Official Study Title: ST. JUDE ELIOT: PHASE 1 EVALUATION OF LY2606368, A MOLECULARLY-TARGETED CHK1/2 INHIBITOR THERAPY, IN COMBINATION WITH CYCLOPHOSPHAMIDE OR GEMCITABINE FOR CHILDREN AND ADOLESCENTS WITH REFRACTORY OR RECURRENT GROUP 3/GROUP 4 OR SHH MEDULLOBLASTOMA BRAIN TUMORS

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Informed Consent for Research

ST. JUDE ELIOT: PHASE 1 EVALUATION OF LY2606368, A MOLECULARLY-TARGETED CHK1/2 INHIBITOR THERAPY, IN COMBINATION WITH CYCLOPHOSPHAMIDE OR GEMCITABINE FOR CHILDREN AND ADOLESCENTS WITH REFRACTORY OR RECURRENT GROUP 3/GROUP 4 OR SHH MEDULLOBLASTOMA BRAIN TUMORS

NOTE: "You" refers to 'you' or 'your child' throughout this document. If you are the guardian of a minor or of a person under legal disability who is being asked to take part in this study, you may give consent on his/her behalf.

Key Information

To start we want to highlight the risks and study requirements that we think you should know before deciding if you want to take part in this research study. If you're still interested, we'll then get into more detail.

In this section, we will briefly explain the following:

A. Why are you being asked to volunteer in this study?

You are being asked to take part in this clinical trial, a type of research study, because you have a brain tumor called medulloblastoma that has grown despite treatment (refractory) or has come back after treatment (recurrent). You have already been treated with chemotherapy and/or radiation and your tumor has not changed or is now growing.

B. What is the usual approach to this cancer?

People who are not in a study are usually treated with surgery, radiation, or FDA-approved drugs. Sometimes, combinations of these are used and your doctor can explain which may be best for you. These treatments can reduce symptoms and may stop the tumor from growing for several months or longer. However, right now, there are no therapies that are known to be very effective for your type of tumor.

C. Why is this study being done?

We are testing a new experimental drug, prexasertib, in combination with chemotherapy drugs in hopes of finding a treatment that may be effective against tumors that have come back or that have not responded to standard therapy.

Key Information

D. What will happen if you decide to take part in the study?

You have already completed the first part of the study called "screening." The testing showed that based on your tumor type, you will receive treatment on Stratum A, which is a combination of prexasertib (the study drug), and cyclophosphamide. Cyclosphosphamide is commonly used to treat medulloblastoma

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

The most common side effects of the study drug, prexasertib, are tiredness, weakness, anemia and bruising/bleeding. When prexasertib is administered in combination with chemotherapy (i.e. cyclophosphamide), overlapping side effects (i.e. anemia, tiredness, blood count suppression) may be exaggerated. The side effects of the other chemotherapy drugs will be described in later consents.

A potential benefit of treatment on this study is that it may cause your tumor to stop growing or to shrink for a period of time. It may lessen the symptoms, such as pain, that are caused by the tumor.

F. How many people will take part in this study?

Up to 50 children and young adults will take part in this study at St. Jude, and an additional 50 children and young adults will take part in three other hospitals collaborating on this study.

G. What are your options?

- You may choose to receive other treatment, if available, that is not part of a research study.
- You may choose to take part in a different study, if one is available.
- You may choose not to be treated for medulloblastoma, but you may want to receive comfort care to relieve symptoms.

If you are still interested in taking part in the SJELIOT research study, more detail will be provided in the following pages and later in the treatment consents.

1. Why are you being asked to volunteer for this research study?

You are being asked to take part in this part of the study because the review and tests done on your tumor during screening showed that your tumor can be assigned to the SJELIOT treatment arm that will use prexasertib and cyclophosphamide to treat your tumor.

Prexasertib is considered experimental because it has not been proven to work in a situation like yours. We are using prexasertib because it seems to work against cancer in test tubes and animals. Prexasertib has been used in adults; however, there is a lot that we do not know about it yet. In adults, it has been used in studies for women with breast and ovarian cancer and in patients with advanced solid tumors. Prexasertib has not been used in combination with chemotherapy to treat children with medulloblastoma.

Please take your time in deciding and feel free to discuss it with your family, friends and St. Jude staff. Before agreeing, it is important that you read this consent form that describes the study. After you understand the study and if you agree to take part, you will be asked to sign this consent form. You will be given a copy to keep.

