Subject No.: _____

Completed by / Date:
_____

INFORMATION AND CONSENT FORM
AND
AUTHORIZATION TO USE AND DISCLOSE PERSONAL AND HEALTH INFORMATION

Sponsor:	Jupiter Orphan Therapeutics
Study Title:	**A PHASE 1 STUDY TO ASSESS THE PHARMACOKINETICS AND SAFETY OF ASCENDING DOSES OF JOTROL ORAL GELCAPS IN HEALTHY SUBJECTS, AND TO DETERMINE THE INFLUENCE OF FOOD**
Protocol Number:	**202016**
Principal Investigator: (Study Doctor)	David J. Wyatt, M.D.
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PART 1

INTRODUCTION, DESCRIPTION, STUDY DURATION

(1) Introduction

You are invited to participate as a subject in a clinical research study. Your participation in this study is voluntary. You have the right to decide not to participate in it or to withdraw at any time without penalty or loss of benefits. During the study, you will be informed as soon as possible of any new information on the study drug that might affect whether you want to continue participating in the study. The study doctor or a designated study staff member can decide to withdraw you from the study, without your consent, if they judge that it would be better for your health, if you do not follow the instructions given to you, or for other reasons. If you are withdrawn from the study by the study doctor or study staff, the reason for your withdrawal will be explained to you. At the time of your withdrawal from the study, you will be asked to undergo additional tests for your safety; one last blood sample may also be collected to measure the amount of study drug in your body.

In total, there will be approximately 24 healthy non-smoking adult subjects participating in this study. This Information and Consent Form is intended to give you an overview of this clinical research study and what it involves. It may contain words that you do not understand. Please ask the study doctor or a member of the study staff to explain any words or information that you do not understand.

If you decide to participate in this study, you will be asked to sign and date this Information and Consent Form. This will confirm that you have been informed of the nature of the study and what it involves but does not take away any of your legal rights.

The Sponsor, Jupiter Orphan Therapeutics, is paying Syneos Health to cover the costs of conducting this study.

(2) General description of the study

This study involves a drug called resveratrol, which is being developed as a gelcap called JOTROL for the treatment of Mucopolysaccharidosis type I (MPS1), Friedreich's ataxia (FA) and or Alzheimer's Disease. MPS1 is an inherited disease-causing damage to multiple organs, and which can lead to short stature, severe abnormalities in the development of bones and cartilage, impaired vision and hearing, swelling of liver and spleen, and intellectual disability. FA is an inherited disease-causing progressive damage to the nervous system. Initially characterized by impaired muscle coordination such as gait disturbance that worsens over time, FA can lead to gradual loss of strength and sensation in the arms and legs, muscle stiffness, impaired speech, hearing, vision, heart diseases, and diabetes. Alzheimer's disease is a form of dementia (mental disorder characterized by a loss of memory, judgment and capacity to think, and changes in personality) that primarily afflicts older patients.

The JOTROL gelcap contains trans-resveratrol (common name: resveratrol) as active ingredient. Resveratrol is naturally found in an abundant amount in red wine, grape berry skins, seeds and, particularly in dried roots of some plants.

Although resveratrol has been evaluated in human studies before, JOTROL has never been given to humans in any standardized clinical trial. In this study, it will be the first time ever that JOTROL is being given to humans. The safety and tolerability of the study drug in humans is unknown at this time. JOTROL is an "investigational" drug product, which means that JOTROL has not been approved for use by the United States Food and Drug Administration (FDA) outside of research studies. JOTROL is therefore considered experimental.

The JOTROL gelcap contains 100 mg of resveratrol.

The purposes of this study in healthy volunteers are to:

- Evaluate how much and how quickly the study drug is taken up, and eliminated by the body when JOTROL is administered as a single dose at different dose levels ranging from 200 mg resveratrol to a resveratrol dose currently estimated at 1000 mg.
- Evaluate how much and how quickly the study drug is taken up and eliminated by the body when administered as gelcaps under fasting conditions and after a meal.

The study will be divided into 2 parts (4 periods in total). All eligible subjects will participate in Study Part 1. You may not be invited to participate in the second part of the study.

