Study Title: GLP-1 Receptor Agonists Post-Bariatric Surgery (GRABS) 0 Pilot Trial
Version Date: 08/15/24
PI: Jason Samuels M.D.

Name of participant: _____ Age: _____

The following is given to you to tell you about this research study. Please read this form with care and ask any questions you may have about this study. Your questions will be answered. Also, you will be given a copy of this consent form.

Key Information:
The first section of this document contains some key points that the research team thought you would find important. The study is described in more detail after this section. If you do not understand something, please ask someone.

Key information about this study:
The purpose of this study is to collect information needed to understand if a potential treatment, Tirzepatide (medication administered by a small shot under the skin) can improve weight loss after someone undergoes bariatric surgery. Tirzepatide is currently approved for the treatment of type 2 diabetes and obesity. This study will enroll up to 30 people at Vanderbilt University Medical Center (VUMC). Patients who participate in this study will either receive the treatment drug Tirzepatide, or continue with your current post-bariatric surgery care.

Obesity can increase the risk of other serious health problems including diabetes, heart disease, high blood pressure, and cancer. In this study, we are testing to see if Tirzepatide is safe and effective to take to take twelve months after someone undergoes bariatric surgery. We are also testing to see if Tirzepatide will increase weight loss. No one knows if the drug being studied will improve weight loss after bariatric surgery.

If you agree to be in the study, you will be in the study for about 48 weeks. The study involves up to 3 in-person study visits in addition to your usual bariatric follow-up visit one year after surgery. You will also receive a phone call from a research nurse or study personnel 6 times. You will be asked to complete a survey asking about any symptoms you may have every 4 weeks for a total of 8 surveys. You will receive the study drug for 24 weeks. Dosage will be increased every 4 weeks by a standard schedule until you reach the maximum dose. Your dose may be decreased if you are having significant side effects. We will measure your vital signs. We

will draw blood and collect urine. If you are a woman and can have children, we will do a urine pregnancy test to make sure you are not pregnant.

At three of your visits, you will also complete a mixed meal test. In a mixed meal test, you will be asked to drink a liquid meal with sugar, fat, and protein. The purpose of this test is to determine how your body's ability to digest food changes over time after bariatric surgery while you are taking the study drug, Tirzepatide. During the test, you will have a catheter placed in one of your veins in your arm and your blood will be drawn multiple times from this catheter. Each test will take about five hours.

Detailed Information:
The rest of this document includes detailed information about this study (in addition to the information listed above).

You are being asked to take part in this research study because you have undergone bariatric surgery with the purpose of losing weight. Your body mass index (BMI) at one year after surgery is over 30 kg/m^2. A BMI over 30 is considered obesity and 35 is considered severe obesity. Studies have shown that many patients with a BMI of 30 or more are at greater risk of heart disease, diabetes, fatty liver, and other diseases related to obesity.

You do not have to be in this research study. You may choose not to be in this study and get other treatments without changing your healthcare, services, or other rights. You can stop being in this study at any time. If we learn something new that may affect the risks or benefits of this study, you will be told so that you can decide whether or not you still want to be in this study. Your medical record will contain a note saying you are in a research study and may contain some research information about you. Anyone you authorize to receive your medical record will also get this information.

Side effects and risks that you can expect if you take part in this study:
A risk of taking part in this study is the possibility of a loss of confidentiality or privacy. Loss of privacy means having your personal information shared with someone who is not on the study team and was not supposed to see or know about your information. The study team plans to protect your privacy.

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Like all drugs, Tirzepatide can have side effects, which are problems caused by the study drug. We do not expect everyone who takes Tirzepatide to have side effects. People in the study will be carefully monitored to see if side effects are happening. The list below shows the side effects that people have had in other studies. During the study, we will carefully monitor for the side effects listed below and other ones.

Common side effects (≥10% of patients):

- Nausea (sick to the stomach)
- Diarrhea (loose stool)
- Vomiting (throwing up)
- Constipation (difficulty passing stool)
- Abdominal pain (pain of the stomach)
- Fatigue (tiredness)
- Headache (pain in the head)
- Heartburn
- Belching or burping (noisy release of air from the stomach)

Uncommon side effects (1%-10% of patients):

- Decreased appetite
- Weight loss
- Injection site reaction (redness, pain or swelling)
- Abdominal distension (feeling of fullness or tightness in the abdomen)
- Flatulence (passing of gas)
- Hypotension (drop in blood pressure)
- Tremors (shaking)
- Dizziness (feeling like you or your head are spinning)
- Tingling (paresthesia)
- Eye irritation (feelings of dryness, itchiness, pain, or grittiness in the eye)
- Tachycardia (fast heart rate)

Rare (<1% of patients)

- Serious allergic reactions (swelling of your face, lips, tongue or throat, severe rash or itching or very rapid heartbeat, problems breathing or swallowing, fainting, or feeling dizzy.
- Gallbladder problems (pain in your upper stomach, yellowing of skin or eyes (jaundice), fever, clay-colored stools)

Black Box Warning: Tirzepatide carries a black box warning as mandated by the FDA. The warning is for the theoretical risk for development of a type of cancer of the thyroid known as medullary thyroid cancer. This is due to data from studies in animals which found a higher rate of these rare cancers when animals were given medications in the same family as Tirzepatide. It is unknown whether this risk is present in humans as well at this time.