2. Who is sponsoring this study?

This study is being sponsored by St. Jude Children's Research Hospital. Eli Lilly (Lilly) will provide the study drug, prexasertib, at no charge. Lilly may receive information about you related to the study.

The principal investigator (researcher) in charge of this study is Dr. Giles Robinson who can be reached by phone at 901-595-3300, if you have any questions or concerns about this research.

3. What is the purpose of this study?

We are testing new experimental drugs such as prexasertib in the hopes of finding a treatment that may be effective against tumors that have come back or that have not responded to standard therapy in patients that are between 1 year and 25 years of age at the time of study enrollment.

The goals of this part of the study are:

- To find the highest safe dose of prexasertib that can be given with cyclophosphamide without causing severe side effects;
- To learn what kind of side effects the treatments can cause;
- To learn more about the pharmacokinetics (how your body handles the drugs) and pharmacodynamics (the effects of the drugs on your body and how the drugs work) of the drugs used in this study;
- To learn more about the biology and genetics of medulloblastoma tumors and if we can predict which tumors will or will not respond to treatment;
- To determine whether prexasertib with cyclophosphamide is a beneficial treatment for your tumor.

Up to 50 children and young adults will take part in this study at St. Jude, and an additional 50 children and young adults will take part in three other hospitals collaborating on this study.

4. What will be done in this study?

Since the screening exams, tests, and procedures show that you can be in this part of the research study, you can now choose to take part and start treatment.

Cyclophosphamide will be given into the vein (IV) as an infusion over 60 minutes twice during a 4 week period on Days 1 and 15. The day after cyclophosphamide, prexasertib will be given into the vein (IV) as an infusion over 60 minutes on days 2 and 16.

This entire 4-week period is called a cycle.

You may continue to receive prexasertib and cyclophosphamide for up to 26 cycles (about 2 years) unless you develop serious side effects or your tumor worsens.

Drug	How the drug will be given	Days
Cyclophosphamide	Into the vein (IV	Days 1 and 15
Prexasertib	Into the vein (IV)	Days 2 and 16

After chemotherapy (after Day 16), you may also get another drug called a "growth factor" (filgrastim or peg-filgrastim), which will be given to help your blood counts recover. Growth factors are given by vein or as a shot just under the skin (SubQ).

The doses of the drugs for the first children enrolled on the study will be based on the side effects seen in adults. Between 2 and 6 children will receive the drugs at each dose. If the side effects are not too severe, the next group of children will receive higher doses. Dosing is done this way because we do not yet know the best dose to use in children. If you are enrolled early in this study you may receive a lower dose than those who are enrolled later. A lower dose may be less likely to have any effect on your tumor. Your doses will not be increased. If you are enrolled in this study at a high dose level you may be more likely to have side effects. If you have bad side effects, your doses may be decreased. Up to eight different doses of prexasertib and cyclophosphamide may be studied.

During the study you will have tests and procedures to check for side effects, and to check how your tumor is responding to the treatment. These tests are part of regular cancer care (standard of care), but you may have them more often because you are on the study.

Standard of care tests and evaluations:

- History and physical exam
- Blood and urine tests
- Electrocardiogram (ECG) to measure the electrical activity of your heart
- Echocardiogram (ECHO) to measure heart function

- Magnetic resonance imaging (MRI) of the brain and spine
- Lumbar puncture (spinal tap) to check for tumor cells in the fluid surrounding your brain and spinal cord, if clinically indicated

There are some extra tests that you will need to have if you take part in this study because they are an important part of this study. These tests are for research, and would not be done if you were not in this study.

Required Research Tests:

- Pharmacokinetics (PK) of prexasertib – required research

  This is a research test that is required to be in the study. Additional PK samples may also be taken, but only if you consent for additional testing. This is discussed in the "Optional Research Testing" later in this consent.

  During the first cycle, blood samples will be collected to measure the amount of prexasertib in your blood at different time points before and after you take this drug. This will help us determine how your body processes and gets rid of the drug. These samples can be collected from your central line.

