This model informed consent form has been reviewed 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

AINV18P1

A Phase 1 Study of Palbociclib ([redacted]), a CDK 4/6 Inhibitor, in Combination with Chemotherapy in Children with Relapsed Acute Lymphoblastic Leukemia (ALL) or Lymphoblastic Lymphoma (LL)

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 have been diagnosed with acute lymphoblastic leukemia (ALL) or lymphoblastic lymphoma (LL). The ALL or LL has come back after treatment (relapsed), or is not responding to treatment (it 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 goal of this study is to see if this treatment plan will improve the outcome of children with relapsed ALL or LL by increasing the percentage of patients who achieve remission after one month of therapy without causing intolerable side effects.

The treatment involves cancer fighting medicines called chemotherapy plus palbociclib. The treatment on this study takes about 32 days.

The dose 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 palbociclib at each dose. If the side effects are too severe, the next group of children will receive a lower dose. Dosing is done this way because we do not yet know the best dose to use in children. Whatever dose you start at, your dose will not be increased.

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

Common side effects of chemotherapy include nausea, vomiting, hair loss, and fatigue (tiredness). Drugs may be given to try to prevent or decrease nausea and vomiting. Hair loss is usually temporary but very rarely it may be permanent. Some chemotherapy may make people permanently unable to have children. On rare occasions, people can get a second cancer from chemotherapy. This usually happens years after the chemotherapy is finished.

This treatment study uses the investigational drug palbociclib.

The full list of risks for drug palbociclib are available in the section What side effects or risks can I expect from being in the study?

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

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 ALL or LL disease 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 have been diagnosed with ALL or LL that has come back after treatment (relapsed), or is not responding to treatment (it is refractory).

ALL and LL are types of cancer that occur in white blood cells. ALL or LL are considered high risk because they can progress or return quickly. The term, risk, refers to the chance of the cancer coming back after treatment.

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, and Switzerland. The PEP-CTN is the group within COG that consists of 21 hospitals based in the United States and Canada, and participation in this study will be limited to these hospitals as well

as Loma Linda University Medical Center, Lucile Packard Children's Hospital Stanford University, Johns Hopkins University/Sidney Kimmel Cancer Center, UNC Lineberger Comprehensive Cancer Center, Laura and Isaac Perlmutter Cancer Center at NYU Langone, University of Oklahoma Health Sciences Center, Cook Children's Medical Center, and Primary Children's Hospital.

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 ALL or LL disease 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 point.

Why is this study being done?

This study will test how well palbociclib given with chemotherapy works in children and young adults with relapsed or refractory ALL or LL. This study is testing palbociclib in combination with the following chemotherapy drugs: vincristine, prednisone or prednisolone, pegaspargase and doxorubicin. This combination of chemotherapy drugs is called reinduction chemotherapy since the purpose is to get rid of as many of the cancer cells as possible after ALL or LL has come back. Palbociclib is experimental because it has not been proven to work in a situation like yours.

Palbociclib works by stopping your cancer cells from growing. We are using palbociclib because it has shown promising activity against leukemia in test tubes and animals and it has been highly effective and approved by the US Food and Drug Administration (FDA) for the treatment of other cancers in adults. We do not know if palbociclib will work in ALL or LL. While palbociclib has been used to treat a lot of adults, it has been used in only a small number of children and there is a lot that we do not know about it yet.

The overall goals of this study are to:

- **This treatment plan is being tested to see if it will improve the outcome of children with relapsed ALL or LL by increasing the percentage of patients who achieve remission after one month of therapy without causing intolerable side effects.**
- **To find a safe dose of palbociclib that can be given with chemotherapy without causing severe side effects;**
- **To learn what kind of side effects palbociclib can cause;**
- **To learn more about how palbociclib works on leukemia and lymphoma cells;**
- **To determine whether palbociclib combined with intensive reinduction chemotherapy is a beneficial treatment for your leukemia or lymphoma.**

What will happen on this study that is research?

