Consent Form – Part 1-Cohort B

Study Title for Study Participants: Testing the ability of MLN0128 to get into the tumor in patients with brain cancer.

Official Study Title for Internet Search on http://www.ClinicalTrials.gov: Pilot Study of MLN0128 in Preoperative Recurrent Glioblastoma (GBM) Patients

What is the usual approach to my brain cancer?

You are being asked to take part in this study because you have a type of brain cancer called glioblastoma which has grown or has recurred and requires surgery. You have already been treated with surgery, radiation, and chemotherapy. People who are not in a study are usually treated with more chemotherapy and additional surgery if appropriate. Sometimes, combinations of these are used and your doctor can explain which may be best for you. These treatments can reduce symptoms and may stop the tumor from growing for several months or more.

What are my other choices if I do not take part in this study?

If you decide not to take part in this study, you have other choices. For example:

- you may choose to have the usual approach described above
- you may choose to take part in a different study, if one is available
- you may choose not to be treated for cancer, but you may want to receive comfort care to relieve symptoms.

Why is this study being done?

One reason that chemotherapy drugs might not work is that the drugs may not be able to get into the brain tumor and kill cancer cells. The purpose of this study is to determine how much the study drug, called MLN0128, reaches the brain tumor. This study is only for people who require surgery for their brain tumor. MLN0128 is not FDA-approved to treat brain cancer but it has slowed tumor growth in several types of tumors in animals.

There will be about 10 people taking part in this study.

What are the study groups?

All study participants will receive one dose of the study drug, MLN0128, in the form of pills that are taken by mouth 2-4 hours prior to scheduled surgery to remove brain tumor. The study doctor will tell you how many pills you should take. The number of pills you take and the time they are taken, should be written down in a pill diary that the study doctor will give you.

During your surgery a portion of your tumor will be taken to measure the concentration of the drug in your tumor.

After recovery from surgery, within 30 days, all patients will receive MLN0128 every week to look at side effects and determine how you respond to the study drug . The study doctor will tell you how many pills you

should take. The number of pills you take each week, and the time they are taken, should be written down in a pill diary that the study doctor will give you.

Every 28 days you will return to the clinic to see the study doctor again. The study doctor supplies the pills during the clinic visits. Empty bottles, any remaining pills, and the pill diary should be returned to the study doctor at each visit.

How long will I be in this study?

You will continue to receive the study pills and be in the study until your tumor grows, or you have side effects that cause your condition to worsen, or you desire to stop treatment. After you stop taking the study pills, your doctor will continue to watch you for side effects and follow your condition for at least 30 days.

What extra tests and procedures will I have if I take part in this study?

Most of the exams, tests, and procedures you will have are part of the usual approach for your cancer. However, if you choose to take part in the study, then you will need the following extra procedures. They are not part of the usual approach for your type of cancer.

Before you begin the study:

You will need to have the following extra exams, tests and procedures:

- Collection of one extra blood sample for studies of drug levels in your blood.

During the study:

- Collection of two extra blood samples around the time of surgery and eight additional samples during the first two days of your post-surgical treatment for studies of drug levels in your blood.
- Collection of pieces of cancer tissue from your tumor during surgery to measure the amount of study drug in your tumor and to look at certain features of the tumor. These samples are required in order for you to take part in this study. The tissue will be collected during your normal surgery to remove the tumor.

Neither you nor your health care plan/insurance carrier will be billed for the collection or processing of the research blood samples and tumor tissue that will be used for this study.

What possible risks can I expect from taking part in this study?

If you choose to take part in this study, there is a risk that you may:

- Lose time at work or home and spend more time at the hospital or doctor's office than usual

The pills used in this study may affect how different parts of your body work such as your liver, kidneys, heart, and blood. The study doctor will be testing your blood and will let you know if changes occur that may affect your health.

There is also a risk that you could have side effects from the study drug.

Here are important points about side effects:

- The study doctors do not know who will or will not have side effects.
- Some side effects may go away soon, some may last a long time, or some may never go away.

- Some side effects may interfere with your ability to have children.
- Some side effects may be serious and may even result in death.

Here are important points about how you and the study doctor can make side effects less of a problem:

- Tell the study doctor if you notice or feel anything different so they can see if you are having a side effect.
- The study doctor may be able to treat some side effects.
- The study doctor may adjust the study drugs to try to reduce side effects.

The tables below show the most common and the most serious side effects that researchers know about. There might be other side effects that researchers do not yet know about. If important new side effects are found, the study doctor will discuss these with you.

