Consent and Authorization Document

A Phase II Study to Evaluate the Efficacy and Safety of Selinexor in Patients with Myelofibrosis Refractory or Intolerant to JAK1/2 Inhibitors (ESSENTIAL)

You are being asked to take part in a research study. Before you decide whether or not to participate, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with friends and relatives if you wish. Ask the research doctor or staff if there is anything that is not clear or if you would like more information. Take time to decide whether or not to volunteer to take part in this research study.

Once you know about the study, you will make a decision about whether to take part. If you decide to take part, you'll be asked to sign this form. Your decision to take part in this study is voluntary which means you are free to decide to join this study or not to join this study.

BACKGROUND

You are being asked to take part in this study because you have a condition called myelofibrosis and other drug(s) that you have tried have either not worked well or have caused too many side effects or side effects which are too severe. In this study you will be given a drug called selinexor. The main reason for the study is to determine the effect that selinexor will have on your disease.

Selinexor (KPT-330) has not been approved by the U.S Food and Drug Administration (FDA), or any other agency, so it is being considered "investigational" for use in this study. An investigational drug is a drug that is being tested and is not approved for sale in the United States by the U.S. Food and Drug Administration (FDA).

The study is being conducted by Dr. Srinivas Tantravahi at Huntsman Cancer Institute of the University of Utah. Karyopharm Therapeutics, Inc. is supplying the study drug, selinexor, and funding for this study.

The chest X-ray and MRIs (Magnetic Resonance Imaging) that are to be performed as part of this study are considered standard of care and would be done regardless of your participation in this research study. If you are unable to have an MRI you will have a CT (Computerized Tomography) scan. CT scans are not considered standard of care and would be done for research purposes.

STUDY PROCEDURES

If you decide you would like to take part in the study and you sign this informed consent form, you will have screening tests and procedures done to make sure you are eligible to participate.

Screening Period

- Medical history will be collected as well as details about what medications, vitamins, and supplements you are currently taking.
- You will have a physical exam and a measure of your vital signs, including height, weight, body surface area (BSA), and body mass index (BMI).

- You will have an evaluation of your ability to perform everyday activities (performance status).
- You will answer questionnaires about how you are feeling and your disease.
- You may have an optional eye exam.
- You will have a MRI to assess your current disease, unless you are unable to have an MRI, then you will have a CT scan. You will also have a chest X-ray.
- You will have an ECG (Electrocardiogram) to check your heart function.
- You will have your blood drawn for standard lab testing to ensure you are healthy enough to take part. If you are a female with the potential of becoming pregnant, you will have a pregnancy test. You will also have tests done to check different components of your cancer and blood, including genetics, which will be compared to samples that will be collected later. In addition to your standard of care labs, we are going to collect approximately 6 teaspoons for research purposes. You will have a bone marrow aspirate and biopsy. These will be checked to help give us information about your cancer and its genetic components. A bone marrow aspirate is a test in which your skin is numbed, and a needle is inserted into the bone to remove part of the liquid bone marrow. A piece of the bone is also removed (bone marrow biopsy) and tested.
- You will have a nutritional consultation.

Treatment Period

Once it is decided that you are able to enroll into this study, you will begin study treatment. The study is divided up into segments of time called "cycles". For this study, a cycle will be 28 days. Selinexor will be given to you as oral tablets, and should be taken once a week. You will take the tablets either at the clinic on visit days, or at home. You will take a 40 mg dose, unless directed otherwise by your doctor and/or study team. It should be taken with at least 4 ounces (120 mL) of fluids (water, juice, etc.) at approximately the same time each day. Selinexor tablets should be swallowed whole (not crushed). You may also be given medications to help with common known side effects before you take your first dose.

You will come to the clinic on Day 1 of each cycle for your study treatment and Day 15 for lab testing. On your first cycle only, you will also come on or around days 8 and 22 for procedures and tests. You will also return for Day 15 of each cycle through cycle 6 for lab testing and every 3 months after that unless your doctor feels it is necessary for you to return for follow up sooner. Some of the procedures are being done as part of your routine cancer care. Some are being done because you are participating in this study. By participating in this study, you may be required to spend extra time at each visit. Ask your study team for more information about how long each visit may be. You will continue on the study treatment as long as you are receiving clinical benefit from the treatment as determined by the study doctor. Treatment will be stopped if your disease gets worse, you have intolerable side effects, you decide to stop, or your doctor decides it would be in your best interest to stop, or the study is terminated by the study sponsor or drug supplier. Your study team will give you more information about your treatment plan.

