STANFORD CONSENT FORM with HIPAA

COHORT 1 – Infigratinib plus Tamoxifen

Are you participating in any other research studies? _____ Yes _____No

CONCISE SUMMARY / INTRODUCTION TO RESEARCH STUDIES

This section is called the Concise Summary, and is intended to give you important information that will help you make an informed decision about whether or not to participate in this research study.

- You are invited to voluntarily participate in a research study of infigratinib. The part of the study you are invited to participate in is Cohort 1 evaluating infigratinib plus tamoxifen.
- You were selected as a possible participant in this study because you have advanced breast cancer with certain characteristics known as "hormone receptor-positive," and "HER2-negative."
    - "Advanced" means your breast cancer spread outside of the breast and local lymph nodes, or cannot be readily removed by surgery. Advanced cancers may be hard to treat.
    - "Hormone receptor-positive" means that the cancer expresses receptors for a female sex hormone, ie, either estrogen and/or progesterone.
    - "HER2-negative" means that there is a change in one of your genes that may affect the fibroblast growth factor receptor (FGFR) pathway, which plays an important role in cancer.
- Infigratinib is an experimental ("investigational") therapy to be used in combination with FDA-approved chemotherapy agents to treat hormone receptor-positive, HER2-negative advanced breast cancer, and your consent to participate is requested. Because this is a research study, infigratinib will be given to you only during this study and not after the study is over.
- This research study is in addition to, and does not replace, your regular medical care. Infigratinib will be added to your regular medical care.
- The purpose of this research is to study if infigratinib, when used in combination with FDA-approved chemotherapy agents, has an acceptable safety profile. This information may help improve patient care. Your participation in this study will help answer the research question.

- Reasonably-foreseeable risks or discomforts include eye problems, loss or thinning of hair, inflammation inside the mouth, stomach or intestinal side effects, and high phosphorus and/or calcium in the blood. More detailed information is provided later in this document, in the section "Possible Risks, Discomforts, and Inconveniences."
- If you take part in this study, you agree not to eat grapefruit, grapefruit juice, grapefruit hybrids, pomegranates, star fruits, pomelos, Seville oranges, or products containing juice of these fruits within 7 days of starting treatment and through the entire treatment period.
- If you take part in this study, you may have to take a phosphate-lowering agent such as sevelamer.
- If you take part in this study, your blood and tissue specimens will be retained for future research use.
- Alternatives to participation in this study is not to participate, ie, receive the same or different treatment, but without infigratinib. You should be aware that there are other effective treatments that are available to you without participating in this research study. By participating in this research study, you may be foregoing other treatment options known to provide clinical benefit for your cancer.
- Ask any questions you wish about this study. If you want, you may discuss this with your family, friends, or your other doctors. You can have a copy of this document to discuss with them.
- If you decide to participate, you can stop your participation at any time. If you want to stop your participation in the study, tell the study doctor or anyone on the study team. If you wish to withdraw your specimens from future research, you need to state this in writing.
- If you stop your participation in the study, your medical care may be compromised. You should discuss this decision with the study doctors, who will help you identify alternate care.

This document is to be used as a guide for a discussion between you and your Study Doctor and the study team. This form, called an informed consent document, was designed to help you understand why this study is being done; what part of the study is "research" or "experimental;" what will be asked of you if you choose to participate; possible risks; any inconveniences or discomforts you may experience; and other important information. This document is intended to provide the information that a

potential participant might want to have in order to make an informed decision about whether to participate in the research study. If you have any questions or would like additional information, please ask the person obtaining consent or any other member of the study team.

If you choose to participate, this form may also be helpful as a reference or reminder about your role in the study, and whom to contact if you have any questions at any time during your participation.

If you decide to take part in this research study, you will be asked to sign this consent form before any study-related activities are performed. You will receive a copy of the signed consent document for your records.

PURPOSE OF RESEARCH

The study team hopes to learn if infigratinib, a drug that targets the FGFR cancer pathway, can be safely added to current anti-hormonal therapies, specifically those including tamoxifen (Nolvadex or Soltamox).

The use of infigratinib in this research study is investigational ("experimental"). The word "investigational" means that infigratinib is not currently approved by the US Food and Drug Administration (FDA) for use in the United States to treat your type of breast cancer, but has been approved for research studies. This study is being conducted under an application submitted to FDA, called an "Investigational New Drug Application" or "IND." Infigratinib will be provided for this study by the drug manufacturer QED Therapeutics, Inc. Tamoxifen (Nolvadex or Soltamox) are used in this study according to their FDA-approved labeling.

Your doctor recommends hormonal therapy as the best treatment choice that is available to you at this time. Your normal medical care for this type of breast cancer could include tamoxifen or possibly other FDA-approved agents. Using current therapies, some patients with advanced solid tumors such as yours receive treatment benefit, but are not cured of their disease.

Your normal medical care would also include medical exams, blood tests, and medical scans to check the status of your cancer such as positron emission tomography (PET); computed tomography (CT); or magnetic resonance imaging (MRI) scans.

If you decide to stop participating in this study, you should notify Jennifer Caswell-Jin, MD, at 650-724-3250 or a study team member.

This research study is looking for up to 12 people in each of 2 treatment groups, and then an additional 12 subjects at the end to gain experience with safety and statistical efficacy for up to a total of 33 people with breast cancer. There will be up to 12 participants in your cohort, Cohort 1, infigratinib plus tamoxifen. This study is being conducted at Stanford University only.

VOLUNTARY PARTICIPATION

Your participation in this study is entirely voluntary. Your decision not to participate will not have any negative effect on you or your medical care. You can decide to participate now, but withdraw your consent later and stop being in the study without any loss of benefits or medical care to which you are entitled.

DURATION OF STUDY INVOLVEMENT

The study schedule includes a screening period, which may take up to 21 days; up to 18 cycles of treatment (each cycle is about 28 days / 1 month); and a follow-up period for 30 days after the last study treatment, for a total of about 20 months. You will continue to be monitored for more than 30 days after treatment ends, if you continue to have unresolved side effects from the drug. After the first 18 cycles of treatment, additional treatment may be allowed in certain situations.

PROCEDURES

It may be harmful to enter this study while receiving some medications, therefore, you may need to stop taking certain medications. Your Study Doctor will review your medications and provide you with specific instructions.

Research studies are usually dividing into at least 3 parts, typically consisting of:

1. Testing to see if you are eligible to participate in the study (“Screening”);
2. Testing during study treatment to monitor your health and the effects of the study treatment (“Study Evaluation Procedures”); and
3. Testing after your treatment is complete (“Follow-up”).

Testing/procedures for each of these parts are described separately below.

Some of these examinations, tests, or procedures may be part of your regular medical care, and/or and may be done even if you do not join the study. If you have had some of them recently, they may not need to be repeated.

Before you join this study, Dr. Caswell-Jin and/or the research study team will review this document with you, and ask you to sign this informed consent document. After you have signed this document and received a signed copy, the study will begin with a Screening Visit.

You are assigned to Cohort 1 (infigratinib plus tamoxifen). Events and timepoints occurring during the study period are described in further detail on the following pages.

Screening Visit

If you choose to participate and sign this consent document, the first activity will be Screening. During the Screening Visit, you will be asked to have the following tests and activities or assessments. After the results of the screening tests are assessed, you may be registered to the study as a participant. Study drug treatment can start within 7 days of study registration.

