Participant Informed Consent for Clinical Research

Study title for participants: AG-120 in People with IDH1 Mutant Chondrosarcoma

Official study title for internet search on http://www.ClinicalTrials.gov:
Phase II Study of AG-120 in IDH1 Mutant Chondrosarcoma

Subtitle: Main Consent

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If you are the parent or legal guardian of the person who is being asked to participate in this research study, you may give consent on his or her behalf. The word "you" in this document refers to your child, if the participant is a minor, or to a person with a cognitive impairment for whom you are the Legally Authorized Representative (LAR).

Overview and Key Information

Why is this study being done?

We are asking you to take part in a clinical research study. We do research studies to try to answer questions about how to prevent, diagnose, and treat diseases like cancer.

You are being asked to take part in this research study because you have chondrosarcoma (cancer of the bone and/or soft tissue) that may have spread outside your bone (advanced or metastatic chondrosarcoma) or has come back (recurrent chondrosarcoma). In addition, your chondrosarcoma has a change (mutation) in a gene called IDH1 (isocitrate dehydrogenase 1). The researchers think that the study drug, AG-120, may help people with your disease because of how the drug has worked in people with other types of cancer that have IDH1 mutation.

We are doing this study to see whether AG-120 is an effective and safe treatment for people with advanced/metastatic or recurrent chondrosarcoma that has IDH1 mutation.

Taking part in this study is your choice.

You can choose to take part or not to take part in this study, and you can change your mind at any time. Whatever choice you make, you will not lose access to your medical care or give up any legal rights or benefits.

This document presents important information to help you make your choice. Please take time to read it carefully. Talk with your doctor, family, or friends about the risks and benefits of taking part in this study. It's important that you have as much information as you need, and that all your questions are answered.

What is the usual approach to my chondrosarcoma?

People who are not in a study are usually treated with surgery, if the tumor is operable (can be accessed and removed by surgery). There is currently no standard chemotherapy option for people with advanced chondrosarcoma that cannot be removed by surgery. In some cases, your doctor may recommend radiation and chemotherapy treatments. Your doctor can explain which treatment may be best for you. These treatments can reduce symptoms and may stop your tumor from growing and spreading.

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

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

What will happen if I decide to take part in this study?

Participants with chondrosarcoma that cannot be removed by surgery

If you decide to take part in this study and you have advanced or metastatic chondrosarcoma that is inoperable (cannot be removed by surgery), you will take the AG-120 by mouth daily until the side effects become too severe, your disease gets worse, the study doctor decides that it is best for you to stop taking the study drug, or the study ends.

After you finish study treatment, the study doctor will continue to follow your condition for 28 days after your last dose of study drug and watch you for side effects. You will return to the clinic within 30 days of your last dose for an End-of-Treatment visit. After this visit, the study team will follow your health (by calling you or having you come to the clinic) every 3 months for 3 years after your last dose.

Participants with chondrosarcoma that can be removed by surgery

If your chondrosarcoma is recurrent and operable (can be removed by surgery), you will take the AG-120 by mouth daily until the day before your surgery (unless you need to stop sooner because of side effects, worsening of your disease, or other reasons). Surgery may occur 4 months or more after you have started taking study drug.

You will have a follow-up visit 4 weeks after your surgery so the study doctor and study team can check on the progress of your disease. If the surgery is successful and removes all your disease, you will not continue study drug. If you have any signs of disease after your surgery, the study doctor may have you continue study drug until you need to stop because of side effects, worsening of your disease, or other reasons.

If you stop study drug after your surgery, the study team will check on your health every 8 weeks until 56 weeks after your surgery, and then every 3 months for 3 years after your surgery. If you continue study drug, you will follow the treatment and follow-up schedule described above for participants whose cancer cannot be removed with surgery.

What are the risks and benefits of taking part in this study?

There are both risks and benefits to taking part in this study. It is important to think carefully about these as you make your decision.

Risks

We want to make sure that you know about a few key risks right now. We will also give you more information in the *What risks can I expect from taking part in this study?* section of this consent form.

If you choose to take part in this study, there is a risk that the study drug may not be as good as the usual approach for treating your cancer.

There is also a risk that you could have side effects from the study drug. These side effects may be worse, and they may be different than you would have with the usual approach for your cancer.

Some of the most common side effects that the study doctors know about are:
- Tiredness (fatigue)
- Diarrhea
- Nausea
- Increase in number of white blood cells (blood cells that help fight infection)
- Fever and fever with very low white blood cell counts
- Swelling of arms and legs
- A decrease in number of red blood cells, which may make you feel weak or tired (anemia)

There may be some risks that the study doctors do not yet know about.