  At each time point, about 1 mL (less than ½ teaspoon per time point) of blood will be drawn:

  - Day 2: 4 blood samples will be collected – before prexasertib starts, at the end of the infusion of the drug, and at 3 and 6 hours after the drug is given.
  - Day 3: 1 blood sample
  - Day 4: 1 blood sample
  - Day 5: 1 blood sample
  - Day 6: 1 blood sample
  - Day 7: 1 blood sample

5. How long will I be in this part of the study?

You may continue to receive this treatment for up to 2 years (up to 26 cycles) unless you develop serious side effects or your tumor worsens.

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

Risks of the study

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

- Lose time at school, work or home and spend more time in the hospital or doctor's office than usual;
- Be asked sensitive or private questions which you normally do not discuss.

The drugs used in this study may affect how different parts of your body work such as your liver, kidneys, heart, and blood. Your St. Jude doctor will be testing your blood and will let you know if changes occur that may affect your health. There is also a risk that you could have side effects.

Here are important points about side effects:

- Your St. Jude doctor does not know who will or will not have side effects.
- Some side effects may go away soon, some may last a long time, or some may never go away.
- Some side effects may interfere with your ability to have children.
- Some side effects may be serious and may even result in death.

Here are important points about how you and your St. Jude doctor can make side effects less of a problem:

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

Side effects can be increased when chemotherapy drugs are combined, as they are in this study. If you need emergency information about an adverse reaction to a drug, you may contact your St. Jude doctor at 901-595-3300.

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

Risks and side effects related to PREXASERTIB include:

COMMON, SOME MAY BE SERIOUS In 100 people receiving prexasertib, more than 20 and up to 100 may have:
• Tiredness, weakness • Anemia which may cause tiredness, or may require blood transfusion • Bruising, bleeding

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving prexasertib, from 4 to 20 may have:
• Nausea • Diarrhea • Vomiting • Loss of appetite, weight loss • Infection, especially when white blood cell count is low • Change in heart rhythm • Headache

Risks and side effects related to PREXASERTIB continued

RARE, AND SERIOUS In 100 people receiving prexasertib, 3 or fewer may have:
• Fever • Dehydration • Rash • Constipation • Severe blood infection • Dizziness • Reaction during or following infusion of the drug which may cause fever, chills, rash, low blood pressure • Nose bleed • Pain in belly • Swelling in arms and legs • Flushing • Chills • Dry mouth • Changes in taste • Sores in mouth • Heartburn • Pain in muscles • Numbness, tingling or pain of the arms and legs

Some drugs or supplements may interact with your treatment plan. Talk to your doctor, pharmacist, or study team before starting any new prescription or over-the-counter drugs, herbals, or supplements and before making a significant change in your diet. Supplements may come in many forms, such as teas, drinks, juices, liquids, drops, capsules, pills, or dried herbs. All forms should be avoided. Certain prescription medications that interact with your liver enzymes must also be avoided during the study.

Lastly, drugs that prolong the QTc interval (a heart rhythm disorder that can cause irregular heart rhythm or arrhythmias) should not be taken on the day of prexasertib dosing. Your doctor may prescribe drugs that prolong the QTc interval only if they are medically necessary and no alternatives are available. Please make sure your study doctor is aware of all medicines and supplements (including prescription and over-the-counter) you are taking and do not start new medications without talking to you study doctor first.

Possible risks and side effects of CYCLOPHOSPHAMIDE:

COMMON, SOME MAY BE SERIOUS In 100 people receiving cyclophosphamide, more than 20 and up to 100 may have:
• Infection, especially when white blood cell count is low • Blood in urine • Nausea, vomiting, diarrhea, loss of appetite, pain in belly • Sores in mouth • Absence of menstrual period which may decrease the ability to have children • Hair loss, skin changes, rash, change in nails

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving cyclophosphamide, from 4 to 20 may have:
• Fluid around the heart • Scarring of the lungs which may cause shortness of breath • Damage to the bone marrow (irreversible) which may cause infection, bleeding, may require transfusions • Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Loss or absence of sperm which may lead to an inability to father children • Stuffy nose

RARE, AND SERIOUS In 100 people receiving cyclophosphamide, 3 or fewer may have:
• Damage to the heart or heart failure which may cause shortness of breath, swelling of ankles, cough or tiredness • Swelling of the body including the brain which may cause dizziness, confusion • A new cancer including cancer of bone marrow (leukemia) caused by chemotherapy • Severe skin rash with blisters and peeling which can involve the mouth and other parts of the body

Risks of overlapping toxicities

When prexasertib is administered in combination with chemotherapy (i.e. cyclophosphamide), overlapping side effects (i.e. anemia, tiredness, blood count suppression) may be exaggerated.