The treatment involves a cancer fighting medicine called palbociclib plus chemotherapy. The treatment on this study takes about 32 days. At the end of study treatment your doctor will discuss further treatment options with you. Further treatment may include some type of additional chemotherapy followed by a bone marrow (stem cell) transplant, if possible.

Palbociclib is an experimental medication that will be given by mouth once daily on Days 1-21. Therapy will also consist of a combination of other standard anticancer medicines, described below.

Procedures common to all patients with relapsed/refractory ALL or LL are described in **Attachment 1**. Treatment that is standard for ALL or LL are described in **Attachment 1**.

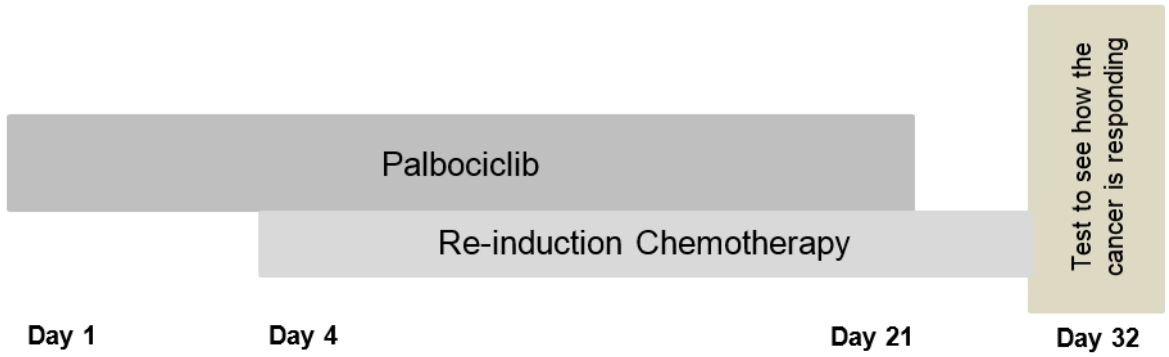
Some parts of the treatment on this study are different from standard therapy. These parts are experimental and are described below.

Dose Confirmation
The palbociclib dose 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 palbociclib at each dose. If the side effects are too severe, the next group of children will receive a lower dose. Dosing is done this way because we do not yet know the best dose to use in children. Whatever dose you start at, your dose will not be increased.

You will be given specific instructions regarding how to take these medicines on this study. Palbociclib is given by mouth once daily on Days 1-21. Palbociclib should be taken with food. If you vomit after taking the medication, the dose will not be repeated.

You will also be given a medication diary to fill out if you are at home each time these oral medicines are taken. Most people receiving this treatment, however, will be treated in the hospital. Use the diary to record the date and time you take the drug, and any side effects you 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 the cycle. This will help us know how much of the drug you take and how it made you feel.

Diagram of Treatment that is Research
This chart shows the treatment on this study.



Palbociclib will be given by mouth once daily on Days 1-21. Therapy will also consist of combinations of other anticancer medicines which are described below.

The standard anticancer medicines in this trial are: doxorubicin, vincristine, pegaspargase, prednisone or prednisolone, cytarabine (ara-C) hydrocortisone and methotrexate. All of these drugs have been used extensively in the treatment of ALL or LL. Prednisone or prednisolone will be given by tablet or liquid taken by mouth (orally). Pegaspargase, vincristine and doxorubicin will be given into the bloodstream through a needle inserted into a vein or through a central line. In addition, cytarabine, hydrocortisone and methotrexate will be used to treat the brain and spinal cord. The drugs used to treat the brain and spinal cord will be given through a needle inserted into the spinal fluid surrounding the spinal column (this is called a “spinal tap”).

Vincristine will be given IV weekly for 4 weeks, doxorubicin will be given once on Day 4 and pegaspargase will be given IV on Days 5 and 18. Prednisone or prednisolone will be given by mouth for 28 days. A spinal tap will be done on Days 1 (cytarabine OR cytarabine, hydrocortisone, and methotrexate), 18 (methotrexate) and 32 (methotrexate). Your doctor will let you know if you will only receive cytarabine on Day 1 or if you will receive cytarabine, hydrocortisone, and methotrexate (the combination of these 3 drugs is called “intrathecal triple therapy”). Only patients with a high amount of leukemia in their spinal fluid will receive intrathecal triple therapy instead of intrathecal cytarabine on Day 1. Additional spinal taps with intrathecal triple therapy will be done weekly if leukemia is detected in the spinal fluid at diagnosis.