Benefits
Studies in people with blood cancers have shown that taking AG-120 can stabilize cancer for a longer period of time than the usual approach. However, we do not know whether this will happen in people with your type of cancer. It is unlikely that the study drug will work in everyone with your cancer. AG-120 may help your cancer, or your cancer may stay the same, or even get worse. What we learn from this research may help other people in the future.

If I decide to take part in this study, can I stop later?
Yes, you can decide to stop participating in the study at any time.

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

If you decide to stop, let the study doctor know as soon as possible. It's important that you stop safely. This may mean slowly stopping the study drug to avoid a sudden unsafe change or risk to your health.

If you stop, you can decide whether to let the study doctor or a member of the study team continue to contact you to ask questions about your health. We will not be able to withdraw information about you that has been used or shared with others before you informed us of your decision to stop.

Are there other reasons why I might stop being in the study?
Yes. The study doctor may take you off the study if:

- Your health changes, and the study is no longer in your best interest
- New information becomes available, and the study is no longer in your best interest
- You do not follow the study rules
- For women who are able to have children: You become pregnant while you are in the study
- The study is stopped by the National Cancer Institute (NCI), Institutional Review Board (IRB), Food and Drug Administration (FDA), or the study sponsor, Memorial Sloan Kettering Cancer Center (MSK). The study sponsor is the organization that oversees the study.

It is important that you understand the information in this informed consent document before you make a decision about participating in this clinical trial. Please read, or have someone read to you, the rest of

this document. If there is anything that you don't understand, ask the study doctor or nurse for more information.

What is the purpose of this study?

This study will test how effective and safe AG-120 is in people with advanced/metastatic or recurrent chondrosarcoma that has IDH1 mutation.

IDH1 is a type of protein involved in the process of providing energy to your body's cells. In diseases like sarcoma, an abnormal form (mutated form) of the IDH1 protein is present in the diseased cells. When IDH1 is present in this abnormal form, it produces too much 2-hydroxyglutarate (2-HG), a substance present in low levels in normal cells. When there is too much 2-HG in normal cells, immature cells may be unable to function normally, which may result in chondrosarcoma. AG-120 may stop the formation of abnormal IDH1 protein, which may reduce 2-HG levels in diseased cells to levels like those in normal cells. AG-120 targets only the abnormal IDH1 protein (and not the normal form).

The FDA has approved AG-120 to treat acute myeloid leukemia with IDH1 mutation. The FDA has not approved the drug for the treatment of advanced/metastatic or recurrent chondrosarcoma that has IDH1 mutation. This study involves an investigational use of AG-120.

The study drug will be provided by Servier Pharmaceuticals, Inc, the study drug manufacturer.

Up to 17 people will take part in this study at Memorial Sloan Kettering Cancer Center (MSK).

What are the study groups?

Study participants will be divided into two study groups depending on their disease status. All study participants will receive the same treatment: oral (by mouth) doses of the study drug, AG-120.

- Group 1 will include participants diagnosed with advanced/metastatic and inoperable (cannot be removed by surgery) chondrosarcoma.
- Group 2 will include participants diagnosed with recurrent and operable chondrosarcoma.

Your study doctor will tell you which group you are in.

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

Before you begin the main part of the study:

The study doctor will review your medical records (including your results from past genetic testing) and the results of new exams, tests, and procedures to see if it is safe for you to take part in the study. This first part of the study is called screening. Most of the screening exams, tests, and procedures are part of the usual care that you would have if you were not in a study.

The tests and procedures that will be done only for research purposes, or that may be done more often because you are participating in this study, are listed below.

- A sample of your tumor tissue will be collected to confirm your diagnosis and for research testing. You will be required to have a new biopsy procedure to take part in this study. You will sign a separate consent form for the biopsy procedure being done to collect the sample. The doctor doing the biopsy will explain what will happen, including any risks or possible side effects that

may result from collecting the sample. More information about the risks of this procedure is provided in the *What risks can I expect from taking part in this study?* section of this consent form.

