MAYO CLINIC

Name and Clinic Number

Approval Date: **September 7, 2018**
Not to be used after: **March 13, 2019**

RESEARCH PARTICIPANT CONSENT AND PRIVACY AUTHORIZATION FORM

Study Title: OBERTO-101, A Phase 1, Multiple dose, Multicenter, Open-label Study to Evaluate Safety, Tolerability and Immunogenicity of Subcutaneous Injection of PolyPEPI1018 Vaccine as an Add-on Immunotherapy to the Standard-of-Care Maintenance Therapy in Subjects with Metastatic Colorectal Cancer (OBERTO)

IRB#: 18-000848

Principal Investigator: Joleen Hubbard, M.D., and Colleagues

Please read this information carefully. It tells you important things about this research study. A member of our research team will talk to you about taking part in this research study. If you have questions at any time, please ask us.

Take your time to decide. Feel free to discuss the study with your family, friends, and healthcare provider before you make your decision.

To help you decide if you want to take part in this study, you should know:

- Taking part in this study is completely voluntary.
- You can choose not to participate.
- You are free to change your mind at any time if you choose to participate.
- Your decision won't cause any penalties or loss of benefits to which you're otherwise entitled.
- Your decision won't change the access to medical care you get at Mayo Clinic now or in the future if you choose not to participate or discontinue your participation.

For purposes of this form, Mayo Clinic refers to Mayo Clinic in Arizona, Florida and Rochester, Minnesota; Mayo Clinic Health System; and all owned and affiliated clinics, hospitals, and entities.

If you decide to take part in this research study, you will sign this consent form to show that you want to take part. We will give you a copy of this signed and dated form to keep. A copy of this form will be put in your medical record.

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CONTACT INFORMATION

You can contact …	At …	If you have questions about …
Principal Investigator: Joleen Hubbard, M.D.	**Phone:** (507) 284-2511 **Institution Name and Address:** Mayo Clinic 200 First St SW Rochester, MN 55905	▪ Study tests and procedures ▪ Research-related injuries or emergencies ▪ Any research-related concerns or complaints ▪ Withdrawing from the research study ▪ Materials you receive ▪ Research-related appointments
Mayo Clinic Institutional Review Board (IRB)	**Phone:** (507) 266-4000 **Toll-Free:** (866) 273-4681	▪ Rights of a research participant
Research Subject Advocate **(The RSA is independent of the Study Team)**	**Phone:** (507) 266-9372 **Toll-Free:** (866) 273-4681 **E-mail:** researchsubjectadvocate@mayo.edu	▪ Rights of a research participant ▪ Any research-related concerns or complaints ▪ Use of your Protected Health Information ▪ Stopping your authorization to use your Protected Health Information
Research Billing	**Rochester, MN:** (507) 266-5670	▪ Billing or insurance related to this research study

Other Information:

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

1. Why are you being asked to take part in this research study?

You are being asked to participate in this research study because you have metastatic colorectal cancer.

It is expected that approximately 15 subjects will be enrolled in this study, with10 participants being enrolled at Mayo Clinic.

2. Why is this research study being done?

The purpose of this study is to determine if an experimental drug, PolyPEPI1018 vaccine, is safe in the treatment of this disease, in addition to the standard treatment. PolyPEPI1018 has not been previously used in humans.

PolyPEPI1018 is a peptide vaccine. The 6 peptides in PolyPEPI1018 contain 12 novel and distinct selected epitopes which are derived from 7 conserved cancer testis antigens (CTAs) that act in combination to activate T cells against CRC antigens in a high proportion of patients. A **peptide vaccine** is any peptide which serves to immunize an organism against a pathogen. Peptide vaccine is often synthetic and mimics naturally occurring proteins from pathogens.

3. Information you should know

Who is Funding the Study?

Treos Bio ZRT is funding the study. Treos Bio ZRT will pay the institution to cover costs related to running the study.

4. How long will you be in this research study?

If you decide to participate in this study, you will be asked to make a total of 16 visits to the study site over the next approximately 41 weeks.

If you have participated in the first part of the OBERTO study and have already signed the informed consent for a single-dose vaccination, by signing the present informed consent form you accept to roll over into the present, multiple doses study and complete a total of 16 visits. You do not need to start over again, you will just continue from your last visit (for example, if you have already completed Visit 6 you will start from Visit 7).

