MC1633 / 16-010066

Phase II Trial to Evaluate the Efficacy of the FASN Inhibitor, TVB-2640, in Combination with Trastuzumab plus Paclitaxel or Endocrine Therapy in Patients with HER2+ Metastatic Breast Cancer Resistant to Trastuzumab-based Therapy

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RESEARCH PARTICIPANT CONSENT AND PRIVACY AUTHORIZATION FORM

Study Title: MC1633, Phase II Trial to Evaluate the Efficacy of the FASN Inhibitor, TVB-2640, in Combination with Trastuzumab plus Paclitaxel or Endocrine Therapy in Patients with HER2+ Metastatic Breast Cancer Resistant to Trastuzumab-based Therapy – MAIN STUDY

IRB#: 16-010066

Principal Investigator: Tufia C. Haddad, 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 form to keep. A copy of this form will be put in your medical record.

CONTACT INFORMATION

You can contact …	At …	If you have questions about
Principal Investigators: Tufia Haddad, M.D. **Arizona** Brenda Ernst, M.D. **Florida** Alvaro Moreno-Aspitia, M.D.	**Phone:** (507) 284-2511 **Institution Name and Address:** Mayo Clinic Rochester 200 1st St SW Rochester, MN 55905 **Phone:** (480) 301-8000 **Address:** Mayo Clinic Arizona 13400 E. Shea Blvd Scottsdale, AZ 85259 **Phone:** (904) 953-7290 **Address:** Mayo Clinic Florida 4500 San Pablo Rd Jacksonville, FL 32224	▪ 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 Participant Advocate **(The RPA is independent of the Study Team)**	**Phone:** (507) 266-9372 **Toll-Free:** (866) 273-4681 **E-mail:** researchparticipantadvocate@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 ▪ Withdrawing from the research study

You can contact …	At …	If you have questions about
Patient Account Services	**Toll-Free:** (844) 217-9591	▪ 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 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.

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

You are being asked to participate in this study because you have advanced breast cancer and some of the standard drugs used to treat your cancer are no longer effective.

The plan is to have about 75 people take part in this study at Mayo Clinic.

2. Why is this research study being done?

In this study we want to find out more about the effectiveness and side effects of a new drug for breast cancer, TVB-2640. Everyone in this study will receive TVB-2640 which is still experimental and isn't approved by the U.S. Food and Drug Administration (FDA). However, the FDA has allowed the use of this drug in this research study. We don't know all the ways that this drug may affect people. It is unknown if participation in this study will help you, but we hope the information from this study will help us develop better treatments for breast cancer in the future.

3. Information you should know

Who is Funding the Study?
The Department of Defense is funding the study. The Department of Defense will pay the institution to cover the costs related to running the study. 3V Biosciences will provide the study drug (TVB-2640).

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

The total length of time that you will be on the study depends on if and for how long, you respond to the treatment. Each treatment cycle is 28 days. You may continue to receive treatment for as long as your doctor feels that your cancer has not become worse, or until you have side effects that you cannot tolerate, for a maximum of up to 3 years. You will return for a final study visit approximately 28 days after your last dose.

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

Before beginning any research procedure you will sign this informed consent form.

You are being asked to participate in this study because your cancer is no longer responsive to the combination of trastuzumab (Herceptin) and taxane-based chemotherapy (paclitaxel or docetaxel) or trastuzumab and endocrine therapy. If you agree to participate you will receive treatment with a combination of 3 drugs: TVB-2640, trastuzumab (Herceptin), and paclitaxel (Taxol); OR TVB-2640, trastuzumab (Herceptin), and your current endocrine therapy.

TVB-2640 is a drug that targets a protein called FASN. In laboratory studies with breast cancer cells that are resistant to trastuzumab (Herceptin) and paclitaxel or trastuzumab and endocrine therapy, blocking FASN with TVB-2640 helps trastuzumab (Herceptin) and paclitaxel (Taxol) or trastuzumab and endocrine therapy become effective again and destroy breast cancer cells.

TVB-2640 is a drug to be taken by mouth each day continuously during each 28-day cycle. TVB-2640 is to be taken at least 2 hours after the last food consumption and at least 1 hour before next food consumption. Each dose should be separated by 24 hours (±4 hours). Trastuzumab (Herceptin) will be given by an intravenous infusion once weekly (on Days 1, 8, 15 and 22) of a 28-day cycle.