Common side effects from acetaminophen (Tylenol):

- Nausea
- Vomiting
- Stomach pain
- Loss of appetite
- Constipation

Risks of Other Protocol Specified Medications or Procedures

Blood Draw

Pain, redness, soreness, bruising, or infection may occur at the needle stick site. Rarely, some people may faint.

Mixed Meal Test

Occasionally patients who drink a high carbohydrate beverage after bariatric surgery may develop symptoms of dumping syndrome including flushing, nausea, vomiting, abdominal discomfort, and diarrhea.

Beneficial effects that might result from this study:

The benefits to science and humankind that might result from this study: Researchers will learn more about this drug and how it may help patients with severe obesity lose weight. Personal benefits: You may personally lose more weight by taking the study drug. This may decrease

your risk of diseases related to obesity such as diabetes, heart disease, or high cholesterol. If you have these diseases, you may be more likely to be able to stop taking medications for these other diseases.

Procedures to be followed:

Screening Visit (1)

Visit -1

This occurs prior to study enrollment. We will review your medical record and determine if you qualify for this study. We will ask you about your medical history and your family history of endocrine cancers. If you indicate your interest in the study, you will also have:

- A phone call with a member of the research study to discuss the study in detail.
- During the phone call, this consent form is reviewed, all questions answered, and you will be asked to sign an electronic copy. You will be given a copy of the consent form. This will occur prior to any study test/procedures being performed.
- You will be given an appointment for your visit 0.
- You will be given instructions on fasting and medications to withhold prior to visit 0b and future visits that require fasting.

Visit 0 once you have consented you will be asked to present to the Clinical Research Center after having fasted for 8 or more hours and the following will take place at this visit:

- You will have labs drawn to check your blood count, vitamin levels, liver and kidney function and electrolyte levels.
- Physical exam including vital signs (heart rate, blood pressure, oxygen level, height, weight, waist circumference).
- If you are a woman and can have children, we collect urine to check if you are pregnant. We will tell you the results.
- Pregnancy test if you are a woman and can have children.
- Vital signs including heart rate, blood pressure, weight, and waist circumference.
- An intravenous catheter will be placed.

- You will drink 1 bottle of "Ensure Plus" drink in 30 minutes or less. This will be mixed with 500 mg of acetaminophen to measure the rate of movement of food through your intestines.
- Blood draw of about or up to 85 ml (about 6 tablespoons) over 4 and a half hours after consuming the drink to check your health and for this research study. Some blood may be stored for future research purposes.
- You will be given dates and instructions for visit 4 and 8.
- You will be given dates and instructions for visits 0D, 4D, and 8D.
- You will be given the study drug as well as instructions on its use.

Visit 0D, 4D, and 8D – DEXA Scan - After each visit to the Clinical Research Center you will also undergo an x-ray that will measure your bone density, muscle mass, and fat mass. The Dual-energy X-ray Absorptiometry (DXA) is a special type of X-ray that measures the mineral density of the bones of the whole body (except head). You should not take any calcium tablets within 2 hours before the scheduled DXA scan This xray will take 30 minutes to an hour. You will lay flat on a table while an xray machine will take pictures of your body from the neck down to your feet. The total amount of radiation that you would receive by participating in this study is equal to that of 34 days of radiation from the natural surroundings, or less than 1% of the amount allowed in a year for people who are exposed to radiation as part of their work.

Visit 4 Clinical Research Center visit

Visit 4 for this visit you will be asked to present to the Clinical research center after having fasted for 8 or more hours and the following will take place at this visit:

- Pregnancy test if you are a woman and can have children.
- Vital signs including heart rate, blood pressure, weight, and waist circumference.
- An intravenous catheter will be placed.
- You will drink 1 bottle of "Ensure Plus" drink in 30 minutes or less. This will be mixed with 500 mg of acetaminophen to measure the rate of movement of food through your intestines.
- Blood draw of about or up to 85 ml (about 6 tablespoons) over 4 and a half hours after consuming the drink to check your health and for this research study. Some blood may be stored for future research purposes.

- For those in randomized to the study drug arm, you will stop the study drug after this visit, if you have not already done so.
- You will be asked to return all used or unused syringes of the study drug.

