CHILDREN'S ONCOLOGY GROUP

The world's childhood cancer experts

NCI Pediatric Early Phase Clinical Trials Network

A program funded by the National Cancer Institute of the National Institutes of Health

Pediatric Early Phase Clinical Trial Network (PEP-CTN) and Developmental Therapeutics (DVL) Chair
Brenda J. Weigel, M.D.
weige007@umn.edu

PEP-CTN and Developmental Therapeutics (DVL) Vice Chair
Elizabeth Fox, M.D.
elizabeth.fox@stjude.org

PEP-CTN Operations Data & Statistics Center Director
Thalia Beeles, MPH
tbeeles@childrensoncologygroup.org

PEP-CTN Statistician
Charles G. Minard, Ph.D.
minard@bcm.edu

PEP-CTN and DVL Chair's Office
University of Minnesota/ Masonic Cancer Center
Masonic Children's Hospital
420 Delaware Street, SE
MMC 366
Minneapolis, MN 55455

P 612 626 5501
F 612 624 3913

Children's Oncology Group Group Chair
Douglas S. Hawkins, MD
Seattle Children's Research Institute
Mailstop: JMB 9
1900 9th Avenue
Seattle, WA 98101
P 206 884 1107
doug.hawkins@seattlechildrens.org

PEP-CTN Operations Data & Statistics Center
800 Royal Oaks Drive
Suite 210
Monrovia, CA 91016

P 626 241 1500
F 626 445 4334

A National Cancer Institute-supported member group of the National Clinical Trials Network

April 15, 2022

Martha Kruhm, MS, RAC
Head, Protocol and Information Office
Operations and Informatics Branch
Cancer Therapy Evaluation Program
Division of Cancer Treatment and Diagnosis
National Cancer Institute
Executive Plaza North Room 730
Bethesda, MD 20892

Dear Ms. Kruhm,

Please find attached Amendment #1 to **PEPN2112**, *A Phase 1/2 Study of BAY 1895344 (elimusertib, IND#152153, NSC#810486) in Pediatric Patients with Relapsed or Refractory Solid Tumors.*

The primary purpose of this amendment is to provide clarifications on eligibility criteria. This amendment also provides updates to sample processing and shipping instructions.

Administrative changes have been made; specific changes are detailed in the Summary of Changes table below. Minor administrative updates (such as the correction of typographical errors, spelling, or updates to the numbers of referenced sections) are tracked in the protocol but not specified.

Please contact us if you have any further questions.

Sincerely,

Samuel Baird, MPH, Protocol Coordinator (for)

Michael Ortiz, M.D., **PEPN2112** Study Chair, and
Brenda Weigel, M.D., PEP-CTN Chair
Elizabeth Fox, M.D., PEP-CTN Vice Chair.

SUMMARY OF CHANGES: CONSENT

In accordance with the above discussion, the following specific revisions have been made to the protocol. Additions are in **boldfaced** font and deletions in strikethrough font.

#	Section	Comments
1.	Throughout	Updated version date.
2.	Overview	• Emphasized that relapsed or refractory cancer is necessary for eligibility on Part A • Replaced the word "~~mutated~~" with "**changed**" that is more appropriate for lay-language.
3.	Additional Required Research Study Tests; Risks associated with required study tests	• Clarified that there are **12** required PK samples for Part A and not ~~14~~ • Clarified quantity of blood collected for PK samples in Part A is for **24**mL and not ~~28~~. • Clarified the required knee X-rays, to provide better information to patients and to be consistent with the protocol. • Removed sentence stating that all required research studies will be paid by through the study, as Knee X-rays will no longer be compensated for by the study but be billable through insurance. • Under WGS, ALT, TERT and C-circles, replaced the word "~~mutated~~" and "~~mutations~~" with "**changed**" that is more appropriate for lay-language.
4.	Additional Optional Research Study Tests	Clarified the amount of blood needed for ctDNA testing, to be consistent with the protocol.
5.	What are the Costs?	Removed language stating that Knee X-rays will be covered by the research study, based on updated coverage analysis, and replaced with language to clarify that Knee X-rays will be billable to the patient and/or insurer.

CHILDREN'S ONCOLOGY GROUP
NCI Pediatric Early Phase Clinical Trials Network
A program funded by the National Cancer Institute of the National Institutes of Health

This model informed consent form has been reviewed by the DCT/NCI and is the official consent document for this study. Institutions must use the sections of this document that are in bold type in their entirety. Editorial changes to these sections may be made as long as they do not change information or intent. If the local IRB insists on making deletions or more substantive modifications to any of the sections in bold type, they must be justified in writing by the investigator at the time of the institutional audit.

SAMPLE RESEARCH INFORMED CONSENT/PARENTAL PERMISSION FORM

PEPN2112, A Phase 1/ 2 Study of BAY 1895344 (elimusertib, IND#152153, NSC#810486) in Pediatric Patients with Relapsed or Refractory Solid Tumors

A Study to See if BAY 1895344 (elimusertib) is Safe for Patients with Relapsed or Refractory Solid Tumors

If you are a parent or legal guardian of a child who may take part in this study, permission from you is required. The assent (agreement) of your child may also be required. When we say "you" in this consent form, we mean you or your child; "we" means the doctors and other staff.

Overview

You are being asked to take part in this research study because you are:

<u>For Patients on Part A:</u>
You are at least 1 year of age and less than 18 years of age, have been diagnosed with an Ewing Sarcoma, Alveolar Rhabdomyosarcoma, or other solid tumor originating outside of the brain or spinal cord (non-CNS primary) including lymphoma that exhibits a specific DNA Damage Response (DDR) mutation. DDR is a process your body takes to repair DNA, and when this process is stopped, or changed, your body can no longer fix damaged DNA. This allows cancer to grow throughout your body. Additionally, your cancer must have either come back ("relapsed") or does not respond to therapy ("is refractory") to be eligible for Part A.