Study Part 1:

This study part involves the administration of single doses of JOTROL under fasting conditions. It will be divided in 3 periods in which the study drug will be administered at increasing dose levels. Dose levels will be administered one after the other, beginning with the lowest dose level (200 mg resveratrol). The following JOTROL doses are planned to be administered:

Periods	**Planned JOTROL doses**
Period 1	Total JOTROL dose: 2 × 100 mg gelcaps (200 mg of resveratrol)
Period 2	Total JOTROL dose: 5 × 100 mg gelcaps (500 mg of resveratrol)
Period 3	Total JOTROL dose: 10 × 100 mg gelcaps (1000 mg of resveratrol)

Each dose level (or period) will be separated from the previous by at least 14 days. After the procedures are completed for a given period, a Safety Review Committee (composed of at least the Study Doctor, an independent third party physician, and a Sponsor's medical representative) will review all information collected for this dose level to decide if it is safe to continue the study with the next planned dose level. If the Safety Review Committee judges that it is not safe to proceed with the next planned dose level, the next dose level may be decreased, the previous dose level may be repeated, or the part of the study that you are participating in may be stopped. If that part of the study is stopped, your participation may be cancelled.

Study Part 2:

Even if you have participated in study Part 1, you may not be offered to participate in Part 2. Only 16 subjects who have completed study Part 1 will be invited to participate in this study part during which they will be administered JOTROL at the highest dose level used during study Part 1 after eating a breakfast high in calories and fat. This is referred to as Period 4. Administration

of the study drug in Period 4 (study Part 2) will be separated from the one of Period 3 (study Part 1) by at least 14 days.

This study should last approximately 1 month for subjects participating in study Part 1 only and 1.5 months for subjects participating in both study parts. Each of the 4 study periods involves a stay of approximately 3 days at Syneos Health (including 2 nights), during which you will not be allowed to leave the site or receive visitors. The first 3 periods form the study Part 1 while study Part 2 consists of Period 4 only. You will be sharing the clinical facilities, including bedrooms, with other subjects, which could reduce your privacy. Each study drug administration will be separated from the previous by at least 14 days to ensure that the study drug you took during one period is no longer in your body when you begin the next period.

PART 2

RISKS OF SIDE EFFECTS

(1) Risks of side effects

Participation in a clinical research study involves some unforeseeable risks of side effects that could occur. The frequencies listed below are not predictive of what could happen during the study. They result from a limited number of studies, usually performed in subjects receiving multiple doses of the study drug. Please be aware that the side effects mentioned below could occur at a frequency higher or lower than indicated, and some side effects not indicated below could also occur. Unless otherwise stated, the side effects listed below are anticipated to be temporary, and it is anticipated that they will disappear by the end of the study.

(2) Risks associated with the study drug formulations

Following the administration of oral (by mouth) resveratrol during clinical studies, resveratrol was well-tolerated. Side effects possibly related to resveratrol are gastrointestinal symptoms such as nausea and diarrhea, when resveratrol was given at repeated doses above those planned to be administered in this study.

The following side effects were seen in 2% to 15% (except if otherwise stated) of the 64 subjects with mild to moderate Alzheimer's disease and in equal or greater frequency than in the placebo (dummy pill that looks similar to resveratrol but does not contain the active ingredient) group are listed below. These subjects were taking resveratrol 500 mg once daily for 52 weeks, with a 500-mg increments every 13 weeks, ending with 1000 mg twice daily (total daily dose of resveratrol: 2000 mg).

<u>Gastrointestinal disorders (42%)</u>

- Diarrhea (41%)
- Nausea

<u>General disorders</u>

- Weight loss (17%)
- Fall (34%)

Nervous system disorders (39%)

- Headache

The following side effects were seen in 2% to 15% (except if otherwise stated) of the 13 subjects with Friedreich's ataxia taking resveratrol 500 mg twice daily (total daily dose: 1000 mg) for 12 weeks and of the 14 subjects with Friedreich's ataxia taking total daily dose of 5 gm of resveratrol for 12 weeks.

Cardiac disorders

- Rapid and irregular heartbeat
- Increase in the level of substances (called enzymes) in blood that may indicate heart problems

Gastrointestinal disorders

- Loose stools
- Abdominal pain/cramps
- Bloating
- Flatulence
- Diarrhea
- Nausea
- Indigestion/upset stomach
- Constipation

Infections

- Urinary tract infection (23%)
- Tonsillitis (inflammation of tonsil)
- Inflammation of the sinus (sinusitis)

Kidney and urinary disorders

- Proteins in urine

Liver, gallbladder or pancreas disorders

- Increase in the level of substances (called enzymes) in blood that may indicate liver problems

Nervous system disorders

- Headache (31%)
- Fatigue (23%)

Respiratory disorders

- Upper respiratory tract infection (31%)

Skin disorders

- Skin rash
- Swelling of the lower limbs

Please note that these side effects were reported in subjects with mild to moderate Alzheimer's disease or with Friedreich's ataxia and receiving daily doses of resveratrol that are a multiple of the planned doses in the present study. In addition, during this study, you will receive JOTROL only 3 to 4 times at least 14 days apart.