Electronic visit 1, 2, 3, 5, 6, and 7. At weeks 6, 12, 18, 30, 36, and 42, you will receive a call from a clinic nurse or researcher to:

- Discuss any changes to your health since your last visit.
- Check to see if you are taking the study drug correctly and without problems.
- Check to see if you are having any problems.
- Ensure you have completed the weekly surveys and address any issues raised by the survey.
- Provide counseling related to any side effects from the study drug.
- Ensure you have received the study drug from the investigational drug pharmacy and answer any questions regarding its administration.
- At visit 7, if you have not already done so, you will receive a date for your visit 8 appointment at the Clinical Research Center You will be given instructions on fasting and medications to withhold prior to visit 8.

Visit 8 – Study completion visit. This visit will be the end of your study enrollment. For this visit you will be asked to present to the Clinical research center after having fasted for 8 or more hours and the following will take place at this visit:

- Vital signs including heart rate, blood pressure, weight, and waist circumference.
- An intravenous catheter will be placed.
- You will drink 1 bottle of "Ensure Plus" drink in 30 minutes or less. This will be mixed with 500 mg of acetaminophen to measure the rate of movement of food through your intestines.
- Blood draw of about or up to 85 ml (about 6 tablespoons) over 4 and a half hours after consuming the drink to check your health and for this research study. Some blood may be stored for future research purposes.

Monthly symptom testing: you will receive a link via the My Health at Vanderbilt app on a weekly basis. The link will take you to a secure, online survey with 20 questions asking you

about any symptoms you have that may be related to the study drug. You will be asked to complete this within 48 hours of receiving the survey.

Medication changes during the study.
Those randomized to the 'control' arm will continue following the standard recommendations for maintaining your weight after bariatric surgery. After your initial screening tests, if you are randomized to the Tirzepatide arm, you will begin either the study drug Tirzepatide at 2.5 mg weekly. At week 4 we will increase your dose to 5 mg. At that point, we will begin adjusting the doses every 4 weeks depending on how well you tolerate the study drug. Your dose will not increase above 15 mg. You will continue the final dose for 4weeks. These changes to your dose are done to determine the best dose to balance weight loss with side effects. Occasionally patients experience significant side effects preventing us from increasing the dose or even requiring that we decrease the dose. We will work with you to avoid that by using other medications to treat these side effects such as medications that treat nausea and vomiting, constipation, or other symptoms. After 24 weeks of taking the drug, you will stop the medication. However, you will remain in the study so that we can observe any changes to your symptoms and your weight for another 24 weeks.

Payments for your time spent taking part in this study or expenses:
All participants, regardless of which intervention they receive will be paid per the study incentive program. For this program, participants will receive $50 for each mixed meal tolerance test they complete up to 3 total tests per person. Additionally, participants who complete all 8 surveys will be paid $100 one time after completing the final survey.

Costs to you if you take part in this study:
If you agree to take part in this research study, you and/or your insurance will not have to pay for the tests and treatments that are being done only for research. However, you are still responsible for paying for the usual care you would normally receive for the treatment of your illness. This includes treatments and tests you would need even if you were not in this study. These costs will be billed to you and/or your insurance.

You have the right to ask what it may cost you to take part in this study. If you would like assistance, financial counseling is available through the Vanderbilt Financial Assistance Program. The study staff can help you contact this program. You have the right to contact your

insurance company to discuss the costs of your routine care (non-research) further before choosing to be in the study. You may choose not to be in this study if your insurance does not pay for your routine care (non-research) costs and your doctor will discuss other treatment plans with you.

Payment in case you are injured because of this research study:
If it is determined by Vanderbilt and the Investigator that an injury occurred as a direct result of the tests or treatments that are done for research, then you and/or your insurance will not have to pay for the cost of immediate medical care provided **at Vanderbilt** to treat the injury. There are no plans for Vanderbilt to pay for any injury caused by the usual care you would normally receive for treating your illness or the costs of any additional care. There are no plans for Vanderbilt to give you money for the injury.

Who to call for any questions or in case you are injured:
If you should have any questions about this research study or if you feel you have been hurt by being a part of this study, please feel free to contact Dr. Jason Samuels at (615) 322 – 4504, ext 24504. If you cannot reach the research staff, please page the study doctor at (615) 835-9163.

For additional information about giving consent or your rights as a person in this study, to discuss problems, concerns, and questions, or to offer input, please feel free to call the VUMC Institutional Review Board Office at (615) 322-2918 or toll free at (866) 224-8273.

Reasons why the study doctor may take you out of this study:
The study doctor may stop you from taking part in this study at any time:
1. if it is in your best interest,
2. if you do not follow the study procedures, or
3. if the study is stopped.

If you are removed from the study, your study doctor will discuss with you stopping procedures and your future care.