Risks of tests and procedures

Like most medical tests, there are some risks and discomforts. The following describes the most common risks of these tests and procedures. Your doctor or nurse will also discuss with you in detail any risks or discomforts of the procedures or test(s) you will be scheduled to undergo.

Blood tests: If blood needs to be drawn from a vein in your arm, this will cause some pain and may result in bruising at the site of the needle stick. If a bruise does form at the end of the needle puncture site, it will generally go away on its own without any treatment. If you have a central venous catheter, drawing blood from this line is associated with a small chance of infection, which could require treatment with antibiotics or, rarely, removal of the line.

Lumbar puncture (spinal tap): A lumbar puncture has a small risk of infection, bleeding, nerve damage, or headache. Leakage of spinal fluid into the tissue can cause a severe headache that lasts for days to weeks. Subjects will be given medications to numb the pain and blur the memory before the test since it is painful. The pain is usually brief but occasionally may linger. Sometimes this procedure is done while the subject is under general anesthesia.

MRI of brain and spine: MRI scans are common standard imaging tests used in the diagnosis and monitoring of many diseases. Although these tests have been in use for many years, their long-term effects on the body are still being learned. The most common discomfort is the length of time a person must lay still or flat while a scan is being performed. Uncommonly, some people may have allergic reactions to dyes injected for some of these tests. Uncommon allergic reactions may result in rash, difficulty breathing, low blood pressure or other severe complications. Please let your doctor or nurse know if you have previously had an allergic reaction.

EKG and echocardiogram: These procedures are associated with very little discomfort. Some people with sensitive skin may develop rashes where the EKG wires are taped on their skin.

History and physical examination and urine tests: There are no physical risks associated with these screening procedures.

Loss of privacy: Very rarely, personal information from your records could be given out by accident. This might make you upset, embarrass you or affect your ability to get insurance. To stop this from happening, we:

- Store records apart from names or other personal information,
- Allow only members of the study team to see the records,
- Store electronic data only on computers protected with a password and encryption software,
- Report study results on the whole group and never identify one single person in any reports.

Benefits

The potential benefit of the treatment with prexasertib and cyclophosphamide is that it may cause your cancer to stop growing or to shrink for a period of time. It may lessen the symptoms, such as pain, that are caused by the cancer. It is extremely unlikely that this treatment will cure your cancer. Because there is not much information about this drug combination's effect on cancers in humans, we do not know if you will benefit from taking part in this study. Information learned from this study may help future patients with cancer.

7. What are the risks to pregnancy, to an unborn child, and to the ability to have children when taking part in this study?

You should not become pregnant or father a baby while on this study because the drugs in this study can affect an unborn baby. Women should not breastfeed a baby while on this study. Your

doctor will talk to you about what kind of birth control methods to use and how long to use them. Some methods might not be approved for use in this study.

It is important you understand that you need to use birth control while on this study. Men and women treated or enrolled on this study must also agree to use adequate contraception prior to the study, for the duration of study participation, and 4 months after completion of prexasertib and cyclophosphamide chemotherapy.

8. Can you stop taking part in this study?

You may refuse to be in this research study or stop at any time. The decision will not affect your care or your relationship with your doctor or St. Jude. If available, you may receive routine medical care at St. Jude Children's Research Hospital.

9. Can you be taken out of this study without your consent?

Your St. Jude doctor may take you out of the study:

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

10. What are your other options?

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

- You may choose to receive other treatment, if available, that is not part of a research study.
- You may choose to take part in a different study, if one is available.
- You may choose not to be treated for medulloblastoma, but you may want to receive comfort care to relieve symptoms.

11. How much will it cost you?

If you have health care coverage, we will bill your health care insurer for all standard of care services, tests, and procedures. Billing your health care insurer impacts your annual deductible and life-time maximum, if any. This may affect your health care coverage to some extent if you go to another health care provider or institution in the future.

At St. Jude, you will not be responsible for or receive bills for co-pays, co-insurance, deductibles, or similar patient-liability amounts, or for the cost of medical care not covered by your health insurer. This includes research-only costs. Research-only tests and procedures will not be billed to you or your health care insurer.

