The Ohio State University Combined Consent to Participate in Research and HIPAA Research Authorization

Study Title: A Phase 1b/2 Study of TP-0903 in Patients with Acute Myeloid Leukemia and FLT3 mutations

Principal Investigator: Dr. Uma Borate

Sponsor: The Ohio State University

- **This is a consent form for research participation.** It contains important information about this study and what to expect if you decide to participate. Please consider the information carefully. Feel free to discuss the study with your friends and family and to ask questions before making your decision whether or not to participate.
- **Your participation is voluntary.** You may refuse to participate in this study. If you decide to take part in the study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your usual benefits. Your decision will not affect your future relationship with The Ohio State University. If you are a student or employee at Ohio State, your decision will not affect your grades or employment status.
- **You may or may not benefit as a result of participating in this study.** Also, as explained below, your participation may result in unintended or harmful effects for you that may be minor or may be serious depending on the nature of the research.
- **You will be provided with any new information that develops during the study that may affect your decision whether or not to continue to participate.** If you decide to participate, you will be asked to sign this form and will receive a copy of the form. You are being asked to consider participating in this study for the reasons explained below.

Key Information About This Study
The following is a short summary to help you decide whether or not to be a part of this study. More detailed information is listed later in this form.

Acute Myeloid Leukemia (AML) is a type of blood cancer. There are different types of AML which are characterized by different genetic mutations. One type of mutation is the FLT3 mutation (fms-like tyrosine kinase 3), which is commonly seen in AML patients and will be studied in this study. This type of AML is associated with poor outcomes. Doctors are researching ways to target this mutation to help improve these outcomes.

This study is testing an investigational drug called TP-0903. TP-0903 has not been approved by the Food and Drug Administration (FDA) to treat patients with AML. In this study, TP-0903 will be tested to determine if it is safe and effective in patients with AML.

The expected duration of the treatment part of the study is 12-18 months, however, this time may vary depending on how your disease responds. There is also a follow-up period that could last up to 5 years.

An important risk to note in this study is that the study drug, TP-0903, may cause low blood cell counts. As with all research, there are risks to participation and not all risks may be known.

You may or may not benefit from participating, but the information gained in this study may help doctors treat patients with AML in the future.

1. Why is this study being done?

You are invited to take part in a clinical trial, a type of research study, because you have Acute Myeloid Leukemia (AML). For the purposes of this research, you will be referred to as a "participant."

Sumitomo Dainippon Pharma Oncology, Inc. (SDPO), is supporting this research study by providing funding for this study and providing the study drug TP-0903.

This study is testing the investigational drug called TP-0903. Investigational means that the FDA has not approved this drug for the treatment of this disease or illness. This study is being done to determine if the study drug, TP-0903, is safe and effective in treating Acute Myeloid Leukemia (AML).

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

Approximately 40-46 patients will take part in this study.

3. What will happen if I take part in this study?

If you agree to take part in the study and sign the consent form, you will be "screened" for the study. This means that you will have tests and procedures completed to determine if you are "eligible" (meet all requirements) to participate in the study. You will be asked questions about your medical history and you will need to tell the study staff about all medications you are taking. After reviewing your health information and test results, the study doctor will determine if you can be in the study. Once you receive a stem cell transplant or stop your study treatment, you will be followed for up to 5 years.

Study Procedures

Screening (tests and procedures done before you can participate in the study)
At study screening, you will read and discuss this Informed Consent Form. If you agree to take part in the study, you will sign and date the last page of this form.

You will have tests and procedures performed to find out if you can be in this study. Some of these may be completed as part of your standard medical care. They include:

- Your medical history including any medications you are currently taking
- A physical exam including height and weight
- Vital signs including blood pressure, heart rate, and temperature
- Blood and urine will be taken for laboratory tests including a serum pregnancy test for female patients
- 12-lead electrocardiogram (ECG)
- Bone marrow core biopsy and aspiration
- You will have an assessment to determine how well you can carry out daily living activities (ECOG Assessment)

If you agree to participate, while in the study you will be responsible for following the study directions given to you by the study staff.

Treatment Procedures (occur after you have been enrolled into the study)
Treatment will be given based on a 28-day cycle.

TP-0903 alone for AML patients with FLT3 Mutations and Relapsed/Refractory Disease:
TP-0903 Monotherapy (up to 4 cycles, each cycle is defined as 28 days):
During this period, you will receive a starting dose level of 50mg of TP-0903 orally (by mouth) every day from Day 1 to Day 21 during each cycle (up to 4). A lower dose level of 37 mg orally (by mouth) every day from Day 1 to Day 21 during each cycle will be considered if 50mg dose is not tolerated.

