RESEARCH SUBJECT CONSENT FORM

TITLE: A Phase 1/2 Trial for Patients with Newly Diagnosed High Grade Glioma Treated with Concurrent Radiation Therapy, Temozolomide, and BMX-001

PROTOCOL NO.: BMX- HGG-001- Phase 2
WIRB® Protocol #20151095

SPONSOR: BioMimetix JV, LLC

INVESTIGATOR: Name
Address
City, State, Zip Code
Country

STUDY-RELATED PHONE NUMBER(S): Name
Number(s) (24 Hours)
[24-Hour Number Required]

You are being invited to take part in a research study. A person who takes part in a research study is called a research subject, or research participant.

Concise Summary

Your consent is being sought for a research study. Your participation is voluntary.

The purpose of the study is to test the effect of the investigational study drug (BMX-001) in combination with radiation therapy and temozolomide. This is a combination Phase 1/ Phase 2 study. The Phase 1 portion of the study was conducted to help determine the safety of the drug as given in humans for the first time as well as to establish the best dose to be given for the Phase 2 portion of the study. Phase 1 is completed, if you decide to participate you will be taking part in Phase 2. Phase 2 is a randomized study. You will be randomly assigned (like the flip of a coin) to receive either BMX-001 and participate in Arm A or participate in Arm B (without BMX-001). Overall survival will be measured and side effects will be evaluated. This study will also assess the effect of BMX-001 in terms of protecting your brain from the worsening of cognitive (thinking) abilities and quality of life that is sometimes experienced when undergoing treatment with radiation therapy and temozolomide (Temodar®) for high grade glioma. It is thought BMX-001 may be effective in preventing memory and thinking problems after radiation therapy, although there is no proof of this yet. In this study, subjects are randomized to get either the investigational agent BMX-001 with radiation therapy and temozolomide or just temozolomide and radiation therapy alone. BMX-001 is injected under the skin. The first dose is given a couple of days before radiation therapy (RT) starts, and then twice a week for 8 weeks. You will continue to be part of this study for as long as you are receiving care for your high grade glioma. There are risks to this study drug that are described in this document. Some risks include irritation at the injection site, feeling tired, a temporary

drop in blood pressure and in rare incidences a skin reaction.

The study will also collect information on your quality of life, side effects of the treatment, survival and neurocognitive effects before and after temozolomide and radiation therapy is given. You have other options instead of being in this study such as receiving alternative investigational drugs, choosing an alternative chemotherapy treatment, you could also choose to receive the standard therapy for this disease, and you can also choose to receive no therapy at this time and receive care to help you feel more comfortable.

If you are interested in learning more about this study, please continue reading below.

What should I know about this research?

- Someone will explain this research to you.
- This form sums up that explanation.
- Taking part in this research is voluntary. Whether you take part is up to you.
- You can choose not to take part. There will be no penalty or loss of benefits to which you are otherwise entitled.
- You can agree to take part and later change your mind. There will be no penalty or loss of benefits to which you are otherwise entitled.
- If you don't understand, ask questions.
- Ask all the questions you want before you decide.

Why is this research being done?

The purpose of this research is to study the effect of the investigational study drug (BMX-001) in combination with radiation therapy and temozolomide. BMX-001 is investigational, which means that it is not approved by the Food and Drug Administration (FDA). BMX-001 is an investigational new class of compound that would be termed "a redox-active metalloporphyrin." This drug was designed to mimic the body's most powerful antioxidant enzymes and is a potent anti-inflammatory that acts by blocking multiple steps in the inflammatory cascade. By inhibiting the inflammatory cascade BMX-001 is expected to protect normal tissues from the inflammatory side-effects of radiation and chemotherapy while at the same time acting as an antioxidant that will have an inhibitory effect on the growth of tumor. Overall survival will be measured and side effects will be evaluated. This study will also assess the effect of BMX-001 in terms of protecting your brain from the worsening of cognitive (thinking) abilities and quality of life that is sometimes experienced when undergoing treatment with radiation therapy and temozolomide (Temodar®) for high grade glioma. BMX-001 is thought to reduce the toxicities (bad side effects) of radiation therapy to the brain.

You are being asked to take part in this research study because you have been newly diagnosed with a malignant (cancerous) brain tumor.

Research studies are voluntary and include only people who choose to take part. Please read this consent form carefully and take your time making your decision. As your study doctor or study staff discusses this consent form with you, please ask him/her to explain any words or

information that you do not clearly understand. We encourage you to talk with your family and friends before you decide to take part in this research study. The nature of the study, risks, inconveniences, discomforts, and other important information about the study are listed below.