5. What will happen to you while you are in this research study?

At your first visit (Visit 1), the following procedures will be performed to determine if you are suitable to participate in the study:

- If you agree to participate in the study, you will be required to sign this informed consent form before any study activities take place.
- Your doctor/staff will discuss all of the requirements for the study and any conditions that will prevent you from being eligible to participate in the trial
- Your medical history will be reviewed
- Your prior cancer treatments will be reviewed
- Your medication history will be reviewed
- Your doctor will perform a complete physical examination and vital signs (heart rate, oral temperature, breathing rate, sitting blood pressure, height and weight) will be taken
- Your doctor will assess your ability to perform daily activities
- A biopsy (a small sample of your tumor tissue) of your tumor will be taken to look for the presence of specific cells called tumor infiltrating lymphocytes or TILs. A biopsy is obtained by taking a small piece of your tumor tissue using a large needle (core biopsy).Alternatively, a small section of your tumor may be removed by cutting it out surgically (excisional biopsy) or with a special round shaped knife (punch biopsy). Your study doctor will explain the details of the procedure depending on how the biopsy will be obtained. This research may help scientists better understand how these TILs affect the treatment of this type of cancer in the future.
- A computed tomography (CT) scan will be performed to assess the extent of your disease and to see if you can participate in this study

- Your doctor/staff will collect about 1-2 tablespoons of blood for laboratory tests to check your overall health and organ functions (such as liver, heart, kidneys, pancreas)
- Your doctor/staff will collect about 1 tablespoon of blood for laboratory tests to check tumor biomarkers that are found in the blood and may be related to your reaction to the study drug
- Your doctor/staff will collect at least 2 tablespoons of your blood to study how your body's immune system responds to certain ingredients of the vaccine. Treos Bio ZRT may store any of this remaining blood sample for up to 2 years after the study completion for additional scientific exploration of how your body's immune system responds to certain ingredients of the vaccine.
- Your doctor/staff will collect at least 2 tablespoons of your urine for laboratory tests to check the health of your urinary tract and kidneys
- If you are a female and able to get pregnant, you will have a urine pregnancy test. Your doctor/staff will tell you the result of this test

The Principal Investigator will review the results of these tests and procedures. If you aren't eligible, the Principal Investigator will tell you why.

If you enter the study, additional procedures will also be performed according to the following schedule:

Visit 2:

- Your doctor/staff will administer 1 mL of the study vaccine beneath your skin in 4 injection sites
- You must remain at the clinic for at least 1 hour after the last injection to see if there are any changes in the areas where you were received the vaccine. Your vitals will be taken before the first injection and 1 hour after the last injection.
- Your doctor/staff will give you a diary to document any changes at the injection sites, physical fatigue, and your body temperature during the first two weeks after Visit 2.
- Your doctor/staff will review your current medications
- Your doctor will perform a complete physical examination and vital signs (heart rate, oral temperature, breathing rate, sitting blood pressure) will be taken
- Your doctor/staff will collect about 1-2 tablespoons of blood for laboratory tests to check your overall health and organ functions (such as liver, heart, kidneys, pancreas)
- Your doctor/staff will collect about 1 tablespoon of blood for laboratory tests to check tumor biomarkers that are found in the blood

- Your doctor/staff will collect at least 2 tablespoons of your blood to study how your body's immune system responds to certain ingredients of the vaccine. Treos Bio ZRT may store any of this remaining blood sample for up to 2 years after the study completion for additional scientific exploration of how your body's immune system responds to certain ingredients of the vaccine.
- Your doctor/staff will collect at least 2 tablespoons of your urine for laboratory tests to check the health of your urinary tract and kidneys
- If you are a female and able to get pregnant, you will have a urine pregnancy test. Your doctor/staff will tell you the result of this test.
- A buccal swab (collecting cells from the inside of your cheek) will be obtained.

Visit 3, Visit 5, Visit 8, Visit 10, Visit 13, & Visit 15

- Your doctor will perform a brief (to check for any new or previously identified signs or symptoms) physical examination and vital signs (heart rate, oral temperature, breathing rate, sitting blood pressure) will be taken
- Your doctor/staff will collect at least 2 tablespoons of your blood to study how your body's immune system responds to certain ingredients of the vaccine. Treos Bio ZRT may store any of this remaining blood sample for up to 2 years after the study completion for additional scientific exploration of how your body's immune system responds to certain ingredients of the vaccine.
- Your doctor/staff will collect your diary at Visits 3, 8, and 13
- Your doctor/staff will review your current medications
- Your doctor/staff will check to see if there are any changes in the areas where you received the vaccine

