic Visit | $15 | $10 | | | | $25 |
| **10** | Monitoring Clinic Visit | $15 | $10 | | | | $25 |
| **12** | Monitoring Clinic Visit | $15 | $10 | | | | $25 |
| **14** | Monitoring Clinic Visit | $15 | $10 | | | | $25 |
| **18** | Monitoring Clinic Visit | $15 | $10 | | $15 | | $40 |
| **22** | Monitoring Clinic Visit | $15 | $10 | | | | $25 |
| **26** | Monitoring Clinic Visit | $15 | $10 | | | | $25 |
| **32** | Monitoring Clinic Visit | $20 | $10 | | $15 | | $45 |
| **32** | Completion Bonus | | | | | $100 | $100 |
| | | | | | **Study Total:** | | **$610** |
| **N/A** | Referral Bonus | | | | | $20^ | $20 |
| | | | | | **Total w/ Referrals** | | **$630** |

**Note: [1] Only applies if you opt to receive $10 travel reimbursement for that visit**
**^ Table shows compensation for two successful referrals.**

**HOW DOES TRAVELING VIA THE RIDE SERVICE WORK?** You may elect to use "Roundtrip", which is a car ride service that partners with Lyft to coordinate roundtrip rides to study appointments. Study staff will schedule each ride using your first name, last name, and phone number via Roundtrip's HIPAA compliant platform. You will receive two reminder calls within 24-48 hours prior to your study visit. The first will serve to confirm your visit, interest in using the ride service, and preferred pickup/drop-off locations. The second will serve to notify you of your ride's pickup time. If the study staff cannot reach you by 5pm the day prior to your study visit, your ride will be cancelled. You will still be permitted to attend the visit and will receive $10 to cover your travel expenses. If you need to cancel a previously confirmed ride, you must do so by contacting the study staff immediately, preferably by 5pm the day before your appointment. If you fail to notify study staff within this timeframe, you may no longer be permitted to use the ride service at future study visits.

**WILL I HAVE TO PAY FOR ANYTHING?** There will be no charge to you for participating in this research study. You and/or your health insurance may be billed for the costs of medical care during this study if these expenses would have happened even if you were not in the study or if your insurance agrees in advance to pay.

**WHAT HAPPENS IF I AM INJURED OR HURT IN THE RESEARCH PROGRAM?** In the event that you are hurt or injured as a result of participation in this research study, please contact the investigator listed on page one of this form. We will offer you the care needed to treat injuries directly resulting from participation in this research study. We may bill your insurance company or other third parties, if appropriate, for the costs of the care associated with these injuries; however, you may also be responsible for some of these costs. The sponsor will pay for the treatment of any injuries or illnesses as a result of the investigational product. Additionally, the sponsor will pay for treatment of any injuries or illnesses resulting from correctly performed procedures that are otherwise not covered by insurance. However, the sponsor will not compensate for treatment of injuries if they result from the failure of the study team, study team negligence, the progression of any underlying conditions, or events from

any approved or standard-of-care therapies. There are no plans for the University of Pennsylvania to pay you or provide other compensation for the injury. You do not give up your legal rights by signing this form.

**WHEN IS THE RESEARCH PROGRAM OVER? CAN I LEAVE BEFORE IT ENDS?** This research study is expected to end after all participants have completed all visits and all information has been collected. This study may also be stopped at any time by the study Sponsor or the Food and Drug Administration (FDA) without your consent if:

- The Principal Investigator feels it is necessary for your health or safety. Such an action would not require your consent, but you would be informed if such a decision was made and the reason for this decision.
- You have not followed study instructions.
- The Sponsor or Principal Investigator has decided to stop the study.

If you decide to participate, you are free to leave the research study at any time. Withdrawal will not interfere with your future care at the University of Pennsylvania.

**WHAT HAPPENS TO MY COLLECTED SAMPLES AND DATA?** Urine samples collected for drug screening and/or pregnancy testing will be discarded once that testing is completed and will not be stored. The saliva samples used to examine by-products of nicotine will be discarded at the end of the study. Blood samples will be used to analyze exploratory cardiovascular risk markers at different time points throughout the study. We would also like to store some of your blood and the information you provide (such as demographic information, smoking behavior, survey responses, and food intake information) for possible use in future research. The information and blood you provide in this study could be useful to future researchers who want to learn more about nicotine addiction and/or better ways to help people quit smoking. This future research would be reviewed and approved by the University of Pennsylvania Institutional Review Board, the committee responsible for approving all research at the University of Pennsylvania. Your data and/or blood will not be used in future research without this approval process.

Permission to store your information and blood for use in future research is optional and you can indicate your choice at the end of this consent form. Your information and blood samples will be labeled and stored with an identification number only (not your name). The next section of the consent form provides additional information on how we will protect your information and keep it confidential. You may withdraw your permission at any time by contacting study staff and letting us know you no longer want your information and samples to be stored for use in future research. It is possible your samples may be used in future research for commercial profit. If so, you will not share in or benefit from this commercial profit. Additionally, individual research results obtained as part of future research will not be shared with you.