- We will study your tissue sample to improve our understanding of the way changes in genes can affect the risk of cancer and other diseases. Genes are the "blueprints" for our bodies. Sometimes genes may have changes that occur during your lifetime that can affect the way a gene works. These changes (mutations) may cause cells to grow rapidly and abnormally, and become a cancer that you cannot pass on to your family members (somatic mutation). However, some people develop cancer because they were born with a mutation in a gene. People who develop cancer because of a genetic mutation usually inherit this genetic change from their mother or their father (germline mutation). Other family members (brothers, sisters, and children) may share this same mutation. Most people with cancer did not develop their disease because of an inherited mutation.
- We will look for changes in your genes using a test called Whole Genome Sequencing or Whole Exome Sequencing (WGS/WES). Your data may be used to learn more about cancer and other diseases. Data from large numbers of people can help researchers learn how changes in the order (sequence) of genes might affect a disease or a person's response to treatment, identify possible links between diseases, and provide new ideas for drug development and personalized therapies
- After your research test sample has been studied, if any part of it is left over, the material will be stored for an indefinite period of time for use in future research. Your sample, including your DNA, may be used or stored for as long as it is useful for research purposes.
- Neither you nor your doctor will be given the results of any genetic research testing done on your sample. If you or your family are interested in learning more about inherited risk factors for cancer, ask your study doctor for a referral to MSK's Clinical Genetics Service.

- Blood samples will be collected (about 3 tablespoons) from a vein in your arm to perform genetic testing, and participants in Group 1 will also have biomarker testing.
  - A biomarker is a biological molecule found in blood, other body fluids, or tissues that is a sign of a normal or abnormal process, or of a condition or disease. A biomarker may be used to see how well the body responds to a treatment for a disease or condition.
  - We will collect a blood sample for a research test that shows whether altered (mutated) cancer genes in your tumor can also be found in your blood. Small pieces of genes free-floating in blood are called cell-free DNA (cfDNA). We will track the amount of cfDNA from your tumor that is found in your blood at different times during and after treatment, which may be related to your response to the treatment.
- Blood collection (less than 1 teaspoon) to measure how well your blood clots (coagulation tests)
- Echocardiogram (ECHO) to test the blood flow through your heart. This procedure will use ultrasound sound waves to create a picture of your heart.

During the study:

<u>All participants</u>

You will take AG-120 by mouth daily as instructed by your study doctor. You will take study drug during 28-day treatment Cycles. There will not be a break between Cycles. You will come to the clinic or have telehealth visits on Days 1 and 15 of Cycles 1 and 2. After that, you will have at least one clinic visit

every other month for the rest of the time you are taking study drug. After Cycle 4, you will be able to have protocol assessments completed locally every other month.

The study team will give you a pill diary so that you can write down, every day, when you take your medication. Your study doctor or nurse will review your completed diary at the beginning of each Cycle. Bring your diary and your bottle(s) of study medication to every clinic visit, even if the bottle is empty.

Group 1 (participants with chondrosarcoma that cannot be removed by surgery)
You will take the AG-120 by mouth daily until the side effects become too severe, your disease gets worse, the study doctor decides that it is best for you to stop taking the study drug, or the study ends.

Group 2 (participants with chondrosarcoma that can be removed by surgery)
You will take the AG-120 by mouth daily for at least 4 Cycles until the day before your standard-of-care surgery (unless you need to stop sooner because of side effects, worsening of your disease, or other reasons). Surgery may occur 4 months or more after you have started taking study drug. The study doctor will let you know when you will need to stop treatment and have surgery to remove the tumor. It is possible that treatment with the study drug may cause your cancer not to be able to be removed by surgery, so speak with the study doctor to understand all the risks of taking part in this study.

If you do not have surgery or there is still cancer in your body after surgery, you may continue to receive the study drug, if your study doctor thinks it's in your best interest.

Exams, Tests, and/or Procedures
You will have exams, tests, and/or procedures during the main study. The procedures that will be done only for research purposes, or that may be done more often because you are participating in this study, are listed below.

- A required biopsy will be performed for research purposes following dosing on Cycle 2, Day 15 (C2D15). The tissue sample collected will be used for genetic and biomarker research.
- You will be asked to have an optional biopsy for research purposes if your disease worsens (disease progression). You will find more information about this optional biopsy in the *Optional Study* section of this consent form.
- Group 2: If you have surgery during the study, a sample of the tumor tissue will be collected for research
- Blood collection (about 3 tablespoons) from a vein in your arm for research purposes
    - Group 1: cfDNA blood samples will be collected on C2D15, C4D1, C6D1, C8D1, and C12D1
    - Group 2: cfDNA blood samples will be collected on C2D15, C3D1, and D4D1
    - Group 1: Biomarker blood samples will be collected on C2D1, C2D15, C3D1, and C4D1
    - Group 2: Biomarker blood samples will be collected on C2D1, C2D15, C3D1, and C4D1

End-of-Treatment and follow-up visits:

Group 1
After your last dose of the study drug, the study doctor will watch you for 28 days leading up to your End-of-Treatment (EOT) visit. The study doctor and the study team will then check on your condition (by calling you or having you come to the clinic) every 3 months for up to 3 years after your last dose.

