CONSENT AND RESEARCH AUTHORIZATION TO DONATE BLOOD AND TISSUE SAMPLES FOR FUTURE RESEARCH PURPOSES YALE UNIVERSITY SCHOOL OF MEDICINE – YALE-NEW HAVEN HOSPITAL 200 FR. 4

Study Title: An Open-Label, Phase I/II, Dose-Escalation Study Evaluating the Safety and Tolerability of GDC-0032 in Patients with Locally Advanced or Metastatic Solid Tumors or Non-Hodgkin's Lymphoma and in Combination with Endocrine Therapy in Patients with Locally Advanced or Metastatic Hormone Receptor-Positive Breast Cancer

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Funding Source: Genentech, Inc.
Researchers: Genentech, Inc., its research partners, collaborators, assignees, licensees or designees.

Invitation to Participate

This is a research study. Your study doctor or the study staff will explain the research study to you. The research study includes only patients who choose to take part. Please take your time to make your decision about taking part in this study. You may discuss your decision with your family and friends. You can also discuss it with your health care team. If you have any questions, you can ask your study doctor for more explanation. In this consent form, "you" refers to the patient.

Taking part in this study is voluntary. No matter what you decide to do, it will not affect your participation in Study PMT4979g or your medical care.

Purpose:

You are being asked to take part in this optional study because you have already agreed to take part in and have signed an Informed Consent Form for Genentech Study PMT4979g, in which you will receive the study drug GDC-0032. Genentech is the sponsor of Study PMT4979g and this separate optional study.

All patients enrolled in the main study will be asked to take part in some of the optional research assessments. In addition, many other patients who are taking part in other Genentech research studies will be asked to provide blood and tissue samples for future research related to disease therapy and diagnostics. Your samples will be stored in the Genentech sample repository along with many other samples collected from patients taking part in Genentech research studies.

Introduction:

Approximately 623-723 patients will be taking part in Study PMT4979g. The study is divided into two phases, Phase I and Phase II. If you are being asked to participate in Phase I or Phase II of this study, you will be given this consent form. There are two stages to the Phase I portion of this study: Stage 1 (dose escalation) and Stage 2 (expansion). Thirty-four patients will take part in Stage 1 and will be asked to take part in this optional research. Approximately 529-629 patients will take part in Stage 2 and will be asked to take part in some of the optional research assessments. Approximately 60 patients will take part in the Phase II portion and will be asked to take part in some of the optional research assessments.

For Study PMT4979g you are going to have blood drawn. When you were first diagnosed, you may have had a biopsy or excision of tissue that contained a sample of your tumor. In addition, if you have any non–study-related, medically indicated procedures during the course of Study PMT4979g, there may be leftover (unused) tissue or bodily fluids. Your blood, tissue, and/or fluid samples may hold important clues that might help researchers to understand more about cancer and why people do or do not respond to treatments. The study sponsor, Genentech Inc. would like to collect a sample of your blood, a section of your tumor tissue, and/or fluids for further research.

If you decide to take part in this additional study, your samples and related medical information collected during Study PMT4979g will be used by the study sponsor researchers and partners for research related to cancer, related diseases, or how GDC-0032 works in the treatment of cancer and related diseases and may help develop new treatments or diagnostic tests in the future. Your samples may be analyzed for the presence of markers that might predict whether your tumor responds or is resistant to GDC-0032. This research may include analyses of DNA, RNA, or proteins associated with the PI3K pathway. Additional studies such as sequencing of genes related to the PI3K pathway may also occur.

About This Research:

Information from this research will be from all of the patients who take part in this study as a group and not just from your samples.

The Study Doctor will replace your name with a code number and provide both the blood sample and your health information to the Researchers. The researchers will place your coded information in a database and will store ("bank") your samples. It may take many years to complete this research, so your samples will be stored indefinitely or until they are all used up. Your blood, tissue, and/or fluid samples and related medical information will be used only for research and will not be sold. Your sample(s) will not be used for genetic testing to determine or predict risk of diseases that you do not currently have. Your samples will not be used for research involving human cloning (growing human tissue from this material). Your health information collected from the main clinical trial will be kept on file in accordance with the Researchers' retention policies.

Procedures:

Optional Tumor Biopsies –

If your doctor determines that you have tumor tissue that may be obtained with a minimum of risk and discomfort to you, you are being asked to undergo tumor biopsies to provide a small sample of your tumor tissue. These biopsies may be required to determine eligibility for some patients taking part in the study and may be optional for other patients taking part in the study (dependent upon the cohort you enter).