The following AEs were more frequently reported by subjects in the 5 g/day resveratrol group: loose stools, diarrhea, and abdominal pain/cramps. In another study conducted in subjects with hepatic metastasis given 5 g/day, the most commonly reported side effects were episodes of light diarrhea, nausea, anal pruritus (itching), and symptoms of hypersensitivity (allergic reactions).

Other side effects have been reported. Any side effect, rare or not, may worsen and be life-threatening.

(3) Allergic reaction risks

With any medication, there is a small but real risk of allergic reactions that can be fatal. These reactions usually start shortly after taking the study drug. If you have a very serious allergic reaction, you may be at risk of death. Some symptoms of allergic reactions are:

- Skin itching, redness, rash
- Difficulty breathing
- Dizziness and fainting
- Swelling around the mouth, throat or eyes
- A fast pulse
- Sweating

If you experience any of the reactions mentioned above, you must immediately inform the Syneos Health study staff or proceed to the nearest hospital emergency department.

(4) Risks associated with study procedures

Blood collections

Among other known risks of side effects in a clinical research study, there are those related to the use of needles for blood collection and catheter (intravenous – IV) insertion: pain, bruising and swelling at the site of blood collection, fainting for a short period, and, very rarely, nerve damage or infection at the needle insertion site.

Electrocardiograms

Electrocardiogram(s) (recording of the electrical activity of the heart or "ECG") will be done during this study. Electrodes (small sticky patches) will be placed on your body. There is no pain or risks related to an ECG. However, removing the electrodes may cause skin irritation. In some areas, it may be necessary to shave a small spot of body hair so the adhesive patches can be properly placed on your body.

Contagious diseases

Finally, although we try to make sure that all subjects are healthy upon participation in the study, the risk of contagious infection is increased because you will be in contact with a number of people during your stay at the site.

(5) Risks associated with pregnancy

Women:

If neither you nor your male partner is surgically sterile (male partner vasectomized since at least 6 months) and if you are not post-menopausal (absence of menses for at least 12 months), you are required to avoid becoming pregnant while you are participating in this study since there may be risks to you or the fetus associated with the use of resveratrol during pregnancy.

You are therefore required to use one of the following methods of contraception for the time specified prior to taking the study drug, throughout the study and until 30 days following the last study drug intake:

- Male condom with spermicide applied intravaginally, for at least 21 days before taking the study drug.
- Intrauterine contraceptive device without hormone release system placed at least 4 weeks before taking the study drug.

Except abstinence, no method of contraception is 100% effective. If you think you may have become pregnant even though you used required contraception while in the study, you should contact the study doctor or the study staff immediately (see telephone number at the first page of this form). Follow-up information about the pregnancy and the outcome will be collected and documented.

PART 3

SUBJECT'S SCREENING SESSION

In order to participate in a clinical research study at Syneos Health, you must first (1) undergo a general medical examination, (2) provide a blood sample, (3) provide a urine sample, and (4) possibly undergo other tests and exams to determine your eligibility. This screening session is expected to last 1 to 3 hours. Some results of the tests and exams performed during this screening session could be used by Syneos Health as the screening tests and exams required for another study.

(1) Medical examination

The medical examination involves:

1. A complete medical questionnaire (for example, past surgery, current condition, medication intake),
2. A general physical examination,
3. Recording of your demographic data (for example, height, weight, etc.),
4. Measurement of your vital signs (for example, blood pressure, heart rate, respiration rate, oral temperature),
5. Recording of the electrical activity of your heart (an ECG).

The physical examination will involve, among other things, an examination of the armpit areas, groin, and the lower legs and ankles to check for swelling of the lymph glands and/or circulation.

(2) Blood draw

A blood sample is necessary to verify your general health status and to detect a possible HIV, Hepatitis B or Hepatitis C infection. A positive result for any of these tests must be reported to the Public Health authorities, as required by law. The total amount of blood collected during the screening session will not exceed 25 mL (about 2 tablespoons).

(3) Urine sample

A urine sample is necessary to verify your health status and to screen for drugs or medications of abuse. It will also be used to verify if you have smoked.

(4) Other tests, exams, samples

a) If you are a woman, you will undergo a urine pregnancy test.
b) Additional samples may be required to repeat analyses or to measure other blood components. You will be informed if new, additional blood measurements are required.
c) You could be asked to come back again to Syneos Health to repeat a test.