General information: Information about you, such as date of birth; gender (sex); and ethnic origin ("demographic information")

Medical history: Your complete medical history will be reviewed, including:

- Review of all medicines and/or supplements you are taking or have been taking
- Questions about any medical symptoms you are having
- Surgery and cancer history, including tumor diagnostic testing
- Reproductive status

Physical examination: A complete physical exam will be performed, including:

- Your vital signs, including height; weight; breathing rate; heart rate; blood pressure; temperature; and other measurements
- General examination of your body systems, such as heart and lungs; ear, nose, and throat; skin; muscles and joints; stomach and gastrointestinal tract; and nervous system
- You will be asked how well you are able to perform normal daily living activities (such as bathing, driving, shopping, working, etc)

Blood collection: Blood collection will typically be from a vein in your arm, using a blood collection needle. This is called venipuncture. If you have an implanted venous access port, this may be used for blood collection. Standard aseptic (clean) techniques will be used. Up to about 3 tablespoons (45 mL) of blood will be collected for:

- **Serum pregnancy test** (if you are a woman who can become pregnant). The pregnancy test must be negative within 7 days before the 1st dose of the study drugs.

- **Complete blood count (CBC) with differential**, including red blood cells (RBC, oxygen-carrying cells): white blood cells (WBC, infection-fighting cells); platelets; and other blood components.
- **Serum chemistry, including a "Complete Metabolic Panel,"** consisting of tests for blood chemicals that indicate how well your body and organs are working, and if you have any significant diseases.
- **Tumor-typing tests** to determine if your tumor classifies as integrative cluster 2 (IC2) or 6 (IC6), based on the results of an FDA-approved test called FoundationOne (F1CDx).
- **Blood levels** (about 0.6 tablespoons, 10 mL) of the DNA changes in your body. This will be collected before you receive the first dose treatment with the study drug on Study Day 1, Day 15, as well as at the end of your treatment. Some of these blood samples will be used for research tests, and some will be stored for future study.

Urine collection: Urine will be collected for standard tests for waste products ("urinalysis") that indicate how well your body is working, and if you have any significant diseases. A urine pregnancy test (if you are a woman who can become pregnant), may be substituted for a serum pregnancy test. The pregnancy test must be negative within 7 days before the 1st dose of the study drugs.

Electrocardiogram (ECG or EKG): An ECG scan will be performed according to standard practice to measure and record the electrical activity of your heart. This assessment is performed entirely from outside the body, meaning you do not have to have an injection or incision (noninvasive). An ECG scan is a non-radiation procedure. The procedure is called a 12-lead ECG because 12 wires will be attached to your chest near your heart, and at your wrists/arms and ankles/legs with adhesive pads. You will be asked to lie still during the procedure. A computer will make a recording of your heart's electrical activity, which will tell doctors information about how well your heart is working. The results of this test may be used in combination with other imaging procedures described below.

Echocardiogram (ECHO) scan: A transthoracic ECHO scan will be performed according to standard practice to evaluate your heart's function and structures. This assessment is performed entirely from outside the body, meaning you do not have to have an injection or incision (noninvasive). An ECHO scan is a non-radiation procedure, and is similar to the sonogram procedure a woman might have during pregnancy. A microphone-like device called a transducer will send out ultrasound waves into your chest. Like a dog whistle, ultrasound is too high for you to hear. The ultrasonic sound waves "echo" off of the heart structures, and a computer converts the echoes into images. Generally, no calming medications (sedation) or fasting are needed. Tell the study team if you have any medical devices implanted, such as a pacemaker. Electrodes will be attached to your skin to record the echoes. The ECHO technician will place a gel

on your chest. The technician will apply varying amounts of pressure with the transducer probe. The amount of pressure should not be uncomfortable, but if it does, tell the technician.

Eye exam: An eye exam will be conducted, consisting of standard procedures for visual acuity testing; slit lamp examination of the anterior eye segment; intraocular pressure; dilated fundoscopy; and retinal optical coherence tomography (OCT). Additional examinations such as specular microscopy (that enables a magnified, direct view of the corneal epithelium) and corneal pachymetry may be performed as clinically indicated. If significant eye problems are found, you will not be able to participate in this study.

CT imaging for tumor assessment: A radiologic evaluation (an "X-ray"), called a computed tomography (CT scan) with contrast, will be performed according to standard practice within 28 days before the expected 1st day of treatment. The scan will be of your chest, abdomen, and pelvis, and is called a CT-CAP scan. These scans look at the extent and activity of your cancer. You may be asked to not drink or eat anything ("fast") for several hours before the scan. The scan appointment will take about 30 to 60 minutes. This baseline scan is part of your regular medical care for a patient with an advanced solid tumor.

Tumor biopsy: A specimen of tissue that is taken from your body for laboratory testing, such as from the tumor or skin, is called a "biopsy." A biopsy specimen will be collected, and may be obtained with a hollow needle (the specimen is called a needle or core biopsy); scalpel; a special cutting instrument called a "punch;" or other appropriate cutting instrument. There will be at least 2 tumor biopsies as part of this study: one before starting treatment (either at the same time as, or in addition to, your diagnostic biopsy confirming eligibility) and one on treatment. Tumor biopsies will be collected if the study doctors decide it is safe and possible, and will not be taken if they decide that there is more than minimal additional risk. In addition to assessing the status of your cancer, this tumor specimen may be used for many research purposes, and may be stored for future studies. Fresh tumor specimens can be used to create cell cultures that allow investigators to study drug response and tumor evolution in the lab using live cells. For example, investigators can treat the cell culture with new combinations of drugs to see how the cells respond. Tumor specimen can also be used to evaluate DNA, RNA, or protein patterns, including in response to treatment. For example, investigators can look for ways that the tumor responds to the treatment that might suggest new combinations of treatment that could work better.

- In addition, you may have tumor specimens from biopsies and surgeries you have undergone in the past stored at Stanford, or at another hospital. You may also undergo additional biopsies or surgeries as part of your clinical care in the future. If there are stored specimens available from these past or future procedures that is not

needed for your diagnostic purposes, the study team may obtain it for future research purposes to study the DNA, RNA, and/or proteins in the specimens. Your samples and de-identified clinical information may be sent outside of Stanford for analysis. By signing this consent form, you are providing authorization for release of stored tissue specimens from outside hospitals or institutions to our study team.

Future Use of Private Information and/or Specimens

Research using tissue, such as a specimen of your tumor and blood, is an important way to try to understand human disease. This research study may include the testing and study of genes, also known as DNA, and related materials called RNA, proteins, and/or metabolites. This type of testing is also called "genetic analysis" or called "pharmacogenomic research." Previously-collected tumor specimens may also be used for this. You are being given this information because the Study Doctors want to save private information and/or specimens for future research.

There are several things you should know before participating in this study and allowing your blood and tumor specimens to be studied. This subject is complicated, and there are many considerations. Ask for more information if you do not understand any part of this information.