Visit 7 and Visit 12

- Your doctor/staff will administer 1mL of the study vaccine beneath your skin in 4 injection sites
- You must remain at the clinic for at least 1 hour after the last injection to see if there are any changes in the areas where you received the vaccine. Your vitals will be taken before the first injection and 1 hour after the last injection.
- Your doctor/staff will give you a diary to document any changes at the injection sites, physical fatigue, and your body temperature during the first two weeks after Visit 7 and Visit 12.
- Your doctor/staff will review your current medications
- Your doctor will perform a complete physical examination and vital signs (heart rate, oral temperature, breathing rate, sitting blood pressure) will be taken

Visit 4, Visit 6, Visit 9, Visit 11, Visit 14, & Visit 16

- Your doctor/staff will review your current medications
- Your doctor/staff will perform a complete physical examination and vital signs (heart rate, oral temperature, breathing rate, sitting blood pressure) will be taken
- Your doctor/staff will check to see if there are any changes in the areas where you received the vaccine
- Your doctor/staff will collect about 1-2 tablespoons of blood for laboratory tests to check your overall health and organ functions (such as liver, heart, kidneys, pancreas)
- Your doctor/staff will collect about 1 tablespoon of blood for laboratory tests to check tumor biomarkers that are found in the blood
- Your doctor/staff will collect at least 2 tablespoons of your blood to study how your body's immune system responds to certain ingredients of the vaccine. Treos Bio ZRT may store any of this remaining blood sample for up to 2 years after the study completion for additional scientific exploration of how your body's immune system responds to certain ingredients of the vaccine.
- Your doctor/staff will collect at least 2 tablespoons of your urine for laboratory tests to check the health of your urinary tract and kidneys
- Your doctor/staff will collect your diary
- If you are a female and able to get pregnant, you will have a urine pregnancy test. Your doctor/staff will tell you the result of this test.
- A CT scan will be performed to assess the extent of your disease
- At Visits 6, 11 and 16 another biopsy of your tumor will be taken to check for the presence of TILs in your tumor

If you are not familiar with any of these procedures, please ask your study doctor to explain how they are performed.

After you complete the last visit (Visit 16), your study doctor will decide what medical treatment you should receive. To complete the study findings, your long term survival status may also be obtained from public sources.

What is expected from you?

When deciding whether to participate, consider whether you are able and willing:

- To follow the study rules
- To commit the time required to keep appointments
- To tell the study doctor truthfully about your complete medical history
- To report any new problems, illnesses, or changes in medication during the study
- To complete the study diary and return it at your scheduled visits

6. What are the possible risks or discomforts from being in this research study?

All drugs may cause certain side effects and discomforts. The most common and expected side effects and discomforts expected for the PolyPEPE1018 are skin reactions, including redness, pain, swelling, warming of the skin, itchiness, and rash, at the injection sites and flu-like symptoms, including fever, chills, weakness, dizziness, nausea or vomiting, muscle ache, fatigue, headache, and occasional breathing difficulties. There may also be side effects and discomforts that are not yet known.

Blood Collection:
When a sample of your blood is drawn for laboratory tests, you may experience some temporary discomfort, bruising, swelling and/or, in rare circumstances, infection at the needle site.

Risks of CT:
You will receive radiation when your CT is done. The amount of radiation you will receive has a low risk of harmful effects.

Tumor Biopsy Risks:
You will sign a separate consent form before the biopsy is done. This will be a standard surgical consent form from the institution where the biopsy procedure takes place. A biopsy is a safe procedure when performed by an experienced doctor. Serious problems are rare. Possible risks can include:

Pain
Pain at the biopsy site is the most common complication after a biopsy.

Bleeding
A small amount of bleeding from the biopsy site can be expected. Excessive bleeding may require you to be hospitalized for a blood transfusion or surgery to stop the bleeding.

Infection
Rarely, bacteria may enter the abdominal cavity or bloodstream and cause an infection which could require antibiotics.

Accidental injury to a nearby organ
In rare instances, the needle may stick another internal organ, such as the gallbladder, intestines, kidney, or a lung.

Are there any reproductive risks?

Women: It is not known if the study treatment may affect an unborn child or nursing infant. For this reason, if you are breastfeeding, pregnant, or plan to become pregnant, you may not participate in this study. If you are capable of becoming pregnant, you must use an acceptable method of birth control throughout the entire study (see below).

Pregnancy: If you become pregnant during your participation in the study, your participation in the study may be stopped. However, data information about your pregnancy may be collected. You/your partner may be requested to sign a separate informed consent form prior to collection of data about the outcome of the pregnancy and associated outcome for scientific or security reasons.

Men: It is not known if the study treatment may affect your sperm or an unborn child. For this reason, you must use an acceptable method of birth control throughout the entire study (see below) and not donate sperm for 3 months from the day of the treatment. If your partner becomes pregnant, she may be requested to sign a separate informed consent form for the collection of data about the pregnancy and the outcome of the pregnancy.