12. Will you be paid for your time or expenses?

You will not be paid for your time or expenses. Also, your samples and/or information may be used to develop a new product or medical test, which may be sold. If this happens, you will not receive any payments for these new products.

13. What if there is a problem?

If you have any questions about this study or if you are injured because of this study, contact Dr. Robinson at 901-595-3300 immediately. If you are injured from being in this research study. St. Jude will offer you reasonable and necessary medical treatment for that injury. If you need more care than St. Jude can provide or if you prefer to seek treatment elsewhere, we will help you find medical care somewhere else. St. Jude may bill your insurance company or other third parties, if appropriate. It is not the hospital's policy to provide payment for other types of costs, such as lost wages, disability, or discomfort if you are injured from being in this study. You are not giving up any of your rights by signing this consent form.

14. How will new findings related to your participation in this study be shared with you?

The researcher will tell you of any new information learned during your study participation which might cause you to change your mind about continuing the study.

15. How will you find out the results of the study?

The researcher will give you information about the overall results of this study. Whether you will know your personal test results will be discussed in another part of this document. St. Jude researchers share information with people in studies in many ways including:

- Articles on www.stjude.org
- In newsletters
- In medical or scientific journals
- In the media
- A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by the U.S. Law. This website will not include information that can identify you. At most the website will include a summary of the results. You can search this website at any time.

16. What about privacy and confidentiality?

When you first registered at St. Jude, you received a copy of the St. Jude Notice of Privacy Practices. It tells how your PHI (protected health information) may be used or given to someone outside the hospital. You have the right to read the Notice of Privacy Practices before you sign this form. It may have changed since you first registered at St. Jude. You can find it at the bottom of every page on the St. Jude Internet website: www.stjude.org.

A decision to take part in this research means that you agree to let the research team use and share your PHI with other researchers for purposes of the study explained above. This information will be kept indefinitely. You have the right to see, copy, and ask for changes to your protected health information that will be used or given out. However, research information may not be seen until the end of the study.

Federal agencies such as the Food and Drug Administration (FDA), the Office for Human Research Protections (OHRP), the National Institutes of Health (NIH), and St. Jude Children's Research Hospital Institutional Review Board (IRB), your insurance company and other health benefits plan (if charges are billed to these plans), as well as other regulatory agencies, committees, or persons involved in overseeing research studies may review your research and medical record.

Researchers and study staff are required by law to report suspected child abuse, threat of harm to self or others, and certain diseases that spread from person to person.

If you consent to take part in this study, the records obtained while you are in this study as well as related health records will remain strictly confidential at all times. The information will be held securely on paper and electronically at your treating hospital and the main hospital site managing this research. Your name will not be passed to anyone else outside the research team or Lilly. You will be allocated a trial number, which will be used as a code to identify you on all trial forms. Any research-related information about you which leaves the hospital will have your name and address removed so that you cannot be recognized.

Your records will be available to people authorized to work on the trial but may also need to be made available to people authorized by the Sponsor, which is the organization responsible for ensuring that the study is carried out correctly. The data will be sent with your unique participant trial number, and all personal identifiers will be removed, so you cannot be identified from it.

By signing the consent form, you agree to this access for the current study and any further research that may be conducted in relation to it, even if you withdraw from the current study. The information collected about you may also be shown to authorized people from the US Regulatory Authority (the Food and Drug Administration); this is to ensure that the study is carried out to the highest possible scientific standards.

17. Permission to use your data/information: Authorization/HIPAA

If you sign this document, you give permission to Dr. Robinson and his staff at St. Jude Children's Research Hospital to use or disclose (release) your health information that identifies you for the research study described in this document.

The health information that we may use or disclose (release) for this research includes information from your medical record, results of physical examinations, medical history, lab tests, and medical tests and procedures.

The health information listed above may be used by and/or disclosed (released) to all researchers and their staff at St. Jude Children's Research Hospital.

St. Jude Children's Research Hospital is required by law to protect your health information. By signing this document, you authorize St. Jude Children's Research Hospital to use and/or disclose (release) your health information for this research. Those persons who receive your health information may not be required by Federal privacy laws (such as the Privacy Rule) to protect it and may share your information with others without your permission, if permitted by laws governing them. Your personal health information may be shared with:

- the Food and Drug Administration (FDA)
- the Office for Human Research Protections (OHRP)
- the National Institutes of Health (NIH)
- St. Jude Children's Research Hospital Institutional Review Board (IRB)
- Eli Lilly and their designated representatives

You do not have to sign this Authorization, but if you do not, you may not receive research-related treatment.