**WHO CAN SEE OR USE MY INFORMATION? HOW WILL MY PERSONAL INFORMATION BE PROTECTED?** While we cannot guarantee total privacy, we will do our best to make sure that the personal information in your research record is kept private. Your information will be labeled with an identification number only (not your name). Only authorized university personnel will be able to link your identification number with your name. Your samples will be stored in our private bank, which can be accessed only by authorized study personnel.

Every attempt will be made by the investigators to keep all information collected in this study strictly confidential. We will store your information in a secure room with limited access. We will control access to the computer files that hold this information. All electronic data will be encrypted and held within a secured network. Remote study sessions will be conducted via phone or via BlueJeans, which is a HIPAA-compliant platform with security features including a room lock to ensure that communications within the platform remain private. Your personal information would only be given out if required by law. If information from this research study is published or presented at scientific meetings, no names or other identifying information will be used.

A description of this clinical trial will be available on http://www.clinicaltrials.gov, as required by U.S. Law. This web site will not include information that can identify you. At most, the web site will include a summary of the results. You can search this web site at any time.

**WHAT INFORMATION ABOUT ME MAY BE COLLECTED, USED OR SHARED WITH OTHERS?**

- Name, address, telephone number, email address
- Date of birth
- Social Security Number (W-9 form)
- Medical Record Number
- Some personal information that may be considered sensitive, such as medical history, psychological history, alcohol use history, etc.
- Results from physical examinations, questionnaires, or procedures as outlined in this consent form

**WHY IS MY INFORMATION BEING USED?** Your contact information is used by the research team to contact you during the study. Your personal health information and results of procedures are being collected as part of this research study. In some situations, personal health information might be used to help guide your medical treatment.

**WHO MAY USE AND SHARE INFORMATION ABOUT ME?** The following individuals and organizations may use or disclose your personal health information for this research study:

- The Principal Investigator (PI) and the research team
- The University of Pennsylvania Institutional Review Boards (the committees charged with overseeing research on human subjects) and the University of Pennsylvania Office of Regulatory Affairs
- The University of Pennsylvania Office of Clinical Research (the office that monitors research studies)
- Authorized members of the University of Pennsylvania, the UPHS, and School of Medicine workforce that may need to access your information in the performance of their duties (for example, research oversight and monitoring)

**ELECTRONIC MEDICAL RECORDS AND RESEARCH RESULTS**

**What is an Electronic Medical Record?**

An Electronic Medical Record (EMR) is an electronic version of the record of your care within a health system. An EMR is simply a computerized version of a paper medical record.

If you are receiving care or have received care within the University of Pennsylvania Health System (UPHS) (outpatient or inpatient) and are participating in a University of Pennsylvania research study, results of research-related procedures (i.e. laboratory tests, imaging studies, and clinical procedures) may be placed in your existing EMR maintained by UPHS. Once placed in your EMR, these results are accessible to appropriate UPHS workforce members that are not part of the research team. Information within your EMR may also be shared with others who are determined by UPHS to be appropriate to have access to your EMR (e.g. health insurance company, disability provider, etc.). No results from this research study or research data will be shared with you or placed in your EMR.

**WHO, OUTSIDE THE SCHOOL OF MEDICINE, MIGHT RECEIVE MY INFORMATION?**

The following entities are supporting and overseeing the research and the sponsor:

- Novo Nordisk (company that manufactures, markets, and distributes liraglutide)
- The Abramson Cancer Center at the University of Pennsylvania
- The Food and Drug Administration (FDA)
- The National Institutes of Health (NIH)

The following entity is managing participant transportation and has access to first name, last name, and phone number only:

- Roundtrip

The Principal Investigator or research staff will inform you if there are any changes to the list above during your active participation in the study. Once your personal health information is disclosed to others outside of UPHS or the School

of Medicine, it may no longer be covered by federal privacy protection regulations. This does not mean that all personal identifying information is being disclosed. Generally, if information has to be released it contains only initials and birth date, or only a unique number, not complete contact information. Any such additions will be subject to Penn UPHS and School of Medicine procedures to protect your privacy.

**HOW LONG MAY THE SCHOOL OF MEDICINE USE OR DISCLOSE MY PERSONAL HEALTH INFORMATION (PHI)?** Your authorization for use of your personal health information for this specific study does not expire.
Your information may be held in a research repository or database. However, UPHS and the School of Medicine may not re-use or re-disclose information collected in this study for a purpose other than this study unless:

- You have given written authorization to do so
- The University of Pennsylvania Institutional Review Board grants permission after ensuring that appropriate privacy safeguards are in place
- As required by law

**CAN I CHANGE MY MIND ABOUT GIVING PERMISSION FOR USE OF MY INFORMATION?** You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the Principal Investigator of the study. Even if you withdraw your permission, the Principal Investigator may still use your information that was collected prior to your written withdrawal request. If you withdraw your permission, you will not be able to stay in the study.