Providing direct medical benefit to you is not the main purpose of this study. The purpose of the Phase 2 is to see if adding the study drug, BMX-001 will provide benefit as compared to the standard of care treatment alone. Please carefully read the sections on risk and benefits below.

This is a combination Phase 1/ Phase 2 study. The Phase 1 portion of the study was conducted to help determine the safety of the drug as given in humans for the first time as well as to establish the best dose to be given for the Phase 2 portion of the study. Phase 1 is completed, if you decide to participate you will be taking part in Phase 2.

Please tell the study doctor or study staff if you are taking part in another research study.

About 160 subjects will take part in this research at up to 10 clinical centers.

How long will I be in this research?

If you receive the study drug, BMX-001 (subjects in Arm A), you will first receive it a few days before, or on the day you start radiation therapy. You will then continue to receive the study drug twice a week for the next 8 weeks, approximately 6 weeks during your radiation therapy, and then for 2 more weeks afterwards. Subjects who do not receive the study drug (Arm B) will have a few study visits less than the subjects in Arm A. All subjects will be followed after 8 weeks of being in the study, every 8 weeks for up to 12 cycles of adjuvant temozolomide. We expect that your taking part in this research will last as long as you are receiving treatment for your high grade glioma at [Institution]. You may remain in this study, as long as your tumor does not get larger (progresses) or there are no bad side effects.

The study doctor may also take you off the study if new scientific developments occur that indicate the treatment is not in your best interest, or he/she feels that this treatment is no longer in your best interest.

We will tell you about new information that may affect your health, welfare, or willingness to stay in this study.

You can choose to stop participating at any time without penalty or loss of any benefits to which you are entitled. However, if you decide to stop participating in the study, we encourage you to talk to your doctor first.

What happens to me if I agree to take part in this research?

Screening

If you agree to be in this study, you will be asked to sign and date this consent form. Many of these procedures will take place up to three weeks before you start the study drug or before you start radiation treatment. You will have the following tests and procedures to make sure that you are eligible:

- Vital signs, including blood pressure
- History and physical exam including a full neurological exam (brain and nervous system function)
- Blood draw (by needlestick) for hematology (blood counts), blood chemistry tests, and blood clotting ability
- Blood pregnancy test, if you are female of childbearing potential, within 2 days of starting the study drug
- Tumor measurement using MRI (scan that uses magnets)
- An Electrocardiogram (ECG)
- Assessments of Quality of Life (used to evaluate the general well-being of individuals)
- Neurocognitive Testing (used to evaluate the ability to think and reason). You will be evaluated for neurocognitive performance using computerized and paper standard neurocognitive testing.
- Pictures of your hair to evaluate for possible hair loss associated with radiation therapy. These pictures are not required and will only be done with your consent.

After completion of the screening process, the doctor will determine whether you are eligible to participate in the treatment part of the study. If you are eligible and you choose to participate, you will be enrolled in the study. If you do not meet the eligibility requirements, you cannot take part in this study, in which case your doctor will inform you of other options that are available to you.

The tests during screening and throughout the study are explained in more detail below:

Magnetic Resonance Imaging Scans (MRIs)/Diffusion Tensor Imaging (DTI): MRIs use a magnet and radio waves to make diagnostic medical images of the body. As this test uses a magnet, it is possible that the magnet could attract certain types of metal within your body. Therefore, we will carefully ask you about metal within your body (this includes certain dyes found in tattoos). If there is any question about potentially hazardous metal within your body, you will be excluded from the study. The MRI involves entering a large room in which a magnet is present. You will be placed on a narrow bed and then slid into a small tunnel approximately 6 feet in length and 25 inches in diameter. You will be asked to lie still for about one hour on this bed. You will hear a loud machine-like noise. You may be asked to have a harmless monitoring device applied during the study. During the study, you can have voice contact and physical contact with someone in attendance if you desire. You may be given a dye intravenously (through a vein) in order enhance the MRI image.

As part of this trial, the MRI performed will be modified (called Diffusion Tensor Imaging or DTI), in order to study improved ways to evaluate your condition. Your MRI scans as part of this trial will be slightly longer (less than 10 minutes) than routine MRIs. There will be no extra injections or cost to you that comes from this modified scan. We use MRIs to study tumor progression and DTIs to study white matter protection.

Electrocardiogram *(ECG):* ECG is a diagnostic tool that is routinely used to assess the electrical and muscular functions of the heart. This will be done at the screening visit (for all subjects) and for subjects in Arm A also on the first day you receive the study drug and during weeks 1 and 4,

before and about 60 minutes after the initial study drug injection.