For patients who previously received paclitaxel (Taxol), it will be given by an intravenous infusion once weekly for 3 weeks in a row followed by a rest week (on Days 1, 8, and 15) of a 28-day cycle.

For patients who previously had endocrine therapy, it will continue as currently prescribed.

You will be given a diary to record when you take your study drug, TVB-2640. You will need to return to Mayo Clinic every month for a re-evaluation before receiving your next cycle of treatment. You will be asked to return your diary, empty pill bottle and any remaining study drug supply at the end of each cycle.

If you agree to be in the study, you will be asked to participate in the following:

Time	What will happen
Pre-Study	• Routine physical exam • Routine blood tests • Pregnancy testing for childbearing women • Adverse event assessment • CT/MRI scan to document tumor size • Echocardiogram • ECG • Eye examination • Research blood collection
Day 1 of each cycle (every 4 weeks or 28 days)	• Routine physical exam • Routine blood tests • Adverse event assessment • Review of your medication diary
Prior to treatment on Days 8, 15 and 22 of each cycle	• Routine blood test to ensure your blood counts are normal • After Cycle 2, you may have some of this testing with your local health provider
Day 8 of Cycle 1	• Research blood collection (about 1 teaspoon)
Day 1 of Cycle 2 (prior to treatment)	• Research blood collection (about 1 teaspoon) • Research tumor biopsy
Before every even numbered cycle (i.e. Cycle 2, 4, 6, etc.)	• Echocardiogram
Every other cycle starting with Cycle 3 (i.e. Cycle 3, 5, 7, etc.)	• CT/MRI scan to document tumor size
At the end of protocol treatment or progression	• Routine physical exam • Routine blood tests • Adverse event assessment • CT/MRI scan to document tumor size

Time	What will happen
Follow-up after study discontinuation	• After you stop the study medication, you will be contacted by the study team during a clinic visit or by telephone every 6 months for a maximum of 3 years after you started treatment.

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

Risks of TVB-2640

Likely risks of *(events occurring greater than 20% of the time)*

- Fatigue
- Loss of appetite
- Redness, swelling, discomfort of the palms of the hands and soles of the feet ("Hand foot syndrome")
- Dry skin
- Hair loss
- Constipation
- Nausea
- Vomiting
- Cough
- Shortness of breath

Less likely risks of *(events occurring less than or equal to 20% of the time)*

- Diarrhea
- Dehydration
- Abdominal pain
- Dry eye
- Redness and itching of the eyes or eyelids (conjunctivitis and blepharitis)
- Watery eyes
- Eye pain
- Blurred vision
- Dizziness
- Low red blood cell count (Anemia)
- Low platelet count

- Infections
- Peeling and cracking of the skin of the hands and feet
- Rash
- Fever
- Abnormal taste
- Swelling of the extremities
- Joint aches or pain
- Itching
- Mouth sores
- Numbness and tingling of the hands and feet
- Headache
- Not feeling hungry, not wanting to eat (decreased appetite)
- Increased triglycerides

Rare but serious risks of *(events occurring less than 2-3% of the time)*

- Inflammation of the cornea, uvea or iris (components of the eye)
- Cataract

Risks of Herceptin (Trastuzumab)

Likely risks of Trastuzumab *(events occurring ≥10% of the time)*

- Common cold symptoms (Nasopharyngitis and rhinitis)
- Infections (Pneumonia, urinary tract infection, etc.)
- A low number of white blood cells, which are the infection fighting cells, which could put you at risk for infection (Neutropenia)
- A low number of oxygen-carrying red blood cells (anemia)
- Weakness (Asthenia)
- Feeling tired (Fatigue)
- Fever (Pyrexia)
- Weight changes (Gain or loss)
- Decreased appetite (Anorexia)
- Difficulty in sleeping (Insomnia)
- Sensation of lightheadedness or vertigo (spinning sensation) (Dizziness)
- Inflammation of the sinuses (Sinusitis)
- Tingling, burning, or prickling sensation (Paresthesia)
- Reduced sense of touch (Hypoesthesia)
- Distorted taste (Dysgeusia)
- Pink eye (Conjunctivitis)