Genes are in every cell of your body. Your genes were inherited from your biological parents and carry instructions for the body to grow, develop, and survive. Genes are made of a substance called DNA. Most genes and DNA are identical among human beings, but there are small variations between different people. These small genetic differences are why people have their own unique characteristics, such hair color, eye color, height, and other characteristics. Some traits affected by genetics are not visible, such as why different people have different responses, including side effects, to the same drug, or are more likely to get certain diseases or conditions. The proteins in your body were determined by your genes, and control how your body works. Differences in genes and therefore proteins can affect the way a disease develops, the way drugs act against the disease, or the way your body uses the drugs.

The purpose of this type of research is to understand the cause of disease, such as cancer, or the body's response to the treatments (such as safety findings or drug level patterns). In this study, the genetic research is being done to try to:

- Discover new and better ways of treating breast tumors that have FGFR gene changes, including to find out if the study drugs were effective against your cancer, why it was effective, and if there are any characteristics of the cancer that predicted whether or not the drugs would be effective.
- Why some tumors respond to therapy and others do not, and to identify markers of therapeutic resistance to certain treatments.

You are not required to agree to provide the specimen for this genetic testing, but agreeing to provide this biopsy specimen is required to participate in this study. If you do not wish to agree, the Study Doctor will discuss treatment options with you.

The specimens collected in this study may be used for future research projects, including projects that are undetermined and may include "full genome sequencing" (ie, all your genes). The results of future studies could trigger the need to test or re-test the genetic research specimens; therefore, the specimens and data generated from them will be held by the sponsor or their partners for many years. These specimens, and the data generated from them, may be shared with other researchers or entered into databases, provided confidentiality is upheld (you are not identified). The information in these databases may be kept forever, however, information that could directly identify you will not be included in these databases.

Genetic Information Data Sharing

Information from analyses of your coded specimens and your coded information will be put into one of the National Institutes of Health (NIH) databases along with information from the other research participants, be shared broadly with the scientific community and be used for unspecified future research. These databases will be accessible by the Internet. Only anonymous information from the analyses will be put in a completely public database, available to anyone on the Internet, and may be used for any research purpose.

No traditionally-used identifying information about you, such as your name; address; telephone number; or Social Security Number, will be put into the public database. While the public database will not contain information that is traditionally used to identify you, people may develop ways in the future that would allow someone to link your genetic or medical information in our databases back to you. For example, someone could compare information in our databases with information from you (or a blood relative) in another database and be able to identify you (or your blood relative). It also is possible that there could be violations to the security of the computer systems used to store the codes linking your genetic and medical information to you. Data cannot be retrieved once distributed to others.

However, your privacy is very important to us and we will use safety measures to protect it. Despite all of the safety measures that we will use, we cannot guarantee that your identity will never become known.

Although you will be told the results of study tests that are part of your regular medical care, the genetic testing described here will not be used for decisions about your medical care, and there may be no results from this genetic research for many years, therefore the results of the genetic testing may not be given to you, your doctor, or any other staff at the study center.

Providing genetic information to others

Sometimes patients have been required to furnish information from genetic testing for health insurance, life insurance, and/or a job. A Federal law, the Genetic Information Nondiscrimination Act of 2008 (GINA), generally makes it illegal for health insurance companies, group health plans, and employers with 15 or more employees to discriminate against you based on your genetic information.

Be aware that that GINA 2008 does not specifically protect you against genetic discrimination by companies that sell life insurance; disability insurance; or long-term care insurance.

Handling of your Blood and Tissue Specimens

Some of your specimens will be sent outside of Stanford for analysis. Other parts of your specimens and the data from them will be stored at Stanford, using a unique subject identifier, called an OnCore subject number that is associated with the study and linked to your personal identifiers, such as your name and medical record number (MRN). Only authorized personnel at Stanford will be able to associate you with the unique subject identifier (OnCore number).

Because the specimens are linked to your personal health identifiers (PHI), you have the right to withdraw consent for the usage of these samples at any time. The investigators might retain the specimens as part of your routine clinical care, but the specimens will not be used for additional research.

Any of your tissue that is used in research may result in new products, tests or discoveries. In some instances, these may have potential commercial value and may be developed and owned by the Investigators, Stanford University and/or others. However, donors of tissues do not retain any property rights to the materials. Therefore, you would not share in any financial benefits from these products, tests or discoveries.

Your specimens and anonymized data information may be sent outside of Stanford for analysis. “Anonymized” means that the specimens and data will not have your name and identification on them, but they could be re-identified.

Women of Childbearing Potential

Women of childbearing potential must be receiving a contraception treatment called luteinizing hormone (LH)-releasing hormone agonist (such as goserelin acetate or leuprolide acetate) initiated at least 28 days prior to study enrollment.

Study Treatment Period

Treatment administration

During the study treatment period, treatment will be administered as 28-day cycles (4 weeks). Your study visits will be on Day 1 of each cycle, except there will be extra study visits on Cycle 1 Day 4, Cycle 1 Day 15, and Cycle 2 Day 15. The following is a treatment summary for Cohort 1.

- Infigratinib daily by mouth at the assigned dose (125 or 100 or 75 mg). Infigratinib is provided as hard gelatin capsules. Monthly treatment schedule is 3 weeks of treatment, following by 1 week with no treatment.
- Tamoxifen administration 20 mg/day by mouth continuously starting on Day 1, 4 hours after infigratinib. Tamoxifen is provided as a pill.

Tests and procedures

The following tests and procedures will be performed at your clinical visits. Not every test or procedure will be conducted at every visit.

Medical history: Your medical history will be updated as described above. You will be asked about all the medications that you are taking, and if you have had any adverse medical experiences.

Physical examination: A physical exam as described above.

Blood collection: Blood will be collected as described above for evaluations and research tests. Up to about 4 tablespoons (60 mL) of blood will be collected. If you are a female of childbearing potential, the pregnancy test will be repeated on Day 1 of Cycle 1 before you start treatment and if a potential pregnancy is suspected.

Electrocardiogram (ECG or EKG): As described above, on Day 1 (± 3 days) of Cycles 2, 4, 6, then Day 1 (± 3 days) of every 6th cycle.

Echocardiogram (ECHO): As described above, on Day 1 (± 3 days) of Cycle 2.

Eye exam: As described above, on Day 1 (± 14 days) of Cycles 2, 3, 4, 6 then on Day 1 (± 14 days) of every 3rd cycle.

Tumor biopsy: A 2nd tumor biopsy will be performed, as described above, on Day 15 (± 3 days) of Cycle 1. Any other time while on treatment is also acceptable.

CT imaging for tumor assessment: A CT-CAP as described above will be performed on Day 1 (± 7 days) of Cycle 3, then on Day 1 (± 7 days) of every other cycle (every 2 cycles). After 12 months of therapy, this can be spaced out to every 12 weeks (3 cycles) at the Investigator's discretion.

Adverse event monitoring will be performed as part of the procedures described above. During the treatment period, the Study Doctors will monitor you for any potential side effects. If the side effects are severe, the Study Doctors may temporarily stop study medication; change the dosage of your study medication; or withdraw your medication completely.

If, at any time, you have any symptom; side effect; or injury affecting you physically or mentally during the study, **you should tell the Study Doctors or nurses right away**, even if you do not think it was caused by the study medication.

If you have to go to the hospital for any reason, please tell the hospital staff that you are participating on a research study, and give them the contact information for the study team. You may be provided with a card with the study team contact information.

Study Follow-up Period

When the decision to discontinue your treatment is made by you and/or your doctor, and approximately 30 days after your treatment is complete, the following tests and procedures will be conducted.