You will be called 3 days after your first dose of selinexor to ensure that you are feeling okay and to make any changes to medications that you were given for possible side effects.

Study Procedures during the Treatment Period:

- You will have physical exams and measures of your vital signs including weight and body mass index (BMI). You will also be asked about any changes in medications that you are taking and changes in how you are feeling to check for potential side effects.
- Evaluations of your ability to perform everyday activities (performance status).
- You will also be asked to complete a questionnaire about any symptoms you are having and how you have been feeling once a week. This will either be at a clinic visit, or at home if you don't have a clinic visit that week.
- You may have an optional eye exam.
- You will have MRIs, unless you are unable to have an MRI for any reason, then you will have CT scans. These will be done at weeks 12 and 24. Unless your disease gets worse before week 24, in which case you will have one at the time it gets worse. If you continue to receive clinical benefit from the study drug, you will continue on the study and have an MRI or CT scan at months 9, 12, and 18.
- If your doctor feels it is necessary, you will have ECGs done.
- You will have blood draws collected for the following reasons. There may be one or more blood draws during a clinic visit:
  - Standard lab testing for safety.
  - To look at the immune system components of your blood as well as genetic components and how they have changed since starting treatment.
  - To see how your cancer is responding to the treatment.
- Bone marrow aspirate and biopsy – At 6 months, 18 months, and yearly thereafter until treatment discontinuation you will have a bone marrow aspirate and biopsy. These will be checked to help give us information about your cancer and its genetic components and how they may have changed since you were on treatment.

End of Treatment

This visit will take place 5 to 9 days after you go off of study treatment. The following procedures will be done:

- You will have physical exams and measures of your vital signs including weight and body mass index (BMI). You will also be asked about any changes in medications that you are taking and changes in how you are feeling to check for resolution of any side effects you may have experienced, and assess for any new ones.
- Evaluations of your ability to perform everyday activities.
- You will also be asked to complete a questionnaire about any symptoms you are having and how you have been feeling.
- You may have an optional eye exam.
- You will have an MRI, unless you are unable to have an MRI for any reason, then you will have a CT scan unless you had a scan within 6 weeks of this visit.
- You will have an ECG.
- You will have a blood draw (approximately 6 tsp for research) collected for the following reasons:
  - Standard lab testing for safety.

  - To look at the immune system components of your blood as well as genetic components and how they have changed since starting treatment.
- Bone marrow aspirate and biopsy – At end of treatment, you will have a bone marrow aspirate and biopsy. These will be checked to help give us information about your cancer and its genetic components and how they may have changed since you were on treatment.

Follow-up

You will be contacted by phone every 3 months to check on your disease status and to see how you are feeling and to see if you have started any new treatments for approximately 24 months. If you have recently had a clinic visit this information may be collected from your medical record.

RISKS

Selinexor

The side effects listed below are based on the information known to Karyopharm, the drug supplier, from previous studies of the study drug and which may or may not be related to the study drug. Not all patients have these side effects. It is possible that new side effects of the study drug not described here may occur in this study. If these new side effects are determined to be significant and that all patients should be informed of them, you will receive this information at that time. If you do not understand what any of these side effects mean, please ask the study doctor or study staff to explain these terms to you.

Very common side effects (≥ 10%):

In 100 people receiving selinexor more than 10 people may have:

- Nausea
- Vomiting
- Diarrhea
- Weight loss
- Constipation
- Fatigue and asthenia – loss of energy; weakness
- Decreased appetite
- Dehydration
- Abdominal pain
- Dysgeusia – change in taste
- Shortness of breath
- Cough
- Dizziness
- Fever
- Blurred Vision
- Headache
- Difficulty falling asleep
- Low platelets in the blood (thrombocytopenia), which may increase the risk of bleeding