(5) Abnormal results

Any abnormal result in the exams, tests, and analyses mentioned above may affect your eligibility to participate in a study. You will be informed of any significantly abnormal result obtained during the screening session or during the study and, if necessary, you will be referred to a health professional.

PART 4

STUDY CONDUCT

(1) Study Procedures

For each period, you will have to show up at Syneos Health on Day -1 at a time specified by the clinic staff.

The following tests will be done upon admission:

- Urine analysis to screen for drugs or medications of abuse;
- Urine cotinine test to confirm that you have not smoked;
- Alcohol breath test;
- Blood pregnancy test

A positive result for one of these tests will automatically result in withdrawal from the study.

In addition to the above tests, blood sample will be collected to verify your general health status upon admission in Period 4 only.

Study Part 1:

The next morning in each of the first 3 study periods, after you have fasted for at least 10 hours, you will be asked to swallow JOTROL gelcaps containing 100 mg of resveratrol, at doses ranging from 200 mg to 1000 mg. The following doses are planned to be administered:

- Period 1: 2 x 100 mg JOTROL oral gelcaps, total resveratrol dose 200 mg
- Period 2: 5 x 100 mg JOTROL oral gelcaps, total resveratrol dose 500 mg
- Period 3: 10 x 100 mg JOTROL oral gelcaps, total resveratrol dose 1000 mg

Doses in Period 2 and 3 may be modified upon decision of the Safety Committee.

Study Part 2 (Period 4):

Sixteen (16) subjects who complete Part 1 of the study may be invited to participate in Part 2 of the study, if deemed eligible by the study doctor.

The next morning, after you have fasted for at least 11 hours, you will have 30 minutes to eat a breakfast in its entirety and then you will be asked to swallow JOTROL gelcaps containing 100 mg of resveratrol, at a maximum dose of 1000 mg (10 x 100 mg JOTROL oral gelcaps, total resveratrol dose 1000 mg). The exact dose to be administered will be selected following collection and analysis of data from study Part 1. The clinical staff will advise you on the exact dose to be administered before dosing. The breakfast will consist of 2 eggs fried in butter, 2 slices of toast with butter, 2 strips of bacon, hash brown potatoes, and about 1 cup of whole milk.

Throughout the study, the study drug will be administered with 240 mL (about 1 cup) of water and a hand and mouth check will be performed to ensure consumption of the study drug. You must not crush or chew the gelcaps, they must be swallowed as a whole.

In each of the 4 periods:

A total of 17 blood samples will be collected to measure the amount of study drug in your body, over a period of 32 hours. In the hours following study drug administration, blood draws could be done close to one another. There will be 1 blood samples taken at night, which will interrupt your sleep, so you will not get a full night's rest. Blood draws will be done using needle puncture or a catheter (for the first 14 blood collections). A catheter (IV) is a flexible tube inserted into the vein that allows taking several blood samples without repeated needle insertion into the skin. The total volume of blood collected should not exceed **733** mL (about **three** cups) for the whole study and **605** mL (about 2 **and half** cups) for subjects participating in Part 1 only. In comparison, a blood donation generally represents approximately 450 mL (2 cups or 1 pint) of blood, and it is done in 1 day.

Five (5) blood samples over a period of 24 hours will be collected for potential RNA analysis, iduronidase activity (how your body breaks down certain molecules), frataxin mRNA, and other possible investigational tests.

Genes are made up of deoxyribonucleic acid (DNA), the genetic material that is found in all cells of your body and containing instructions that your body reads to understand how it should be built and work. In order to send its instructions, DNA needs to be transcribed into ribonucleic acid (RNA). RNA is a molecule implicated in various biological processes, including protein synthesis. There are proteins involved in absorption, breaking down, and elimination of ingested substances. Studying RNA may help understand differences among individuals in the way they respond to the study drug, as well as helping in the development of new drugs or improvement of existing drugs. Therefore, this study includes collecting blood samples for RNA analysis. The blood samples will also be used for iduronidase activity measurement, and other possible investigational tests. Iduronidase is a protein involved in many processes in the body. A deficiency in this protein activity leads to the accumulation of some substances in the body cells that may result in diseases that might be severe.