Blood Tests: In total, 18 ml approximately 4 teaspoons of blood will be drawn from your arm by a needlestick for the evaluations before starting study drug during the screening period. During the course of the study, complete blood count (CBC) tests will be drawn (approximately 1 teaspoon) weekly, beginning at Week 2, while you are receiving radiation therapy and temozolomide and for 2 weeks afterward, and then on days 21 and 28 while you are receiving adjuvant (added) temozolomide (that is, temozolomide the first 5 days of each 28-day cycle). Blood chemistry (CMP) tests also will be drawn (approximately 1 teaspoon of blood) weekly beginning at Week 2, while you are receiving radiation therapy and temozolomide and for 2 weeks afterward, and then at day 21 of each cycle while you are receiving adjuvant temozolomide (that is, temozolomide the first 5 days of each 28-day cycle).

A blood test to determine how well your blood clots will be drawn during the screening period (less than 1 teaspoon of blood [3 mL]).

For women of childbearing potential, a blood test to rule out pregnancy will be done during the screening period within 48 hours prior to starting the study drug. Approximately 1 teaspoon of blood will be taken to perform this test.

In total, approximately 14 teaspoons (70 mL) of blood will be drawn during the study period when you are receiving radiation therapy and temozolomide for standard clinical blood tests such as CBC and CMP tests. In total approximately 36 teaspoons (180 mL) will be drawn over a 12-month period while you will be receiving adjuvant temozolomide for standard clinical blood tests, such as CBC and CMP tests.

Quality of Life: Assessed by using patient report outcomes (PROs). PROs refer to the subjective report of symptoms, concerns, and feelings. This will be evaluated using questionnaires. These questionnaires will ask questions about your mood, sleep, thoughts, feelings, physical function, thinking, and overall well-being. Questionnaires will be on paper and will be completed with pen.

Neurocognitive Testing: Testing will be performed on the computer, with a tester, and/or on paper. For the computer testing, the program consists of verbal and visual memory tests, attention tests, reasoning tests and speed of processing tests. You will use a laptop computer or iPad to complete these tests. No previous exposure to computers, tablets or computer testing is needed to complete the test. For the tests that you complete on an iPad, the verbal responses you provide during the tests will be audio recorded. These audio recordings will be used by the representatives of the sponsor to make sure that your responses are recorded correctly. The audio recordings will be retained for the period of time specified for all other study data or as required by law.

Please see the chart in the "Study Procedure" section below for the frequency of Quality of Life and Neurocognitive Testing evaluations you will have while participating in this study.

It will take approximately two hours to complete neurocognitive testing and to fill out the questionnaires.

You will not receive the results of the neurocognitive testing you perform during the study.

Additional tests may be done at the discretion of your physician as part of your regular care throughout the study. These exams and tests will be done to monitor the effects of study drugs.

Optional Photographs to Assess Hair Loss: In order to assess potential hair loss from radiation therapy, photographs may be taken of your scalp. The photographs will be taken of the craniotomy surgical incision site and surrounding area. The camera will be held approximately 6-48 inches from the incision. There will be no identifiers on the photographs. Up to 6 photographs may be taken at any one time-point. Photographs will not include your entire face (will not include your eyes, nose, mouth). The photographs will be taken by the PI or trained staff and may be uploaded to the electronic medical record, kept in a separate electronic research file or on paper. The photographs may be uploaded to the electronic medical record by using electronic applications for iPhones or for iPads or tablets. These applications allow for the photograph to be uploaded directly and are not stored on the device taking the picture. If you agree to have your photograph taken, the study team will take the photograph of your craniotomy incision site at baseline (when you go on study), after you complete radiation and temozolomide (2-4 weeks after completion) and approximately every 8 weeks while you are on the study.

Whether or not you decide to have these pictures taken you can still participate fully in all other aspects of the study as described in this consent form. While the photographs will not include your face, (eyes, nose or mouth) and will not have your name or other personal identifiers, there is a risk that the photo could be left on the individual employee or work Phone or the institution device.

I consent to have pictures of my scalp as described above: _____ (initials) _____ Date

I do NOT consent to have pictures taken my scalp as described above: _____ (initials) ____ Date

Study Procedures

This is a randomized study. You will be randomly assigned (like the flip of a coin) to receive either BMX-001 and participate in Arm A or participate in Arm B (without BMX-001). You have a 1 in 2 chance of receiving the study drug (BMX-001). You cannot choose your study group. If you are randomized to receive BMX-001, less than 12 weeks after surgery for your malignant brain tumor, you will receive a loading dose (which is a higher dose given in two injections) of BMX-001 injected under your skin (on your torso, upper leg or upper arm) the day before you start radiation therapy and temozolomide. Thereafter, you will receive a lower dose (given in one injection) injection of BMX-001 under your skin twice each week for the approximately 6 weeks that you will be receiving radiation therapy and temozolomide, along with 2 weeks after chemoradiation. This will be the end of your treatment with BMX-001. The total planned number of doses of BMX-001 that you will receive will be 17 doses.