- Increased tear production (Lacrimation)
- Swelling of the extremities (Peripheral edema)
- Hot flashes
- Shortness of breath (Dyspnea)
- Nosebleed
- Cough
- Runny nose
- Feeling sick to your stomach (Nausea)
- Loose stools (Diarrhea)
- Throwing up (Vomiting)
- Indigestion
- Constipation
- Inflamed or sore mouth
- Sore throat
- Rash
- Development of bald spots (Alopecia)
- Reddening, swelling, numbness and peeling skin on palm of hand (Palmar-Plantar Erythrodysesthesia)
- Fingernail or toenail disorder
- Body pain (muscles, chest, joints, abdomen, back, bone, headache)
- Chills
- Feeling sad or blue (Depression)

Less common risks of Trastuzumab *(events occurring ≥1% but <10% of the time)*

- Rapid heartbeat (Tachycardia)
- High blood pressure (Hypertension)
- Damage to the heart (Abnormal rhythms, palpitations damage to heart muscle or cardiomyopathy)
- Cardiac failure (Congestive heart failure)
- Low blood pressure (Hypotension)
- Asthma
- Lung problems (Fluid accumulation and pneumonia)
- Acne
- Skin problems (dermatitis, itching)
- Arthritis
- Muscle spasms

Rare but serious risks of Trastuzumab *(events occurring less than 2-3% of the time)*

- Allergic reaction (including life-threatening reactions-low blood pressure, shortness of breath, and death)
- Lung inflammation (Wheezing and Pneumonitis)
- Inflammation of the pancreas (Pancreatitis)
- Deafness
- Jaundice
- Hypersensitivity reactions including anaphylaxis, infusion reactions pulmonary events, exacerbation of chemotherapy-induced neutropenia, and thrombosis.

Long term effects of trastuzumab remain unclear. If additional information becomes available regarding both long term and short-term safety concerns that could affect your willingness to take part in this study.

Special Cases
Congestive heart failure with symptoms of shortness of breath and edema (swelling) has been observed in patients who have received trastuzumab alone and with cytotoxic chemotherapy. There is a possibility that administration of trastuzumab may increase the risk of getting this side effect. For this reason, your heart will be carefully followed during this study.

It is known that trastuzumab may cause harm to an unborn fetus. This toxicity may be due to either the trastuzumab itself or the preservation benzyl alcohol, a preservative that has been known to cause toxicity in newborns. This drug should not be given to anyone with a known sensitivity to benzyl alcohol.

You should not get pregnant up to 6 months from stopping the drug. Trastuzumab can harm the fetus causing fetal malformation and death from severe oligohydramnios (loss of fluid in the sac surrounding the fetus in the uterus).

Risks of Paclitaxel (if applicable)

Likely risks of paclitaxel are those that occurred greater than 20% of the time:

- Loss of appetite.
- Nausea and vomiting.
- Diarrhea.
- Loss of body fluids, which may upset the balance of minerals in the body (dehydration).
- Redness, soreness, and/or irritation of the linings of the mouth, throat, and digestive system.

- Temporary decrease in the number of white blood cells (leucopoenia and neutropenia; with a potential risk of infection). This may increase the risk of developing a life-threatening infection. Please contact your doctor immediately if you feel ill or feverish.
- Hair loss.
- Peripheral neuropathy (a form of damage to the nerves supplying the hands and feet that leads to numbness, the feeling of "pins and needles," and/or muscle weakness). Most but not all subjects experienced improvement of their symptoms following discontinuation of paclitaxel treatment.
- Temporary decrease in the number of red blood cells (anemia; with a potential risk of fatigue or generally feeling unwell).

Less likely risks of paclitaxel are those that occurred less than or equal to 20% of the time:

- Pain in the bones, joints, and/or muscles.
- Low blood pressure.
- Dizziness (lightheadedness), which may impact your ability to drive or use machinery. Please avoid these activities if there is any concern.
- Blurred vision.
- Sensation of seeing flashing lights.
- Skin rash.
- Elevated liver function tests (increased levels of liver enzymes in the blood which may suggest injury to the liver).
- Temporary decrease in the number of red blood cells (anemia; with a potential risk of fatigue or generally feeling unwell).
- Temporary decrease in the number of platelets (thrombocytopenia; with a potential risk for bleeding and bruising).