COMMON, SOME MAY BE SERIOUS In 100 people receiving MLN0128, more than 20 and up to 100 may have:
• Diarrhea, nausea, vomiting • Tiredness • Swelling of the body • Loss of appetite • Increase in blood glucose (sugar): Glucose is what the body uses for energy, and it is regulated or controlled in the body by insulin levels. Too much glucose can cause dehydration, excessive thirst, the need to urinate frequently and other symptoms • Rash

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving MLN0128, from 4 to 20 may have:
• Anemia which may require blood transfusion • Dry mouth • Sores in mouth which may cause difficulty swallowing • Bruising, bleeding • Dehydration • Changes in taste • Itching

RARE, AND SERIOUS In 100 people receiving MLN0128, 3 or fewer may have:
• Heart stops beating • Abnormal heartbeat which may cause fainting • Kidney damage which may require dialysis

Let your study doctor know of any questions you have about possible side effects. You can ask the study doctor questions about side effects at any time.

Reproductive risks: You should not get pregnant, breastfeed, or father a baby while in this study and for 30 days after your last dose of study pills. The study pills used in this study could be very damaging to an unborn baby. Check with the study doctor about what types of birth control, or pregnancy prevention, to use while in this study.

There can also be a risk in finding out new genetic information about you. New health information about inherited traits that might affect you and your blood relatives could be found during a study.

What possible benefits can I expect from taking part in this study?

This study has only a small chance of helping you because we do not know if the study drug, MLN0128, is effective. This study may help researchers learn things that may help other people in the future.

Can I stop taking part in this study?

Yes. You can decide to stop at any time. If you decide to stop for any reason, it is important to let the study doctor know as soon as possible so you can stop safely. If you stop, you can decide whether or not to let the study doctor continue to provide your medical information to the organization running the study.

The study doctor will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

The study doctor may take you out of the study:

- If your health changes and the study is no longer in your best interest
- If new information becomes available
- If you do not follow the study rules
- If the study is stopped by the sponsor, IRB or FDA.

What are my rights in this study?

Taking part in this study is your choice. No matter what decision you make, and even if your decision changes, there will be no penalty to you. You will not lose medical care or any legal rights.

For questions about your rights while in this study, call the _____ *(insert name of center)* Institutional Review Board at _____ *(insert telephone number). (Note to Local Investigator: Contact information for patient representatives or other individuals at a local institution who are not on the IRB or research team but take calls regarding clinical trial questions can also be listed here.)*

What are the costs of taking part in this study?

The MLN0128 pills will be supplied at no charge while you take part in this study. The cost of getting the pills ready and giving it to you is also provided at no charge. It is possible that the MLN0128 pills may not continue to be supplied while you are on the study. Although not likely, if this occurs, your study doctor will talk to you about your options.

You and/or your health plan/insurance company will need to pay for all of the other costs of treating your cancer while in this study, including the cost of tests, procedures, or medicines to manage any side effects, unless you are told that certain tests are supplied at no charge. Before you decide to be in the study, you should check with your health plan or insurance company to find out exactly what they will pay for.

You will not be paid for taking part in this study.

What happens if I am injured or hurt because I took part in this study?

If you are injured or hurt as a result of taking part in this study and need medical treatment, please tell your study doctor. The study sponsors will not offer to pay for medical treatment for injury. Your insurance

company may not be willing to pay for study-related injury. If you have no insurance, you would be responsible for any costs.

If you feel this injury was a result of medical error, you keep all your legal rights to receive payment for this even though you are in a study.

Who will see my medical information?

Your privacy is very important to us and the researchers will make every effort to protect it. Your information may be given out if required by law. For example, certain states require doctors to report to health boards if they find a disease like tuberculosis. However, the researchers will do their best to make sure that any information that is released will not identify you. Some of your health information, and/or information about your specimen, from this study will be kept in a central database for research. Your name or contact information will not be put in the database.

There are organizations that may inspect your records. These organizations are required to make sure your information is kept private, unless required by law to provide information. Some of these organizations are:

- The study sponsor and Millennium, the drug company supporting this study.
- The Institutional Review Board, IRB, is a group of people who review the research with the goal of protecting the people who take part in the study.
- The Food and Drug Administration and the National Cancer Institute in the U.S., and similar ones if other countries are involved in the study.

Where can I get more information?

You may visit the NCI Web site at http://cancer.gov/ for more information about studies or general information about cancer. You may also call the NCI Cancer Information Service to get the same information at: 1-800-4-CANCER (1-800-422-6237).

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.

Who can answer my questions about this study?

You can talk to the study doctor about any questions or concerns you have about this study or to report side effects or injuries. Contact the study doctor _____ *(insert name of study doctor[s])* at _____ *(insert telephone number).*

My Signature Agreeing to Take Part in the Study

I have read this consent form or had it read to me. I have discussed it with the study doctor and my questions have been answered. I will be given a signed copy of this form. I agree to take part in the study.

Participant's signature_____

Date of signature_____