Medical history: As described above. You will be asked about all the medications that you are taking, and if you have had any adverse medical experiences.

Physical examination: A physical exam as described above.

Blood collection: Blood will be collected as described above for evaluations and research tests. This will be done one time at the discontinuation of your treatment. If you are a female of childbearing potential, the pregnancy test will will be done one time at the discontinuation of your treatment.

Electrocardiogram (ECG or EKG): As described above. This will be done one time at the discontinuation of your treatment.

Echocardiogram (ECHO): As described above. This will be done one time at the discontinuation of your treatment.

Eye exam: As described above. This will be done one time at the discontinuation of your treatment.

CT imaging for tumor assessment: A CT-CAP as described above will be performed one time at the discontinuation of your treatment if they were not done in the previous 4 weeks.

Adverse event monitoring will be performed as part of the procedures described above during the follow-up period.

PARTICIPANT RESPONSIBILITIES

As a participant, your responsibilities include:

- Follow the instructions of the Protocol Director and study team.
- Be sure to tell the study team about all of your present and past diseases, allergies and any drugs or **medications you have been or are taking**.
- Do not take additional medications (including over-the-counter medications or supplements) without consulting your study doctor. This is for your safety. Additional medications include all prescription drugs, over-the-counter (OTC) drugs, herbal preparations, and nutritional supplements. These may interact with the study drug infigratinib. There are numerous medications that may interfere with the effect of the study drugs. **Before starting the study treatments, while you are on the study, and for 30 days after your last dose of study treatment, do not take any other medications, even if prescribed by another doctor, without discussing with the study doctors**.
- **Do not consume** grapefruit, grapefruit juice, grapefruit hybrids, Seville oranges, pomegranates, star fruits, pomelos, or any products containing the juice of these fruits.
- Most people taking infigratinib will develop high phosphorus in the blood. You must follow the study doctor's instructions on avoiding high-phosphate foods (maintain a low phosphorus diet) and taking phosphate binder medications (eg, sevelamer).
- It is important to tell your doctor about any pre-existing eye problems you have, as your doctor may decide to change your treatment. If you experience any eye changes or problems, contact the study doctors or team immediately. It is important that you do not drive a car or work with machinery if you begin to experience any visual changes while on the study.
- Ask questions as you think of them.
- Tell the Protocol Director, or any Study Doctor or study team member if you change your mind about staying in the study.
- Tell the Protocol Director, or any Study Doctor or study team member about any side effects, doctor visits, or hospitalizations that you may have.

- If you are a woman able to have children and are sexually-active with men, use barrier contraception (ie, diaphragm, cervical cap, male or female condom, spermicidal foam, sponges or film) for intercourse while taking infigratinib and for 3 months following the last dose of infigratinib. You **must** use barrier contraception regardless of any other form of birth control you continue to use.
- If you are a sexually-active man, use a condom during intercourse while taking infigratinib and for 3 months following the last dose of infigratinib. Men must use a condom even if they have had a vasectomy, and even during intercourse with a male partner.
- Tell the Protocol Director, or any Study Doctor or study team member if you believe you might be pregnant or have gotten your partner pregnant. If you are a woman and experience a miss in menses cycle ("miss your period"), you must inform the Protocol Director or study team.
- Keep your study appointments. If it is necessary to miss an appointment, please contact the Protocol Director, or any Study Doctor or study team member to reschedule as soon as you know you will miss the appointment.
- Take the Study Drugs as instructed.
- Maintain control of the Study Drugs, and keep them in a safe place where children cannot access them. Follow any additional storage instructions that you are provided with.

WITHDRAWAL FROM THE STUDY

If you first agree to participate and then you change your mind, you are free to withdraw your consent and discontinue your participation at any time. Your decision will not affect your ability to receive medical care for your disease and you will not lose any benefits to which you would otherwise be entitled.

If you decide to withdraw your consent to participate in this study, you should notify Jennifer Caswell-Jin, MD, at 650-724-3250 or a study team member. If you withdraw after starting treatment with the study drugs, your Study Doctor will need to check on your health status afterwards. If you do not want the Study Doctor to check on your health status after withdrawing from the study, you should say so. Upon your request to the Protocol Director, any remaining biological samples that have been collected from you will be destroyed. However, any data collected before you withdrew will be retained and used to complete the research.

To help you safely finish your participation in the study, the Study Doctors may ask you to have more tests and you will be asked to come into the clinic for an End-of-Treatment Visit within 14 days of stopping the Study Drugs. The Study Doctor will

discuss your treatment options with you at this time. If your participation in the study is ended, you must return all study-related supplies, including unused Study Drugs.

If you withdraw from the study, or the study medication is stopped for any reason,

- Your cancer may get worse.
- To help you leave the study safely, the Study Doctors may ask you to have more tests.
- The Study Doctors may also ask if you wish to take part in the follow-up portion of the study. If you agree to continue with the follow-up portion of the study, information about your health will continue to be collected as described above in the Follow-up Procedures section.
- The Study Doctor will discuss with you the different withdrawal decisions, including your options for continued treatment.
- If your participation in the study ends, you must return all study-related supplies, including unused Study Drug.
- Data and information from your participation may not be removed from the research study database and may continue to be used to complete the research analysis. This is discussed in more detail under the heading “Authorization To Use Your Health Information For Research Purposes” on the following pages.

Your treatment in this study can continue until one of the following occurs:

- You withdraw your agreement to continue to take part in this research study;
- The Study Doctor withdraws you from the study, and the study medication is stopped, with or without your consent, for one or more of the following reasons:
  - Failure to follow the instructions of the Protocol Director and study team
  - The Study Doctor decides that continuing your participation could be harmful to you, or otherwise not in your best interest
  - Your cancer becomes worse (tumor progression)
  - If you have bad side effects during treatment, or if you or your doctor otherwise decide that the side effects are too severe or undesirable
  - You need treatment with drugs or procedures not allowed in the study
  - You have become pregnant; intend to become pregnant; or are nursing a child during this study
  - The study is stopped by the drug manufacturer, QED Therapeutics; their collaborator the Helsinn Group; the Study Doctor; the Stanford Institutional Review Board (the IRB, a group of people who review the research to protect your rights), or by a regulatory agency such as the US FDA

- Other administrative reasons
- Unanticipated circumstances

When your participation in this study ends, you may be asked to return for a final visit to have some end-of-study evaluations or tests, or to allow medical information to be collected about your health after the trial treatment is stopped. After you finish the study, or stop taking the Study Drugs for any other reason, you may continue to be checked regularly (physical exams; blood tests; tumor measurements; X-rays; other scans, etc) if you continue to have significant side effects from the treatment. This is called follow-up. Your Study Doctor will follow your progress, in accordance with good medical care, for as long as it is felt to be necessary by both you and the doctor, unless you ask otherwise. Many if not all of these procedures will be part of your regular continued medical care. In addition, further treatment outside the study will be discussed with you.

POSSIBLE RISKS, DISCOMFORTS, AND INCONVENIENCES

This section describes the reasonably-foreseeable risks, discomforts, and inconveniences that you may experience while participating in this study. These may make you sick, feel uncomfortable, or even harm you. These deserve careful thought.