Rare but serious risks of paclitaxel are those that occurred less than 2-3% of the time:

- Inflammation of the lungs that may cause shortness of breath (pneumonitis).
- Escape of the drug from the vein injection site (with mild local swelling, tenderness, and/or chronic skin sores).
- Severe skin reaction that may require hospitalization.
- Liver dysfunction (increased bilirubin; with a possibility of skin yellowing).
- Confusion.
- Inflammation of the pancreas.
- Seizures.
- Abnormal heart rhythms.

- Allergic reactions during chemotherapy administration (hives, itching, wheezing, a severe drop in blood pressure, and difficulty breathing. A severe allergic reaction can be life threatening and requires immediate medical attention).
- Development of a hole in the wall of the bowel that may be life threatening.

Many side effects go away shortly after both drugs are stopped, but in some cases side effects can be serious, long lasting, or may never go away. There may be a risk of death. Some side effects may not be known. Side effects may range from mild to life-threatening. Other drugs may be given to make side effects less serious and less uncomfortable. Talk to the researcher and/or your healthcare provider about side effects and ask any other questions.

Risks of TVB-2640 in Combination with Paclitaxel (if applicable)
In a phase I study of TVB-2640 in combination with paclitaxel, the rate of pneumonitis or inflammation of the lungs was 9%. Pneumonitis may be detected prior to the onset of symptoms (shortness of breath), incidentally noted on a CT or MRI scan. More commonly, pneumonitis causes symptoms such as shortness of breath or dry cough. Severe cases of pneumonitis, resulting in the need for supplemental oxygen and 1 death have been reported. The other potential risks associated with this combination therapy are listed previously for each agent separately.

Risks of Endocrine Therapy (if applicable)
If you are taking an aromatase inhibitor (anastrozole, exemestane, or letrozole) or fulvestrant as part of this trial, your doctor will talk to you about the specific risks of the drug you are taking.

The most common side effects from aromatase inhibitors are the same as the symptoms of menopause and include:

- Hot flashes
- Night sweats
- Vaginal dryness
- Muscle and joint pain

Serious side effects include:

- Osteoporosis – thinning of the bones, which may be easier to break
- Heart problems – especially if you are already at risk or have already been diagnosed with heart problems

Blood Draws
The risks of drawing blood include pain, bruising, lightheadedness, and/or fainting, or rarely, infection at the site of the needle stick.

Biopsies
Biopsies are normally performed under the guidance of an imaging technique. Each procedure requires a separate consent prior to the biopsy. The risks may include:

- Pain and discomfort. The amount of pain and discomfort will vary, depending on the location of the biopsy site. These risks can be discussed with the study doctor.
- Minor bleeding at the biopsy site.
- Tenderness at the biopsy site.
- Scarring at the biopsy site.
- Rarely, an infection at the biopsy site.

- Lidocaine, a numbing drug, may burn or cause a rash, redness or soreness where you get the shot. There is a small risk that this drug may cause problems with heart rhythm.

Although uncommon, problems from biopsies can be life threatening. Some potentially serious problems from bleeding or organ damage may occur. These might require surgical repair.

Skin or chest biopsy
Likely: local discomfort and minor bleeding
Rare: moderate or major bleeding. Infection and allergic reaction to the numbing medicine also occur rarely.

Lymph node biopsy
Likely: local discomfort and minor bleeding
Rare: moderate or major bleeding, need for blood transfusion, lung collapse, hospitalization due to bleeding or other complications, infection, damage to bowels, damage to nearby organs, allergic reaction to the numbing medicine.

Liver biopsy
Likely: local discomfort and minor bleeding
Rare: moderate or major bleeding, need for blood transfusion, lung collapse, hospitalization due to bleeding or other complications, infection, damage to bowels, damage to nearby organs, allergic reaction to the numbing medicine

Bone biopsy
Likely: local discomfort and minor bleeding
Rare: moderate or major bleeding, need for blood transfusion, lung collapse, hospitalization due to bleeding or other complications, infection, damage to bowels, damage to nearby organs, allergic reaction to the numbing medicine.

Lung biopsy
Likely: local discomfort and minor bleeding
Possible (approximately 10% risk): partial lung collapse which may be associated with shortness of breath, pain with inspiration, and need for hospitalization.
Rare: moderate or major bleeding, need for blood transfusion, complete lung collapse, hospitalization due to bleeding or other complications, infection, cough, damage to nearby organs, allergic reaction to the numbing medicine. In the event of complete lung collapse, shortness of breath, pain with inspiration, chest tube placement and hospitalization are likely.