The EOT and follow-up procedures that will be done only for research purposes, or that may be done more often because you are participating in this study, are listed below.

- cfDNA blood samples (about 1 tablespoon) will be collected at EOT
- Biomarker blood samples (about 1 tablespoon) will be collected at EOT

Group 2
You will have a follow-up visit 4 weeks after your surgery so the study doctor and study team can check on the progress of your disease. If the surgery is successful and removes all your disease, you will not continue study drug. If you have any signs of disease after your surgery, the study doctor may have you continue study drug until you need to stop because of side effects, worsening of your disease, or other reasons.

If you stop study drug after your surgery, the study team will check on your health every 8 weeks until 56 weeks after your surgery, and then every 3 months for 3 years after your surgery. If you continue study drug, you will follow the treatment and follow-up schedule described above for participants whose cancer cannot be removed with surgery.

The EOT and follow-up procedures that will be done only for research purposes, or that may be done more often because you are participating in this study, are listed below.

- cfDNA blood samples (about 1 tablespoon) will be drawn at your first follow-up visit after surgery and every third follow-up visit for 2 years or until EOT
- Biomarker blood samples (about 1 tablespoon) will be collected at EOT

Study Calendars that show how often you will have these exams, tests, and procedures are provided at the end of this consent form. The calendars also include exams, tests, and procedures that are part of your usual care.

Will I receive the results of my research tests?
Neither you nor your doctor will receive the results of any tests done for research purposes during this study.

What risks can I expect from taking part in this study?
If you choose to take part in this study, there is a risk that:

- You may lose time at work, school, or at home, and you may spend more time than usual in the hospital or doctor's office
- You may be asked sensitive or private questions that you do not usually discuss
- There may be a risk in finding out new genetic information about yourself. New health information about inherited traits that might affect you or your family (blood relatives) could be found during a research study.
- As part of this study, we will perform a genetic test designed to find out if your tumor has the genetic changes being analyzed in this study. If your tumor has these genetic changes, we will assign you to a study group based on the genetic features of your tumor. Because this genetic test is still in development, there is a risk that the test results could be wrong. If the test results are wrong, you may be included in this study even though it may not offer the best treatment option

for you. Or you may be excluded from the study even though it may offer a good treatment option for you.

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

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

Important information about side effects:

- The study doctors do not know who will or will not have side effects.
- Some side effects may go away soon, some may last a long time, and some may never go away.
- Some side effects may make it difficult for you to have children.
- Some side effects may be mild. Others may be very serious, and may even result in death.

Important information about how you and the study doctor can make side effects less of a problem for you:

- If you notice or feel anything different, tell the study doctor. He or she can check to see if you are having a side effect.
- The study doctor may be able to treat some side effects.
- The study doctor may adjust the study drug to try to reduce your side effects.

If you have recurrent and operable chondrosarcoma (Group 2), there is a risk that your disease may grow while you are receiving study treatment. Surgery to remove your disease may no longer be possible.

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

Possible side effects of AG-120:

Common, some may be serious In 100 people receiving AG-120, more than 10 and as many as 100 may have:
• Tiredness (fatigue) • Diarrhea • Nausea • Increase in number of white blood cells (blood cells that help fight infection) • Fever • Fever with very low white blood cell counts • Swelling of arms and legs • A decrease in number of red blood cells, which may make you feel weak or tired (anemia) • Shortness of breath • Fluid in or around the lungs or heart • Constipation • Pain in joints • Vomiting • Cough • Decreased appetite

Common, some may be serious In 100 people receiving AG-120, more than 10 and as many as 100 may have:
• Decreased appetite • Skin rash • Weakness • Pneumonia • Low blood pressure • Mouth blisters/sores • A decrease in number of platelets (blood cells that help with clotting) • Headache • Low blood levels of magnesium (symptoms may include weakness, muscle cramp and/or irregular heartbeat) • Stomach area (abdominal) pain • Low blood level of potassium (possible weakness) • Dizziness • Nose bleed • Back Pain • Itching • High blood levels of uric acid (possible painful joints and/or kidney failure) • Difficulty sleeping • Chest pain • Loss of Strength • Low number of red blood cells, which can cause tiredness and shortness of breath (and may require a blood transfusion) • Low sodium counts (a type of body salt that helps control blood pressure and the function of muscles and nerves)

Occasional, some may be serious In 100 people receiving AG-120, between 4 and 10 may have:
• Irregular heart rhythms (prolonged QT interval) • Severe infection throughout the body (sepsis) • Tumor lysis syndrome (TLS), which has occurred in people taking AG-120 for advanced blood cancers. TLS results from the rapid breakdown of cancer cells in response to treatment. This breakdown can result in problems with many of the body's normal functions, and may cause weakness, low blood pressure, muscle cramps, kidney damage, irregular heartbeat, and/or other organ damage. TLS can be life-threatening. One participant in a study involving AG-120 died from kidney failure related to TLS. • Isocitrate dehydrogenase (IDH) differentiation syndrome, which has been seen in people receiving drugs targeting leukemia. IDH differentiation syndrome may include one or more of the following symptoms: unexplained fever, shortness of breath, high counts of white blood cells (blood cells that fight infection), high counts of platelets (blood cells that help with clotting), and/or fluid in or around the lungs or heart. Some of these symptoms may require further medical intervention and could be life-threatening.