**WHAT IF I DECIDE NOT TO GIVE PERMISSION TO USE AND GIVE OUT MY HEALTH INFORMATION?** You will not be able to participate in this research study.

**WHO CAN I CALL WITH QUESTIONS, COMPLAINTS OR IF I'M CONCERNED ABOUT MY RIGHTS AS A RESEARCH PARTICIPANT?** If you have questions, concerns, or complaints regarding your participation in this research study or if you have any questions about your rights as a research participant, you should speak with the Principal Investigator listed on page one of this form. If a member of the research team cannot be reached, or you want to talk to someone who is not directly involved with the study, you may contact the Office of Regulatory Affairs with any questions, concerns, or complaints at the University of Pennsylvania by calling 215-898-2614.

When you sign this form, you are agreeing to take part in this research study. This means that you have read the consent form, your questions have been answered, and you have decided to volunteer. Your signature also means that you are permitting the University of Pennsylvania Health System and the School of Medicine to use your personal health information collected about you for research purposes within our institution. You are also allowing the University of Pennsylvania Health System and the School of Medicine to disclose that personal health information to outside organizations or people involved with the operations of this study. A copy of this form will be given to you.

**STORING BLOOD SAMPLES FOR USE IN FUTURE RESEARCH:**
Please check YES and initial if you give permission for us to store some of your blood from this study for use in future research. Please check NO and initial if you **do not** give us permission to store some of your blood from this study for use in future research.

☐ **YES** ☐ **NO** **Participant Initials: _____**

**Name of Research Participant:**

PRINT NAME: _____

SIGNATURE: _____ DATE: _____

**Name of Person Obtaining Consent:**

PRINT NAME: _____

SIGNATURE: _____ DATE: _____



*IRB Approval From: 10-06-2021 To: 10-05-2022*

| | Intake | Pre-Quit Period | | | | | Monitoring Period | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Study Week | | | | | | | | | | | | | | |
| **Study Procedures** | | 1 | 2 | 3 | 4 | 5 | 6* | 7 | 8 | 10 | 12 | 14 | 18 | 22 | 26 | 32[5] |
| *Medication* | | | | | | | | | | | | | | | | |
| Review Non-Study Medications | x | x | x | x | x | x | x | x | x | x | x | x | x | x | x | x |
| Symptoms Evaluation Checklist | | x | x | x | x | x | x | x | x | x | x | x | x | x | x | x |
| Liraglutide or Placebo | | x[1] | x | x | x | x | x | x | x | x | x | x | x | x | x | x |
| Study Medication Adherence | | | x | x | x | x | x | x | x | x | x | x | x | x | x | x |
| *Intake, Lab, & Clinic Visits* | | | | | | | | | | | | | | | | |
| Informed Consent | x | | | | | | | | | | | | | | | |
| Medical History | x | | | | | | | | | | | | | | | |
| Brief Physical Examination | x | | | | | | | | | | | | | | | |
| Height | x | | | | | | | | | | | | | | | |
| Urine Pregnancy Test | x[2] | x[2] | x[2] | x[2] | x[2] | x[2] | x[2] | x[2] | x[2] | x[2] | x[2] | x[2] | x[2] | x[2] | x[2] | x[2] |
| CO Measurements, Weight, Blood Pressure, HR, Blood Glucose Monitoring, Study Questionnaires, Psychiatric Assessments | x | x | x[6] | x[6] | x[6] | x | x[6] | x[6] | x[6] | x[6] | x[6] | x[6] | x | x[6] | x[6] | x |
| Urine Drug Screen | x | x | | | | x | | | | | | | | | | |
| Food-Related Computer Tasks | x | x | | | | x | | | | | | | | | | |
| Blood Sample Collection | x | x | | | | x | | | | | | | x | | | x |
| Schedule 24-Hr Dietary Recalls | x[3] | | | | x[3] | | | | | | | x[3] | | | x[3] | |
| Saliva Sample Collection | | | | | | | | x[4] | | | | | | | | x[4] |
| Impact of COVID-19 on Smoking Survey | x | | | | | | | | | | | | | | x | |
| *Smoking Cessation Counseling* | | | | | | | | | | | | | | | | |
| Pre-Quit Counseling Session | | | | | | x | | | | | | | | | | |
| Target Quit Date Session | | | | | | | x | | | | | | | | | |
| Booster Counseling Session | | | | | | | | x | x | x | x | | x | | x | |

CO = Carbon Monoxide reading; HR = Heart Rate
* = Target Quit Date
[1] = Participants will be randomized to receive either liraglutide or placebo
[2] = Female participants only
[3] = Three 24-hour dietary recall assessments will be completed over the phone prior to the next visit
[4] = Based on smoking behavior, participants may be asked to provide a saliva sample
[5] = Four weeks after the last study visit, participants will be contacted by phone to assess smoking status and any delayed side effects
[6] = Measure will not be completed if session is conducted remotely.