<u>For Patients in Part B:</u>

- You are at least 1 year of age and less than 31 years of age and have been diagnosed with an Ewing Sarcoma or Alveolar Rhabdomyosarcoma that has relapsed or is refractory.
- Or, you are at least 1 year and less than 22 years of age and have been diagnosed with another non-CNS primary solid tumor including lymphoma that exhibits a specific DNA Damage Response (DDR) mutation that has relapsed or is refractory.

Taking part in this study is voluntary. You may choose not to be in this study. If you decide not to be in this study, you will not be penalized, and you will not lose any benefits to which you are entitled. You will still receive medical care.

The overall goals of this study are:

- **This is called a Phase 1/2 study because the goal is to find the highest dose of BAY 1895344 (elimusertib) that can be given without causing severe side effects;**
- **To learn what kind of side effects BAY 1895344 (elimusertib) may cause;**
- **To learn more about the pharmacology (how your body handles the drug) of BAY 1895344 (elimusertib);**
- **To determine whether BAY 1895344 (elimusertib) is helpful in treating patients with relapsed and refractory solid tumors**

In Part A of the study, if you are less than 18 years of age you will receive a dose of BAY 1895344 (elimusertib) that is similar to the recommended dose in adults with cancer, but the dose will be based on your body size. If the starting dose has side effects that are severe or not acceptable, your dose will be decreased, and future children and adolescents may start the drug at a lower dose. Therefore, if you are enrolled when the study initially begins to enroll children and adolescents, you may receive a higher dose than those who are enrolled later. If you are enrolled in this study at a higher dose you may be more likely to have side effects. If you have bad side effects, your dose may be decreased. Two different doses of BAY 1895344 (elimusertib) may be studied in children and adolescents younger than 18 years of age.

In Part B of the study, if you are at least 18 years of age you will receive the same dose that was recommended to adults. If you are less than 18 years of age you will receive the dose of BAY 1895344 (elimusertib) that was found during Part A of the study to be safe in children and adolescents less than 18 years. If the dose that you start in Cycle 1 has side effects that are severe or not acceptable, your dose may be decreased during Cycle 1 or later cycles.

All people who receive cancer treatment are at risk of having side effects. In addition to killing tumor cells, cancer therapy can damage normal tissue and produce side effects.

This study uses the investigational drug BAY 1895344 (elimusertib). Common side effects of this drug are anemia, nausea, tiredness, bruising, bleeding, and infection. Some less common but notable side effects are diarrhea, vomiting, loss of appetite and sensitivity to sunlight which may lead to increased risk of sunburn. It is very important that you use sun protection on days BAY 1895344 (elimusertib) is given and for 3 days after receiving BAY 1895344 (elimusertib). This includes applying sunblock (at least SPF 30+), wearing long sleeves, wearing a hat and sunglasses, and avoiding direct and indirect sunlight (including sunlight through a window). The full list of risks for BAY 1895344 (elimusertib) are available in Possible Side Effects of BAY 1895344 (elimusertib). You can ask your study doctor questions about side effects at any time.

If your bones are not fully mature, BAY 1895344 (elimusertib) may increase your risk of the area near the ends of your long bones growing excess tissue. We will be monitoring for this by taking X-rays of the affected knees throughout the study, until those areas have stopped growing tissue and have closed. If excess tissue is found with these X-rays, a more detailed image of the knee will be obtained with the use of an MRI. Where an X-ray can show us your bones, MRIs can show us your bones, muscles and other tissues. This will help confirm if there

are changes in the bone or tissue around the knees including extra tissue or widening of the part of the bone where bone growth occurs and whether or not therapy on BAY 1895344 (elimusertib) should be stopped.

We hope that this study will help you personally, but we do not know if it will. The potential benefits to you associated with participation in this study are described in the section Are there benefits to taking part in the study?

You have a choice between another treatment for your relapsed or refractory solid tumor and this clinical trial. The rest of this form provides detailed information about the study and what to expect should you decide to participate.

Why am I being invited to take part in this study?

You are being asked to take part in this research study because you are in one of the groups of patients described below.

For Patients on Part A:
You are at least 1 year of age and less than 18 years of age, have been diagnosed with an Ewing Sarcoma, Alveolar Rhabdomyosarcoma, or other solid tumor originating outside of the brain or spinal cord (non-CNS primary) including lymphoma that exhibits a specific DNA Damage Response (DDR) mutation, and has either relapsed or is refractory to other treatments.

For Patients in Part B:

- You are at least 1 year of age and less than 31 years of age and have been diagnosed with an Ewing Sarcoma or Alveolar Rhabdomyosarcoma that has relapsed or is refractory to other treatments.

- Or, you are at least 1 year and less than 22 years of age and have been diagnosed with another non-CNS primary solid tumor including lymphoma that exhibits a DDR mutation that has relapsed or is refractory to other treatments.

This study is called a clinical trial. A clinical trial is a research study involving treatment of a disease in human patients. This study is being carried out by the Children's Oncology Group (COG) Pediatric Early Phase Clinical Trial Network (PEP-CTN). COG is an international research group that consists of more than 200 hospitals that treat children with cancer in the United States, Canada, Australia, New Zealand, and Switzerland. The PEP-CTN is the group within COG that consists of 21 hospitals based in the United States, and participation in this study will be limited to these hospitals for Part A, but up to an additional 21 sites based in the United States, Canada and Australia may be added for Part B.

It is common to enroll children and adolescents with cancer in a clinical trial that seeks to improve cancer treatment over time. Clinical trials include only people who choose to take part. You have a choice between another treatment for relapsed or refractory cancer and this clinical trial.

Please take your time to make your decision. You may want to discuss it with your friends and family. We encourage parents to include their child in the discussion and decision to the extent that the child is able to understand and take part.