If your malignant brain tumor does not appear to get worse 2-4 weeks after radiation therapy, but not greater than 8 weeks, you will begin standard of care adjuvant (added) temozolomide per standard dosing. The temozolomide will be daily for 5 days, days 1-5 of each cycle. Each cycle will be 4 weeks. The dose of temozolomide will be reduced if you have an adverse event (bad

effect) that the study doctor attributes to temozolomide. You will receive the drug temozolomide by mouth in a fasting state (nothing to eat for one hour prior to each dose and for two hours after each dose). The actual number of temozolomide capsules you take will vary depending upon your height and weight.

The charts below show what evaluations you will have during this study. The left-hand column tells you which evaluations will be done and the right-hand column shows the relative time frame within the part of the study.

Evaluations Prior to the start of RT and TMZ/ Loading Day (First BMX-001 Dose for subjects in Arm A)

Medical History and Physical with full Neurological Examinations
Toxicity Assessment
Vital signs, including blood pressure
Electrocardiogram (ECG) – Arm A only
MRI (DTI/Susceptibility Imaging)

Evaluations During Radiation Therapy/Temozolomide +/- BMX-001

Medical History and Physical with full Neurological Examinations	Every 2 weeks
ECG -Arm A only	First day of BMX-001, Week 1 and Week 4 before and 60 minutes after the injection.
Vital signs, including blood pressure	Every week
Complete Blood Count (CBC) with differential (blood count test)	Weekly
Comprehensive Metabolic Panel (CMP)- blood chemistry test	Weekly
Toxicity assessment	Continuous

Evaluations During Adjuvant Temozolomide

History and Physical with Neurological Examination	Every 8 weeks
CBC with differential	About at days 21 and 28 of each 28 day cycle
CMP	About on day 21 of each 28 day cycle
MRI of the brain	Every 8 weeks
Toxicity (adverse event or bad effect) assessment	Continuous [a]
Quality of Life Assessments	Every 8 weeks
Neurocognitive Testing	Every 8 weeks [b]
MRI (DTI/Susceptibility Imaging)	Before starting adjuvant temozolomide and 6 months after completion of radiation therapy

[a] You should contact your study doctor at any time to let him or her know of any bad side effects that you might be having.

[b.] Some additional neurocognitive tests will be performed before the start of the first cycle of adjuvant temozolomide, and about 6 and 12 months after you complete radiation therapy.

Optional Photographs for Hair Loss Evaluation

Photographs of your scalp (optional)	Baseline 2-4 weeks after radiation therapy Approximately every 8 weeks while on the study

After the completion of treatment, we will continue to contact you to see how you are doing.

What are my responsibilities if I take part in this research?

If you take part in this research, you will be responsible for following the guidelines included in this informed consent form.

Could being in this research hurt me?

Side effects of study drugs and procedures may be mild or they may severe enough to be life threatening. They may resolve (stop) after you stop the study drug or procedure or they may continue. Adding BMX-001 to standard of care therapy may interfere with the effectiveness of radiation or chemotherapy.

As a result of your participation in this study, you are at risk for the following side effects:

BMX-001 may cause some, all or none of the side-effects listed below. BMX-001 has only been given to animals before. Side effects are dose-dependent and the relatively low doses of this drug planned in this study have not been associated with side effects in animals other than those related to the color of the injected drug.

The most common side effects (expected to occur in more than 30% of subjects) are:

- Red to brown discoloration of the skin at the injection site which may take up to several weeks to resolve
- Irritation at the site of the injection of the drug under the skin
- Transient tachycardia (fast heart beat) after receiving the study drug

Less common side effects (expected to occur in 10-30% of subjects) are:

- Pain at the site of the injections of the drug under the skin
- Local histamine release which could be caused by the study drug. This could cause pruritus (itching), erythema (redness), edema (swelling), urticaria (welts). This is expected to resolve within a couple of hours of injection.

Rare side effects (expected to occur in less than 10% of subjects) are:

- Temporary hypotension (low blood pressure)
- Malaise or "not feeling well" for a few hours
- Prolongation of the QT interval after the loading dose. This is a condition in which your heart muscle takes slightly longer than normal to recharge between beats. This can be seen on an ECG, and is called a prolonged QT interval. We will monitor this by performing ECGs before and after study drug administration the first day you receive the drug and then twice (or more if indicated by your doctor) during BMX-001 treatment. Many drugs are known to cause this. For more information about this please discuss with your study doctor.