You might experience negative effects related to the study drug while participating in the study. All research participants taking part in the study will be watched carefully for any negative effects; however, the study team does not know all the effects that the study drug may have on you. The study team may give you medicines to help reduce negative effects. These effects may be mild or serious. Many side effects go away when treatment is stopped, but in some cases, it is possible that the side effects could be serious, long-lasting, permanent, or may even be life threatening or fatal. In addition, because this is a research study, there may be risks that are not yet known ("unforeseeable"). You should discuss the side effects listed below with your study doctor before joining the study.

If you have any questions, you should contact Jennifer Caswell-Jin, MD, at 650-724-3250 or a study team member.

The negative events that are the most likely to happen to you if you take part in this study are listed below. The study drugs and procedures in this study may have risks that are not known at this time. You must tell the Study Doctor or study team about all side effects that you have. It is important that you report all symptoms and side effects that you experience as soon as they occur, whether or not you think they are caused by the study drug. If you are not honest about your side effects, it may not be safe for you to stay in the study. Your Study Doctor may give you medications to try to help lessen some of the side effects. All patients in the study will be monitored for side effects.

If you experience serious problems, you may be asked to return to the study center for more tests. If you experience any of the following symptoms of an allergic reaction, contact the Study Doctor or the Study Team immediately. An allergic reaction, if not treated promptly, can become life-threatening.

- Difficulty breathing; shortness of breath; or wheezing
- Swelling of the face, mouth, lips, gums, tongue or neck
- Rash, hives, or blisters
- Increased heart rate (a fast pulse or tachycardia)
- Abnormal or increased sweating
- Dizziness and fainting

Potential side effects of infigratinib

Infigratinib has been administered at the dose and schedule to be used in this study (up to 125 mg, 3 weeks on / 1 week off) to more than 400 people with advanced cancer. Some of the most important potential side effects to be aware of are:

- High phosphorus in the blood. Most people who take infigratinib (about 64%) will develop high phosphorus, and may need to go on a low phosphorus diet and/or take a phosphorus-lowering medicine called sevelamer to control their phosphorus level. Most people who developed high phosphorus while on infigratinib did not have any associated symptoms, but high phosphorus can cause muscle or joint pains or cramps and other symptoms in some people.
- High calcium in the blood. This is less common than high phosphorus (approximately 14%), but can occur. Most people who developed high calcium while on infigratinib did not have any associated symptoms, but high calcium can cause constipation, abdominal pain, nausea or vomiting, low appetite, and other symptoms in some people.
- Eye problems. About half of people taking infigratinib have eye effects. All participants will undergo a detailed eye examination at the start of the study, after 1 month, 2 months, 3 months, 5 months on therapy, and subsequently about every 3 months during the study. If significant and/or persistent changes from baseline are found while you are on study, you may need to discontinue from the study. It is important to tell your doctor about any pre-existing eye problems you have and visual changes that occur while taking infigratinib, as your doctor may decide to change or stop your treatment. It is important that you do not drive a car or work with machinery if you begin to experience any visual changes while on the study.

Most of the eye problems on infigratinib were generally manageable. The most common eye problems seen were dry eye (22%) and blurred vision (10%). More serious eye problems can occur, in about 3% of people. For example:

- Less than 1% of people developed symptomatic cataract causing vision to be worse than 20/40.
- Less than 1% of people developed corneal inflammation or a corneal ulcer, causing vision to be worse than 20/40.
- Less than 1% of people developed vision worsening to worse than 20/40 that was caused by other reasons, ie, not caused by cataract or corneal inflammation.

- Inflammation of the inside of the mouth ("stomatitis"). This was seen in 37% of people taking infigratinib, and was severe (interfering with being able to eat or drink) in 5%.
- Stomach or intestinal side effects. 36% developed constipation, 27% developed diarrhea, and 28% developed nausea at some point on therapy. In most people, these side effects were manageable.
- Hair loss or thinning. 27% of people noted this.

Beyond the effects listed above, the following negative events occurred in at least 10% of the people who took infigratinib at the dose and schedule in this study. For some of these effects, it is not clear if people developed these symptoms because of infigratinib, because of their cancer, or for some other reason:

- Tired feeling (fatigue) (40%)
- Decreased appetite (anorexia) (30%)
- Dry mouth (23%)
- Altered taste (21%)
- Vomiting (21%)
- Joint pain (17%)
- Stomach pain (15%)
- Trouble breathing (15%)
- Weight loss (13%)
- Hand/foot syndrome (palmar-plantar erythrodysaesthesia syndrome) (14%)
- Dry skin (12%)
- Fever (12%)

- Back pain (12%)
- Leg or arm pain (12%)
- Cough (11%)
- Nail disorder (13%)
- Headache (11%)
- Lack of energy (10%)
- Nosebleeds (10%).

Other less common side effects of uncertain relatedness that were observed in less than 10% of individuals include:

- Eyelash changes (8%)
- Loss of eyelashes (madarosis) (2%)
- Shortness of breath (1%)
- Cough (1%)
- Pain while peeing (1%)
- Acne (1%)
- Inflamed colon (1%)
- Temporary increase in the time it takes for the heart to recharge between beats (measured via electrocardiogram [ECG], and most often without symptoms (1%)
- Painful and swollen gums (1%)
- Anxiety (0.5%)
- Abnormal deposit of calcium salts in body tissues and small blood vessels of the fat and skin tissues (calcinosis/calciphylaxis) (0.5%)

There are also laboratory abnormalities that may occur. Most of these would be detected by blood tests, would not cause any symptoms, and would be reversible. In rarer cases, they could require stopping the drug or potentially even hospitalization. These laboratory abnormalities may indicate:

- Worsening kidney function (24%)
- Increased liver enzymes (16%)
- Decreased red blood cell count, which can cause fatigue or shortness of breath (18%)

- Decreased phosphorus, usually due to the medication given to treat increased phosphorus levels (13%)
- Increased pancreas enzymes (11%)
- Low sodium level (11%).
- Decreased parathyroid hormone (1%)
- Increased or decreased blood sugar (0.5 to 1%)
- Decreased activity of the thyroid gland (hypothyroidism) (0.5%)

Deaths during infigratinib treatment

Of the 458 people who took infigratinib at the dose and schedule used in this study at the time of this report, there have been 2 deaths for reasons possibly-related to infigratinib. One of these people died from a cardiac arrest and one died from a lack of blood flow to the intestines.

Other risks from infigratinib:

Since infigratinib is an investigational drug, there may be other risks that are unknown.

It is important that you report all symptoms and side effects that you experience as soon as they occur, whether or not you think they are caused by the study treatment and whether or not you think they are serious.

Potential side effects of sevelamer

Sevelamer is likely to be administered while you are taking infigratinib, to help manage high phosphorus in the blood, a common side effect of infigratinib. Sevelamer is an FDA-approved drug, and its drug package insert provides a complete listing of warnings and precautions.

The most common adverse events of sevelamer include nausea; vomiting; stomach pain; loss of appetite (anorexia); upset stomach; gas; bloating; diarrhea; constipation; tired feeling (fatigue); itching (pruritus); and joint pain .

Potential side effects of tamoxifen

Tamoxifen is an FDA-approved drug, and its drug package insert provides a complete listing of warnings and precautions.

The most common adverse events occurring in patients receiving tamoxifen are hot flashes, mood disturbances, vaginal bleeding, nausea, and fluid retention.