What is the current standard of treatment for this disease?

We are asking if you want to participate in this study because there is not a standard treatment for your cancer at this time.

Why is this study being done?

BAY 1895344 (elimusertib) is experimental because it has not been proven to work in a situation like yours. We are using BAY 1895344 (elimusertib) because it seems to work against cancer in test tubes and animals. BAY 1895344 (elimusertib) has been used in adults, but there is a lot that we do not know about BAY 1895344 (elimusertib).

This is a Phase 1/2 study because the goal is to find the highest dose of BAY 1895344 (elimusertib) that we can give safely. We are testing new experimental drugs such as BAY 1895344 (elimusertib) in the hopes of finding a treatment that may be effective against cancer that has come back, or that has not responded to standard therapy. This study looks at how well BAY 1895344 (elimusertib) works when given to children and young adults with refractory or recurrent solid tumors and lymphomas which contain specific genetic changes. BAY 1895344 (elimusertib) is experimental because it has not been proven to work in a situation like yours. We are using BAY 1895344 (elimusertib) because it seems to work against cancer in test tubes and animal models. BAY 1895344 (elimusertib) has been used in adults but there is a lot that we do not know about it yet in children.

The overall goals of this study are:

- **To find the highest dose of BAY 1895344 (elimusertib) that can be given to patients less than 18 years of age without causing severe side effects;**
- **To learn what kind of side effects BAY 1895344 (elimusertib) may cause;**
- **To learn more about the pharmacology (how your body handles the drug) of BAY 1895344 (elimusertib);**
- **To determine whether BAY 1895344 (elimusertib) is helpful in treating patients with relapsed or refractory solid tumors.**

What will happen on this study that is research?

The treatment involves the use of a drug called BAY 1895344 (elimusertib). The treatment on this study can continue for up to about 24 months. It is divided into 2 phases of therapy with the first phase being called Part A and the second phase being called Part B. You will either participate in Part A or Part B of the study, depending on your age and diagnosis, as described in "Why am I being invited to take part in this study?"

Part A:
You are at least 1 year of age and less than 18 years of age, have been diagnosed with Ewing Sarcoma, Alveolar Rhabdomyosarcoma, or any non-CNS primary solid tumor including lymphoma that exhibits a specific DDR mutation, and your cancer is either relapsed or is refractory, and is either evaluable or measurable.

The dose for the first children enrolled on the study will be based on the dose and side effects seen in adults. Between 2 and 6 children will receive BAY 1895344 (elimusertib) at this dose. If the side effects are too severe, the next group of children will receive a lower dose. If the side effects are not too severe, then the lower dose level will not be tested.

If you are enrolled early in this study you may receive a higher dose than those who are enrolled later. If you are enrolled in this study at a higher dose you may be more likely to have side effects. If you have bad side effects, your dose may be decreased. Two different doses of BAY 1895344 (elimusertib) may be studied.

Part B:
You are being asked to take part in this research study because you are at least 1 year of age and less than 31 years of age and have been diagnosed with Ewing Sarcoma or Alveolar Rhabdomyosarcoma, or you are at least 1 year of age and less than 22 years of age and have been diagnosed with any non-CNS primary solid tumor including lymphoma that exhibits a specific DDR mutation, and your tumor has either relapsed or is refractory, and is measurable.

BAY 1895344 (elimusertib) is given by mouth two times a day, and the tablets must be swallowed whole. BAY 1895344 (elimusertib) should be taken on an empty stomach 1 hour before or 2 hours after food. If you vomit after taking the medication, the dose should not be repeated.

You will be given specific instructions regarding how to take these medicines. You will also be given a medication diary to fill out at home each time these oral medicines are taken. Use the diary to record the date and time you take the drug, and any side effects you may experience. Also record in the diary other medications and/or supplements you are taking and whether you vomited or missed a dose. This diary should be returned to the clinic, along with the medication bottle (even if it is empty) weekly during Cycle 1 and then at the end of every cycle. This will help us know how much of the drug you take and how it made you feel.

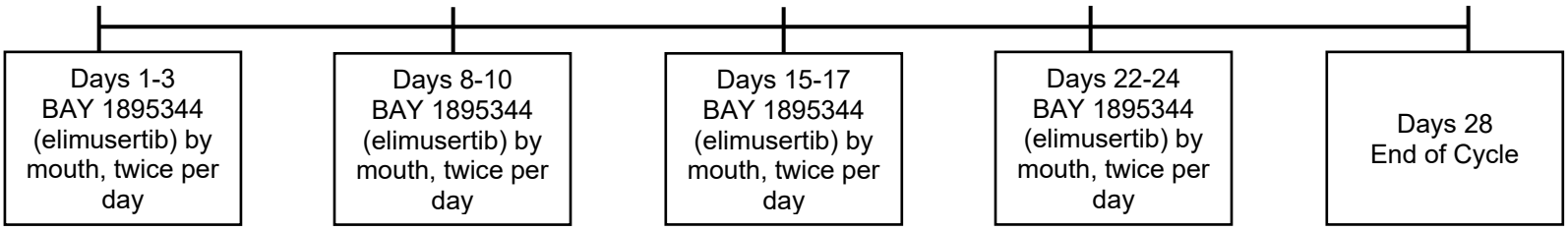
Blood will be drawn to perform tests to see how your body handles the drug and to monitor for side effects. Imaging studies will be done to monitor the tumor.

Treatment with BAY 1895344 (elimusertib) is experimental and is described below.

Summary of Study Treatments

If the exams, tests, and procedures show that you can be in the study, and you choose to take part, BAY 1895344 (elimusertib) will be given by mouth twice a day for 3 days straight, followed by 4 days without taking the drug. This will be repeated over the course of a 28-day period. This entire 28-day period is called a cycle. You may continue to receive BAY 1895344 (elimusertib) for up to 26 cycles, which will last about 24 months, unless you develop serious side effects or your tumor worsens.