Additional possible side effects are:

- Red to dark color of urine
- Light-activated skin rash in response to sun exposure
- It is also possible that previously unobserved and unexpected side effects could occur.

Temozolomide may cause some, all or none of the side effects listed below (Arm A and Arm B).

The most common side effects (occurring in more than 30% of subjects) were:

- Fatigue
- Nausea
- Hair loss

Less common side effects (occurring in 10-30% of subjects) were:

- Thrombocytopenia (low platelets)
- Loss of appetite
- Headache
- Constipation
- Diarrhea
- Vomiting
- Rash
- Swelling in extremities

Rare side effects (occurring in less than 10% of subjects) were:

- Abdominal and/or breast pain
- Dry skin, skin redness, and/or itching
- Inflammation of the mouth, throat and/or sinuses
- Dizziness, weakness
- Confusion, memory impairment
- Anxiety, depression
- Joint and muscle pain
- Trouble sleeping
- Change in sense of taste
- Blurred vision
- Coughing or shortness of breath
- Urinary incontinence/frequency, urinary tract infection
- Weight increase
- Seizures/convulsions
- Adrenal hypercorticisim (elevated hormone levels)
- Low white blood cell (WBC) count
- Allergic reaction, sometimes severe
- Anemia (decreased number of red blood cells), which may cause symptoms of shortness

of breath, weakness, and fatigue.

Rare and Serious

- Liver damage which may cause yellowing of eyes and skin and swelling and may result in liver failure

Rarely, unusual ("opportunistic") infections have occurred. Rare cases of erythema multiforme (skin condition) have been reported which got better after temozolomide was stopped and, in some cases, recurred upon restarting treatment with temozolomide.

Very rare side effects have included secondary cancers including leukemia and myelodysplastic syndrome (MDS). MDS is a disorder of the bone marrow in which blood cells that do not function normally are produced.

Reproductive studies have not been done with temozolomide. Immature sperm and testicular atrophy (wasting away) occurred in studies with rats and dogs, using doses of temozolomide ¼ and 5/8 of the recommended human doses. In animal studies temozolomide caused death and multiple malformations of unborn young in rats and rabbits exposed during pregnancy.

Risks and Side Effects of Radiation Therapy: The radiation you will receive is considered standard of care for your tumor. The amount of radiation you will receive by participating in this study is the same as for patients with the same disease who are not taking part in this study.

Early side effects of radiation that may start while you are receiving radiation include hair loss, scalp redness, inflammation of the ear canals, and fatigue. In a few patients, radiation contributes to headaches or nausea. Rarely, tumors may swell during radiation causing neurological symptoms such as weakness on one side, visual loss, or changes in mental function. There is a small chance of long-term effects from radiation, occurring months or years after completion. These may include worsening of mental function, hearing, vision, strength and coordination. Rarely, radiation may cause the development of benign or malignant tumors around the brain or skull. It is unknown whether temozolomide increases the risk of any of the early or late side effects of radiation.

MRI: There have been no ill effects reported from exposure to the magnetism or radio waves used in this test. However, it is possible that harmful effects could be recognized in the future. A known risk is that the magnet could attract certain kinds of metal. Therefore, we will carefully ask you about metal within your body (this includes certain dyes found in tattoos). If there is any question about potentially hazardous metal within your body, you will be excluded from the study. We will also keep the examining room locked so that no one carrying metal objects can enter while you are in the scanner.

The most common side effects of the MRI contrast agents are local warmth/pain at the injection site, nausea and/or vomiting. Serious allergic reactions are very rare, may occur and may be life-threatening. A rare but serious adverse reaction has been observed in patients that received a gadolinium-based contrast material during MRI examinations, a reaction called nephrogenic systemic fibrosis (NSF). Patients with kidney disease are at increased risk of developing NSF. NSF may cause skin thickening, joint pain and/or swelling. In rare cases NSF can lead to lung and heart problems and cause death. To minimize the likelihood that you will be affected, you will have a blood test to measure your kidney function. If your blood test is abnormal, you will not be permitted to receive gadolinium.

Blood Draws: The collecting of blood samples to monitor your health and do PK throughout this study may cause mild discomfort or pain from the needle puncture and possible bruising or mild bleeding. The risk of infection is slight and will be further reduced by keeping the puncture site clean and dry.

Drug and Food Interactions: For your safety, you must tell the study doctor or nurse about all the prescribed medical food and drugs, herbal products, over-the-counter (OTC) drugs, vitamins and natural remedies that you are taking before you start the study and before taking any of these products while you are on the study.

Neuro-Cognitive Testing: There are few physical risks associated with this type of testing. Frustration with completing the mental tasks is the most common risk of this testing. Some individuals can feel stressed and anxious during testing. You should discuss these feelings with your physician if you are concerned.