You have the right to decide not to participate in the RNA analysis and other investigational tests. However, because these analyses are part of the study, if you do not agree to participate in these tests, you cannot participate in this clinical research study. Blood samples will be sent to an external laboratory where your RNA will be analyzed, and the other tests will be done. These samples will be labeled with a code that will be kept by the investigator, so that you can not be identified. Procedures will be done for the long-term preservation of these samples until planned tests have been done. Therefore, samples will be retained for up to 2 years, until exhausted or until the Sponsor requests destruction. If you withdraw consent, your banked specimens will be promptly disposed of. However, the data will not be discarded if analyses have been completed before you withdraw consent.

For study Part 1 only, 3 additional blood samples (approximately 2 tablespoons per sample) in each period will be collected, from at most (maximum) 10 subjects, for the evaluation of immune cells in your blood.

For Part 1 (Periods 1, 2, and 3), urine samples will be collected at 6 different time intervals from 2 hours before dosing until 32 hours after dosing.

A study doctor will be reachable at all times during the study. If deemed necessary by the study staff, additional tests or blood draws could be performed to ensure your safety.

(2) Post-study procedures

The following procedures will be performed on the last study day to check your overall health:

- Blood and urine tests;
- Vital signs;
- ECG;
- Urine pregnancy test for female subjects

We recommend that you stay on our premises for 5 minutes following a blood draw. Please mention to the study staff if you feel sick or believe you are having side effects of any kind.

Even after the study is completed, Syneos Health may contact you within a few weeks after the last study day to clarify information or to ask you to come back for additional tests for your safety.

PART 5

STUDY RESTRICTIONS

(1) Food and fluids

You will have to follow a standard diet during your stay at Syneos Health:

- Study Part 1 (Periods 1, 2, and 3): No food will be allowed from at least 10 hours before to at least 4 hours after taking the study drug, for a total of at least 14 hours.
- Study Part 2 (Period 4): No food will be allowed at least 11 hours before receiving a breakfast high in fat and calories. You will also be fasting for 4 hours after the administration of study drug.
- Except for fluids provided with the critical breakfast (study Part 2 only) and water given with the study drug, no fluids will be allowed from at least 1 hour before to at least 1 hour after taking the study drug.

(2) Physical activity

You will be free to engage in normal activities after administration of study drug. Lying down or sleeping will be prohibited for the first 2 hours (study Part 1) and 4 hours (study Part 2) after taking the study drug, unless it is required for your health or by study procedures. Performing vigorous physical activity will be prohibited during your stay.

(3) Other restrictions to prevent possible interactions with the study drug

It is important that you follow all the restrictions listed in the table below. Not following these restrictions could have consequences on your health or on the study results.

Prohibited product	Restriction before the study	Restriction during the study
Prescription medication*	14 days before the first study drug administration	Throughout the study
Over-the-counter products* (other than the occasional use of acetaminophen [up to 2 g daily])	14 days before the first study drug administration	Throughout the study
Hard drugs (for example, cocaine, PCP, crack, heroin, amphetamines)	1 year before the screening visit	Throughout the study
Soft drugs (for example, marijuana)	3 months before the screening visit	Throughout the study
Food containing poppy seeds (muffins, bagels and cakes)	24 hours before the admission	None

Natural health products (including herbal remedies, homeopathic products, traditional medicines, probiotics, food supplements such as vitamins, minerals, amino acids, essential fatty acids, and protein supplements used in sports)	14 days before the first study drug administration	Until after the last blood draw of each period
Drugs known to induce or inhibit liver drug metabolism, including St. John's wort	30 days before the first study drug administration	Until after the last blood draw of the study
Depot injection or an implant of any drug	3 months before the first study drug administration	Throughout the study
Grapefruit, starfruit, pomegranate, pineapple, or pomelo products (fresh, canned or frozen)	7 days before study drug administration in each period	Until after the last blood draw of each period
Alcohol-based products	24 hours before the admission in each period	Until after the last blood draw of each period
Food or beverages containing caffeine (for example, coffee, tea, chocolate, cola beverages or decaffeinated products) or energy drink	48 hours before study drug administration in each period	Until after the last blood draw of each period
Tobacco products	3 months before the screening visit	Throughout the study
Foods rich in resveratrol (for example grapes, peanuts and their derived-products including wines and juices)	7 days before administration of study drug in each period	Until after the last blood draw of each period

***** For certain drugs, the restriction period may be longer than indicated in the table. A study doctor will evaluate all medications you took before the beginning of the study to make sure that the restriction periods are appropriate.

PART 6

SAFETY INSTRUCTIONS, COMPENSATION, CONFIDENTIALITY, AND SUBJECT'S RIGHTS

(1) Safety instructions

If you do not follow the study restrictions, you should tell the study staff as soon as possible.