What will happen if you decide to stop being in this study?
If you decide to stop being part of the study, you should tell your study doctor. Deciding to not be part of the study will not change your regular medical care in any way. If you decide to stop

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being part of the study, you should tell your study doctor. Deciding to not be part of the study will not change your regular medical care in any way.

Confidentiality:
The study funder VUMC may share your information and/or samples, without identifiers, to others or use them for other research projects not listed in this form. Vanderbilt University Medical Center, Dr. Samuels, and his study staff will comply with all laws regarding the privacy of such information. There are no plans to pay you for the use or transfer of this de-identified information.

It is the intent of the study doctor, study staff, and Vanderbilt University that the health data that is shared will not be able to identify you. You will be identified by a code and personal information from your records will not be released without your written permission.

You will not be identified by name in any published reports about this study or in any other scientific publication or presentation. Information about you collected for this study may be shared with other researchers. It may also be used for other research studies. We will make sure that your identity cannot be linked to the information we share. We will not ask you for additional permission before sharing the information.

Vanderbilt University Medical Center may use the health data and/or samples sent to them:
1) To develop new tests
2) For other activities (such as development and regulatory)
3) As part of research activities related to the study of diseases and the development of drugs and tests used to treat diseases.
4) To allow outside researchers to use data and specimens that does not identify you.

There is a risk that if people outside the study get your health data, they could misuse it for purposes other than those outlined in this consent. The study team has strict privacy and confidentiality protection procedures in place to prevent this from occurring so the chance of this happening to you is extremely small.

Privacy:

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Any samples and information about you may be made available to others to use for research. To protect your privacy, we will not release your name. You will not receive any benefit as a result of the tests done on your samples. These tests may help us or other researchers learn more about the causes, risks, treatments, or how to prevent this and other health problems.

Your samples may be used to make new products or tests. These may have value and may be developed and owned by the study staff, Vanderbilt University, VUMC, and/or others. If this happens, there are no plans to provide money to you.

At any time, you may ask in writing to have your sample destroyed. You should contact Dr. Samuels or his study staff at

Jason M Samuels, M.D.
1161 21st Avenue South
Medical Center North, D-5203
Nashville, TN 37232-2730

to have your sample destroyed and no longer used for research. We will not be able to destroy research data that has already been gathered using your sample. Also, if your identity was removed from the samples, we will not be able to locate and destroy them. There will be no costs to you for any of the tests done on your samples. You will not be paid for the use of your samples.

Study Results:
Study results will not be shared directly with participants but will be available through publication in medical journals.

Participation in future studies
Data from this study might be used for future research. We would like to contact you regarding new clinical trial options. By signing this form, you will allow qualified professional persons from our research team to contact you in the future to ask if you want to participate in any studies. You have no obligation to participate in any study.

Authorization to Use/Disclose Protected Health Information
What information is being collected, used, or shared?

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To do this research, we will need to collect, use, and share your private health information. By signing this document, you agree that your health care providers (including both Vanderbilt University Medical Center and others) may release your private health information to us, and that we may use any and all of your information that the study team believes it needs to conduct the study. Your private information may include things learned from the procedures described in this consent form, as well as information from your medical record (which may include information such as HIV status, drug, alcohol or STD treatment, genetic test results, or mental health treatment).

Who will see, use or share the information?
The people who may request, receive or use your private health information include the researchers and their staff. Additionally, we may share your information with other people at Vanderbilt, for example if needed for your clinical care or study oversight. By signing this form, you give permission to the research team to share your information with others outside of Vanderbilt University Medical Center. This may include the sponsor of the study and its agents or contractors, outside providers, study safety monitors, government agencies, other sites in the study, data managers and other agents and contractors used by the study team. We try to make sure that everyone who sees your information keeps it confidential, but we cannot guarantee that your information will not be shared with others. If your information is disclosed by your health care providers or the research team to others, federal and state confidentiality laws may no longer protect it.

Do you have to sign this Authorization?
You do not have to sign this Authorization, but if you do not, you may not join the study.

How long will your information be used or shared?
Your Authorization for the collection, use, and sharing of your information does not expire. Additionally, you agree that your information may be used for similar or related future asthma or obesity research studies.

What if you change your mind?
You may change your mind and cancel this Authorization at any time. If you cancel, you must contact the Principal Investigator in writing to let them know by using the contact information provided in this consent form. Your cancellation will not affect information already collected in

the study, or information that has already been shared with others before you cancelled your authorization.

If you decide not to take part in this research study, it will not affect your treatment, payment or enrollment in any health plans or affect your ability to get benefits. You will get a copy of this form after it is signed.

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STATEMENT BY PERSON AGREEING TO BE IN THIS STUDY

I have read this consent form and the research study has been explained to me verbally. All my questions have been answered, and I freely and voluntarily choose to take part in this study.

Date	Signature of patient/volunteer

Consent obtained by:

Date	Signature
	Printed Name and Title