Confidentiality: There is also the potential risk of loss of confidentiality. Every effort will be made to keep your information confidential; however, this cannot be guaranteed. Some of the questions we will ask you as part of this study may make you feel uncomfortable. You may refuse to answer any of the questions and you may take a break at any time during the study. You may stop your participation in this study at any time.

There may be risks, discomforts, drug interactions or side effects that are not yet known.

For those of Reproductive Potential

Female

Being a part of this study while pregnant may expose the unborn child to significant risks, some of which may be currently unforeseeable. Therefore, pregnant women will be excluded from the study. If you are a woman of childbearing potential, a blood pregnancy test will be done (using 1 teaspoon of blood drawn from a vein by needle-stick), and it must be negative before you can continue in this study. If sexually active, you must agree to use appropriate contraceptive measures for the duration of the study and for 12 months afterwards. Medically acceptable contraceptives include: (1) surgical sterilization (such as a tubal ligation or hysterectomy), (2) approved hormonal contraceptives (such as birth control pills, patches, implants or injections), (3) barrier methods (such as a condom or diaphragm) used with a spermicide, or (4) an intrauterine device (IUD). Contraceptive measures such as Plan B$^{(TM)}$, sold for emergency use after unprotected sex, are not acceptable methods for routine use. If you do become pregnant

during this study or if you have unprotected sex, you must inform your study physician immediately.

Male
Your participation in this research may damage your sperm, which could cause harm to a child that you may father while on this study. Such harm may be currently unforeseeable. If you are sexually active, you must agree to use a medically acceptable form of birth control in order to be in this study and for 12 months afterward. Medically acceptable contraceptives include: (1) surgical sterilization (such as a vasectomy), or (2) a condom used with a spermicide. Contraceptive measures such as Plan B(TM), sold for emergency use after unprotected sex, are not acceptable methods for routine use. You should inform your partner of the potential for harm to an unborn child. She should know that if pregnancy occurs, you will need to report it to the study doctor, and she should promptly notify her doctor.

Will it cost me money to take part in this research?

There will be no additional costs to you as a result of being in this study. However, routine medical care for your condition (care you would have received whether or not you were in this study) will be charged to you or your insurance company. You may wish to contact your insurance company to discuss this further. In order to make sure that tests and studies done solely for research purposes are charged correctly, we will carefully monitor your charges as long as you are participating in this study. These tests and studies are not a part of routine care, and people who are not part of the study do not usually have them performed. Please talk to the research team if you would like to know more about which tests and studies are being done solely for research purposes.

BMX-001 is provided free of charge by BioMimetix, JV LLC while you are on study. Temozolomide is commercially available and will not be supplied free of charge. Radiation therapy is standard of care and will not be supplied free of charge.

1. The ECGs are research-related costs and will not be charged to you or your insurance. The MRI for DTI/Susceptibility Imaging may or may not be covered, please discuss with your study doctor.

If you do not sign this consent form, you will continue to receive care, but not as a part of this study.

Will being in this research benefit me?

We cannot promise any benefits to you or others from your taking part in this research. However, possible benefits to you may include protection against cognitive decline caused by radiation therapy and/or reduction and/or remission of your high grade glioma. Additionally, a potential benefit may include protection against development of thrombocytopenia (a condition in which you have a low blood platelet count) which is caused by treatment with TMZ. About 15% of the subjects receiving TMZ as part of standard therapy for HGG develop thrombocytopenia. These subjects are at risk for a bleeding complication and may have their cancer therapy interrupted to allow recovery of the bone marrow. However, because this clinical protocol is experimental, it

cannot be guaranteed that subjects will receive any benefit as a result of participating in this research study.

We hope that in the future the information learned from this study will benefit other people with your condition.

During this research project, new information regarding the risks and benefits of the study may become known to the investigators. If this occurs, they will tell you about this new information. New information may show that you should no longer participate in the research. If this occurs, the persons supervising the research will stop your participation in it. In either case, you will be offered all available care that suits your needs and medical conditions.

What other choices do I have besides taking part in this research?

Instead of being in this study, you have these options:

- You could choose to receive alternative investigational drugs.
- You could choose to receive an alternative chemotherapy treatment.
- You could choose to receive the standard therapy for this disease.
- You could choose to receive no therapy at this time and receive care to help you feel more comfortable. If you choose this option, you may reconsider at any time, and this decision will in no way affect the regular care that you receive.

Please talk to your doctor about these and other options.

What happens to the information collected for this research?