Birth Control: Birth control methods considered acceptable for this study include hormonal contraceptives or an intrauterine device combined with at least 1 of the following forms of contraception: a diaphragm, cervical cap, or condom.
It is important that you tell the study doctor immediately if you or your partner becomes pregnant during the study. The doctor will talk with you about what you should do.

7. Are there reasons you might leave this research study early?

Your participation in this study is voluntary. You do not have to take part, and you may discontinue your involvement at any time without penalty or loss of benefits to which you are otherwise entitled. If you decide to leave the study before the last study visit, tell the study doctor and follow instructions. It may be helpful if you could explain your reasons. You may receive standard treatment and no prejudice will be shown towards you for medical care or participation in future research.

In addition, your study doctor or the sponsor may withdraw you from the study for your own safety, even if you wish to continue to participate, for example:

- If you need additional medication
- If you experience a study-related injury or unacceptable vaccine site reaction
- If you do not follow the study rules
- If you become pregnant
- If you develop a condition that the study does not allow
- If at the request of your primary care provider, she/he thinks the study is no longer in your best interest
- If the study has ended
- If at the request of the health authority, institutional review board/independent ethics committee, investigator, or pharmaceutical supporter

If your participation in the study is stopped early, you may be asked to complete end-of-study procedures (such as a final physical examination and laboratory tests) for your own safety.

Your study doctor will inform you in a timely manner of any new information learned during the study that may affect your willingness to continue your participation.

8. What if you are injured from your participation in this research study?

Where to get help:

If you think you have suffered a research-related injury, you should promptly notify the Principal Investigator listed in the Contact Information at the beginning of this form. Mayo Clinic will offer care for research-related injuries, including first aid, emergency treatment and follow-up care as needed.

Who will pay for the treatment of research related injuries:

The Sponsor, Treos Bio ZRT will offer to pay for medical treatment of research-related injuries directly resulting from the proper application of the study drug. The Sponsor may decide not to pay for several reasons. The Sponsor may not pay if the Sponsor concludes the injury happened because you did not follow the study directions or the injury resulted from your actions. The Sponsor may not consider the worsening of an existing health condition to be a research-related injury. In the case of injury resulting from your participation in this study, you do not lose any of your legal rights to seek payment by signing this form. Contact the Principal Investigator, who can help you obtain this reimbursement.

9. What are the possible benefits from being in this research study?

If the study drug is effective, it may control, reduce, or eliminate your cancer. It is possible that you may not personally benefit from your participation in this study. However, by taking part, you will provide new information that may benefit other patients in the future.

10. What alternative do you have if you choose not to participate in this research study?

Vaccination with PolyPEPI1018 is not alternative to any standard treatment, but in addition to standard treatment. If you decide not to participate in this study, you may still receive the standard treatment(s) for your metastatic colorectal cancer. Your study doctor will discuss these options with you.

11. What tests or procedures will you need to pay for if you take part in this research study?

You won't need to pay for tests and procedures which are done just for this research study. These tests and procedures are:

- Study Vaccine PolyPEPI1018 and its administration
- Physical exams
- Blood and urine tests performed for this study
- Tumor Biopsy
- CT Imaging
- Buccal swab
- Pregnancy Testing (if applicable)

However, you and/or your insurance will need to pay for all other tests and procedures that you would have as part of your clinical care.

You will also be responsible for any co-payments and deductibles.

If you have billing or insurance questions call Research Billing at the telephone number provided in the Contact Information section of this form.

12. Will you be paid for taking part in this research study?

You may be reimbursed, up to $39 per visit, for any reasonable travel expenses (bus/train/taxi fares) incurred as a result of taking part in this study on production of a receipt.

13. What will happen to your samples?

Biological samples will be collected, processed and reported as necessary for the purposes of the study.

Genetic Testing for Certain Genetic Markers

In addition to the experimental vaccine, Treos Bio ZRT plans to study certain genetic markers in your body and assess their relationship with your immune system's response. These genetic markers will be studied using the biological sample collected via the buccal swab at Visit 2.

Remaining blood samples will be stored at ViroStatics Porto Conte Ricerche srl SP 55 Porto Conte/capo Caccia km 8400 - CP 84 Loc. Tramariglio – 07041 Alghero (SS), Italy for up to 2 years after study completion for additional scientific exploration of how your body's immune system responds to certain ingredients of the vaccine. Only the sponsor and the lab personnel at ViroStatics will have access to the samples and results. If and when the additional scientific exploration (testing) will be conducted, the retained samples will be handled in the same manner as that required for processing the original samples. After 2 years past the study completion, any remaining samples will be destroyed. You have the right to be informed of any plans for new analyses on retained identifiable samples that are not currently foreseen and you have the right to refuse further analyses. You have the right to withdraw consent to use/store your samples, including requesting destruction of the sample, as long as the link to your identity has not been broken. You do not have to explain your reason for deciding to withdraw samples. Your information, samples and test results will always be treated in a confidential manner.