Before taking any medication (prescription or over the counter), you need to check first with the study doctor or study staff if this medication is safe for you to take. In case a healthcare professional (for example, a doctor, pharmacist or dentist) recommends you to take medication for a health problem or if you need to have a medical procedure (for example, a surgery) while

participating in this study, you should inform the healthcare professional that you are taking part in a clinical research study on a study drug called JOTROL (resveratrol).

Upon leaving the Syneos Health facility, if you feel dizzy or drowsy, you should not perform activities requiring mental alertness, judgment and physical coordination such as driving or operating machinery until you feel secure and safe to do so.

(2) Study-related injury

In case of injury or disease because of your participation in this study, you will receive appropriate medical care. The sponsor is committed to cover all necessary and related medical costs not covered by your private medical insurance (if any).

To pay medical expenses, the sponsor will need to know some information about you like your name, date of birth, and Medicare Beneficiary Identifier (MBI). This is because the sponsor has to check to see if you receive Medicare and if you do, report the payment it makes to Medicare.

If you suffer a serious or lasting injury as a result of participation in this study, it may affect your ability to obtain private health insurance, your employability, and/or quality of life. No compensation other than that mentioned in this Information and Consent Form is planned.

In no way does signing and dating this consent form waive your legal rights nor does it relieve Syneos Health, the study staff, sponsor or others involved in the study from their legal and professional responsibilities.

(3) Benefits

No direct benefits can be anticipated from participating in this clinical research study. The tests provided may help you learn about your general health. This study may help doctors and scientists learn things about the study drug that will help others.

(4) Alternatives to being in the study

You are being asked to take part in this study because you are healthy. The only option is not to take part in this study.

(5) Compensation

You will not receive compensation for your participation in the screening visit.

You will receive compensation for the time and inconveniences related to your participation in this study. Details about the amount of compensation and the payment schedule specifying the specific amounts and timing of payments are outlined in Appendix 1 provided with this Information and Consent Form.

If you do not complete the entire study, the amount you receive will depend on the portion of the study you completed, even if the study is cancelled or stopped by the sponsor or Syneos Health.

There are no costs for you: any expenses and costs associated with the study are covered by the sponsor.

(6) Voluntary participation / Withdrawal

You are encouraged and have the right to ask questions at any time concerning potential and/or known risks of this study. Your participation in this study is voluntary. You have the right to decide not to participate in it or to withdraw at any time without penalty or loss of benefits. The study doctor will inform you of any new significant information, when it becomes available, which may affect your willingness to continue to participate in this study. This new information may mean that you can no longer participate in this study. It could also mean that the sponsor may suspend or prematurely end the study. If this occurs, the study staff supervising the study will stop your participation.

(7) Data retention

If you decide to withdraw from the study, or if the study doctor or a study staff decides to withdraw you from the study for safety reasons, for not following the requirements of the study, or for any other reason, the data collected up to the time of your withdrawal from the study remains part of the study database and may not be removed.

(8) Confidentiality

Syneos Health takes necessary steps to protect the privacy of your personal information. The use and disclosure of your study records will be done in accordance with the Authorization to Use and Disclose your Personal and Health Information presented in Appendix 2 of this Information and Consent Form or when disclosure is required by law. You will be asked to sign and date this authorization before taking part in the study.

Outside of Syneos Health, you will be identified at all times by a number and your initials, unless there is an emergency situation and/or a representative of Syneos Health has to communicate with your primary doctor. If the results of the study are published, your identity will remain confidential.

As part of this clinical research study, the study doctor will collect personal information about you and your health. You have the right to check your study records and request changes if the information is not correct.

The above-mentioned study data will be available for confidential consultation and may be accessed by representatives of Syneos Health in the United States and outside of United States, by representatives of the study sponsor, various regulatory agencies such as the U.S. Food and Drug Administration (FDA), as well as the Institutional Review Board, Advarra.

While every effort will be made to protect the privacy of your information, absolute confidentiality cannot be guaranteed. This does not limit the duty of the study doctor and the study staff to protect your privacy.

In addition, should you require medical care or hospitalization during the course of the study, Syneos Health's representative may contact the treating physician with your consent, except that consent may not be requested if there is an emergency situation.