Your private information and your medical record will be shared with individuals and organizations that conduct or watch over this research, including:

- The research sponsor, BioMimetix JV, LLC
- People who work with the research sponsor
- Government agencies, such as the Food and Drug Administration
- The Institutional Review Board (IRB) that reviewed this research
- The Data Safety Monitoring Board

Study records that identify you will be kept confidential as required by law. Federal Privacy Regulations provide safeguards for privacy, security, and authorized access. Except when required by law or for your care, you will not be identified by name, social security number, address, telephone number, or any other direct personal identifier in study records disclosed outside of [Institution]. An exception to this is that your date of birth, the dates that you complete the questionnaires, your audio recorded neurocognitive testing sessions, and other study procedures and computer internet protocol (IP) addresses will be included in the information sent to VeriSci (previously called NeuroCog), a group outside of [Institution] that collects this data on our behalf. The results of the neurocognitive tests conducted on the iPad and the audio recordings included with them will be stored on a secure cloud based server maintained

by VeraSci. The electronic files, including the audio files, will be retained for the period of time specified for all other study data or as required by law. For all records disclosed outside of the clinical center, you will be assigned a unique code number. The key to the unique code number will be maintained electronically on a secure network, which is accessible only to key personnel for the study and is password protected.

As part of the study, the study team will report the results of your study-related laboratory tests and imaging to BioMimetix JV, LLC. Additionally, tests used to diagnose your cancer will be reported to the sponsor. Tests to be provided to the sponsor would include laboratory tests such as your blood counts and tests to measure the function of your liver and kidneys, pathology reports, neurological tests, and radiographic studies including MRI scans of your head. As part of the study, your date of birth, dates of procedures and initials may also be reported to BioMimetix JV, LLC and people working with BioMimetix JV, LLC. In addition, your records may be reviewed in order to meet federal or state regulations. Reviewers may include representatives from the Food and Drug Administration, representatives of BioMimetix JV, LLC, the Western Institutional Review Board [and the [Institution IRB]]. In addition, the data and conduct for this study will be monitored by an outside committee called a Data Safety Monitoring Board (DSMB). Data about your participation will be shared with the DSMB members for their review of overall safety of the study drug. Data shared may have dates of treatment, test/procedures, diagnosis, and your initials and study ID.

If any of these groups review your research record, they may also need to review your entire medical record.

The images from the modified MRI scans and any MRI scan obtained to follow your brain tumor performed within three months of the modified scans may be sent outside of the clinical center to research collaborators located at Duke University (the imaging analysis center for this study), or others such as neuroimaging researchers, grant funding agencies and/or foundations, such as the National Institutes of Health, and/or to other databases organized by the National Cancer Institute, such as the National Cancer Imaging Archive. For tests to be useful, limited identifiers like test dates and diagnosis are necessary. By signing this consent form you authorize [Institution] to send out these specific identifiers in any MRI images that are sent outside of [Institution].

As part of this study, [Name] and his or her study team will ask you to have certain tests and radiographic studies. Some of these blood and radiographic studies would have been done as part of your regular care. These test results will be used both to treat you and to complete this research. These test results will be recorded in your medical record and will be reported to BioMimetix JV, LLC. Results of tests and studies done solely for this research study and not as part of your regular care will also be included in your medical record.

The study results may be retained in your research record forever. Any research information in your medical record will also be kept indefinitely.

This information may be further disclosed by the sponsor of this study, BioMimetix JV, LLC. If disclosed by the sponsor, the information is no longer covered by the federal privacy regulations. We protect your information from disclosure to others to the extent required by law. We cannot promise complete secrecy.

If this information is disclosed to outside reviewers for audit purposes, it may be further disclosed by them and may not be covered by the federal privacy regulations. While the information and data resulting from this study may be presented at scientific meetings or published in a scientific journal, your identity will not be revealed.

We may publish the results of this research. However, we will keep your name and other identifying information confidential.

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.

Data or specimens collected in this research might be deidentified and used for future research or distributed to another investigator for future research without your consent.

Who can answer my questions about this research?

If you have questions, concerns, or complaints, or think this research has hurt you or made you sick, talk to the research team at the phone number listed above on the first page.

This research is being overseen by an Institutional Review Board ("IRB"). An IRB is a group of people who perform independent review of research studies. You may talk to them at (800) 562-4789, help@wirb.com if:

- You have questions, concerns, or complaints that are not being answered by the research team.
- You are not getting answers from the research team.
- You cannot reach the research team.

- You want to talk to someone else about the research.
- You have questions about your rights as a research subject.

What if I am injured because of taking part in this research?

Immediate necessary medical care is available at [Institution] in the event that you are injured as a result of your participation in this research study. However, there is no commitment by [Institution], BioMimetix, JV, LLC or your physicians to provide monetary compensation or free medical care to you in the event of a study-related injury.