If you agree to have tumor tissue taken, you will undergo the first biopsy before starting treatment with GDC-0032. A doctor (pathologist) will look at the tissue biopsy sample to determine whether or not the sample has enough cancer cells to conduct research tests. If the sample does not have enough cancer cells, you will not be asked to undergo additional biopsies. If the sample has enough cancer cells, you will be asked to undergo another biopsy about 15–21 days (Phase I: Stage 1 or Stage 2, Cohorts A–X) or 29–44 days (Phase II) after you have started daily treatment with GDC-0032. On the day of the second biopsy, you will be told when to take your daily dose of the study drug. In addition, you are being asked to have an optional tumor biopsy procedure at the time that your disease gets worse. Tests done on this biopsy may help explain why the study drug has stopped working. Depending on when

your biopsy is scheduled, you may also have approximately 1 teaspoon of additional blood drawn at the time of the biopsy to determine changes in GDC-0032 levels in your blood. If you have already had blood taken on the day of your biopsy, this additional blood will not be obtained. The tissue will be analyzed to see if there are changes in the proteins associated with the PI3-kinase (PI3K) pathway and other effects as a result of taking GDC-0032. If you do not have tumor tissue that can be obtained in this way or you do not wish to undergo the biopsy to obtain this tissue, you may still participate in the main Study PMT4979g.

Some patients must have a mutation or amplification in the PI3K gene in their tumor sample to take part in this study. You will be asked to undergo a new tumor biopsy if we cannot determine whether the PI3K gene in any prior tumor biopsy samples has a mutation or amplification. If you refuse the new tumor biopsy, you may not be allowed to participate in the study.

<u>Optional Research on Leftover Blood, Bodily Fluids, and Tissue samples taken in Study PMT4979g –</u>

- For Study PMT4979g, you will have blood, bodily fluids, and tissue samples taken during the clinic visits. Genentech would like to use any leftover blood samples for research tests. Your samples may be used to help researchers to: **Better understand why certain people are more likely to respond to medicines such as GDC-0032**
- **Better understand how and why cancer and related diseases act differently in different people**
- **Develop new treatments for cancer or related diseases**
- **Find reasons why certain people are more likely to have side effects to medicines such as GDC-0032**
- **Find out how medicines such as GDC-0032 are processed by people's bodies and how such treatment may affect people's bodies**
- **Develop better ways for preventing diseases or treating diseases earlier**
- **Develop or improve tests that help with detection or understanding of cancer and related diseases, to help identify the right medicine for the right patient**

Since this research will be done on leftover blood samples only, there is no additional procedure (blood draw) and therefore no additional risk.

Optional Research Studies on Leftover Blood, Bodily Fluids and Tissue Samples obtained for Other Purposes –

If you have any non–study-related, medically indicated procedures during the course of Study PMT4979g that result in leftover tissue or bodily fluids, Genentech would like to collect your unused tissue or bodily fluids to use in research studies related to GDC-0032 activity against tumors, mechanisms of resistance to GDC-0032, and side effects due to GDC-0032. If you do not wish your leftover samples to be collected, you may still participate in the main study. All patients are being asked to participate in these optional research studies on leftover samples obtained for other purposes.

Your doctor will explain the medically indicated procedure. If you agree to allow Genentech to use any leftover tissues or fluids from the medical procedures, the samples will be stored and used for research related to GDC-0032 and the PI3K pathway.

Since this research will be done on leftover samples only, there is no additional procedure (blood draw or biopsy) and therefore no additional risk.

If the procedures are done on days that are not close to or at the regular study visits, then you may be asked to have approximately 1 teaspoon of blood drawn to examine the level of GDC-0032 in your blood.

Risks:

Tumor Biopsies –

If you choose to allow collection of your tumor tissue, your doctor will explain the risks of the procedure to you for you to decide if you want to participate. As with any procedure there are risks and discomforts.