Diagram of Treatment for a single cycle



Treatment Tables

The treatment described below is the full study treatment for a single cycle of BAY 1895344 (elimusertib).

Method for Giving Drug

- **PO** - Drug is given by tablet swallowed through the mouth.

Treatment with Experimental Drug

Drug	How the drug will be given	Days
BAY 1895344 (elimusertib)	PO tablet* twice daily	1-3; 8-10; 15-17; 22-24

*Tablet must be swallowed whole

Additional Required Research Study Tests

We would also like to do some extra tests called pharmacokinetic studies and correlative studies. Pharmacokinetic studies help us determine how much of the BAY 1895344 (elimusertib) is in your blood. Correlative studies help us evaluate the effects BAY 1895344 (elimusertib) has on your body and on the tumor. These tests will help us learn more about BAY 1895344 (elimusertib) and may help patients who receive this drug in the future. The information learned from these studies would not change the way you are treated, and the results of these tests will not be given to you.

The following tests will be done because you are part of this study. If you were not in the study you would probably not have these tests.

Pharmacokinetic Studies (Required):
Pharmacokinetic studies help us determine how your body processes and gets rid of a drug. We want to learn more about how children and young adults process the drug BAY 1895344 (elimusertib). Some information already exists on how adults handle the drug, but less information exists for children and adolescents.

For patients enrolled on Part A of the study, a total of 12 blood samples will be collected for the pharmacokinetic tests. These samples will be taken before the drug begins on Cycle 1, day 1 and then again at 1 hour, 2 hours, 4 hours, 8 hours after taking BAY 1895344 (elimusertib). Additionally, samples will be taken before the drug begins on Cycle 1, day 3 and again, 1 hour after taking BAY 1895344 (elimusertib). Samples will also be collected before the drug begins on Cycle 1, day 10 and then again at 1 hour, 2 hours, 4 hours, 8 hours after taking BAY 1895344 (elimusertib).

For patients enrolled on Part B of the study, a total of 6 blood samples will be collected for the pharmacokinetic tests. These samples will be taken before the drug begins on Cycle 1, day 1 and 1 hour after taking BAY 1895344 (elimusertib). In the same fashion, an additional 2 samples will be collected for Cycle 1, day 3 and for Cycle 1, day 10.

Each sample is about 2 mL or roughly ½ teaspoon for each sample. In total, about 24 mL or 5 teaspoons of blood will be collected if you are participating in Part A, and 12 mL, or 3 teaspoons of blood if you are participating in Part B. The information learned from this research will not change the way you are treated, and the results of these tests will not be returned to you.

Knee X-Rays (Required):
BAY 1895344 (elimusertib) is associated with a risk of growing excess tissue in the growth plates of bones, which are the areas where bones grow. If you are at an age to continue to grow, you will receive a knee X-ray, before starting therapy on BAY 1895344 (elimusertib) to determine if your bones are still growing.

If the X-ray shows that your leg bones are still growing, we will share this information with you and continue obtaining knee X-rays to ensure that excess tissue does not begin to appear within the bones around the knees. These additional X-rays will be obtained after the first cycle of therapy, then every 3 cycles and at the end of the study treatment, until it is determined that your leg bones have completed growing.

If after receiving BAY 1895344 (elismusertib), excess tissue is shown to be growing around your knees in these X-rays, you may have more frequent X-rays taken as determined by your doctor to monitor the growth. A Magnetic Resonance Image (MRI) may also be obtained that will allow your doctor to view the growth in greater detail. If your doctor is concerned about the growth after your MRI, your doctor may make the decision to discontinue your treatment with BAY 1895344 (elismusertib) and you may be removed from the study.

Archival Tumor Tissue for Immunohistochemistry for Ataxia Telangiectasia Mutated (ATM) (Required):
ATM and ATR are two genes that are responsible for repairing damage to your DNA within your cells. ATM can be turned off just within tumor cells, helping the spread of cancer. Since DNA needs to be repaired in all cells, tumor cells which have ATM turned off are particularly dependent upon ATR to repair their DNA. BAY 1895344 (elimusertib) blocks ATR so your normal cells will still be able to repair their DNA with ATM but the cancer cells, which already have ATM turned

off, will not be able to effectively repair their DNA and should therefore be able to be killed more easily. By determining if you have ATM present in your tumor tissue before you begin BAY 1895344 (elimusertib), we can better understand if BAY 1895344 (elimusertib) is effective in ATM-deficient childhood tumors.

As part of your regular care, your doctor may have removed some tumor tissue to see if you have cancer and/or to treat a tumor that has come back after treatment. This is known as archival tumor tissue. We would like to keep some of the tissue that is left over to do special tests, such as the one described above, that may indicate how BAY 1895344 (elimusertib) is working to treat your tumor. The tissue will be sent directly to the lab for testing and will not be sold. There will be no biopsy procedure done to collect this sample unless it will already be collected for routine clinical care.

The information learned from this research will not change the way you are treated, and the results of these tests will not be returned to you. The research done with your tissue may help us learn more about BAY 1895344 (elimusertib) but may help children and young adults who receive this drug in the future.

Central Review (Required):
Copies of the scans used to diagnose the cancer and the pathology reports to diagnose your cancer will be sent to a central review center to help confirm findings. The results of these reviews will not be returned to you.

Additional Optional Research Study Tests
We would also like to do some extra, optional tests called correlative and pharmacodynamic studies. Correlative and pharmacodynamic studies help us evaluate the effect of BAY 1895344 (elimusertib) on your body and on the tumor. These tests will help us learn more about BAY 1895344 (elimusertib) and may help children who receive this drug in the future.