During the study you will have tests and procedures to check for side effects and see how your ALL or LL is doing. These tests are part of regular cancer care, but you may have them more often because you are on the study:

- Physical exam
- Blood tests
- Spinal taps
- A repeat bone marrow at the end of therapy
- Repeat studies to evaluate your cancer (CT, MRI, PET/CT, etc.) at the end of therapy

When bone marrow testing is being done as part of your standard testing on Day 32, 5mL or 1 teaspoon will be collected for minimal residual disease (MRD) testing. This type of testing is used to see whether there are any leukemia cells present after therapy. These bone marrow samples are required from all patients with leukemia and are considered a standard way to measure the response to treatment.

Copies of the scans used to diagnose your cancer and some of the tissue already taken may be sent to a central review center as part of COG quality control. COG does this to double check the hospitals’ results.

Details of treatment are summarized below:

Prior to starting study	• Get routine blood tests, bone marrow tests, spinal tap, imaging
Day 1	• Start palbociclib once daily for Days 1-21

	• Receive Intrathecal cytarabine (IT ARAC) OR Intrathecal Triple Therapy (ITT) on Day .Your doctor will let you know which drugs you'll receive.
Day 4	• Continue palbociclib once daily for Days 1-21 • Receive Intrathecal Triple Therapy (ITT) if CNS leukemia present • Receive doxorubicin • Begin receiving prednisone or prednisolone on Days 4-31 • Receive vincristine
Day 5	• Continue palbociclib once daily for Days 1-21 • Continue prednisone or prednisolone on Days 4-31 • Receive pegaspargase
Day 11	• Continue palbociclib once daily for Days 1-21 • Continue prednisone or prednisolone on Days 4-31 • Receive Intrathecal Triple Therapy (ITT) if CNS is present at the start of treatment • Receive vincristine
Day 18	• Continue palbociclib once daily for Days 1-21 • Continue prednisone or prednisolone on Days 4-31 • Receive Methotrexate (IT MTX) if CNS leukemia is not present at the start of treatment • Receive Intrathecal Triple Therapy (ITT) if CNS leukemia present • Receive vincristine • Receive pegaspargase
Day 25	• Continue prednisone or prednisolone on Days 4-31 • Receive Intrathecal Triple Therapy (ITT) if CNS leukemia present • Receive vincristine
Day 31	• Complete prednisone or prednisolone on Days 4-31
Day 32	• Receive Methotrexate (IT MTX) if CNS leukemia is not present at the start of treatment • Assess response to treatment

Research Study Tests and Procedures

Correlative Study	Required/Optional?	Sample Volume	
		Volume per sample	Total
Pharmacokinetic Study (PK)	Required	3-4 ml	36-48 ml
Bone Marrow And Peripheral Blood Studies (ALL Only)	Optional	Bone marrow samples (5 mL) Peripheral Blood Day 4 (15 mL if weight > 10 kg, 10 mL if weight ≤ 10 kg)	Bone marrow samples (10 mL) Peripheral Blood Day 4 (15 mL if weight > 10 kg, 10 mL if weight ≤ 10 kg)

Total Volume	44-61 mL

Required Research Study Tests

We would like to determine how much palbociclib is in your blood (pharmacokinetics). Each sample is about 3-4 mL (a little less than 1 teaspoon) of blood. Blood samples for pharmacokinetics will be taken on the following schedule: Days 1 and 11: before palbociclib is given and at 1, 2 and 4, 8 and 24 hours post-dose of palbociclib. Twelve samples will be taken over the course of the study. These samples are required from all patients on study. The pharmacokinetic test will be done because you are part of this study. If you were not in the study you would probably not have this test.