- Decrease in red blood cells (anemia) causing fatigue
- Decrease in white blood cells (leukopenia), which may increase the risk of infection
- Decrease in neutrophils (a specific type of white blood cell that helps fight infections)
- Pneumonia
- Low blood sodium which may increase the risk of seizures
- Low potassium which may cause weakness, muscle cramps and spasms
- Peripheral edema – swelling in extremities due to accumulation of fluid, usually in legs
- High blood sugar which may cause fatigue, increased thirst/hunger, frequent urination, weight loss, numbness and tingling in hands/feet

Common side effects (≥ 1-10%):

In 100 people receiving selinexor about 1 to 10 people may have:

- Rash
- Eye disorders including cataract (new or worsened), dry eye, visual impairment, seeing flashes of light
- Night sweats
- Dry mouth
- Stomatitis – a condition that causes painful swelling and sores inside the mouth
- Dyspepsia – indigestion
- Chills
- Hypotension – low blood pressure
- Hypertension
- Tachycardia – fast heart rate
- Nosebleed
- Contusion (bruise due to body injuries such as fall)
- Electrolyte disturbances including:
    - Low phosphate which may cause muscle weakness and fatigue
    - Low magnesium which may cause muscle twitches and cramps
    - Low calcium which may cause numbness and tingling in hands/feet/face, muscle stiffness and cramps
    - High potassium which may cause muscle weakness, palpitations or irregular heartbeats and chest pain
- Low albumin (which may cause swelling especially of the hands/feet, weakness or exhaustion)
- Peripheral neuropathy – weakness, numbness, and pain from nerve damage, usually in the hands and feet
- Decrease in lymphocytes – a specific type of white blood cell that are part of your immune system
- Increase of creatinine in the blood due to a reduction of kidney function, often related to dehydration
- Elevated liver enzymes including alanine aminotransferase increased, aspartate aminotransferase increased, blood alkaline phosphatase increased

- Elevated pancreatic enzymes including high amylase and high lipase
- Muscle weakness
- Febrile neutropenia – fever in the absence of a normal white blood cell response that may mean you have an infection
- Respiratory tract infection (including upper)
- Urinary tract infection
- Sepsis (including septic shock) – potentially life-threatening complication of an infection
- Pain in joints and muscles
- Malaise (a general feeling of being ill or bodily weakness)
- Muscle spasms
- Gait disturbance
- Hair loss
- Itching
- Depression
- Syncope – fainting
- Cognitive disorder
- Mental status changes including confusion

Uncommon side effects (> 0.1-1%):

In 1,000 people receiving selinexor about 1 to 10 people may have:

- Tumor lysis syndrome – potentially a life-threatening side effect caused by the rapid breakdown of tumor cells and may cause irregular heartbeat, kidney failure or abnormal blood test results which included elevated uric acid level, elevated serum potassium and phosphorus levels, and a decreased calcium level.
- Enterocolitis infectious (inflammation of digestive tract caused by infection)
- Gastroenteritis (stomach flu)
- Rhinovirus infection (common cold; infection of nose, ear, sinuses; very rarely leading to pneumonia or bronchitis)

Rare side effects (> 0.01-0.1%):

In 10,000 people receiving selinexor about 1 to 10 people may have:

- Acute cerebellar syndrome – symptoms can include a sudden loss of coordination, balance, or slurred speech

Serious adverse effects (≥ 3 cases reported as related by the principal investigator):

- Cardiac failure
- General physical health deterioration
- Multiple organ dysfunction syndrome
- Lung infection
- Bacteremia – bacterial infection in the blood
- Bronchitis – infection of tubes that carry air to and from lungs

- Decreased ejection fraction – reduction in amount of blood pumped out of heart
- Encephalopathy – brain disease, damage, or malfunction, which can present different symptoms that range from mild, such as some memory loss or subtle personality changes, to severe, such as dementia, seizures, or coma.
- Delirium – state of acute confusion
- Acute kidney injury
- Pulmonary embolism – pulmonary embolism occurs when a clump of material, most often a blood clot, gets wedged into an artery in your lungs.
- Hypoxia – an absence of oxygen supply at tissue level

RADIATION RISKS

This research study involves exposure to radiation from 4 possible CT scans that will be done if you are unable to have an MRI. These scans are being done for the research study and are not considered part of your standard care. The risk from this radiation exposure is considered to be small and comparable to other every day risks. This amount does not include any radiation exposures that you may receive from other types of tests.