Stem Cell Transplant:
If your disease responds well, you may be eligible for an allogeneic stem cell transplant. If so, you will stop taking TP-0903 one week prior to admission for the transplant. Stem cell transplantation will be done following The Ohio State University Wexner Medical Center guidelines and will not be detailed in this document. For further details, please talk to your study doctor.

If your disease responds well but you are not eligible for an allogeneic stem cell transplant, you may continue treatment with TP-0903 for as long as you are achieving clinical benefit based on you doctor's judgement.

Follow-up Period
After you receive the stem cell transplant or discontinue the study treatment the study team will follow-up with you every 3 months for up to 2 years from registration and then every 6 months for up to 5 years from registration.
See Table-1 below for a calendar displaying the treatment procedures.

Table 1-Schedule of Assessments

Schedule of Study Assessments	Screening	Cycle1						Cycle 2-Cycle 4							End of Treatment	Follow-Up
		Induction (Day 1- Day 7)														
		D1	D5	D6	D12	D21	D28	D1	D6	D7	D12	D18	D21	D28		
Medical History	X														X	
Physical Exam	X	X	X		X	X		X	X						X	X
Vitals	X	X	X		X	X	X	X	X		X			X	X	X
Electrocardiogram	X	X						x							X	
Pregnancy Test	X														X	
Blood Sample	X	X	X		X		X	X	X		X			X	X	X
Bone Marrow Aspiration & Biopsy	X		X				X							X (Only on C4D28)		
Side Effect Assessment	X		X		X	X	X	X			X			X	X	
TP-0903 Dosing (in clinic/ at home/ inpatient)		X (Daily, Day1-Day21)						X (Daily, Day 1-Day 21)								

4. How long will I be in the study?

Patients may continue treatment indefinitely for as long as clinical benefit is achieved per the investigator's judgment.

After you discontinue therapy for any reason, you will have follow-up visits for up to 5 years from registration.

5. Can I stop being in the study?

You may leave the study at any time. If you decide to stop participating in the study, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled. Your decision will not affect your future relationship with The Ohio State University.

You may be taken off the research study for many reasons including if:

- Your doctor considers it to be in your best interest
- The study treatment or procedures are found to be unsafe or ineffective
- Your condition worsens
- A decision is made to close the study
- Or for any other unforeseen reason that make it necessary to stop your participation in the research study

If you wish to withdraw from the study, please contact the principal investigator, Dr. Uma Borate, at:

Uma Borate, MD
1800 Cannon Drive
Lincoln Tower 1120E
Columbus, OH 43210
614-293-3316
Uma.Borate@osumc.edu

6. What risks, side effects or discomforts can I expect from being in the study?

While participating in this study, you may experience side effects. All cancer treatments can have side effects, which can range from mild and reversible to severe, long-lasting and possibly life-threatening. There is a great deal of variability among side effects of different cancer treatments and between individuals. In a research study, all of the risks or side effects may not be known before you start the study. **You should tell the study doctor right away if you experience any side effects.**

You will be watched closely by your study doctor for any side effects. Your doctor may give you medicines that help lessen side effects. If your doctor decides that it is not safe for you to continue on the study, they may stop your participation.

Please let your study doctor know of any other medications or supplements you are taking. Some medications when taken together with the study medications may either increase the likelihood of side effects or lessen the effectiveness of the study medications.

During the research study, you will be notified of newly discovered side effects or significant findings, which may affect your health or willingness to participate.

Risks and Side Effects of Drug Used in This Study:

TP-0903

TP-0903 may cause low blood cell counts (red blood cells, platelets, and/or white blood cells/neutrophils):

- A low red blood cell count (anemia) may cause difficulty breathing and/or tiredness.
- A low platelet count increases your risk of bleeding (such as nosebleeds, bruising, stroke, and/or digestive system bleeding). You may need platelet transfusions.
- A low white blood cell count increases your risk of infection (such as pneumonia and/or severe blood infection). Infections may occur anywhere and become life-threatening. Symptoms of infection may include fever, pain, redness, and difficulty breathing.
- A low neutrophil count (a type of white blood cell) which increases risk of infection.