Correlative Study	Volume per sample
Pharmacokinetic Study (PK)	3-4 ml
Total Volume	36-48 ml

Optional Research Study Tests (ALL Patients Only)

We would also like to do some tests called biologic studies. These tests are important to help us learn more about effects of palbociclib on leukemia cells and may help children and young adults 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. You can still be in the study if you do not want to do these tests. At the end of this consent form, there is a place to record your decision about taking part in each test.

Biology Studies using Bone Marrow Samples (ALL Patients only)

When bone marrow testing is being done as part of your standard testing before you begin therapy and on Day 32, we would like to request an extra sample (10 mL or about 2 teaspoons) from patients greater than or equal to 10 kg (26.5 pounds) or, 5 mL (about 1 teaspoon) from patients less than 10 kg (26.5 pounds), to evaluate the effect of palbociclib on your leukemia cells. The tests may help us to better learn how this drug may work.

Biology Studies using Blood Samples (ALL Patients only)

During the study, an additional blood sample will be collected on Day 4, after 3 days of palbociclib, to evaluate the effect of palbociclib on leukemia cells in your blood. This blood sample will be collected at the same time standard blood tests are performed to monitor for any side effects from treatment and the status of your disease. The blood samples are 15 mL (about 3 teaspoons) for patients greater than or equal to 10 kg (22 pounds), and 10 mL (about 2 teaspoons) from patients less than 10 kg (22 pounds). The tests may help us to better learn how this drug may work.

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 chemotherapy can damage normal tissue and produce side effects.

The table below show the most common and the most serious side effects that researchers know about palbociclib. 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.

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.

The risks of standard anticancer medicines given on this study are listed in **Attachment 2**.

Common side effects of chemotherapy include nausea, vomiting, hair loss, and fatigue (tiredness). Drugs may be given to try to prevent or decrease nausea and vomiting. Hair loss is usually temporary but very rarely it may be permanent. Some chemotherapy may

make people permanently unable to have children. On rare occasions, people can get a second cancer from chemotherapy. This usually happens years after the chemotherapy is finished.

Side effects can be increased when chemotherapy drugs are combined.

The most common serious side effect from cancer treatment is lowering of the number of blood cells resulting in anemia, increased chance of infection, and bleeding tendency. Low blood counts are described in the COG Family Handbook for Children with Cancer. Parents will be taught more about caring for their child when his or her blood counts are low.

Reproductive risks

Women should not become pregnant while on this study and for at least 3 weeks after the last dose of palbociclib, because the drug(s) in this study can be bad for an unborn baby. Men should avoid fathering a child or donating sperm while on this study and for at least 3 months after the last dose of palbociclib, because palbociclib 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. 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. Also check with your doctor about how long you should not breastfeed after you stop the study treatment(s).

Risks of Study

The use of palbociclib instead of another treatment may cause more complications.

Your other treatment options may include:

- **Getting treatment or care for your cancer without being in a study**
- **Taking part in another study**
- **Focusing on comfort care instead of drugs to treat the tumor**

The palbociclib plus chemotherapy treatment that is being studied could be less effective than another treatment.

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.

The chemotherapy used in this study may affect how different parts of your body work such as your liver, kidneys, heart, and blood. The study doctor will be testing your blood 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 drug/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.

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.

There may be unknown risks, or risks that we did not anticipate, associated with being in this study.

Are there benefits to taking part in the study?

We hope that this study will help you personally, but we do not know if it will.

Potential benefits to you could include:

- May cause your ALL or LL to stop growing or to go into remission for a period of time
- May lesson the symptoms that are caused by the ALL or LL.

With any cancer treatment, sometimes treatment does not make the cancer go away. Or, sometimes treatment makes the cancer go away for a while but the cancer comes back later.

We expect that the information learned from this study will benefit other patients in the future.

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 30 patients.

How long is the study?

People in this clinical trial are expected to receive treatment on this study for about 42 Days. After treatment, you will have follow-up examinations and medical tests.