Rare, and serious In 100 people receiving AG-120, 3 or fewer may have:
• Guillain-Barre Syndrome, which affects the immune system. Symptoms may include weakness, loss of muscle function, numbness, tingling, burning caused by damage to nerves and the nervous system. This can condition may be life threatening as it may cause trouble breathing, and affect your blood pressure and heart rate. • Abnormal liver tests, which may mean that your liver is not functioning properly and may be associated with tiredness and yellowing of the skin and eyes • Leukoencephalopathy, which affects your brain function. Symptoms may include difficulty walking, progressive weakness, acute onset of headache, hypertension, seizures and visual disturbances. This can condition can result in death or severe disability. • Lumbosacral Plexopathy, which affects your nervous system. Symptoms in the lower body may include numbness, pain, muscle weakness, decreased strength in your legs, and/or trouble walking. • Posterior Reversible Encephalopathy Syndrome (PRES), which affects the brain function. Symptoms may include confusion, loss of vision, seizures, high blood pressur, or loss of consciousness.

Possible risks of radiation-based diagnostic imaging: You will have CT scan(s) to guide the biopsy procedure. You will be exposed to low amounts of radiation from the scan(s) performed during this research study. The CT scans provide detailed pictures of the inside of the body using radiation, like an x-ray. Every day, people are exposed to low levels of radiation that comes from the sun and the environment. Scientists think that exposure to too much radiation can be harmful.

The amounts of radiation associated with the scan(s) included in this study are similar to those from standard-of-care imaging procedures. Each year, many thousands of patients routinely undergo similar scans and receive similar doses of radiation with no short- or long-term adverse effects.

Possible risks and discomfort associated with research biopsies: Risks associated with biopsies include pain, redness, swelling, bleeding, bruising, infection, and, rarely, death. The doctor performing the biopsy will explain the details and risks of the procedure, which may vary, depending on how the biopsy sample will be obtained. You will sign a separate consent document before you undergo this procedure.

Reproductive risks: You should not get pregnant, breastfeed, father a baby, or donate sperm while you are in this study. The study drug used in this study could be very damaging to an unborn baby. Check with the study doctor about what types of birth control or pregnancy prevention to use while you are in this study. Female and male participants who are able to have children must use two acceptable method of birth control during the whole study, and for at least 90 days after the last dose of AG-120. This contraception requirement also applies to male participants' sexual partners (if those partners are able to have children).

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

What are my responsibilities in this study?

If you choose to take part in this study, you will need to:

- Keep your study appointments
- Tell the study doctor about:
  - All medications and any supplements you are taking
  - Any side effects from these medications or supplements
  - Any doctor visits or hospital stays outside of this study
  - Whether you have been or are currently in another research study
- Remember to bring your completed pill diary to all your clinic appointments, along with your medication bottle(s), even if the bottle is empty.

Is there a conflict of interest for this study?

The study is sponsored by Memorial Sloan Kettering and funded by Servier Pharmaceuticals. The study also receives support provided by Institut de Recherches Internationales Servier (I.R.I.S.) and the Department of Defense (DOD). There are no known investigator conflicts of interest for this study. In addition, we want you to be aware that one of MSK's leaders, who is not involved in the research or the conduct of this study, is a founder and an Advisory Board Member of Servier Pharmaceuticals and has a financial interest in the company. If you would like to know more about the steps MSK has taken to protect your best interests while you are in this study, please contact the MSK Patient Representative Department at 212-639-7202.

What are the costs of taking part in this study?

You will not have to pay for the study drug or for tests and procedures done only for research purposes, including:

- Blood collection and testing for research purposes (all times you give blood for cfDNA, genetic, and biomarker tests)
- Biopsies for research at screening; Cycle 2, Day 15; and disease progression
- ECHO at screening
- Blood collection at screening for coagulation tests

It is possible that AG-120 may not continue to be supplied while you are in the study. This possibility is unlikely, but if it occurs, your study doctor will talk with you about your options.