Specific warnings for tamoxifen

- Risk of uterine malignancy.
- Risk of increased thromboembolic events – stroke, or blood clots in various areas of the body including the lungs (pulmonary embolism), gastrointestinal tract, kidneys, or legs (deep vein thrombosis).
- Risk of liver cancer and liver abnormalities.
- Tamoxifen can cause fetal harm when administered to a pregnant woman.

In addition, there are other risks and possible discomforts you might experience from the study procedures. The following discusses procedure risks related only to the research, and does not include risks of procedures that should be discussed as part of your regular medical care.

- **Allergic reactions**: All drugs have a potential risk of an allergic reaction, which if not treated promptly, could become life-threatening. You should get medical help and contact the Study Doctors right away if you think you have any of the following symptoms of a serious allergic reaction: trouble breathing, or swelling of the face, mouth, lips, gums, tongue or neck. Other allergic reactions may include rash, hives, or blisters.
- **Blood draws**: A blood draw may cause fainting; inflammation of the vein; stinging, discomfort, or pain; bruising; discomfort; redness; burning; swelling; or bleeding at the site where the needle is placed to draw the blood. There is a slight chance of infection. You may feel dizzy or you may faint. If you feel faint, you should immediately lie down to avoid falling.

- **Tumor biopsy**: The risk of a tumor biopsy depends on the size, type, and location of your cancer. The most common side effects, which are usually minor, include pain, discomfort, bleeding, redness and swelling, scarring, bruising, and/or infection at the site where the biopsy needle is inserted, as well as fever. You may experience dizziness or fainting. Pain and discomfort can last for a couple of hours to a couple of days after the specimen is taken. Significant bleeding and infection may occur, but are uncommon. To reduce these risks, the site of the biopsy will be numbed and sterile techniques will be used. Your doctor may give you antibiotics to prevent or treat any infection. In extremely rare cases, an allergic reaction to the local anesthetic used to numb the biopsy site can occur. Biopsies are routine procedures, and established institutional procedures will be followed. You may be required to sign a separate informed consent form.
- **ECG:** Risks from an ECG can include skin irritation and/or a rash from the gel, or from wearing or removing the patches.
- **ECHO scan**: An ECHO scan is very similar to a sonogram, such as a pregnant woman might receive, and is considered very safe. For some patients, having to lie still on the examination table for the length of the procedure may cause some discomfort or pain.
- **Radiologic imaging: X-ray / CT scans**. A CT scan exposes you to radiation (discussed below). When you are in the scanner, you may experience discomfort or anxiety due to be in the small space inside the machine, or from the loud noises the scanner makes. If you become anxious or concerned in tight spaces, or from loud noises, tell the study team or technician **before the scan**. You may receive a medication to calm you if you need help with this.
- **Radiologic imaging: Radiation exposure from X-ray / CT scans**. This research study involves exposure to radiation from 2 Chest/Abdomen/Pelvis CT exams. This radiation exposure is not necessary for your medical care and is for research purposes only. The additional amount of radiation exposure is about 25 mSv, which is approximately equal to 50% of the limit that radiation workers (for example, a hospital X-ray technician) are allowed to receive in 1 year. This amount of radiation involves minimal risk and is necessary to obtain the research information desired.
- **Radiologic imaging: Injection of contrast agents**: A contrast agent or dye will be injected for the CT scans. Following are the risks associated with injection of contrast agents.
  - Allergic reaction, which can be severe and/or life-threatening.
  - Kidney problems or kidney failure, especially if you are taking Glucophage (metformin, a common medicine for diabetes).
  - After the injection, there is a risk of pain, discomfort, or a burning sensation at the injection site; a flushing or warmth sensation; a salty or metallic taste in the

mouth; a brief headache; or nausea/vomiting. nausea, flushing, warmth, and a salty taste. These effects usually last for a few moments.

- If you are a smoker or exposed to cigarettes or nicotine, you may experience spasms in the arteries of your heart.

- **Pregnancy / Reproductive Risk**: Because your treatment includes chemotherapy, there are risks to a fetus (unborn child) or the pregnant woman, even if it is the man participating in this study. There is a risk that pregnancy could still result despite the responsible use of reliable method of birth control. You must use barrier protection as outlined in "Participant Responsibilities". Detailed information about preventing pregnancy is also provided in that section.
- **Women of childbearing potential**: If you believe you might be pregnant, even if you experience a menses cycle ("have your period"), you must inform the Protocol Director or study team immediately.
- **Genetic research risks:** This research involves genetic studies and information. Procedures have been put into place that are designed to make it very difficult for the results from genetic research to be linked to you. However, even without your name or other identifiers, your genetic information is unique to you, and there is a remote possibility that someone could trace the information in a central database back, and identify you. If a genetic disorder is discovered in your genes, there is a remote possibility that this information could become public and affect you or your family in an unfavorable way, including a possible risk of discrimination by employers or insurance providers.
- **Personal anxiety**: Following are some common concerns that research subjects may have.
  - You may be asked sensitive or private questions which you normally do not discuss. It may be necessary to answer some of these questions related to your health and medical status.
  - You may feel embarrassed during the physical exam. You may request that the physical exam be done by a clinician of the same gender.
  - You may be concerned about your personal information being revealed. Although the Study Team, NCI, NIH, and FDA do their best to protect your personal information, this cannot be absolutely guaranteed.
- **Other risks**: Since infigratinib is investigational ("experimental") when taken alone or in combination with other medications, there may be other risks that are unknown ("unforeseeable") at this time.

It is important that you report <u>all symptoms and side effects</u> that you experience <u>as soon as</u> they occur, whether or not you think they are caused by the study drugs or the study procedures. Contact Jennifer Caswell-Jin, MD at

650-724-3250 or the Study Team via the Nurse Coordinators at 650-498-6000 (24 hours). If you are unable to reach anyone at the number(s) listed above, and you feel you may need medical attention, **call 911** or go to the nearest emergency room.

POTENTIAL BENEFITS

It is possible that your health or medical condition may improve because of your participation in this study. The use of the study treatment, may help to treat your disease. However, there is no guarantee that you will benefit in this or any other way.

Although you may not directly benefit from participation in this study, information learned from this study may help other people in the future, including other people with cancer.

We cannot and do not guarantee or promise that you will receive any benefits from this study.

ALTERNATIVES

You should be aware that there are other effective treatments that are available to you without participating in this research study. By participating in this research study, you may be foregoing other treatment options known to provide clinical benefit for your cancer. The Study Doctors will discuss with you the risks and benefits of these alternatives, including which other treatments might be suitable for you.

You do not have to be in this study to receive treatment for your cancer. Possible alternative treatments and side effects of these treatments depend on the characteristics of your cancer, and the stage and location of your cancer. The effectiveness and side effects of other treatments may be different for different people. Instead of taking part in this study, you may choose to:

- Surgically remove the tumor.
- Receive radiation therapy, but not as part of this study.
- Receive treatment with other chemotherapy drugs, including those that have been approved for use in the US. There are numerous treatments that may or may not be suitable for the specifics of your cancer. The study doctor can discuss these with you.
- Receive treatment with other drugs called targeted therapies, which recognize specific features of cancer, and focus the treatment effect on those cells. There are numerous treatments that may or may not be suitable for the specifics of your cancer. The study doctor can discuss these with you.
- Receive surgery plus 1 or more of the above therapies. There are specific names for the order in which this type of treatment is given.