We would like to continue to find out about your health for about 30 days after your last day of receiving cancer fighting medicine on 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 does not respond to the treatment or gets worse
- 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 you are female and become pregnant

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 3**.

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 government agencies, such as the 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**
- **The drug company supporting the study (the company that make palbociclib) or their designated reviewers.**

In addition to storing data in the study database, data from studies that are publicly funded may also be shared broadly for future research with protections for your privacy. The goal of this data sharing is to make more research possible that may improve people's health. Your study records may be stored and shared for future use in public databases. However, your name and other personal information will not be used.

Some types of future research may include looking at your information and information from other patients to see who had side effects across many studies or comparing new study data with older study data. However, right now we don't know what research may be done in the future using your information. 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.

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.

The drug company will provide palbociclib at no charge while you take part in the study. The drug company does not cover the cost of getting the palbociclib ready and giving it to you, so you or your insurance company may have to pay for this. Costs associated with the intensive reinduction chemotherapy must be covered by you or your insurance company.

Even though it probably won't happen, it is possible that the study may not be able to continue to provide the palbociclib for some reason. If this should occur, other possible options are:

- You might be able to get the palbociclib from the manufacturer or your pharmacy but you or your insurance company may have to pay for it.
- If there is no palbociclib available at all, no one will be able to get more and the study would close.

If a problem with getting palbociclib occurs, your study doctor will talk to you about these options.

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 charged for the costs of the special biology studies that are being done for research purposes only.

Funding support

If you choose to enroll on this study, this institution will receive some money from the Children's Oncology Group to do the research. There are no plans to pay you for taking part in this study.

The drug company that makes palbociclib is providing money to the Children's Oncology Group to do the research.

Money to do this research is also being provided by the Children's Oncology Group Foundation.

This study includes providing specimens to the researcher, there are no plans for you to profit from any new product developed from research done on your specimens.

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.

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 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 health information may be placed in central databases for researchers to use. The databases will not include your name or contact information.

If you decide now that your specimens can be used for research, 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.

The most common risks related to drawing blood from your arm are brief pain and maybe a bruise.

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 blood may be sent to a research laboratory and studied to see the effects of palbociclib on leukemia cells, the tests may help us to better learn how this drug may work.*

*Yes*_____ *No*_____ _____ / _____
Initials *Date*

2.) *My bone marrow may be sent to a research laboratory and studied to see the effects of palbociclib on leukemia cells, the tests may help us to better learn how this drug may work.*

*Yes*_____ *No*_____ _____ / _____
Initials *Date*

Signature

I have been given a copy of all 23 pages of this form. The form includes three (3) 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

Treatment and Procedures Common to all Patients with ALL or LL

Methods for Giving Drugs

Various methods will be used to give drugs:

- **PO** - Drug is given by tablet or liquid swallowed through the mouth.
- **IV** - Drug is given using a needle or tubing inserted into a vein. Drugs can be given rapidly over a few minutes ("push") or slowly over minutes or hours ("infusion").
- **IT** - Drug used to treat the brain and spinal cord is given using a needle inserted through the back into the fluid surrounding the spinal cord.

Central Line

Your doctor may recommend that you get a special kind of IV called a "central line." 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.

Lumbar Punctures ("L.P.s", "spinal taps")

You are familiar with spinal taps since they were done during your (your child's) initial therapy for ALL. Whether you decide to (allow your child to) participate or not on this study, additional spinal taps will need to be done to prevent the leukemia from spreading to the spinal fluid. Spinal taps are painful and may cause headaches. The skin at the site of needle insertion is usually numbed with an anesthetic cream or lidocaine before the procedure is performed. Approximately 1 teaspoon of spinal fluid will be withdrawn prior to injection of the medicines (cytarabine or methotrexate alone, or the combination of methotrexate, cytarabine and hydrocortisone, if leukemia is present in the spinal fluid or brain).

During the study you will have tests and procedures to check for side effects and see how your tumor is doing. These tests are part of regular cancer care, but you may have them more often because you are on the study. Copies of the scans used to diagnose your cancer and some of the tissue already taken may be sent to a central review center as part of COG quality control. COG does this to double check the hospitals' results.