In most patients, biopsies of tumor tissue will be performed with a special needle, called a core biopsy needle. The core biopsy needle allows the doctor to remove a small piece of that tissue that can later be evaluated under a microscope. The safety of biopsies of tumors in internal organs is enhanced by doing this procedure under CT guidance. The CT scan will help the doctor locate the tumor tissue, avoid vital structures like blood vessels, and place the needle into the tumor tissue. Unless the tumor tissue is a lump in the skin or in a lymph node just under the skin (superficial), the tumor biopsies for this optional research will be done under CT scan

guidance. The risks of the tumor biopsy procedure are mainly pain, bleeding, and infection. Depending on the location of the tumor, there is a small risk of injury or damage to the nearby organs or tissues. Your doctor may use a local anaesthetic or a medicine to calm your nerves before or during the biopsy procedure. Your doctor will explain the procedure to you and discuss these comfort measures.

Blood Draws -

If you are asked to have additional blood samples drawn, a minor risk exists of brief discomfort, bruising, bleeding, swelling, or, rarely, infection at the site of needle insertion for the blood collection procedure.

Other Potential Risks -

There are also non-physical risks associated with taking part in this study, such as the risks associated with a loss of privacy or confidentiality. For example, if your identity as a participant in this optional research study or your identifiable genetic or health information were disclosed to unauthorized persons, there is the possible risk of discrimination by employers or insurance providers. The Researchers believe that the risks of such improper disclosure are very small because strict privacy and confidentiality procedures for this research have been adopted. (See the “Privacy and Confidentiality” section of this Informed Consent).

Benefits:

No direct benefit can be promised to you as a result of your participation in this research study, since the research may take many years. Reports about research done with your blood and tissue will not be given to you or your doctor. Any research done will not have an effect on your medical care; however, donating your blood, fluids, and tissue for additional research may eventually benefit other patients.

Economic Considerations:

You will not be paid for your participation in this optional research study.

There are no costs to you or to your health plan/insurance company to take part in this optional study.

Development for Commercial Gain –

Your samples will be owned by Genentech. If a commercial product is developed from this research study, rights to the commercial product will belong to Genentech and its collaborators (persons or companies partnering with Genentech). You and your family will not receive any financial benefits or compensation from or have rights in any developments, inventions, or other discoveries that might come out of this research.

Privacy and Confidentiality:

Your medical information will be kept as confidential as possible within the limits of the law. Your medical information may be given out if required by law. Genentech may use the medical information collected during this study to describe your blood or tissue samples; however, you will not be identified by name or picture. If information from this study is published in a medical journal or presented at scientific meetings, you will not be identified by name, picture, or any other personally identifying information.

Reports about research done with your samples will not be given to you, your study doctor, or any of your doctors. These reports will not be put in your medical record. These reports will not be used to provide genetic information about you or your relatives to people such as insurers and employers unless it is required by law.

Information about your study participation will be entered into your Electronic Medical Record (EMR). Once placed in your EMR, these results are accessible to all of your providers who participate in the EMR system. Information within your EMR may also be shared with others who are appropriate to have access to your EMR (e.g., health insurance company, disability provider.)

The following people and groups of people may look at and/or copy your medical records to make sure that the study is being done properly and to check the quality of the data:

- Genentech study monitors and representatives
- Genentech collaborators and licensees (people and companies partnering with Genentech)

- The Institutional Review Board (IRB) responsible for protecting the rights and safety of the patients who take part in research studies
- Those providers who are participants in the Electronic Medical Record (EMR) system
- The U.S. Food and Drug Administration (FDA) and other government agencies involved in keeping research safe for people

Review of your medical records by these people or groups of people will not violate your confidentiality.

Although you have the right, subject to policies of Yale School of Medicine and Yale New Haven Hospital to access information in your medical records, including information related to the main clinical trial (once that study is complete), the information that is maintained in databases and created during this optional study is for research purposes only. The Researchers will not initiate the return of any of the genetic information to you or your health care provider. **Information resulting from the research will not be entered into your medical records.** At some point, information about the results of the research may be published; however, you will not be identified in any such publication.

It is possible, however, that members of regulatory authorities, such as the United States Food and Drug Administration and other persons required by law may have access to the research results.

The Researchers may use other laboratories, investigators, commercial or academic third parties as their “agents” to assist in this research. If these agents assist in the research, your sample and some of your health information will be shared with them. The Researchers will require that these agents protect your privacy.

A new Federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.

- Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

All health insurance companies and group health plans must follow this law by May 21, 2010. All employers with 15 or more employees must follow this law as of November 21, 2009. Be aware that this new Federal law does **not** protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

In Case of Injury:

If you have any side effects after taking the study drug or are injured during the study, tell your Study Doctor right away. Your Study Doctor will make sure you receive medical treatment.