> *If you are a smoker or have COPD or other chronic pulmonary disease, your risk of complications from a lung biopsy is greater than those who do not smoke or do not have an underlying pulmonary disease.

Some biopsy procedures require imaging studies, such as a CT scan or ultrasound to plan or guide the procedure. These studies would be done even if you were not donating samples for research purposes. However, if the biopsy is done for research, the imaging studies would also be considered research. Your doctor will tell you whether imaging studies are required for your procedure. If you have a CT scan, there is also a small risk of allergic reaction to the dye that may be used during the scan. You could have anxiety or claustrophobia in the scanning machine. Talk to your doctor if you have had problems during a CT scan in the past. There is no radiation from an ultrasound test.

Radiation risk from biopsies
As part of the pre-screening research project, you may be required to have one CT-guided biopsy. The CT-guided biopsy procedure requires exposure to radiation. You will be exposed to additional radiation during the CT scans involving the research use of radiation. The amount of radiation you will receive has a low risk of harmful effects.

Echocardiogram
This test uses sound waves to look at your heart. The person doing the test will press on your chest with a machine to obtain the pictures. The pressure may be uncomfortable.

Unforeseeable Risks:
Many side effects go away shortly after the study drugs are stopped, but in some cases side effects can be serious, long lasting, or may never go away. There may be a risk of death. Some side effects may not be known. Side effects may range from mild to life-threatening. Other drugs may be given to make side effects less serious and less uncomfortable. Talk to the researcher and/or your healthcare provider about side effects and ask any other questions.

Pregnancy and Birth Control:
Women: If you are sexually active and able to become pregnant, you must agree to use two of the birth control methods listed below:

- Hormonal methods, such as birth control pills, patches, injections, vaginal ring, or implants
- Barrier methods (such as a condom or diaphragm) used with a spermicide (a foam, cream, or gel that kills sperm)
- Intrauterine device (IUD)
- Abstinence (no sex)

You must use birth control for the entire study and for at least 7 months after your last dose of study drug.

Men: If you are sexually active, and able to father a child, you must agree to use two of the birth control methods listed below:

- Barrier methods (such as a condom or diaphragm) used with a spermicide (a foam, cream, or gel that kills sperm)
- Hormonal methods used by your partner, such as birth control pills, patches, injections, vaginal ring, or implants
- Intrauterine device (IUD) used by your partner
- Abstinence (no sex)

You must use birth control for the entire study and for at least 7 months after your last dose of study drug.

Confidentiality:
As with all research, there is a chance that confidentiality could be compromised; however, we take precautions to minimize this risk.

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

You may decide to stop at any time. You should tell the Principal Investigator if you decide to stop and you will be advised whether any additional tests may need to be done for your safety.

In addition, the Principal Investigator, the study sponsor, or Mayo Clinic may stop you from taking part in this study at any time:

- If it is in your best interest,
- If you don't follow the study procedures,
- If the study is stopped.

If you leave this research study early, or are withdrawn from the study, no more information about you will be collected; however, information already collected about you in the study may continue to be used.

We will tell you about any new information that may affect your willingness to stay in the research study.

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?

Care for such research-related injuries will be billed in the ordinary manner, to you or your insurance. Treatment costs for research-related injuries not covered by your insurance will be paid by Mayo Clinic.

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

TVB-2640 is an experimental drug. This means that there is no guarantee that TVB-2640 will cure your cancer or even improve your condition. There is a chance that your cancer could improve while you are on the study, and there is a chance that your cancer could get worse while you are on the study. Although no direct health benefit is guaranteed, it is hoped that this study will produce information that may lead to a more effective treatment of cancer.

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

Your participation in this study is optional. There are other treatment options available to you that will be discussed with you by your physician. One of these options may be T-DM1 (also known as trastuzumab emtansine or Kadcyla), an FDA-approved therapy for patients with metastatic HER2+ breast cancer that has progressed or is no longer responsive to trastuzumab (Herceptin) with taxane-based chemotherapy. Patients who have or have not previously received T-DM1 may be eligible for this study. If you have not yet received T-DM1, you can discuss this option with your physician. These options may include other cancer medications or measures to make you comfortable. You do not need to take part in this study to receive treatment for your cancer.