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.

- 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.
- Tests to monitor your heart and lung function.
- 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.
- Spinal Taps to check for cancer cells in the spinal fluid and to give chemotherapy into the spinal fluid. This is described in the COG Family Handbook for Children with Cancer.
- Blood tests
- Physical Exam

Attachment 2

Risks of Chemotherapy Drugs Used to Treat ALL or LL

Possible Side Effects of Asparaginase Erwinia

COMMON, SOME MAY BE SERIOUS In 100 people receiving Asparaginase Erwinia, more than 20 and up to 100 may have:
• **Nausea** • **Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat**

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Asparaginase Erwinia, from 4 to 20 may have:
• **Pain in belly** • **Vomiting** • **Blood clot** • **Fever**

RARE, AND SERIOUS In 100 people receiving Asparaginase Erwinia, 3 or fewer may have:
• **Diarrhea** • **Bleeding** • **Seizure**

Possible Side Effects of Cytarabine (ara-c) when given into the spinal fluid (intrathecal)

COMMON, SOME MAY BE SERIOUS In 100 people receiving cytarabine (ara-c) when given into the spinal fluid, more than 20 and up to 100 may have:
• **Nausea, vomiting** • **Fever** • **Headache**

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving cytarabine (ara-c) when given into the spinal fluid, from 4 to 20 may have:
• **Anemia which may cause tiredness, or may require blood transfusions** • **Infection, especially when white blood cell count is low** • **Bruising, bleeding** • **Tiredness, dizziness, loss of coordination** • **Numbness and tingling of the arms and legs** • **Inflammation of the lining of the brain that can lead to headache, numbness and tingling**

RARE, AND SERIOUS In 100 people receiving cytarabine (ara-c) when given into the spinal fluid, 3 or fewer may have:
• **Seizure** • **Paralysis** • **Blurred vision with a chance of blindness** • **Damage to the brain that may result in a decrease in the ability to learn**

Possible Side Effects of Doxorubicin

COMMON, SOME MAY BE SERIOUS In 100 people receiving Doxorubicin, more than 20 and up to 100 may have:
• **Hair loss** • **Vomiting** • **Red colored urine, saliva, or sweat**

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Doxorubicin, from 4 to 20 may have:
• **Heart failure or heart attack which may cause shortness of breath, swelling of ankles, cough or tiredness which may occur years after the dose** • **Abnormal heartbeat** • **Damage to the lungs which may cause shortness of breath when combined with radiation** • **Infection, especially when white blood cell count is low** • **Bruising, bleeding** • **Anemia which may cause tiredness, or may require transfusion** • **Hepatitis or damage to the liver which may cause yellow eyes and skin, swelling** • **Kidney damage which may require dialysis** • **Swelling and redness at the site of the medication injection or area of previous radiation** • **Belly pain** • **Sores in the mouth or throat** • **Nausea, diarrhea** • **Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat** • **Damage to the skin which may cause pain** • **Cancer of the bone marrow (leukemia) caused by chemotherapy** • **Darkening of the nail beds or skin or hands and feet** • **Loss of nails**

RARE, AND SERIOUS In 100 people receiving Doxorubicin, 3 or fewer may have:
• **Severe blood infection**

Possible Side Effects of Intrathecal Triples (cytarabine, methotrexate, and hydrocortisone) when given into the spinal fluid

COMMON, SOME MAY BE SERIOUS In 100 people receiving intrathecal triples, more than 20 and up to 100 may have:
• **Nausea, vomiting** • **Fever** • **Headache**

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving intrathecal triples, from 4 to 20 may have:
• **Swelling of the brain which may cause blurred vision and/or confusion** • **Damage to the brain which may cause changes in thinking** • **Difficulty with speaking** • **Pain** • **Confusion, dizziness** • **Tiredness** • **Rash**