- Neoadjuvant treatment, which means to receive chemotherapy and/or radiation therapy before surgery. Having one or both of these before surgery may help shrink the tumor, which may be easier to remove during the surgery.
- Adjuvant treatment, which means having a surgery first, then receiving chemotherapy and/or radiation therapy. The goal of adjuvant treatment is to kill any cancer cells that may be left in your body after the surgery. Even if there is no visible sign of cancer cells, your physician may suggest adjuvant treatment to kill remaining microscopic cancer, as this lowers the risk that the cancer may come back or spread.

- Participate in another research study with a different study drug or procedure.
- While your type of cancer may be treatable with currently approved and available medications and procedures, another alternative is to receive only comfort care, also called "palliative care," like painkillers. These types of treatments do not treat your cancer (ie, "are not curative"), and only make you comfortable ("symptom relief;" pain reduction; reduce tiredness, help with appetite problems or other problems caused by cancer). If you think you might prefer comfort care, please discuss this with your family, friends, and doctor. **NOTE**: The Study Doctors do not recommend this decision for you at this time, although it is and will remain your decision.

The Study Doctors will discuss with you the risks and benefits of these alternatives, including which other treatments might be suitable for you.

If you decide that you do not wish to take part in this study and wish to pursue any of these, or other alternatives, this will not change your regular medical care or the other treatment choices in any way.

PARTICIPANT'S RIGHTS

You should not feel obligated to agree to participate. Your questions should be answered clearly and to your satisfaction. If you decide not to participate, tell the Protocol Director. You can also tell any other member of the study team.

You will be told of any significant new information that is learned during the course of this research study, which might affect your condition or your willingness to continue participation in this study. After you hear about this information, you have the right to withdraw from the program.

If medically-relevant information about you or your test results that might affect your future treatment or your willingness to continue participation in this study is obtained, this information will be discussed with you.

You will be told the results of tests that are part of your medical care, but you may not be told the results of the research tests, including any future research tests.

ClinicalTrials.gov

A description of this clinical trial will be available on *http://www.ClinicalTrials.gov*, as required by US 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.

CONFIDENTIALITY

Identifiers might be removed from identifiable private information and/or identifiable specimens and, after such removal, the information and/or specimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from you.

The results of this research study may be presented at scientific or medical meetings or published in scientific journals. Your identity and/or your personal health information will not be disclosed except as authorized by you or as required by law. However, there is always some risk that even de-identified information might be re-identified.

Your research records may be disclosed outside of Stanford, including in computer databases and by other electronic methods, but you will only be identified by your unique study identifier, and not your name. Information linking your study identifier to your name will be kept in a secure location at Stanford and access will be limited to the Study Doctor and authorized members of the Study Team.

Patient information may be provided to federal and other regulatory agencies as required. The US FDA, for example, may inspect research records and learn your identity if this study falls within its jurisdiction.

The purpose of this research study is to obtain data or information on the safety and effectiveness of infigratinib in combination with other chemotherapy agents; the results will be provided to the drug manufacturer QED Therapeutics; their collaborator the Helsinn Group; the Food and Drug Administration (FDA); and other federal and regulatory agencies as required.

CERTIFICATE OF CONFIDENTIALITY

This research is covered by a Certificate of Confidentiality from the National Institutes of Health (NIH). The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research

except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by National Cancer Institute (NCI), an institute of the US National Institutes of Health (NIH), which is funding this project or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

The Certificate of Confidentiality will not be used to prevent disclosure for any purpose you have consented to in this informed consent document, such as research data in your medical record.

Authorization To Use Your Health Information For Research Purposes

Because information about you and your health is personal and private, it generally cannot be used in this research study without your written authorization. If you sign this form, it will provide that authorization. The form is intended to inform you about how your health information will be used or disclosed in the study. Your information will only be used in accordance with this authorization form and the informed consent form and as required or allowed by law. Please read it carefully before signing it.

What is the purpose of this research study and how will my health information be utilized in the study?

The purpose of this research study is to learn about the safety and effectiveness of infigratinib in combination with chemotherapy, and to find the best dose of infigratinib in the combinations. Information from this study will be submitted to the drug manufacturer QED Therapeutics and partner Helsinn Group, and international regulatory agencies including the FDA. The results from this research study are expected to be presented at scientific or medical meetings or published in scientific journals. **You will not be personally identified in the publications, although representatives of the sponsor, FDA, and other international regulatory agencies may need to know who you are**.

Do I have to sign this authorization form?

You do not have to sign this authorization form. But if you do not, you will not be able to participate in this research study including receiving any research-related treatment.

Signing the form is not a condition for receiving any medical care outside the study.

If I sign, can I revoke it or withdraw from the research later?

If you decide to participate, you are free to withdraw your authorization regarding the use and disclosure of your health information (and to discontinue any other participation in the study) at any time. After any revocation, your health information will no longer be used or disclosed in the study, except to the extent that the law allows us to continue using your

information (eg, necessary to maintain integrity of research). If you wish to revoke your authorization for the research use or disclosure of your health information in this study, you must write to:

Jennifer Caswell-Jin, MD
269 Campus Dr; CCSR 1145C; M/C 5769
Stanford Cancer Institute; Stanford University Medical Center
Stanford, CA 94305

What Personal Information Will Be Obtained, Used or Disclosed?

Your health information related to this study, may be used or disclosed in connection with this research study, including, but not limited to identifiers such as your name and initials, address including ZIP code, phone numbers, dates including date of birth, age, biological gender (your sex), race, ethnicity, and other numbers or codes such as your unique study identifier that might identify you. During the study, researchers will also obtain information about your health status, life-style choices, medical history, and medical diagnoses, including family medical history and allergies; your current and past medications or therapies; your physical examination results including height and weight, blood pressure readings, heart rate, breathing rate and temperature; your laboratory test results including blood, urine, and pregnancy tests; results of procedures, such as eye exams, tumor measurements or assessments, medical scans including CT, ECHO, and ECG scans; tumor biopsy; results of genetic and biomarker testing; and medical reports, such as the discharge summary and radiology, post-operative, and pathology reports. **The researchers will also get information from your medical record (including hospital records from the Stanford Healthcare and your referring physician's records).**

Who May Use or Disclose the Information?

The following parties are authorized to use and/or disclose your health information in connection with this research study:

- The Protocol Director, Jennifer Caswell-Jin, MD
- Research Staff
- The Stanford University Administrative Panel on Human Subjects in Medical Research

Who May Receive or Use the Information?

The parties listed in the preceding paragraph may disclose your health information to the following persons and organizations for their use in connection with this research study:

- QED Therapeutics, or their representatives
- Helsinn Group, or their representatives
- The Stanford Data and Safety Monitoring Committee (DSMC); and/or any other unit of Stanford University as necessary
- The Food and Drug Administration (FDA) and/or other state or international regulatory authorities
- The Office for Human Research Protections (OHRP) in the US Department of Health and Human Services (DHHS)
- The US National Institutes of Health (NIH), including the National Cancer Institute (NCI)

Your information may be re-disclosed by the recipients described above, if they are not required by law to protect the privacy of the information.

When will my authorization expire?