The information learned would not change the way you are treated, and the results of these tests will not be given to you. You do not have to do these tests if you do not want to. If you choose to not do these tests, you can still participate in the study. At the end of this consent form, there is a place to record your decision about taking part in each optional test.

The study will cover the costs of the optional research tests.

Tumor Whole Genome Sequencing (WGS) and Alternative Lengthening of Telomeres (ALT) for Telomerase reverse transcriptase (TERT) and C-Circles (Optional):
WGS gives us a clear snapshot of how your DNA has changed to allow cancer to grow inside of your body. Understanding how your DNA has changed will allow us to determine if certain changes may cause BAY 1895344 (elimusertib) to work more effectively.

One way that cancers are able to continue to grow beyond their normal ability is through increasing the length of their telomeres, the protective caps at the ends of DNA. Telomeres can be extended either through a process called ALT as well as by activating a gene called TERT. The ALT process creates abnormal DNA structures called C-circles. We believe that tumors which use ALT to extend their telomeres may make their tumor more sensitive to BAY 1895344 (elimusertib) and so we would like to study this, as well as TERT, within your tumor.

As part of your regular care, your doctor may have removed some archival tumor tissue either at your diagnosis or when your cancer relapsed. If any of this archival tissue is left over and no

longer needed for your medical care, we would like to use it for this optional test. If there is additional frozen tumor available after the WGS test is completed, we would like to use the remaining tumor tissue to look for C-circles and TERT in your tumor.

We would also like to collect tumor tissue after you complete therapy on BAY 1895344 (elimusertib). In total, we are asking for up to three different samples, where one is provided at diagnosis and another at relapse before you start this study and one additional sample given only if you have surgery within 30 days after you complete therapy on BAY 1895344 (elimusertib).

PGBD5 and R-Loops (Optional):
Some childhood cancers are found to express a gene called PGBD5 that helps spread cancer by damaging your DNA. R-loops are abnormal strands of DNA which can form from the rapid spread of cancer. We anticipate that tumors which reveal the presence of PBGD5 or R-loops will be more susceptible to BAY 1895344 (elimusertib).

We would also like to use archival tumor tissue for this optional test, meaning that we are asking for tissue that has already been removed and is no longer needed for your medical care.

pKAP1, pH2AX and pATR for Pharmacodynamics (Optional):
The presence of the genes pKAP1, pH2AX and pATR indicate DNA damage and would help us determine the pharmacodynamics of BAY 1895344 (elimusertib). The pharmacodynamics determine how BAY 1895344 (elimusertib) works within your body, by affecting the presence of these genes in your tumor tissue. These tests would be performed before you start using BAY 1895344 (elimusertib), on archival tumor tissue, and after you stop using BAY 1895344 (elimusertib) if any additional tumor samples are available within 30 days of completing the study. There will be no biopsy procedure done to collect this sample unless it will already be collected for routine clinical care.

Alternative Lengthening of Telomeres (ALT) in circulating tumor DNA (ctDNA) (Optional):
We would like to know whether we can detect ALT within ctDNA. ctDNA are fragments of the cancer's DNA that are released into the blood as it is spread throughout the body. We are asking for your permission to take an additional 10mL or 2 teaspoons of blood for this test. This would be before you start therapy on BAY 1895344 (elimusertib), at the time of enrollment.

Additional Blood for Pharmacokinetics (Optional):
We would like to collect additional blood to more accurately examine the pharmacokinetics of BAY 1895344 (elimusertib). This blood would be collected on Cycle 1, days 1 and 10, 12 hours after your dose of BAY 1895344 (elimusertib) on those days. This would require more time in the clinic and that is why we are giving you the option of providing us these additional samples.

Each sample is about 2 mL or roughly ½ teaspoon of blood.

Archival Tumor Tissue Specimen Biobanking (Optional):
We would like to take some archival tumor tissue that has already been collected for future research. This is called "specimen banking" or "tissue banking." A tissue bank is a lab where specimens (such as tumor, blood or bone marrow) are kept for use in future research studies.

You do not have to provide these samples if you do not want to. You can still be in the study if you do not want to provide these samples. At the end of this consent form, there is a place to record your decision about taking part in banking.

What side effects or risks can I expect from being in the study?

Treatment Risks
All people who receive cancer treatment are at risk of having side effects. In addition to killing tumor cells, cancer therapy can damage normal tissue and produce side effects.

The risks of BAY 1895344 (elimusertib) given are listed in Possible Side Effects of BAY 1895344 (elimusertib).

Risks of Study
The use of BAY 1895344 (elimusertib) instead of other treatments may cause more complications.

BAY 1895344 (elimusertib) treatment that is being studied could be less effective than other treatments.

You may lose time at school, work or home and spend more time in the hospital or doctor's office than usual. You may be asked sensitive or private questions which you normally do not discuss.

BAY 1895344 (elimusertib) may affect how different parts of your body work such as your liver, kidneys, heart, and blood. The study doctor will be testing your blood and will let you know if changes occur that may affect your health.

There is also a risk that you could have side effects from the study drugs/study approach. Here are important points about side effects:

- The study doctors do not know who will or will not have side effects.
- Some side effects may go away soon, some may last a long time, or some may never go away.
- Some side effects may interfere with your ability to have children.
- Some side effects may be serious and may even result in death.

You can ask your study doctor questions about side effects at any time.

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

- Tell the study doctor if you notice or feel anything different so they can see if you are having a side effect.
- The study doctor may be able to treat some side effects.
- The study doctor may adjust the study drugs to try to reduce side effects.
- The study doctor will provide you with information about other drugs you may need to avoid while receiving the study drugs.

This study uses the investigational drug BAY 1895344 (elimusertib). Common side effects of this drug are anemia, nausea, tiredness, bruising, bleeding and infection. Some less common but notable side effects are diarrhea, vomiting, loss of appetite and sensitivity to sunlight which may lead to increased risk of sunburn. It is very important that you use sun protection on days BAY 1895344 (elimusertib) is given and for 3 days after receiving BAY 1895344 (elimusertib).