You and/or your health plan/insurance company will have to pay for all the other costs of treating your cancer while you are in this study. These charges include the costs of insurance co-pays and deductibles, as well as tests, procedures, or drugs that you get during the study to monitor your safety, and to prevent or manage any side effects.

Talk to your insurance provider and make sure that you understand what your insurance pays for and what it does not pay for if you take part in this clinical trial. Also find out if you need approval from your health plan before you can take part in this study.

The study doctor or nurse can help you find the right person to talk to if you are not sure which costs will be billed to you or your insurance provider.

Will I receive payment for taking part in this study?

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

Your biospecimens (blood and tissue) may be used in the development of new tests, drugs, or other products for sale. If they are, you will not receive any payment from the sale of these products.

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

You will get medical treatment if you are injured as a result of taking part in this study.

If you think that you have been injured as a result of taking part in this research study, tell the study doctor or the person in charge of the study as soon as possible. The name and telephone number of the person in charge of this research are listed on the first page of this consent form.

We will offer you treatment for research injuries that happen as a result of your taking part in this study. You and/or your health plan will be charged for this treatment. Medical services will be offered at the usual charge. You will be responsible for any costs not covered by your health plan/insurance company.

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

Who will see my medical information?

Your privacy is very important to us, and the researchers will make every effort to protect it. Trained staff at Memorial Hospital may review your records, if necessary.

Access to your protected health information will be limited to those listed in the Research Authorization form, which is a part of the informed consent process.

Your information may be given out, if required by law. For example, some states require doctors to make a report to the state health board if they find that a participant in a research study has a contagious disease like tuberculosis. However, the researchers will do their best to make sure that any information about you that may be released will not identify you.

In the future, your information (data) and biospecimens may be de-identified, which means that your data and/or biospecimens will be assigned a unique code, and the list that links the code to your name will be stored separately from your biospecimens and data. Your de-identified information and biospecimens may be used for research that has not been described in this consent form, and they may be shared with another investigator for future research. You will not be asked if you agree to take part in future research studies.

If your information from this study is used in any reports or publications, your name and anything else that could identify you will not be used. It is possible that your de-identified information from this study will be shared with other researchers outside of MSK and may be stored in public databases. All requests for data sharing will be reviewed by the study sponsor, and if individual results are included in the data, they will not contain any identifiable information about you, such as your name, address, telephone number, or social security number. Your privacy is very important to us and we use many safety procedures to protect your privacy. However, we cannot guarantee that no one will ever be able to use your information to identify you.

A Federal law, 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

Be aware that this Federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, long-term care insurance, or if you are a member of the military.

Where can I get more information?

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

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

You can talk to the study doctor about any questions or concerns that you may have about this study, or to report side effects or injuries. You may also contact the lead researcher listed on the first page of this consent.

For questions about your rights while you are participating in this study, call the MSK Institutional Review Board (IRB) at 212-639-7592. If you have concerns, complaints, or input on research, or if you would like more information about the informed consent process, please contact the MSK Patient Representative Department at 212-639-7202.

Optional Study:

This part of the consent form describes an optional study that you can choose to take part in. You will not get health benefits from this study. The doctors leading this research hope that the results of this study will help other people with cancer in the future.

The results of this study will not be added to your medical records, and you and/or your study doctor will not be informed of the test results.

You will not be billed for this optional study. You can still take part in the main study even if you do not participate in the optional study. If you sign up for but cannot complete the optional study for any reason, you can still take part in the main study.

Optional collection of tissue for research testing at disease progression

If you choose to take part in this study, you will have an optional biopsy at the time your disease gets worse (disease progression). Researchers will use the information from tests on this new biopsy sample to compare the impact of the study drug before and after treatment and for biomarker research. The sample will also be used for genetic research. Information about genetic research can be found in the *Before you begin the main part of the study* section of this consent form.

You will sign a separate consent form for the biopsy. The doctor doing the biopsy will explain what will happen, including any risks or possible side effects that may result from collecting the sample. More information about the risks of this procedure is provided in the *What risks can I expect from taking part in this study?* section of this consent form.

The results of testing your tumor sample will be used only for research, and not to guide your medical care.

Please check Yes or No. Your medical care will not be affected, no matter what you decide to do.

I agree to have the optional biopsy at disease progression.

❑ Yes ❑ No

This is the end of the section about the Optional Study.

Research Authorization for the Use and Disclosure of Protected Health Information (PHI)

AG-120 in People with IDH1 Mutant Chondrosarcoma

Federal law requires Memorial Sloan Kettering Cancer Center (MSK) to protect the privacy of information that identifies you and relates to your past, present, and future medical conditions (protected health information; PHI). We are committed to protecting the privacy of your information.