Please note that you may change your mind and revoke (take back) this Authorization at any time. Even if you revoke this Authorization, St. Jude Children's Research Hospital may still use or disclose health information they already have obtained about you as necessary to maintain the integrity or reliability of the current research. To revoke this Authorization, you must write to:

HIPAA Privacy Officer
St. Jude Children's Research Hospital
262 Danny Thomas Place, Mail Stop 280
Memphis, TN 38105

This Authorization does not have an expiration date.

18. Further Information and Contact Details for Questions About This Research Study

You are encouraged to ask any questions you wish, before, during or after your treatment. If you have any questions about the study, please speak to your study nurse or doctor, who will be able to provide you with up to date information about the drug(s)/procedure(s) involved. If you wish to read the research on which this study is based, please ask your study nurse or doctor.

If there is anything you do not understand, or have any other questions, please contact the researcher listed below.

IF AT ANY TIME DURING THE STUDY YOU EXPERIENCE ANY DISCOMFORT OR UNUSUAL SYMPTOMS, OR SIDE EFFECTS, PLEASE CONTACT THE DOCTOR LISTED BELOW:

Principal Investigator, Researcher:
Dr. Giles Robinson
St. Jude Children's Research Hospital
262 Danny Thomas Place
Memphis, TN 38105
Telephone: (901) 595-3300

If you require any medical or surgical treatments outside of St. Jude such as with your local doctor or another hospital during this study, your researcher and their team would need to be informed.

You can get more details about your rights as a research participant by calling the St. Jude Institutional Review Board at 901-595-4357 or the Research Participant Advocate at 901-595-4644 or 901-595-1139. The Research Participant Advocate is an individual who is not part of the research study team and is available to you to discuss problems, concerns, and questions. The Advocate can help you obtain information and can relay any input you may have concerning the research to the research study team. If you are outside of the Memphis area, please call toll-free 1-866-583-3472 (1-866-JUDE-IRB).

If you decide you would like to take part, then please read and sign the consent form. You will be given a copy of this information and the consent form to keep. A copy of the consent form will be filed in your patient notes, one will be filed with the study records and one may be sent to the Research Sponsor.

You can have more time to think this over if you are at all unsure.

Thank you for taking the time to read this information sheet and to consider this study.

19. OPTIONAL RESEARCH STUDIES

This section is about optional research studies you can choose to take part in.

You will not get health benefits from any of these optional research studies. There are no costs to you or your insurance or other payers. You will not be paid for taking part. If any of the research leads to new tests, drugs, or other commercial products, you will not share in any profits.

By signing this consent form, you are voluntarily and freely donating your samples such as blood, bone marrow, and tumor to St. Jude Children's Research Hospital and hereby relinquish all property rights, title and interest you may have in those samples.

The researchers leading the optional research studies hope the results will help other people with cancer in the future.

The results from these optional research studies will not be added to your medical record nor will you or your doctor know the results.

You can still take part in the main study even if you say 'no' to any or all of these optional research studies. If you sign up for but cannot complete any of the optional studies for any reason, you can still take part in the main study. If you choose to take part in these studies at a later date, you will be asked to sign a consent form.

Optional Study #1 (participants who weigh ≥ 15 kg only)

Test	Time Point	Purpose
Prexasertib - Optional matched cerebral spinal fluid (CSF) and blood pharmacokinetic (PK) research studies	If you do NOT have an Ommaya reservoir We will collect CSF at the same time you have a CSF sample collected as part of routine care. We would like to take an additional 1mL (less than ½ teaspoon per time point) of CSF and at the same time, collect ½ teaspoon of blood to measure the amount of study drug in the blood to see how this compares to the amount of study drug in your CSF. If you have an Ommaya reservoir: We will collect CSF and blood samples at the following times: • Before you receive prexasertib • At the end of prexasertib infusion • 6 hours after the infusion • 24 hours after the infusion	To study the amount of prexasertib in your CSF and blood over time.