(9) Monitoring

As part of your participation in this study you will be monitored by closed-circuit television (CCTV) during screening, any stay and follow-up visits including exit visit. CCTV cameras are located throughout the screening center, the clinical unit and the eating area/recreation room. CCTV cameras are not placed in the restrooms/washrooms or showers. The purpose of CCTV is to maintain close watch of your health condition while participating in the study to make certain you are safe. By signing and dating this Information and Consent Form you agree to be monitored by closed-circuit television.

(10) Whom to contact about the study

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns or complaints about the study, please contact the study doctor or study staff at the telephone number listed on the first page of this consent document. If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in this research study.

An institutional review board (IRB) is an independent committee established to help protect the rights of research subjects. If you have any questions about your rights as a research subject, and/or concerns or complaints regarding this research study, contact:

- By mail:
  Study Subject Adviser
  Advarra
  6940 Columbia Gateway Drive, Suite 110
  Columbia, MD 21046
- or call **toll free**: 877-992-4724
- or by **email**: adviser@advarra.com

Please reference the following number when contacting the Study Subject Adviser: Pro00046245.

Please note that for matters regarding payment or routine compensation issues, questions should be directed to Syneos Health.

PART 7

ATTESTATION, AUTHORIZATION, COMMITMENT, AND CONSENT

(1) Attestation

I acknowledge I have been given sufficient time to read this Information and Consent Form, ask any question I might have about the information presented and decide whether or not I want to participate in this study.

I acknowledge having received satisfactory answers to questions I have asked.

(2) Authorization

I authorize the confidential consultation of the study data including data collected about me by the organizations described in Part 6.

For my safety, I authorize Syneos Health to contact other clinical research organizations to verify my past or current participation in clinical research studies and in blood donation sessions. I also authorize Syneos Health to disclose to these organizations information relative to my past or current participation in studies conducted by Syneos Health. The exchange of information with other organizations regarding my participation in other clinical research studies may be done with a system that uses my fingerprint.

(3) Commitment

- I will not donate blood or plasma from the screening session, during my participation in this study and for at least 56 days after the end of the study;
- I will attend all scheduled visits on time;
- I will give true information about my medical history;
- I will not participate in another clinical research study during this study and for at least **56** days after the end of the study;
- I will respect all study restrictions and follow all instructions given to me by the study staff;
- **For women:** I will use adequate contraceptive methods for at least 30 days following the last study drug administration;
- I will advise the study staff of any change in my medical condition, minor or major, during the study and for 4 days following the last study drug administration;
- I will comply with Syneos Health rules and requirements.

(4) Consent

The study doctor has my permission to contact my doctor about my participation in this study:

YES _____ NO _____
Initials Initials

First and last name of the doctor to contact: _____

I consent to taking part in the procedures described in this document and confirm that I will be given a signed and dated copy of this form for my records.

_____ _____
Print first name Print last name

_____ Date: | | | - | | | | - | | | | |
Signature D D M M M Y Y Y Y

By signing and dating this document you do not waive any of your legal rights, nor release the study doctor or sponsor from their legal and professional obligations. Signature of this document confirms you have been informed about the nature of the study you are participating in.

PART 8

STUDY DOCTOR'S OR STUDY DESIGNEE'S DECLARATION

I confirm that the subject was given an opportunity to ask any questions about the study. I have answered the subject's questions about study participation and the associated risks and benefits. I have also encouraged the subject to ask additional questions at any time during the course of the study. I confirm that the subject was given a signed and dated copy of the Information and Consent Form.

_____ _____

Print first name Print last name

_____ Date: | | | - | | | | - | | | | |

Signature D D M M M Y Y Y Y

Time of signature *if not recorded electronically*: _____

APPENDIX 1 – COMPENSATION

As a compensation for the time and inconveniences related to your participation in this study, you could receive up to $**2430** for the Part 1 of the study and up to an additional **700**$ for Part 2.

Compensation will be allocated at the completion of each event as follows:

Compensation schedule Part 1	
Periods 1 and 2	
Each onsite stay*	$500
Period 3	
Onsite stay*	$500
Amount for the duration of the study (including washout duration in case you would be selected to participate in Part 2)	$**600****
Amount allowed for completing Part 1***	$330
Total	**$2430**

*If you don't complete the entire stay, you will receive a prorated amount based on the reason you leave the study ($100 / 12 hrs). Please ask your study doctor for more information.

**** This amount for the duration of the study will be given at the last period completed.**

*** This amount will be allocated only to subjects completing the whole study Part 1. Completing the whole study means completing all 3 Part 1 study periods.