If you are enrolled in this study, the excess radiation you will receive is about the same as a uniform whole-body dose of:	The amount of radiation that is **considered safe** for a **radiation worker** (e.g. doctor, nurse, scientist, etc.) to receive in one year:
1.85 rem	**5 rem**

***A "*rem*" is a unit of radiation dose.*

REPRODUCTIVE RISKS

It is likely that the study drug may have a potentially harmful effect on the unborn child. If you are a sexually active and possibly fertile woman, you will be asked to use 2 medically approved methods of birth control (contraception) during the treatment period and for at least 3 months after you finish taking the study drug. Examples of medically acceptable birth control include hormonal contraceptives (oral pills, patches, vaginal ring, injectables or implants), medically prescribed IUDs, and barrier methods, e.g., male and female condoms, cervical cap, diaphragm and sponge. Check with your study doctor about what kind of birth control methods to use. Some methods might not be approved for use in this study. If you suspect that you have become pregnant during the trial, you must notify the study doctor immediately. You should also not breast feed while on this study.

If you are a male that is sexually active with a possibly fertile woman, you must agree to an effective barrier method as listed above while taking the study drug and for 3 months after.

If you think that you, or your partner, may be pregnant at any time while on this study, you must inform your study doctor immediately. You will be asked to take part in monitoring the outcome of your pregnancy and the study doctor will remain in contact with you to determine the conclusion of your

pregnancy. If you are woman and become pregnant while in the study, you will be discontinued from the study.
For more information about risks and side effects, ask your study doctor.

Other Risks and Inconveniences including Genetic Risks
There are also non-physical risks associated with taking part in this study, such as the risks associated with a breach of privacy or confidentiality. For example, if your identity as a participant in genetic research or your identifiable genetic or health information were disclosed to unauthorized persons, there is the possible risk of discrimination by employers or insurance providers. The risks of such improper disclosure are very small because Huntsman Cancer Institute has adopted strict privacy and confidentiality procedures for this research.

Blood draws or IV: Risks associated with drawing blood or putting a needle in your vein might include pain from the puncture, bruising, bleeding, infection, or fainting. Every effort will be made to minimize discomfort.

Genetic Testing
In the United States, the Genetic Information Nondiscrimination Act of 2008 (GINA) prohibits discrimination in health coverage and employment based on genetic information. GINA, together with the Health Insurance Portability and Accountability Act (HIPAA), generally prohibits health insurers or health plan administrators from requesting or requiring genetic information of an individual or the individual's family members, or using it for decisions regarding coverage, rates, or preexisting conditions. The law also prohibits most employers from using genetic information for hiring, firing, or promotion decisions, and for any decisions regarding terms of employment. Utah State Law also offers protection against discrimination in health coverage and employment and employment.

The genetic testing that will be done in this trial is called tumor mutation burden analysis. This will only be done if you consent to the optional tumor testing at the end of this form. You will not receive the results of these tests nor will they be included in your medical records.

UNFORESEEABLE RISKS
Problems or side effects that are not known could also occur. Most side effects are expected to go away after treatment is stopped or interrupted; however, in some cases the side effects may be serious, long-lasting, permanent or lead eventually to death. You will be given any new information when it becomes available that may affect your willingness to start or continue in the study.

BENEFITS
There may not be any benefit to you from your being in the study. The information gained in this study will aid in the understanding of cancer and help in the development of new approaches to its treatment in the future. You will not be compensated for participating in this study or as a result of new treatments or products developed using information obtained in this study.

ALTERNATIVE PROCEDURES

You do not have to be in this study to get help for the type of cancer you have. The study doctor will talk to you about other things you can do for this type of cancer, including the important risks and benefits. Some other things you might do are:

- Use other approved chemotherapy regimens.
- Use other investigational treatments.
- Get supportive care.
- Choose to have no further treatment.

NUMBER OF PARTICIPANTS

Up to 24 patients are expected to be enrolled in this study from the Huntsman Cancer Institute/University of Utah.