Your authorization for the use and/or disclosure of your health information will end on 31 December 2099 or when the research project ends, whichever is earlier.

Will access to my medical record be limited during the study?

To maintain the integrity of this research study, you may not have access to any health information developed as part of this study until it is completed. At that point, you would have access to such health information if it was used to make a medical or billing decision about you (eg, if included in your official medical record).

_____
Printed Name of Adult Participant

_____ _____
Signature of Adult Participant Date

_____
If needed: Printed Name of legally-authorized representative (LAR)

_____ _____
Signature of LAR Date

_____
LAR's Authority to Act for Participant
(eg, parent, guardian, or conservator)

NOTE: *If using the Short Form Consent process for informed consent in another language pursuant to an "Alteration of HIPAA Authorization," neither the participant nor their LAR should sign the HIPAA "Authorization To Use Your Health Information For Research Purposes" above.*

FINANCIAL CONSIDERATIONS

Costs

If you participate in this study, the study will pay for those services, supplies, procedures, and care associated with this study that are not a part of your routine medical care. However, there may be additional costs to you. These include basic expenses like transportation and the personal time it will take to come to the Study Visits.

You and/or your health insurance must pay for services, supplies, procedures, and care that are required during this study for routine medical care. **You will also be responsible for any co-payments and/or deductibles as required by your insurance**. If the costs of a co-payment related to the study are not covered by your insurer, managed care plan or other benefits program, you may be responsible for these costs. If you are unable to pay for such costs, the Protocol Director and/or the Study Team will assist you in applying for supplemental benefits. The study may cover any remaining excessive costs incurred for care or special medications required to continue participation in the study. Participation in this study is not a substitute for health insurance.

Some insurance companies or other 3rd-party payers may not pay for standard-of-care procedures or laboratory tests, including hospitalization, when they are done as part of a research study. You should consult with your health benefit plan to determine whether your medical costs associated with your care during this study are covered.

Payments / Reimbursement

You may be reimbursed for reasonable travel expenses associated with the study visits. Please ask the study team for more details.

Payments or reimbursement may only be made to US citizens, legal resident aliens, and those who have a work-eligible visa. You may need to provide your Social Security Number (SSN) to receive payment. If your SSN is required to receive payment, and you do not wish to provide your SSN, you have the option of declining the payment.

This study includes the collection of research specimens. Any of your specimens which are used in research, including those used in genetic research, may result in new products; tests; or discoveries. In some instances, these products may have commercial value, and may be developed and owned by the study team; Stanford University; QED Therapeutics and partner Helsinn Group (and their affiliates and collaborators) and/or others. However, donors of specimens do not retain any property rights to the specimens or data derived from them. Therefore, you would not share in any financial benefits from these products, tests or discoveries.

Any of your specimens which are used in research may result in new products, tests or discoveries. In some instances, these may have potential commercial value and may be developed and owned by the study team; Stanford University and/or others. However, donors of specimens do not retain any property rights to the materials. Therefore, you would not share in any financial benefits from these products, tests or discoveries.

Funding Source

QED Therapeutics and partner Helsinn Group are helping to pay for (sponsoring) this study, and providing the study drug Infigratinib and/or other materials for this study.

The National Institutes of Health (NIH) / National Cancer Institute (NCI) is providing financial support and/or material for this study.

Consultative or Financial Relationships

None

COMPENSATION for Research-Related Injury

All forms of medical diagnosis and treatment – whether routine or experimental – involve some risk of injury. In spite of all precautions, you might develop medical complications from participating in this study. If such complications arise, the Protocol Director and the research study team will assist you in obtaining appropriate medical treatment. In the event that you have an injury or illness that is directly caused by your participation in this study, care will be provided to you. You will **not** be responsible for any of these costs.

If you receive Medicare benefits, and if the sponsor of this study pays for any study-related treatment, complications or injuries, personal information about you, your treatment, and your participation in this study will be provided to the sponsor, who is required by law to provide it to Medicare.

You do not waive any liability rights for personal injury by signing this form.

CONTACT INFORMATION

Questions, Concerns, Complaints, or to Report an Injury or Side Effect: If you have any questions, concerns or complaints about this research study, its procedures, risks and benefits, or alternative courses of treatment, you should contact the Study Doctors Jennifer Caswell-Jin, MD at 650-724-3250, or a study team member. You should also contact them at any time if you feel you have been hurt by being a part of this study.

If you are unable to reach anyone at the number(s) listed above, and you feel you may need medical attention, call or go to the nearest emergency room.

Independent Contact: If you are not satisfied with how this study is being conducted, or if you have any concerns, complaints, or general questions about the research or your rights as a participant, please contact the Stanford Institutional Review Board (IRB) to speak to someone independent of the research team at 650-723-5244 or toll-free at 1-866-680-2906. You can also write to the Stanford IRB, Stanford University, 1705 El Camino Real, Palo Alto, CA 94306.

Appointment or Alternate Contact: If you need to change your appointment, or if you cannot reach the Study Doctor, please contact Study Team at 650-736-5790.

EXPERIMENTAL SUBJECT'S BILL OF RIGHTS

As a research participant you have the following rights. These rights include but are not limited to the participant's right to:

- Be informed of the nature and purpose of the experiment;
- Be given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be utilized;
- Be given a description of any attendant discomforts and risks reasonably expected;
- Be given an explanation of any benefits to the subject reasonably to be expected, if applicable;
- Be given a disclosure of any appropriate alternatives, drugs or devices that might be advantageous to the subject, their relative risks and benefits;
- Be informed of the avenues of medical treatment, if any available to the subject after the experiment if complications should arise;
- Be given an opportunity to ask questions concerning the experiment or the procedures involved;
- Be instructed that consent to participate in the medical experiment may be withdrawn at any time and the subject may discontinue participation without prejudice;
- Be given a copy of the signed and dated consent form; and
- Be given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element of force, fraud, deceit, duress, coercion or undue influence on the subject's decision.

May we contact you about future studies that may be of interest to you? ___**Yes** ___**No**

Signing your name means you agree to be in this study and that you will receive a copy of this signed and dated consent form.

_____
Printed Name of Adult Participant

_____ _____
Signature of Adult Participant Date

_____
If needed: Printed Name of Legally Authorized Representative (LAR)

_____ _____
Signature of LAR Date

_____
LAR's Authority to Act for Participant (eg, parent, guardian, or conservator)

_____
Printed Name of Person Obtaining Consent (POC)

_____ _____
Signature of POC Date

The following witness line is to be signed only if the consent is provided as a summary form and accompanied by a short-form foreign language informed consent document.

_____
Printed name of witness

_____ _____
Signature of witness Date

(eg, staff, translator/interpreter, family member)

The translated short form must be signed and dated by **BOTH** the participant (or their LAR) **AND** the witness.

The English consent form ("referred to as the "Summary Form" in the regulations"):

- Must be signed by **BOTH** the witness **AND** the Person Obtaining Consent (POC).
- The non-English speaking participant / LAR does **NOT** sign the English consent.
- The non-English speaking participant / LAR should **NOT** sign the HIPAA participant line.
- If the participant / LAR is non-English speaking, the POC must ensure that:
  1) The LAR's Description of Authority is completed, and
  2) Any questions or options presented by the consent form are documented and initialed by the POC on the Summary Form, per the participant's wishes, as they are understood during the consent process.