****** Subjects having extra blood collected for immune cells evaluation will get an additional $100 per period.**

You may be selected as a stand-by subject for Part 1 and should be ready to fully participate in the study as a replacement. If you are selected as a stand-by subject, you will receive $150 if you are asked to stay onsite until study drug administration is completed. If you are not called upon to spend the night at Syneos Health, you will receive $75. You will be paid at the time of leaving the site if you are not called upon to participate in the study.

If you have completed Part 1, you may be selected as a subject for Part 2. If you are dosed in Part 2, you will receive:

Compensation schedule Part 2	
Period 4	
Onsite stay*	$500
Amount allowed for completing Part 2**	$**200**
Total	**$700**

*If you don't complete the entire stay, you will receive a prorated amount based on the reason you leave the study ($100 / 12 hrs). Please ask your study doctor for more information.
**This amount will be allocated only to subjects completing the Part 2 study period.

You may be selected as a stand-by subject for Part 2 and should be ready to fully participate in the **period** as a replacement. If you are selected as a stand-by subject, you will receive $150 as you will be asked to stay onsite until study drug administration is completed.

The amounts mentioned above may be subject to tax withholding and reporting as per Federal and State laws.

APPENDIX 2 – AUTHORIZATION TO USE AND DISCLOSE PERSONAL AND HEALTH INFORMATION

As part of this clinical research study, the study doctor will collect personal information about you and your health. This personal and health information may include your date of birth, gender, ethnicity, information obtained via access to your personal medical records (for example, past medical history and test results), and the results of the study-related tests and procedures described in this Information and Consent Form (for example, laboratory test results, physical exam data, electrocardiogram, etc.). This personal and health information will be kept in the study records.

Syneos Health requires that all study subjects provide authorization for the use and disclosure (release) of personal and health information collected by Syneos Health or otherwise as part of your potential participation in a clinical research study. You do not have to sign and date this authorization to use and disclose your personal and health information, but if you do not, you may not participate in this study.

Your personal and health information may be used by and/or disclosed as follows:

- Outside of Syneos Health, you will be identified at all times by a number and your initials, unless there is an emergency situation and/or Syneos Health is communicating with your primary doctor.
- The study records will be available for confidential consultation by representatives of the study sponsor, various regulatory agencies such as the U.S. FDA, as well as the Institutional Review Board, Advarra. This consultation is done to verify study procedures and/or data, without violating confidentiality of the subjects except to the extent permitted by applicable laws and regulations.
- In the context of this study, study data may also be sent to these persons/organizations upon their request. Some of the persons/organizations that will have access to your personal and health information may be based outside the United States. While every effort will be made to protect the privacy of your information, absolute confidentiality cannot be guaranteed. This does not limit the duty of the study doctor and the study staff to protect your privacy.
- You have the right to check your study records and request changes if the information is not correct.
- If the results of the study are published, your identity will remain confidential.
- Your personal information, including your health information, will be kept by Syneos Health in a database with limited access for a period of at least 2 years after the marketing application for the study drug is approved, or if the application for the study drug is not approved, until at least 2 years after the study is over.

The sponsor and those working for the sponsor may use the data and information sent to them:

- To see if the study drug works and is safe.
- To compare the study drug to other drugs.
- For other research activities related to the study drug.

This authorization does not have an expiration date. You may change your mind and revoke (cancel) this authorization at any time. Even if you revoke this authorization, Syneos Health and the sponsor of the study may still use or disclose your personal and health information they have already obtained as necessary to maintain the integrity or reliability of the current study. To revoke this authorization, you must write to the study doctor at the address listed on the first page of this Information and Consent Form, stating that you are revoking your Authorization to Use and Disclosure your Personal and Health Information. If you revoke your authorization before the study is completed, you will not be allowed to continue your participation in the study. Other than in connection with any testing procedures to be performed in connection with your withdrawal from the study, no new personal or health information that identifies you will be gathered after your written request is received. However, your personal and health information that has already been gathered may still be used and given to others as described in this form.

Your right to access your personal and health information in the study records will be suspended during the study to keep from changing the study results. When the study is over, you can access your study personal and health information.

Authorization

I give permission to Syneos Health and representatives of the study sponsor to use or disclose my personal and health information that may identify me for the clinical research study, as described in this Information and Consent Form. I will receive a signed and dated copy of this form for my records.

Name of the subject:

_____ _____
Print first name Print last name

_____ Date: | | | - | | | | - | | | | |
Signature D D M M M Y Y Y Y

Name of the person obtaining the authorization:

_____ _____
Print first name Print last name

_____ Date: | | | - | | | | - | | | | |
Signature D D M M M Y Y Y Y