PERSON TO CONTACT

If you have questions, complaints or concerns about this study, you can contact Dr. Srinivas Tantravahi at 801-585-0255. If you think you may have been injured from being in this study, please call Dr. Tantravahi at 801-585-0255. The University Hospital Operator can be reached at this number: 801-581-2121 available 24-hours a day. Please ask for the oncologist on call.

Institutional Review Board: Contact the Institutional Review Board (IRB) if you have questions regarding your rights as a research participant. Also, contact the IRB if you have questions, complaints or concerns which you do not feel you can discuss with the investigator. The University of Utah IRB may be reached by phone at (801) 581-3655 or by e-mail at irb@hsc.utah.edu.

Research Participant Advocate: You may also contact the Research Participant Advocate (RPA) by phone at (801) 581-3803 or by email at participant.advocate@hsc.utah.edu.

RESEARCH-RELATED INJURY

If you are injured from being in this study, medical care is available to you at the University of Utah, as it is to all sick or injured people. The University of Utah has not set aside any money to pay the costs for such care. The University will work with you to address costs from injuries. Costs would be charged to you or your insurance company (if you have insurance), or other third party (if applicable), to the extent those parties are responsible for paying for medical care you receive. Since this is a research study, some health insurance plans may not pay for the costs. By signing this consent form you are not giving up your right to pursue legal action against any parties involved with this research. Karyopharm Therapeutics, the drug supplier, is not providing insurance coverage or other compensation to you for this study.

The University of Utah is a part of the government. If you are injured in this study, and want to sue the University or the doctors, nurses, students, or other people who work for the University, special laws may apply. The Governmental Immunity Act of Utah is a law that controls when a person needs to bring a claim against the government, and limits the amount of money a person may recover. See sections 63G -7-101 to -904 of the Utah Code.

VOLUNTARY PARTICIPATION

Taking part in this research study is voluntary. You may decide not to take part or you may leave the study at any time. Refusal to take part or the decision to withdraw from this study will involve no penalty or loss of benefits to which you are otherwise entitled.

Tell the study doctor if you are thinking about stopping or decide to stop, as it may be necessary to do certain tests in order to ensure your safety. If you choose not to return for an assessment, we may ask for medical records from your current general practitioner in order to continue to monitor your health.

If you decide not to continue in the study at any time, your study doctor will arrange for you to receive alternative treatment and any necessary assessments or procedures according to standard of care.

RIGHT OF INVESTIGATOR TO WITHDRAW

Your study doctor may decide to take you off this study at any time without your consent for any of the following reasons:

- if your disease becomes worse and is not responding to the study drug,
- if he or she believes it is in your best interest,
- if you do not follow the study rules,
- if you miss study visits and/or procedures,
- if you have serious side effects,
- if you become pregnant,
- you do not later consent to any future changes that may be made in the study plan; or any other reason.

There is also the possibility that the investigator, may close the study before your participation is complete and without prior warning. If any of these events were to happen, your study doctor would assist with arrangements for your continued care as appropriate.

COSTS AND COMPENSATION TO PARTICIPANTS

Some of the procedures and treatments you'll have while you are on the study are considered "standard of care" for your type of illness. Even though you will be a part of the study, these types of procedures and treatments will be billed to you and/or your insurance company just like regular medical care. Some procedures and treatments you'll have while you are on the study are considered "study related" and are not billed to you and your insurance company. You should ask your study coordinator and treating physician for details about the specific procedures you or your insurance company will be financially responsible for.

Selinexor will be provided to you free of charge in this study by Karyopharm Therapeutics.

NEW INFORMATION
You will be given any new information about the study drugs that may affect your willingness to start or continue in the study as it becomes available.

AUTHORIZATION FOR USE OF YOUR PROTECTED HEALTH INFORMATION
Signing this document means you allow us, the researchers in this study, and other working with us to use some information about your health for this research study.

This is the information we will use and include in our research records:

- Demographic and identifying information like your name, address, telephone number, and email address.
- Related medical information about you like family medical history, allergies, current and past medications or therapies, information from physical examinations such as blood pressure readings, heart rate, temperature, and lab results.
- All tests and procedures that will be done in the study

How we will protect and share your information:
We will do everything we can to keep your information private, but we cannot guarantee this. The research records will be kept in a secured manner and computer records will be password protected. We may need to disclose information about you as required by law.
Study information may be stored with other information in your medical record. Other doctors, nurses, and third parties (like insurance companies) may be able to see this information as part of the regular treatment, payment, and health care operations of the hospital.
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.