I give my permission to use any leftover of my biological samples for the above optional scientific exploration:

☐ Yes ☐ No Please initial here: _____ Date: _____

14. How will your privacy and the confidentiality of your records be protected?

Mayo Clinic is committed to protecting the confidentiality of information obtained about you in connection with this research study.

To protect the data and confidentiality of your data, a code will be used as an identifier. The code will be a registration number assigned specifically to you by the Mayo Clinic Cancer Center Registration Office or Study Sponsor, if applicable. The correlating Mayo Clinic number and your name for reference will be maintained in a secure database accessible by Mayo Clinic assigned research staff.

Future Medical or Pharmaceutical Research:

I additionally allow the use of my coded medical information for future cancer related or PolyPEPI1018 vaccine research such as exploration of how your body's immune system responds to certain ingredients of the vaccine.

☐ Yes ☐ No Please initial here: _____ Date: _____

During this research, information about your health will be collected. Under Federal law called the Privacy Rule, health information is private. However, there are exceptions to this rule, and you should know who may be able to see, use and share your health information for research and why they may need to do so. Information about you and your health cannot be used in this research study without your written permission. If you sign this form, it will provide that permission.

Personal information may be collected about you includes name, address, telephone number, social security number, date of birth, and health plan number.

Health information may be collected about you from:

- Past, present and future medical records.
- Research procedures, including research office visits, tests, interviews and questionnaires.

Why will this information be used and/or given to others?

- To do the research.
- To report the results.
- To see if the research was done correctly.

If the results of this study are made public, information that identifies you will not be used.

Who may use or share your health information?

- Mayo Clinic research staff involved in this study.
- Treos Bio ZRT and its authorized agents

With whom may your health information be shared?

- The Mayo Clinic Institutional Review Board that oversees the research.
- Other Mayo Clinic physicians involved in your clinical care.
- Researchers involved in this study at other institutions.
- Federal and State agencies (such as the Food and Drug Administration, the Department of Health and Human Services, the National Institutes of Health and other United States agencies) or government agencies in other countries that oversee or review research.
- The sponsor(s) of this study and the people or groups it hires to help perform this research.
- A group that oversees the data (study information) and safety of this research.

Is your health information protected after it has been shared with others?

Mayo Clinic asks anyone who receives your health information from us to protect your privacy; however, once your information is shared outside Mayo Clinic, we cannot promise that it will remain private and it may no longer be protected by the Privacy Rule. The study data may be transferred to other countries for processing, including countries not covered by data protection legislation. The laws of your state may provide further protection.

Your Privacy Rights

You do not have to sign this form, but if you do not, you cannot take part in this research study.

While the study is in progress, your access to your study records will be temporarily suspended. You will be able to access your information when the research study is completed. You have the right to see and copy the medical information collected from you in the course of the study for as long as that information is maintained by the study personnel and other entities subject to federal privacy regulation.

If you cancel your permission to use or share your health information, your participation in this study will end and no more information about you will be collected; however, information already collected about you in the study may continue to be used.

If you choose not to take part or if you withdraw from this study, it will not harm your relationship with your own doctors or with Mayo Clinic.

You can cancel your permission to use or share your health information at any time by sending a letter to the address below:

Mayo Clinic
Office for Human Research Protection
ATTN: Notice of Revocation of Authorization
201 Building 4-60
200 1st Street SW
Rochester, MN 55905

Alternatively, you may cancel your permission by emailing the Mayo Clinic Research Subject Advocate at: researchsubjectadvocate@mayo.edu.

Please be sure to include in your letter or email:

- The name of the Principal Investigator,
- The study IRB number and /or study name, and
- Your contact information.

Your permission lasts until 2 years beyond the end of this study, unless you cancel it. Because research is an ongoing process, we cannot give you an exact date when the study will end.

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ENROLLMENT AND PERMISSION SIGNATURES

Your signature documents your permission to take part in this research.

	/ /	: AM/PM
Printed Name	Date	Time

Signature

Person Obtaining Consent

- I have explained the research study to the participant.
- I have answered all questions about this research study to the best of my ability.

	/ /	: AM/PM
Printed Name	Date	Time

Signature