TP-0903 may also cause the following changes in blood counts and lab results:

- Abnormal liver test (possible liver damage)
- Increased blood sugar
- Increased blood levels of potassium (possible kidney failure)
- Decreased blood levels of magnesium (possible abnormal muscle function and/or blood pressure)
- Decreased blood levels of phosphate (possible kidney damage)
- High blood levels of uric acid (possible painful joints and/or kidney failure)
- Low albumin in the blood can cause generalized swelling
- Low blood sodium, can cause confusion, seizures, fatigue and low levels of consciousness
- Decreased blood levels of lymphocytes which may increase risk of infection
- Increased blood levels of liver enzymes (alkaline phosphatase, ALT, AST) which may cause possible liver damage
- Increased blood levels of creatinine which may cause kidney damage
- Decreased blood levels of potassium which may cause heart irregularities and muscle weakness

TP-0903 may cause gastrointestinal tract and other body organ side effects:

- Loss of appetite
- Weight loss
- Heartburn (indigestion)
- Nausea and vomiting
- Diarrhea (sometimes with blood)
- Fatigue (feel tired and as though you have no energy)
- Alopecia (hair loss)
- Chest pain
- High blood pressure
- Red eyes due to inflammation
- Taste changes which may affect the way foods normally taste
- Palpitations
- Abdominal pain
- Constipation
- Dyspepsia (indigestion)
- Discolored feces
- Retching (dry heaving)
- Decreased activity
- Dehydration
- Joint swelling
- Anxiety
- Muscle disorders (such as: muscle pain, back pain, flank pain, muscle spasms, muscle weakness)
- Neurological disorders (such as: dizziness, seizures, encephalopathy- a brain disease that alters the brain function or structure, headaches)

Other Risks and Discomforts

Blood Draws

The risks of having blood drawn include pain, bruising, redness, and rarely, infection. Blood will be drawn by experienced technicians and whenever possible it will be obtained at a time when blood is being obtained for other tests your study doctor has ordered.

Bone Marrow Biopsies/Aspirates

Bone marrow aspiration and biopsy may result in pain and/or discomfort at the site where the procedure was done. The risks associated with the procedure include infection and bleeding. Rarely, nerve damage may occur.

Pregnancy-Related Risks

Because taking part in this study can result in risks to an unborn or breastfeeding baby, you should not become pregnant, breastfeed a baby, or father a child while on this study. You must use birth control during the study if you are sexually active.

- Males: You MUST NOT father a child while you are in this study. This treatment may indirectly affect an unborn child. You and your partner must use an approved form of birth control during this study. Even if you had surgery to prevent pregnancy, the drug may harm an unborn child if your partner gets pregnant. Some surgeries (such as vasectomy or having your tubes tied) may not always work. You and your partner will need to continue to use birth control for 3 months after your last treatment unless your partner has had a surgery (i.e. hysterectomy) that prevents pregnancy, or is more than 2 years post-menopausal.
- Females: If you are pregnant, you will not be enrolled on this study. If you become or suspect that you are pregnant, you must tell your doctor right away. Getting pregnant will result in your removal from this study. You MUST NOT become pregnant while you are on this study. The treatment may harm the unborn child. You and your partner must use an approved form of birth control while on the study. You will need to stay on birth control for 3 months after your last treatment. If you had surgery that prevents pregnancy, or are more than 2 years post-menopausal, then you may not need to practice birth control. Your doctor will talk to you about this.

Birth Control Methods:

The only sure way to prevent pregnancy is to not have vaginal sex. Other birth control methods reduce the risk of pregnancy. Sometimes they do not work. If you are a female who is able to become pregnant, you must agree to use a medically acceptable highly effective method of birth control that is approved by your study doctor during the entire study period. If you are a male, you must use an effective barrier method of contraception if sexually active with a female of child-bearing potential.
Medically acceptable methods include:

- Condoms with contraceptive foam
- Oral, implantable or injectable contraceptives
- Contraceptive patch
- Intrauterine device (IUD)
- Diaphragm with spermicidal gel
- Surgically sterile or post-menopausal partner

The study staff will discuss the options that you may use.

If you think you or your partner is pregnant, you must call your doctor right away. Your doctor will discuss your treatment and the effect on the pregnancy. We will follow the pregnancy until delivery to check for any effects from the drug.

Nursing Risks:

The study drug used in this study may harm a nursing baby. You should not nurse your baby while you are getting the study medicines. The drug used in this study could pass into the breast milk even for some time after you stop taking the study drug. Ask your doctor about the length of time you need to avoid nursing.

Fertility Risks:

The drug used in this study may affect your ability to have children in the future (fertility). If you have reached puberty, your doctor may talk with you about egg banking (for females) or sperm banking (for males).

7. What benefits can I expect from being in the study?

Taking part in this study may or may not benefit you. The results of this study may help researchers learn how to better treat future AML patients.