This includes applying sunblock (at least SPF 30+), wearing long sleeves, wearing a hat and sunglasses, and avoiding direct and indirect sunlight (including sunlight through a window).

If your bones are not fully mature, BAY 1895344 (elimusertib) may increase your risk of the area near the ends of your long bones growing excess tissue. We will be monitoring for this throughout the study by taking X-rays of the affected knees, until those areas have stopped growing tissue and have closed.

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

Possible Side Effects of BAY 1895344 (elimusertib)

COMMON, SOME MAY BE SERIOUS In 100 people receiving BAY 1895344 (elimusertib), more than 20 and up to 100 may have:
• Anemia which may require blood transfusion • Nausea • Tiredness • Bruising, bleeding • Infection, especially when white blood cell count is low
OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving BAY 1895344 (elimusertib), from 4 to 20 may have:
• Diarrhea, vomiting • Loss of appetite
RARE, AND SERIOUS In 100 people receiving BAY 1895344 (elimusertib), 3 or fewer may have:
• None

In addition to the risks described above, there may be unknown risks, or risks that we did not anticipate, associated with being in this study.

Risks associated with required study tests

For the required tests that were described above that include the pharmacokinetic studies and knee X-rays, there are additional risks that you should be aware of.

Pharmacokinetic studies:

We will need to take a small amount of blood from one of your arm's veins. To do this, we will need to use a very-small needle to poke one of your veins and take the small amounts of blood. However, you may experience some pain and discomfort when the needle goes in and out of your arm to get the blood needed for these tests. In general, these tests will take about 5 minutes to complete.

Your doctor may recommend that you get a special kind of IV called a "central line" that may be used to collect these samples. This is a kind of IV placed into a big vein in your body, usually in the chest, that can stay in for a long time. The risks connected with central lines will be explained to you and all of your questions will be answered. If you are to have a central line inserted, you will be given a separate informed consent document to read and sign for this

procedure. A description of the types of central lines is in the COG Family Handbook for Children with Cancer.

Knee X-rays:
If you are still growing, we will take X-rays of your knees to monitor for tissue growth or growth widening associated with the use of BAY 1895344. Excess tissue or widening of the growth plate does not usually cause any symptoms. Rarely, pain, difficulty walking, or inability for the bone to continue to grow can occur, if the tissue growth is not detected. This X-ray is a safe and painless test that uses a small amount of radiation to take a picture of the lower leg. This test typically takes about 15 minutes to complete.

Reproductive risks
Women should not become pregnant and men should not father a baby while on this study because the drug(s) in this study can be bad for an unborn baby. If you or your partner can get pregnant, it is important for you to use birth control or not have sex while on this study and for 3 months + 2 days for men and 6 months + 2 days for women after the last dose of BAY 1895344 (elimusertib). Check with your study doctor about what kind of birth control methods to use and how long to use them. Some birth control methods might not be approved for use in this study. If you are a woman and become pregnant or suspect you are pregnant while participating in this study, please inform your treating physician immediately. Women should not breastfeed a baby while on this study and until 4 months after stopping study treatment.

Are there benefits to taking part in the study?

The potential benefit of the treatment with BAY 1895344 (elimusertib) 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. However, 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.

What other options are there?

Instead of being in this study, you have these options:

- **Getting treatment for your cancer without being in a study.**
- **Taking part in another study.**
- **Getting comfort care, also called palliative care. This type of care helps reduce pain, tiredness, appetite problems and other problems caused by the cancer. It does not treat the cancer directly. Instead it tries to improve how you feel. Comfort care tries to keep you as active and comfortable as possible.**

Please talk to your doctor about these and other options.

How many people will take part in the study?

The total number of people enrolled on this study is expected to be 90. This is divided among parts A and B of the study.

Part A:
There will be a minimum of 4 people, up to a maximum of 23.

Part B:
There will be a minimum of 20 people and a maximum of 67.

How long is the study?

Although it is difficult to predict which, if any, child may benefit, it is possible that people in this clinical trial may receive treatment on this study for up to 2 years.

We would like to continue to find out about your health for about 5 years after you enter this study. By keeping in touch with you for a while after you complete treatment, we can better understand the long-term effects of the study treatments.

You can stop taking part in the study at any time. However, if you decide to stop participating in the study, we encourage you to talk to the study doctor and your regular doctor first. They will help you stop safely.

Your doctor or the study doctor may decide to take you off this study:
- if he/she believes that it is in your best interest
- if your disease comes back during treatment
- if you experience side effects from the treatment that are considered too severe
- if new information becomes available that shows that another treatment would be better for you
- If the tumor gets worse

What about privacy?

We will do our best to make sure that the personal information in your medical record will be kept private. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used. The Children's Oncology Group has a privacy permit to help protect your records if there is a court case. However, some of your medical information may be given out if required by law. If this should happen, the Children's Oncology Group will do their best to make sure that any information that goes out to others will not identify who you are. Information about this Certificate of Confidentiality is included in **Attachment 2**.

Organizations that may look at and/or copy your research or medical records for research, quality assurance and data analysis include groups such as:

- **Children's Oncology Group and research partners**
- **Representatives of the National Cancer Institute (NCI), Food and Drug Administration (FDA), and other U.S. and international governmental regulatory agencies involved in overseeing research.**
- **The Institutional Review Board of this hospital**
- **Pediatric Central Institutional Review Board (CIRB) of the National Cancer Institute**
- **The study sponsor and any drug company supporting the study or their designated reviewers now or in the future.**

What are the costs?

Taking part in this study may lead to added costs to you or your insurance company. There are no plans for the study to pay for medical treatment. Please ask about any expected added costs or insurance problems. Staff will be able to assist you with this.