Genentech will pay for the reasonable costs of immediate care for any physical injury to you that specifically results from the study drug, but only if:

- Genentech and the study doctor agree that your injury resulted from the study drug (GDC-0032) and not from a preexisting medical condition;
- Your injury did not result from a failure to follow study protocol or instructions, or from the negligence, mistakes, or misconduct of the study personnel.

You will not receive any other kind of payment. There are no plans to pay you for such things as lost wages, disability, or discomfort as part of this study. You do not give up any of your legal rights by signing this consent form.

Withdrawal of Consent and Destruction of Samples:

You may withdraw this consent and discontinue your participation in this optional research study described above at any time without affecting your participation in the main clinical trial.

To withdraw your consent, you must contact the Study Doctor, Lajos Pusztai, M.D., 203-737-8309, because only he/she has access to all of your identifying information. If you withdraw your consent for this optional research study during at any time, you may request that you no longer want your blood, tissue, or blood and tissue samples to be stored or used for additional

research. Then, any blood or tissue samples that remain will be destroyed. You do not need to give a reason for changing your mind.

We will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study. When informed of this new information, if you agree to continue in the study, you will be asked to sign an updated consent form.

No matter what you decide to do, it will not affect your participation in Study PMT4979g or your medical care. If you change your mind, and your samples have already been tested, those results will still remain part of the overall research data. Additionally, even if you withdraw or discontinue treatment in Study PMT4979g, you may continue to participate in this separate optional research study. If you choose not to participate or if you withdraw it will not harm your relationship with your own doctors or with Yale-New Haven hospital.

Questions:

We have used some technical terms in this form. Please feel free to ask about anything you do not understand and to consider this optional research study and the consent form carefully – as long as you feel is necessary – before you make a decision.

Do not sign this consent form unless you have had a chance to ask questions and have received satisfactory answers to all of your questions.

If you agree to be in this optional research study, you will receive a signed and dated copy of this consent form for your records.

YOUR CONSENT TO PARTICIPATE IN THE STUDY AND AUTHORIZATION FOR USE AND DISCLOSURE OF YOUR MEDICAL RECORD INFORMATION

OPTIONAL TUMOR BIOPSIES

I willingly consent to undergo a tissue biopsy of my tumor and allow my blood and related medical information collected during Study PMT4979g to be used for the types of research outlined for Optional Tumor Biopsies.

☐ Yes ☐ No

OPTIONAL RESEARCH ON LEFTOVER BLOOD, BODILY FLUIDS, AND TISSUE SAMPLES TAKEN IN STUDY PMT4979G

I willingly consent to allow any leftover samples of my blood and related medical information collected at any time during Study PMT4979g to be used for the types of research outlined for Optional Research on Leftover Blood, Bodily Fluids, and Tissue Samples Taken in Study PMT4979g.

☐ Yes ☐ No

OPTIONAL STUDIES ON OTHER BLOOD, BODILY FLUIDS, AND TISSUE SAMPLES OBTAINED FOR OTHER PURPOSES

I willingly consent to allow my blood and tissue sample and related medical information collected during Study PMT4979g to be used for the types of research outlined for Optional Studies on Other Blood, Bodily Fluids, and Tissue Samples Obtained for Other Purposes.

☐ Yes ☐ No

Authorization and Permission

I have read (or someone has read to me) this form and have decided to participate in the project as described above. Its general purposes, the particulars of my involvement and possible hazards and inconveniences have been explained to my satisfaction. My signature also indicates that I have received a copy of this consent form.

By signing this form, I give permission to the researchers to use and give out information about me for the purposes described in this form. By refusing to give permission, I understand that I will not be able to participate in this research.

Study Participant (print name)	Signature	Date
Person obtaining consent (print name)	Signature	Date
Person obtaining consent (print name) – only if applicable, otherwise blank	Signature	Date
Interpreter/ Witness (print name) – only if applicable, otherwise blank	Signature	Date

If after you have signed this form you have any questions about your privacy rights, please contact the Yale Privacy Officer at (203) 432-5919.

If you have further questions about this project or if you have a research-related problem, you may contact the Principal Investigator, Dr. Lajos Pusztai at 203-737-8309. If you would like to talk with someone other than the researchers to discuss problems, concerns, and questions you may have concerning this research, or to discuss your rights as a research subject, you may contact the Yale Human Investigation Committee at (203) 785-4688.