8. What other choices do I have if I do not take part in the study?

Taking part in this research study is voluntary. Instead of being in this research study, you have other options which may include the following:

- Taking part in another research study, if one is available
- Receiving standard of care treatment
    - Standard of care treatment for your type of cancer includes an anti-cancer drug called gilteritinib
- Receiving comfort care, also called palliative care. This type of care may help to reduce the symptoms caused by cancer, but does not treat the cancer directly
- Receiving no treatment

You may choose not to participate without penalty or loss of benefits to which you are otherwise entitled.

9. What are the costs of taking part in this study?

The study agent, TP-0903, will be provided at no cost to you or your insurance. Tests and procedures performed solely for research will also be provided at no cost. This includes a bone marrow aspiration/biopsy on Cycle 1 Day 5 and research testing on your bone marrow and blood by the central lab. Your study doctor or coordinator can tell you, specifically, which costs are covered by the study.

Most of the care you receive during this study is considered routine for the management of your disease. This routine care will be billed to you and your insurance company in the usual manner. Routine care include the drugs needed to treat side effects or complications. Routine

care also includes hospital stays, doctors' services, lab work, and bone marrow aspirations. You will be responsible for any deductibles, coinsurance or copayments required by your insurance plan as well as any costs not covered by your insurance.

Some insurance companies will not cover routine costs if you are participating in a research study. Others may limit what they pay. Before participating in this study, we recommend that you ask your insurance provider if there are any limitations to your particular plan.

If you are a Medicare Advantage Plan participant (HMO or PPO), original Medicare is billed first for routine, study-related services while you participate in an approved trial. Your Advantage Plan is billed second for their share of your costs. You may or may not have additional out of pocket costs after Medicare or your Advantage Plan pays. Additional information can be obtained from your Advantage Plan and online at:

https://www.medicare.gov/Pubs/pdf/02226-Medicare-and-Clinical-Research-Studies.pdf

10. Will I be paid for taking part in this study?

You will receive no compensation (payment) for taking part in this study.

11. What happens if I am injured because I took part in this study?

If you suffer an injury from participating in this study, you should notify the researcher or study doctor immediately, who will determine if you should obtain medical treatment at The Ohio State University Wexner Medical Center.

The cost for this treatment will be billed to you or your medical or hospital insurance. The Ohio State University has no funds set aside for the payment of health care expenses for this study.

Sumitomo Dainippon Pharma Oncology, Inc. may agree to pay for the reasonable costs of treatment of any adverse reaction or injury to you which, in the reasonable judgment of The Ohio State University and Sumitomo Dainippon Pharma Oncology, Inc., specifically results from the Study Drug. Payment may only be made for expenses that are not covered by your medical or hospital insurance or similar third party payor providing such coverage. Sumitomo Dainippon Pharma Oncology, Inc. will not pay for expenses if the adverse reaction or injury to you was caused by the negligence or misconduct of The Ohio State University or Investigator, or if caused by a pre-existing abnormal medical condition or underlying disease.

12. What are my rights if I take part in this study?

If you choose to participate in the study, you may discontinue participation at any time without penalty or loss of benefits. By signing this form, you do not give up any personal legal rights you may have as a participant in this study.

You will be provided with any new information that develops during the course of the research that may affect your decision whether or not to continue participation in the study.

You may refuse to participate in this study without penalty or loss of benefits to which you are otherwise entitled.

An Institutional Review Board responsible for human subjects research at The Ohio State University reviewed this research project and found it to be acceptable, according to applicable state and federal regulations and University policies designed to protect the rights and welfare of research participants.

13. Will my de-identified information and bio-specimens be used or shared for future research?

Yes, they may be used or shared with other researchers without your additional informed consent.

14. Will my study-related information be kept confidential?

Efforts will be made to keep your study-related information confidential. However, there may be circumstances where this information must be released. For example, personal information regarding your participation in this study may be disclosed if required by state law.

Also, your records may be reviewed by the following groups (as applicable to the research):

- Office for Human Research Protections or other federal, state, or international regulatory agencies;
- U.S. Food and Drug Administration;
- The Ohio State University Institutional Review Board or Office of Responsible Research Practices;
- The sponsor supporting the study, their agents or study monitors; and
- Your insurance company (if charges are billed to insurance).

If we find any new information that significantly impacts your health or may affect your willingness to participate in the research study, we will share it with you. This information may be relayed to you by phone, email, mail, or routine clinic visit. You may be asked to sign a new consent form that includes the new information.