If you enroll in this research study, your protected health information will be used and shared with others, as explained below. MSK must obtain your permission before using or sharing your protected health information for research purposes. This form helps to make sure that you are informed of the ways in which your information will be used or shared in the future.

Carefully read the information below before you sign this form. By signing this form, you agree to the use and disclosure of your information for this research study.

1. What protected health information about me will be used or shared with others during this research?

- Your medical records
- Your research records, including new health information created from study-related tests, procedures, visits, and/or questionnaires
- Any health information or clinical data associated with your biospecimens, if the information or data could be reasonably used to identify you. This information or data will be shared only if you have agreed to it by signing this informed consent document.
- HIV-related information, including any information indicating that you have had an HIV-related test; or that you have HIV infection, HIV-related illness, or AIDS; or any information that could indicate that you may have been exposed to HIV. (New York State requires us to obtain your consent to use or share this information.)

2. Who will use or share my protected health information?

MSK will use and share your protected health information. People and offices that deal with research oversight, quality assurance, and/or billing will be able to use and share your protected health information, including:

- The study's Principal Investigator and Co-Principal Investigator: Ciara Kelly, MBBS and William Tap, MD
- Your research team at MSK, including the participating investigators, research staff, research nurses, fellows/residents, and clerical support staff
- Any healthcare personnel who provide services to you in connection with this study
- Members and staff of MSK's Institutional Review Board (IRB) and Privacy Board (PB)
- Staff of MSK's Clinical Research Administration, which oversees clinical studies, and Clinical Research Information Technology Group, which manages research databases
- Members of MSK's Data Safety Monitoring Board/Committee and the Quality Assurance Committee

3. With whom outside of MSK may my protected health information be shared?

Although all reasonable efforts will be made to maintain the confidentiality of your protected health information, it may be shared with and used by the following:

- The company or organization that provides the funding for the study, Servier Pharmaceuticals, Inc.
- MSK's research collaborators, business partners, subcontractors and agent(s), in the United States or in other countries, working to conduct the study, to monitor the study, or to analyze the study information for this study or for other research about the study drug.
- Other research doctors and medical centers participating in this research.
- Federal and state agencies, and other domestic or foreign government bodies, if required by law and/or necessary for oversight purposes, including:
    - Office for Human Research Protections (OHRP) of the US Department of Health and Human Services (HHS)
    - US Food and Drug Administration (FDA) and other regulatory agencies responsible for oversight of research
    - National Cancer Institute (NCI)/National Institutes of Health (NIH)
- Other qualified researchers, approved by MSK, who may receive individual research results that do not identify you.

Some of the organizations that may receive your protected health information may not have to satisfy the privacy rules and requirements; they may share your information with others without your permission.

4. Why will my protected health information be used by or shared by MSK or others?

The main reasons for the use or sharing of your information include the following:

- To conduct the study, to monitor your health status, to measure the effects of the drug(s)/device(s)/procedure(s) being studied, and to determine the research results
- To ensure that the research meets legal and institutional requirements
- To develop new tests, procedures, and commercial products
- To enhance research databases, so that scientists can design better research studies to develop new therapies for patients and to gain a better understanding of disease
- To assist with MSK medical treatment, billing, or healthcare operations. For example, medical information produced by this research study will become part of your hospital medical record.

5. For how long will my protected health information be used or shared with others?

There is no set date at which your protected health information that is being used or shared for this research study will be destroyed or no longer used. The information used and created during the

study may be analyzed for many years, and it is not possible to know when this analysis will be completed.

6. Statement of privacy rights:

- It is your right to refuse to sign this authorization form. If you do not sign this form, you will not be able to participate in this research study. However, if you do not sign, it will not affect your ongoing medical treatment or healthcare coverage.

- You have the right to withdraw your permission for MSK to use or share your protected health information. Please note that we will not be able to withdraw all the information about you that already has been used or shared with others to carry out research-related activities such as oversight, or information that is needed to ensure the quality of the study. To withdraw your permission, write to the study doctor listed on the first page of this consent form at: Memorial Sloan Kettering Cancer Center, 1275 York Avenue, New York, NY 10065. If you withdraw permission for us to use or share your protected health information, you will not be able to continue to participate in this research study.

- You have the right to request access to your protected health information that is being used or shared during this research and that is related to the research or to payment for the research. However, you may access this information only after the study is completed. You may have access to your medical record at any time. To request this information, please contact the study doctor whose name and telephone number are listed on the first page of this consent form. You may also ask the study doctor to correct any study-related information about you that is wrong.