In the case of injury or illness resulting from this study, emergency medical treatment is available but will be provided at the usual charge. No funds have been set aside to compensate you in the event of injury. However, by signing this form, you are not giving up any legal rights to seek to obtain compensation for injury.

You or your insurance company will be charged for continuing medical care and/or hospitalization.

Participants will not be charged for collection of blood or tumor material performed solely for research. However, the study does not cover the cost of getting the required knee X-rays, so you or your insurance company may have to pay for this.

The NCI will supply the BAY 1895344 (elimusertib) at no charge while you take part in this study. The NCI does not cover the cost of getting the BAY 1895344 (elimusertib) ready and giving it to you, so you or your insurance company may have to pay for this.

Even though it probably won't happen, it is possible that the manufacturer may not continue to provide BAY 1895344 (elimusertib) to the NCI for some reason. If this does happen, other possible options are:

- You might be able to get the BAY 1895344 (elimusertib) from the manufacturer or your pharmacy but you or your insurance company may have to pay for it.

- If there is no BAY 1895344 (elimusertib) available at all, no one will be able to get more and the study would close.

If a problem with getting BAY 1895344 (elimusertib) occurs, your study doctor will talk to you about these options.

If you choose to enroll on this study, this institution will receive some money from the Children's Oncology Group to do the research.

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's Web site at http://www.cancer.gov/clinicaltrials/learningabout.

You will not be paid for taking part in this study. The research may lead to new tests, drugs, or other products for sale. If it does, you will not get any payment.

What are my rights as a participant?

Taking part in this study is voluntary. You may choose not to be in this study. If you decide not to be in this study, you will not be penalized and you will not lose any benefits to which you are entitled. You will still receive medical care.

You can decide to stop being in the study at any time. Leaving the study will not result in any penalty or loss of benefits to which you are entitled. Your doctor will still take care of you.

We will tell you about new information that may affect your health, welfare, or willingness to stay in this study. A committee outside of COG closely monitors study reports and notifies COG if changes must be made to the study. Members of COG meet twice a year to discuss results of treatment and to plan new treatments.

During your follow-up visits after treatment, you may ask to be given a summary of the study results, which will only be available after the study is fully completed. A summary of the study results will also be posted on the Children's Oncology Group website (http://www.childrensoncologygroup.org/). To receive the results, you may either (1) go to the COG website to check if results are available or (2) register your information with the COG on its web site and have an email sent to you when the results are available. Your pediatric oncology team from your hospital can give you additional instructions on how to do this. Please note, that the summary of results may not be available until several years after treatment for all people on the study is completed, and not only when you complete treatment.

Whom do I call if I have questions or problems?

For questions about the study or if you have a research related problem or if you think you have been injured in this study, you may contact Dr. *XXXX* or your doctor at *XXXX*.

If you have any questions about your rights as a research participant or any problems that you feel you cannot discuss with the investigators, you may call *XXXX* Institutional Review Board (IRB) Administrator at *XXXX*.

If you have any questions or concerns that you feel you would like to discuss with someone who is not on the research team, you may also call the Patient Advocate at *XXXX*.

Where can I get more information?

The COG Family Handbook for Children with Cancer has information about specific cancers, tests, treatment side effects and their management, adjusting to cancer, and resources. Your doctor can get you this Handbook, or you can get it at https://www.childrensoncologygroup.org/index.php/cog-family-handbook.

Visit the NCI's Web site at http://www.cancer.gov.

If you are in the United States, you may call the NCI's *Cancer Information Service* at: 1-800-4-CANCER (1-800-422-6237).

Information about long term follow-up after cancer treatment can be found at: http://www.survivorshipguidelines.org/.

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 will get a copy of this form. You may also ask for a copy of the protocol (full study plan).

Specimens for additional optional research tests

The choice to let us use specimens for research is up to you. No matter what you decide to do, it will not affect your care. You can still be a part of the main study even if you say 'No' to taking part in any of these optional research studies.

If you decide that your specimens can be used for research, some of your genetic and health information may be placed in central databases for researchers to use. The databases will not include your name or contact information.

Generally, hospitals will keep some of your tissue. This tissue may be used to help treat your cancer in the future. There is a small risk that when this tissue sample is submitted to the biobank for this optional sample collection, your tissue could be used up.

If you decide now that your specimens can be used for research and banking, you can change your mind at any time. Just contact us and let us know that you do not want us to use your specimens. Then, any specimens that we have will be destroyed.

If you want to learn more about tissue research with specimens, the NCI website has an information sheet called "Providing Your Tissue For Research: What You Need To Know." This sheet can be found at: https://www.cancer.gov/publications/patient-education/providing-tissue. Please read the information below and think about your choices. After making your decisions, check "Yes" or "No", then add your initials and the date after your answer. If you have any questions, please talk to your doctor or nurse, or call our research review board at the IRB's phone number included in this consent.

1.) *My **tumor tissue** may be sent to a COG laboratory and studied for WGS, ALT for TERT and C-circles*

Yes_____ No_____ _____ / _____
Initials Date

2.) *My **tumor tissue** may be sent to a COG laboratory and studied for pKAP1, pH2AX and pATR for Pharmacodynamics*

Yes_____ No_____ _____ / _____
Initials Date

3.) *My **tumor tissue** may be sent to a COG laboratory and studied for PGBD5 and R-Loops*

Yes_____ No_____ _____ / _____
Initials Date

4.) *My **blood** may be sent to a COG laboratory and studied for ALT in ctDNA.*

Yes_____ No_____ _____ / _____
Initials Date

5.) *My **blood** may be sent to a COG laboratory and studied for Additional PK samples.*

Yes_____ No_____ _____ / _____
Initials Date

Specimens for Optional Biobanking

If you agree to Biobanking, your tumor sample will be stored in the *Biopathology Center at Nationwide Children's Hospital, in a locked location*. The Biopathology Center is supported by the NCI. The samples will be kept until they are used up, unless you request that they be destroyed. Some information from your medical record will also be kept in secure databases at the Biobank and updated from time to time. The information and samples will be kept under a code, not your name.