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:

- Pretreatment eye examination
- ECG
- Tumor biopsies
- Research-related blood collections
- Every other echocardiogram (Cycle 2 Day 1, Cycle 6 Day 1, etc.)
- Study drug (TVB-2640)

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. These tests and procedures are:

- Physical exams
- Pregnancy test, if applicable
- Pre-medication prior to treatment, if applicable
- Every other echocardiogram (Baseline, Cycle 4 Day 1, Cycle 8 Day 1, etc.)
- Tumor assessment scans such as a CT, PET, MRI

- Routine clinical blood work
- Standard of care drugs (trastuzumab, paclitaxel, endocrine therapy)

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

If you have billing or insurance questions call Patient Account Services 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 will not be paid for taking part in this study.

13. What will happen to your samples?

The research blood and tumor samples collected during the course of this study will be analyzed to determine if there is a protein in the blood or in the tumor that may be associated with its response to the study drug, TVB-2640. A portion of the tumor samples will be analyzed at Mayo Clinic. A portion of the blood and tumor samples will be analyzed at laboratories external to Mayo Clinic, in collaboration with 3V-Biosciences, the company that makes TVB-2640.

We would like to keep your sample for future research. You can still take part in this current study even if you don't want your sample used for future research. If you agree to give your sample, it will be the property of Mayo Clinic.

Other researchers at Mayo Clinic who aren't involved with this study may ask to use your sample for future research. Researchers at other institutions may also ask for a part of your sample for future studies. If you approve release of your sample by checking 'yes' below, Mayo may send the sample(s) and some information about you to researchers who request them, but Mayo will not send your name, address, phone number, social security number, or any other identifying information with the sample. Your sample will be sent to researchers in a coded format, which protects your identity.

Some future studies may examine your DNA, which is the genetic information you inherited from your parents (genetic testing). The Principal Investigator may contact you if there are findings which may be useful for your health care. You would be given general information on the potential risks, benefits, and costs of choosing to learn about the findings.

Please read the following statements and mark your choices:

I permit leftover samples to be stored and used for future research to learn about, prevent, or treat cancer.

☐ Yes ☐ No Please initial here: _____Date: _____

I permit my samples to be stored and used for future research about other health problems (for example: causes of diabetes, heart disease, and Alzheimer's, or genetic links to alcoholism).

☐ Yes ☐ No Please initial here: _____Date: _____

I permit Mayo Clinic to give my sample and related information to researchers at other institutions:

☐ Yes ☐ No Please initial here: _____Date: _____

There is a very small chance that some commercial value may result from the use of your donated sample. If that happens, you won't be offered a share in any profits.

You may request to have your sample destroyed by writing to the Principal Investigator. The address is found in the "Contact Information" section of this consent form.

Because we cannot predict how your sample will be used in the future, we cannot promise that samples can be retrieved and destroyed.

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. All of your research samples transferred to the sponsor or designee will be labeled with a code number and kept in locked storage. Only your study doctor will be able to link your samples with your identity. No one working with your samples will know your identity. If the results of the research are made public, information that identifies you will not be used.

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.

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.
- 3-V Biosciences, Inc. (Manufacturer and Developer of TVB-2640)
- Department of Defense (DOD)

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 Defense, 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.

In addition, individuals involved in study oversight and <u>not</u> employed by Mayo Clinic may be allowed to review your health information included in past, present, and future medical and/or research records. This review may be done on-site at Mayo Clinic or remotely (from an off-site

location). These records contain information that directly identifies you. However, the individuals will not be allowed to record, print, or copy (using paper, digital, photographic or other methods), or remove your identifying information from Mayo Clinic.

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.

Your Privacy Rights

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

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
Plummer Building, PL 3-02
200 1st Street SW
Rochester, MN 55905

Alternatively, you may cancel your permission by emailing the Mayo Clinic Research Participant Advocate at: researchparticipantadvocate@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 forever, unless you cancel it.

ENROLLMENT AND PERMISSION SIGNATURES

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

Printed Name Date (mm/dd/yyyy) Time (hh:mm am/pm)

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.

Printed Name Date (mm/dd/yyyy) Time (hh:mm am/pm)

Signature