Notice concerning HIV-related information

Individuals/organizations are prohibited from sharing any HIV-related information about you without your approval, unless they are permitted to do so under federal or state law. You have a right to request the list of people who may receive or use your HIV-related information without your authorization.

If you experience discrimination because of the release or disclosure of your HIV-related information, you may contact the New York State Division of Human Rights at 888-392-3644 or the New York City Commission on Human Rights at 212-306-7500. These agencies are responsible for protecting your rights.

Memorial Sloan Kettering Cancer Center
IRB Number: 19-393 A(7)
Approval date: 02-May-2022

Participant Informed Consent/Research Authorization for Clinical Research

Statement of professional obtaining consent
I have fully explained this clinical research study to the participant or to his/her Legally Authorized Representative (LAR). In my judgment, and in that of the participant or his/her LAR, sufficient information, including risks and benefits, was provided for the participant or his/her LAR to make an informed decision. The consent discussion will be documented in the participant's EMR.

Consenting professional must personally sign and date		
Consenting professional's signature		**Date:**
Consenting professional's name (Print)		

Participant's (or Legally Authorized Representative's [LAR's)]) statement
I have read this form that describes the clinical research study. I have also talked it over to my satisfaction with the consenting professional. By signing below, I agree to the following: (1) to voluntarily participate in this clinical research study; (2) to authorize the use and disclosure of my/the participant's protected health information (data about myself/the participant); and (3) to state that I have received a signed and dated copy of this consent form.

Participant/LAR must personally sign and date		
Participant/LAR signature		**Date:**
Participant/LAR name (Print)		
LAR relationship to participant		

Witness signature (if required)

- ❑ Witness for non-English speaking participant: I declare that I am fluent in both English and in the participant's (or LAR's) language, and I confirm that the consent discussion was appropriately interpreted for the participant (or LAR).
- ❑ Other: I confirm that the consent discussion occurred, and that the participant agreed to participate in this study by signing this form, making his/her mark, or verbally agreeing.

Name of witness: _____

Signature of witness: _____ **Date:** _____
(The name of the witness must be documented in the EMR.)

Interpreter (if required)
Name of interpreter (if present): _____
ID number (if phone interpreter): _____
(The interpreter's name or ID number must be documented in the EMR.)

The participant/Legally Authorized Representative must be provided with a **signed copy** of this form.

Study Calendars:

These calendars show the exams, tests, and procedures that will be done as part of this research study, as well as the tests and procedures that are part of your usual care.

Group 1 (participants with chondrosarcoma that cannot be removed by surgery):

Exams/tests/ procedures	Screening	Cycles 1 & 2		C3D1	End of treatment/follow-up	
		D1	D15		End-of-Treatment (EOT) visit	Follow-up every 3 months
AG-120 dosing and diary completion		X	X	X		
Physical exam/Telehealth assessment	X	X		X	X	
Side effect review		X	X	X	X	
Routine blood tests	X	X	X	X	X	
Routine urine tests	X					
Blood or urine pregnancy test, if applicable	X	X		X	X	
Electrocardiogram (EKG)	X	X	X	X	X	
ECHO/MUGA	X					
Tumor imaging (CT or MRI scans)	X	Every 8 weeks until Week 56, and then every 12 weeks until disease progression				
Blood samples for cfDNA	X	X	C2	C4, C6, C8, & C12	X	
Blood samples for research (genetic and biomarker)	X	C2	C2	C3 & C4	X	
Research biopsy	X		C2		Optional	
Follow-up contact						X

Group 2 (participants with chondrosarcoma that is able to be removed by surgery):

Exams/tests/ procedures	Screening	Cycles 1 & 2		C3D1 & C4D1	Post-surgery follow-up (FU)		
		D1	D15		1st FU visit	2nd FU visit	Disease progression/recurrence
AG-120 dosing and diary completion		X	X	X			
Surgery		You may be offered surgery after 4 months of treatment					
Physical exam	X	X		X		X	
Side effect review		X	X	X			
Routine blood tests	X	X	X	X			
Routine urine tests	X						
Blood or urine pregnancy test, if applicable	X	X		X			
Electrocardiogram (EKG)	X	X	X	X	X		
ECHO/MUGA	X						
Tumor imaging (CT or MRI scans)	X	Every 8 weeks until Week 56, and then every 12 weeks until disease progression					
Blood samples for cfDNA	X		C2	C3 & C4	X	X	X
Blood samples for research (genetic and biomarker)		X	X	C3 & C4	X		X
Research biopsy	X		X				Optional
Follow-up contact					Every 8 weeks after 1st FU visit until Week 56, and then every 3 months for 3 years		