RARE, AND SERIOUS In 100 people receiving intrathecal triples, 3 or fewer may have:
• **Seizure** • **Damage to the brain which could lead to coma** • **Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat** • **Bleeding into the space of the spine at the site of the injection** • **Paralysis, weakness** • **Infection**

Possible Side Effects of Methotrexate when given into the spinal fluid (intrathecal)

COMMON, SOME MAY BE SERIOUS In 100 people receiving methotrexate when given into the spinal fluid, more than 20 and up to 100 may have:
• **Nausea** • **Headache**

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving methotrexate when given into the spinal fluid, from 4 to 20 may have:
• **Swelling of the brain which may cause blurred vision, and/or confusion** • **Damage to the brain which may cause changes in thinking** • **Confusion, dizziness** • **Vomiting** • **Rash** • **Tiredness** • **Pain** • **Anemia which may require blood transfusions** • **Infection, especially when white blood cell count is low** • **Bruising, bleeding** • **Difficulty with speaking**
RARE, AND SERIOUS In 100 people receiving methotrexate when given into the spinal fluid, 3 or fewer may have:
• **Seizure** • **Damage to the brain which could lead to coma** • **Paralysis, weakness** • **Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat** • **Bleeding into the space of the spine at the site of the injection**

Possible Side Effects of Pegaspargase

COMMON, SOME MAY BE SERIOUS In 100 people receiving Pegaspargase, more than 20 and up to 100 may have:
• **Nausea, vomiting** • **Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat** • **Chills, fever** • **Tiredness** • **Hives, rash**

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Pegaspargase, from 4 to 20 may have:
• **Blood clot** • **Liver damage which may cause yellowing of eyes and skin** • **Anemia which may require blood transfusions** • **Infection, especially when white blood cell count is low** • **Abnormal heart beat** • **Bruising, bleeding** • **Night sweats** • **Headache**

RARE, AND SERIOUS In 100 people receiving Pegaspargase, 3 or fewer may have:
• **Belly pain, damage to the pancreas**

Possible Side Effects of Prednisone or Prednisolone

COMMON, SOME MAY BE SERIOUS In 100 people receiving prednisone or prednisolone, more than 20 and up to 100 may have:
• **In children and adolescents: decreased height** • **Loss of bone tissue** • **Mood swings** • **Skin changes, acne** • **Swelling of the body, tiredness, bruising** • **High blood pressure which may cause headaches, dizziness, blurred vision** • **Pain in belly** • **Increased appetite and weight gain in the belly, face, back and shoulders** • **Difficulty sleeping**

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving prednisone or prednisolone, from 4 to 20 may have:
• **Blood clot which may cause swelling, pain, shortness of breath** • **Cloudiness of the eye, visual disturbances, blurred vision** • **Glaucoma** • **Infection** • **Non-healing wound** • **Diabetes** • **A tear or a hole in the bowels which may cause belly pain or that may require surgery** • **Damage to the bone which may cause joint pain and loss of motion** • **Numbness and tingling of the arms, legs and upper body** • **Muscle weakness** • **Kidney stones** • **Heartburn**

RARE, AND SERIOUS In 100 people receiving prednisone or prednisolone, 3 or fewer may have:
• **Bleeding from sores in the stomach** • **Broken bones**

Possible Side Effects of Vincristine

COMMON, SOME MAY BE SERIOUS In 100 people receiving vincristine, more than 20 and up to 100 may have:
• **Constipation, nausea, vomiting** • **Hair loss** • **Pain or redness at the site of injection** • **Numbness and tingling of fingers or toes** • **Headache, jaw pain and/or muscle pain** • **Weakness and difficulty walking** • **Swelling of lower legs**

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving vincristine, from 4 to 20 may have:
• **Swelling that may be accompanied by confusion, and dizziness** • **Paralysis, weakness, headache, confusion** • **Drooping eyelids** • **Hoarseness** • **Visual loss** • **Difficulty with balance and hearing**

RARE, AND SERIOUS In 100 people receiving vincristine, 3 or fewer may have:
• **Seizure**

Attachment 3

Certificate of Confidentiality

The Children's Oncology Group has received 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.