This is a publicly funded study. Samples from publicly funded studies are required to be shared as broadly as possible. Qualified researchers can submit a request to use the materials stored in the Biobank. The research may be about your type of cancer, about other cancers, or even about conditions unrelated to cancer. A science committee at the Children's Oncology Group, and/or the National Cancer Institute, will review each request. The goal of this is to make more research possible that may improve people's health. Researchers will not be given your name or any other information that could directly identify you. Your sample will not be sold to third parties. Neither you nor your study doctor will be notified when research will be conducted or given reports or other information about any research that is done using your samples, unless something is discovered that could directly affect your health. If that happens your study doctor will be notified and will decide whether and how to contact you.

Right now, we don't know what research may be done in the future using your samples. This means that:

- You will not be asked if you agree to take part in the specific future research studies using your health information.
- You and your study doctor will not be told when or what type of research will be done.
- You will not get reports or other information about any research that is done using your information.

Unknown future research studies may include sequencing of all or part of your DNA. This is called genomic sequencing. Sequencing allows researchers to identify your genetic code. Changes in your genetic code may just be in your tumor tissue. These are called somatic changes. Changes may also be in your normal tissue and passed down through your family. For example, these genetic changes may be passed down to your children in the same way that eye and hair color are passed down. These are called germline changes. If only tumor tissue is sequenced, we will not know if a genetic change in your tumor is also in your normal tissue. This is why sometimes both normal tissue and tumor tissue are sequenced. This helps researchers understand if a genetic change happened only in your cancer tissue, or in your normal tissue as well.

Some of your genetic and health information may be placed in central databases that may be made available to qualified researchers, along with information from many other people. Information that could directly identify you will not be included.

Even without your name or other identifiers, your genetic information is unique to you. If you agree to Biobanking, there is a risk of a data security breach and that someone could trace the genetic information in a central database back to you. Although this has never happened in real life and we have many safeguards in place to prevent it from happening, the risk may change in the future as people come up with new ways of tracing information. There are laws against the misuse of genetic information, but they may not give full protection. In some cases, misuse of the information could be used to make it harder for you to get or keep a job or insurance.

There can also be risks in learning about your own genetic information. New health information about inherited traits that might affect you or your blood relatives could be found during a study. Sometimes this is upsetting to families or they wish they didn't know the information. We encourage you to discuss this study with your relatives before you decide whether to participate in the Biobanking part.

If you want to learn more about tissue research with banked specimens, the NCI website has an information sheet called "Providing Your Tissue For Research: What You Need To Know." This sheet can be found at: https://www.cancer.gov/publications/patient-education/providing-tissue.

Please read the information below and think about your choices. After making your decisions, check "Yes" or "No", then add your initials and the date after your answer. If you have any questions, please talk to your doctor or nurse, or call our research review board at the IRB's phone number included in this consent.

1) Check YES if you agree to have samples kept (banked) for use in research to learn about, prevent, or treat cancer or other health problems (for example: diabetes, Alzheimer's disease, or heart disease). Check NO if you do not want samples banked.

Yes _____ No _____ _____ / _____
Initials Date

Signature

I have been given a copy of all _____ pages of this form. The form includes 2 attachments.

I have reviewed the information and have had my questions answered.
I agree to take part in this study.

Participant_____Date _____

Parent/Guardian_____Date _____

Parent/Guardian_____Date _____

Physician/PNP obtaining consent_____Date _____

Attachment 1

Study Treatment and Procedures

Methods for Giving Drugs

- **PO** - Drug is given by tablet swallowed through the mouth.

Treatment Tables

The treatment described below is the full study treatment for patients with Ewing Sarcoma, Alveolar Rhabdomyosarcoma, or other solid tumor originating outside of the brain or spinal cord (non-CNS primary) including lymphoma that exhibits a specific DNA Damage Response (DDR) mutation

Drug	How the drug will be given	Days
BAY 1895344 (elimusertib)	PO tablet* twice daily	1-3; 8-10; 15-17; 22-24

*Tablet must be swallowed whole

Standard Tests and Procedures

The following tests and procedures are part of regular cancer care and may be done even if you do not join the study.

- Frequent labs to monitor your blood counts and blood chemistries.
- Urine tests to measure how your kidneys are functioning.
- Pregnancy test for females of childbearing age before treatment begins.
- X-rays and scans to monitor your response to treatment.
- Bone marrow aspiration tests to see if the cancer is responding to treatment. The bone marrow procedure is described in the COG Family Handbook for Children with Cancer.

Attachment 2

Certificate of Confidentiality

The Children's Oncology Group is covered by a Certificate of Confidentiality from the federal government, which will help us protect the privacy of our research subjects. The Certificate protects against the involuntary release of information about subjects collected during the course of our covered studies. The researchers involved in the studies cannot be forced to disclose the identity or any information collected in the study in any legal proceedings at the federal, state, or local level, regardless of whether they are criminal, administrative, or legislative proceedings. However, the subject or the researcher may choose to voluntarily disclose the protected information under certain circumstances. For example, if the subject or his/her guardian requests the release of information in writing, the Certificate does not protect against that voluntary disclosure. Furthermore, federal agencies may review our records under limited circumstances, such as a DHHS request for information for an audit or program evaluation or an FDA request under the Food, Drug and Cosmetics Act.
The Certificate of Confidentiality will not protect against the required reporting by hospital staff of information on suspected child abuse, reportable communicable diseases, and/or possible threat of harm to self or others.