Please circle and initial your choice: I agree to have my CSF and blood used for matched pharmacokinetic research studies.	**YES: _____ Initials** **NO: _____ Initials** **N/A: weighs < 15 kg**

Optional Study #2 (participants who weigh ≥ 15 kg only)

Test	Time Point	Purpose
Cyclophosphamide pharmacokinetic studies	If you agree to take part in this optional research we will collect blood at the following times: Cycle 1 only, Days 1 and 2 • Before you receive cyclophosphamide • At the end of the cyclophosphamide infusion • 3 hours after infusion • 6 hours after infusion • 24 hours after the infusion	To study the amount of cyclophosphamide in your blood over time.
Please circle and initial your choice: I agree to have my blood used for matched pharmacokinetic research studies.		**YES: _____ Initials** **NO: _____ Initials** **N/A: weighs < 15 kg**

Optional Study #3 (participants who weigh ≥ 15 kg only)

Test	Time Point	Purpose
Cyclophosphamide - Optional matched cerebral spinal fluid (CSF) and blood pharmacokinetic (PK) research studies	If you do NOT have an Ommaya reservoir: We will collect CSF at the same time you have a CSF sample collected as part of routine care. We would like to take an additional 1mL (less than ½ teaspoon per time point) of CSF and at the same time, collect ½ teaspoon of blood to measure the amount of study drug in the blood to see how this compares to the amount of study drug in your CSF. If you have an Ommaya reservoir: We will collect CSF and blood samples at the following times: • Before you receive cyclophosphamide • At the end of cyclophosphamide infusion • 3 hours after the infusion • 24 hours after the infusion	To study the amount of cyclophosphamide in your CSF and blood over time.
Please circle and initial your choice: I agree to have my blood used for matched pharmacokinetic research studies.		**YES: _____ Initials** **NO: _____ Initials** **N/A: weighs < 15 kg**

The optional research tests 4, 5 and 6 described below will require that you sign an additional informed consent document, for the TBANK protocol, if you agree to any of these three tests. The TBANK protocol governs the operation of the St. Jude Children's Research Hospital Biorepository. The TBANK informed consent document will provide details about how information gained from these optional research tests will be handled and how possible results will be communicated to you.

Optional Study #4

Test	Time Point	Purpose
Optional Biology Studies – Tumor tissue	At the time of enrollment	Researchers at St. Jude will perform research studies on your tumor sample that was collected at surgery to learn more about the biology and genetics of your tumor. A variety of research tests will be done to learn more about the tumor's specific genes and chromosomes. Genes are pieces of DNA, and most genes contain the information for making a specific protein. Chromosomes are part of cells that contain genetic information. Researchers will also look for new tumor markers that may be important in diagnosing and treating your type of tumor.
Please circle and initial your choice: I agree to have my tumor tissue used for biology research studies		**YES: _____ Initials** **NO: _____ Initials**

Optional Study #5

Test	Time Point	Purpose
Optional Biology Studies – CSF	Researchers at St. Jude will perform research tests on extra cerebrospinal fluid (CSF) that was obtained during routine care. As part of routine care	Researchers at St. Jude will perform research studies on your CSF to learn more about the biology of your tumor. The tests are done to learn

	on this study, CSF will be obtained during a lumbar puncture. Also, CSF may come from surgery called ventriculo-peritoneal (VP) shunt placement that is done in patients with increased pressure in the brain. Some children who already have a VP shunt may have problems related to it and require surgery and access to the CSF. VP shunt surgery is considered a necessary part of care in some patients. We will not perform an extra procedure to obtain CSF just for research. With your permission, we would like to save an extra 1mL (less than ½ teaspoon per time point) of CSF from each sample taken during routine care to help us learn more about the biology and genetics on medulloblastoma.	more about specific genes and chromosomes that may be important in these types of tumors, including variations in genes of participants enrolled on this study. Researchers will also look for tumor markers contained within the CSF. Genetic information from your CSF sample will be compared with genetic information from your tumor sample to help us better understand your tumor.
Please circle and initial your choice: I agree to have my cerebrospinal fluid (CSF) used for biology and genetic research studies		**YES:** _____ **Initials** **NO:** _____ **Initials**