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

15. HIPAA AUTHORIZATION TO USE AND DISCLOSE INFORMATION FOR RESEARCH PURPOSES

I. What information may be used and given to others?

- Past and present medical records;
- Research records;
- Records about phone calls made as part of this research;
- Records about your study visits;
- Information that includes personal identifiers, such as your name, or a number associated with you as an individual;
- Information gathered for this research about:
  HIV / AIDS
  Hepatitis infection
  Other reportable infectious diseases
  Physical exams
  Laboratory, x-ray, and other test results
  Diaries and questionnaires
  The diagnosis and treatment of a mental health condition
- Records about any study drug you received;

II. Who may use and give out information about you?

Researchers and study staff.

III. Who might get this information?

- The sponsor of this research. "Sponsor" means any persons or companies that are:
  - working for or with the sponsor; or
  - owned by the sponsor.
- Authorized Ohio State University staff not involved in the study may be aware that you are participating in a research study and have access to your information;
- If this study is related to your medical care, your study-related information may be placed in your permanent hospital, clinic, or physician's office record;
- Others: Sumitomo Dainippon Pharma Oncology, Inc. (SDPO) , data safety monitoring boards

IV. Your information may be given to:

- The U.S. Food and Drug Administration (FDA), Department of Health and Human Services (DHHS) agencies, and other federal and state entities;
- Governmental agencies in other countries;
- Governmental agencies to whom certain diseases (reportable diseases) must be reported; and
- The Ohio State University units involved in managing and approving the research study including the Office of Research and the Office of Responsible Research Practices.

V. Why will this information be used and/or given to others?

- To do the research;
- To study the results; and
- To make sure that the research was done right.

VI. When will my permission end?

There is no date at which your permission ends. Your information will be used indefinitely. This is because the information used and created during the study may be analyzed for many years, and it is not possible to know when this will be complete.

VII. May I withdraw or revoke (cancel) my permission?

Yes. Your authorization will be good for the time period indicated above unless you change your mind and revoke it in writing. You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the researchers. If you withdraw your permission, you will not be able to stay in this study. When you withdraw your permission, no new health information identifying you will be gathered after that date. Information that has already been gathered may still be used and given to others.

VIII. What if I decide not to give permission to use and give out my health information?

Then you will not be able to be in this research study and receive research-related treatment. However, if you are being treated as a patient here, you will still be able to receive care.

IX. Is my health information protected after it has been given to others?

There is a risk that your information will be given to others without your permission. Any information that is shared may no longer be protected by federal privacy rules.

X. May I review or copy my information?

Signing this authorization also means that you may not be able to see or copy your study-related information until the study is completed.

16. Who can answer my questions about the study?

For questions, concerns, or complaints about the study, or if you feel you have been harmed as a result of study participation, you may contact**:**

Uma Borate, MD
1800 Cannon Drive
Lincoln Tower 1120E
Columbus, OH 43210
614-293-3316
Uma.Borate@osumc.edu

For questions related to your privacy rights under HIPAA or related to this research authorization, please contact the HIPAA Privacy Officer in the College of Medicine at **614-292-2856** or by mail at:
HIPAA Privacy Officer
Suite E2140
600 Ackerman Rd.
Columbus, OH, 43202

For questions about your rights as a participant in this study or to discuss other study-related concerns or complaints with someone who is not part of the research team, you may contact the Office of Responsible Research Practices at 1-800-678-6251.

If you are injured as a result of participating in this study or for questions about a study-related injury, you may contact**:**

Uma Borate, MD
1800 Cannon Drive
Lincoln Tower 1120E
Columbus, OH 43210
614-293-3316
Uma.Borate@osumc.edu

Signing the consent form

I have read (or someone has read to me) this form and I am aware that I am being asked to participate in a research study. I have had the opportunity to ask questions and have had them answered to my satisfaction. I voluntarily agree to participate in this study.

I am not giving up any legal rights by signing this form. I will be given a copy of this combined consent and HIPAA research authorization form**.**

Printed name of participant	**Signature of participant**
	AM/PM
	Date and time
Printed name of person authorized to consent for participant (when applicable)	**Signature of person authorized to consent for participant (when applicable)**
	AM/PM
Relationship to the participant	**Date and time**

Investigator/Research Staff

I have explained the research to the participant or his/her representative before requesting the signature(s) above. There are no blanks in this document. A copy of this form has been given to the participant or his/her representative.

Printed name of person obtaining consent	**Signature of person obtaining consent**
	AM/PM
	Date and time

Witness(es)

Printed name of witness	**Signature of witness**
	AM/PM
	Date and time
Printed name of witness	**Signature of witness**
	AM/PM
	Date and time