In order to conduct this study and make sure it is conducted as described in this form, the research records may be used and reviewed by others who are working with us on this research:

- Members of the research team and University of Utah Health Sciences Center.
- The University of Utah Institutional Review Board (IRB), who reviews research involving people to make sure the study protects your rights.
- Karyopharm Therapeutics, the drug supplier of selinexor, and its authorized agents.
- Government agencies responsible to confirm research accuracy such as the United States Food and Drug Administration (FDA), and the National Cancer Institute (NCI) which is a part of the National Institute of Health (NIH).
- Governmental agencies in other countries where the study drug may be considered for approval.

If we share your identifying information with groups outside of the University of Utah Health Sciences Center, the groups may not be required to follow the same federal privacy laws that we follow. They may also share your information again with others not described in this form.

What if I Decide Not to Take part After I sign the Consent and Authorization Form?
You can tell us anytime that you do not want to be in this study and do not want us to use your health information. You can also tell us in writing. If you change your mind, we will not be able to collect new information about you, and you will be withdrawn from the research study. However, we can continue to use information we have already started to use in our research, as needed to maintain the integrity of the research.

This authorization does not have an expiration date.

You have a right to information used to make decisions about your health care. However, your information from this study will not be available during the study; it will be available after the study is finished.

CONSENT

I have been given adequate time to read and consider the information in this consent form prior to signing (or it has been read to me). All my questions about the study and my participation in it have been answered and I will be given a copy of this signed and dated consent form for my records and continued reference.

My signature below indicates that I voluntarily agree to take part in this research study. By signing this consent form, I do not release the study doctor or his study staff, the institution or the drug supplier from their professional and legal duties.

I authorize the use and disclosure of my health information to the parties listed in the authorization section of this consent for the purposes described above.

I agree to take part in this research study and authorize you to use and disclose health information about me for this study, as you have explained in this document.

_____
Participant's Name

_____ _____ _____
Participant's Signature Date Time

_____
Name of Person Obtaining Authorization and Consent

_____ _____ _____
Signature of Person Obtaining Authorization and Consent Date Time

LANGUAGE INTERPRETER STATEMENT (if applicable):

I confirm that I was present as an interpreter for the duration of the consent process for this research study. I confirm that I am qualified/have the necessary skills to provide interpretation between [insert target language] _____ and English. By signing this form, I confirm that I provided a full and complete interpretation of the exchange between the research staff member named above and the patient named above, to the best of my ability.

Name of Interpreter_____ Employer/Vendor (if applicable) _____

_____ _____ _____
Signature of Interpreter Date Target Language

Information requested for federal grant reporting purposes *(optional)*

Sex/Gender

- ❑ **Male**
- ❑ **Female**

Ethnicity

Do you consider yourself to be Hispanic or Latino? (see definition below)

Hispanic or Latino. A person of Mexican, Puerto Rican, Cuban, South or Central American, or other Spanish culture or origin, regardless of race.

Select one:

- ❑ **Hispanic or Latino**
- ❑ **Not Hispanic or Latino**

Race

What race do you consider yourself to be? SELECT ONE OR MORE OF THE FOLLOWING:

- ❑ **American Indian or Alaska Native.** A person having origins in any of the original peoples of North America (including, Central or South America) who maintains cultural identification through tribal affiliation or community recognition.
- ❑ **Asian.** A person having origins in any of the original peoples of the Far East, Southeast Asia, or the Indian subcontinent, including, for example, Cambodia, China, India, Japan, Korea, Malaysia, Pakistan, the Philippine Islands, Thailand, and Vietnam.
- ❑ **Black or African American.** A person having origins in any of the black racial groups of Africa.
- ❑ **Native Hawaiian or other Pacific Islander.** A person having origins in any of the original peoples of Hawaii, Guam, Samoa, or other Pacific Islands.
- ❑ **White.** A person having origins in any of the original peoples of Europe, the Middle East, or North Africa.
- ❑ **Unknown.**

❑ **Check here if you do not wish to provide some or all of the above information.**

Initial and Date