For questions about the study or research-related injury, contact [Name] at [Number].

Can I be removed from this research without my approval?

Your doctor may decide to take you off this study if your condition gets worse, if you have serious side effects, or if your study doctor determines that it is no longer in your best interest to continue. The sponsor or regulatory agencies may stop this study at any time without your consent. A reason why this might occur includes new identification of an unexpected problem with the study drug. If this occurs, you will be notified and your study doctor will discuss other options with you.

What happens if I agree to be in this research, but I change my mind later?

You may choose not to be in the study, or, if you agree to be in the study, you may withdraw from the study at any time. If you withdraw from the study, no new data about you will be collected for study purposes unless the data concern an adverse event (a bad effect) related to the study. If such an adverse event occurs, we may need to review your entire medical record. All data that have already been collected for study purposes, and any new information about an adverse event related to the study, will be sent to the study sponsor.

Your decision not to participate or to withdraw from the study will not involve any penalty or loss of benefits to which you are entitled, and will not affect your access to health care. If you do decide to withdraw, we ask that you contact [Name] in writing and let him/her know that you are withdrawing from the study. The mailing address is [address].

We will tell you about any new information that may affect your health, welfare, or choice to stay in this research.

Will I be paid for taking part in this research?

Subjects who agree to be in this study will have their external beam radiation treatment at [Institution]. The study sponsor will provide a travel stipend up to the amount of $1,000, to help compensate you for travel expenses associated with undergoing external beam radiation treatment at [Institution] while on this study. The travel stipend will be provided as follows:

$100 for each week of radiation treatment (pro-rated for visits completed up to 6 weeks, for a total of $600), followed by $400 provided at the completion of week 8. Payments will be provided after you have completed the 3rd week of standard radiation treatment here at [Institution]. At that time a check for $300 will be requested and mailed to your home. After you complete week 8, a second check for $700 will be requested and mailed to your home.

In order to receive this stipend, an additional form needs to be completed and a social security number will have to be collected.

Payment received as compensation for participation in research is considered taxable income to the research subject. If payment to an individual exceeds $600 in any one calendar year, [Institution] is required to report this information to the Internal Revenue Service (IRS). Research subject payments to a non-employee of [Institution] exceeding $600 during any calendar year will result in a 1099 (Miscellaneous Income) form being issued to the individual and a copy sent to the IRS.

Statement of Consent:

All subjects unable to consent are required to assent, unless the investigator determines that the capability of the subject is so limited that the subject cannot reasonably be consulted.

Your signature documents your permission for you or the individual named below to take part in

_____	_____
Printed name of subject (not required if subject personally provided consent)	Date
_____	_____
Signature of person obtaining consent	Date

My signature below documents that the information in the consent form and any other written information was accurately explained to, and apparently understood by, the subject, and that consent was freely given by the subject.

Signature of witness to consent process	Date

****For Sites in California****

AUTHORIZATION TO USE AND DISCLOSE INFORMATION FOR RESEARCH PURPOSES

What information may be used and given to others?
The study doctor will get your personal and medical information. For example:

- Past and present medical records
- Research records
- Records about phone calls made as part of this research
- Records about your study visits.

Who may use and give out information about you?
The study doctor and the study staff. [They may also share the research information with [enter SMO company name], an agent for the study doctor. delete if the site does not have an SMO]

Who might get this information?
The sponsor of this research. "Sponsor" means any persons or companies that are:

- working for or with the sponsor, or
- owned by the sponsor.

Your information <u>may</u> be given to:

- The U.S. Food and Drug Administration (FDA),
- Department of Health and Human Services (DHHS) agencies,
- Governmental agencies in other countries,
- The institution where the research is being done,
- Governmental agencies to whom certain diseases (reportable diseases) must be reported, and
- Western Institutional Review Board® (WIRB®)

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

- to do the research,
- to study the results, and
- to make sure that the research was done right.

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

What if I decide not to give permission to use and give out my health

information?
Then you will not be able to be in this research study.

May I review or copy my information?
Yes, but only after the research is over.

May I withdraw or revoke (cancel) my permission?
This permission will be good until December 31, 2060.

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 study doctor. If you withdraw your permission, you will not be able to stay in this study.

When you withdraw your permission, no new health information identifying you will be gathered after that date. Information that has already been gathered may still be used and given to others.

Is my health information protected after it has been given to others?
There is a risk that your information will be given to others without your permission.

Authorization:
I have been given the information about the use and disclosure of my health information for this research study. My questions have been answered.

I authorize the use and disclosure of my health information to the parties listed in the authorization section of this consent for the purposes described above.

AUTHORIZATION SIGNATURE:

_____ _____

Signature of Subject **Date**