Optional Study #6

Test	Time Point	Purpose
Optional contact regarding genetic results	At the time of genetic testing	We may find a genetic condition that we believe explains your medulloblastoma when performing genetic testing on your tumor. It is also possible that we could find a genetic condition that has nothing to do with your cancer history, but that increases the chance for you to develop other medical problems, such as a heart condition. It is important to know that the study team is not actively looking for these conditions. <u>If we do not find them, that does not mean you do not have them.</u> However, if we find one of these conditions, and you choose to learn about these results, then an oncologist, genetics professional, or other medical specialist will discuss them with you. Sometimes, if the information concerns a minor child, and is related to a disease that is serious and that could be prevented or treated before your child turns 18, you may not be able to say "no" to receiving the information. Because the DNA sequencing is being done in a research laboratory and not a clinical laboratory with certified procedures for reporting patient results, we cannot directly release results from this study to you. If we obtain information that we think might be important to you or your family, we may be able to have these results confirmed by a certified clinical lab. A clinical laboratory is authorized to release results from participant's tests for clinical and diagnostic purposes. Most clinical laboratories will ask for fresh blood samples in order to ensure the accuracy of the results. Because regulations limit the full disclosure of individual research results, we may be limited in the information we can provide you at the time we ask for the fresh sample. The results of the clinical testing will be placed in your medical record and we will be able to discuss those results with you.

Please circle and initial your choice	**YES: I want to be informed about genetic results that may point to or reflect an increased risk of disease. I understand that clinical genetic testing will need to be completed before my research results can be considered final and released to me.** **_____** **Initials** **NO: I do not want to be informed about genetic results that may point to or reflect an increased risk of disease.** **_____** **Initials**

Optional Study #7 (participants who weigh ≥ 15 kg only)

Test	Time Point	Purpose
Optional Biology Studies – Blood	Three tubes of blood (total of about 10-16 mL or less than 3 teaspoons total) would be taken shortly after enrollment for these studies.	Researchers at St. Jude will perform research studies on your blood to learn more about the biology of your tumor. The tests are done to learn more about specific genes and chromosomes that may be important in these types of tumors, including variations in genes of participants enrolled on this study. Researchers will also look for tumor markers contained within the blood. Genetic information from your blood sample will be compared with genetic information from your tumor sample to help us better understand your tumor.
Please circle and initial your choice: I agree to have my blood used for biology research studies		**YES: _____** **Initials** **NO: _____** **Initials** **N/A: weighs < 15 kg**

PARENT/GUARDIAN STATEMENT (Required for participants younger than 18 years): I have read this document or it was read to me. I have been encouraged to ask questions and all my questions have been answered. I give permission for my child to be in this research study.

Parent/Legal Guardian Signature	Date	Time AM/PM (circle one)

ASSENT DISCUSSION (Required for participants 7–13 years old):

☐ The research was explained to the minor participant in age-appropriate terms and the minor verbally agreed to take part in the study.

☐ Minor declined to take part in the study. The minor declined for the following reason(s):

_____

☐ An assent discussion was not initiated with the minor for the following reason(s):

- ☐ Minor is under 7 years of age.
- ☐ Minor is incapacitated.
- ☐ Minor refused to take part in the discussion.
- ☐ Other_____

RESEARCH PARTICIPANT STATEMENT (14–17 years old and Adult Participants 18 years and older): I have read this document or it was read to me. I have been encouraged to ask questions and all my questions were answered. I agree to take part in this research study.

Research Participant Signature	Date	Time AM/PM (circle one)

RESEARCHER/DESIGNEE STATEMENT: I have explained the research to the participant and his/her parent(s) or legal guardian(s). The research participant and parent(s)/guardian(s) were encouraged to ask questions and all questions were answered to their satisfaction. A copy of this form has been given to the participant or his/her representative.

Researcher/Designee Signature	Date	Time AM/PM (circle one)

Print Name

Interpreter (if needed)	Date	Time AM/PM

RESEARCH PARTICIPANT ADVOCATE STATEMENT: I observed the informed consent process. The research study, intervention/observation, risks, benefits, and alternatives were presented to the research participant and/or legal guardian(s). They were encouraged to ask questions, and research team members answered all their questions. The participant /parent(s) indicated that they: 1) understood the information presented; and 2) voluntarily consented /agreed to take part in the research.

_____	_____	_____
Research Participant Advocate	Date	Time AM/PM (circle one)

PLEASE FAX CONSENT FORM TO CLINICAL TRIALS OPERATIONS
SCAN and EMAIL to: protocoleligibilityoffice@stjude.org or FAX to: (901) 595-6265