

**CONSENT TO TAKE PART IN A CLINICAL RESEARCH STUDY  
AND  
AUTHORIZATION TO DISCLOSE HEALTH INFORMATION**

**Sponsor / Study Title:** Arisan Therapeutics, Inc./ “A PHASE 1, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, TWO-PART (SINGLE-ASCENDING DOSE AND MULTIPLE-ASCENDING DOSE) STUDY TO ASSESS THE SAFETY, TOLERABILITY, AND PHARMACOKINETICS OF ARN-75039 WHEN ADMINISTERED BY THE ORAL ROUTE IN HEALTHY ADULT SUBJECTS”

**Protocol Number:** ARN-75039-101 (v6.1)

**Principal Investigator:  
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West Bend, WI 53095

**SUBJECT SCREENING #** \_\_\_\_\_

**KEY INFORMATION:**

You are invited to take part in a research study. This research study is studying ARN-75039 as a possible treatment for Lassa virus (LASV) infection. Arisan Therapeutics, Inc. is sponsoring this research study.

You will not receive direct medical benefit from receiving the study drug. You may benefit by having your medical history recorded, undergoing a physical examination, and having blood and urine tests as they apply to this research project.

Just by taking part in this research study, you may be helping future patients by providing important information about the study drug and by contributing to medical knowledge.

The goal of this study is to assess the safety and tolerability of single and multiple doses of ARN-75039 when administered by the oral route at escalating dose levels in healthy volunteers. If you agree to participate in this study, you will be given ARN-75039 or a placebo. ARN-75039 capsules are proposed for the treatment of patients with Lassa virus (LASV) infection. LASV is a type of viral hemorrhagic fever commonly spread by rats, although it can also spread from human to human via contact with contaminated bodily fluids and excretions. The virus typically occurs in West Africa.

This study will measure how safe and tolerable the drug is. In animal studies, small changes in blood tests were seen at doses higher than what is being used in this study, and after stopping the drug, all of those changes went back to what they were before taking the drug.

The following will be collected as a part of this study (more details provided in the additional sections within this consent):

- Medical history and physical examinations (including height and weight measurements for Body Mass Index (BMI, a way to tell if your weight is proportional to your height).
- Assessments of blood pressure, respiratory rate, heart rate, and oral temperature.
- Ophthalmologic examinations (dilated eye exam), (a routine eye exam that uses eye drops to widen your pupils so the doctor can see the back of your eye, or retina).
- A complete history of relevant allergies or drug sensitivities.
- Electrocardiograms (ECG), (a painless recording of the electrical activity of your heart).
- A test of how quickly food travels through your gut
- Pharmacokinetic (PK) blood sampling (blood samples for determination of study drug levels).
- SARS-CoV-2 test
- You will be asked if you have taken any medication recently.
- You will be asked if you have been feeling ill recently.

Clinical laboratory tests (urine and blood samples), including screening for drugs, alcohol, and pregnancy tests (all female subjects), and testing for HIV, hepatitis B and C. Positive results of HIV or hepatitis tests will be reported to local health authorities as required by state law.

Please read this form carefully. Take time to ask the study doctor or study staff as many questions about the study as you would like. The study doctor or study staff can explain words or information that you do not understand. Reading this form and talking to the study doctor or study staff may help you decide whether to take part or not. If you decide to take part in this study, you must sign your name at the end of this form. You cannot take part in this research study until you sign and date this form.

## **WHAT IS A VOLUNTEER INFORMED CONSENT?**

You are being asked to take part in a research study of an experimental drug ARN-75039, in a capsule, that has not been approved by the U.S. Food and Drug Administration (FDA), to find out if the study drug is safe. Before you decide to take part, you should understand the possible benefits and risks associated with this study. This process is known as informed consent and means that you will:

- Receive detailed information about this research study.
- Have a chance to ask and receive answers to any questions you may have.
- Be asked to read and sign this informed consent, once you understand the study and wish to take part.
- Be given a signed and dated copy of this informed consent to keep.

Taking part in this study is entirely voluntary.

If you are participating in the study, you will be expected to cooperate with the study doctor and study staff and to comply with all written or other instructions related to this study.

## **WHY IS THIS DRUG BEING STUDIED?**

This is a clinical research study. This study is sponsored by a pharmaceutical company named Arisan Therapeutics, Inc. based in Carlsbad, California. If you agree to participate in this study, you will be given

ARN-75039. ARN-75039 capsules are proposed for the treatment of patients with Lassa virus (LASV) infection.

The dosage form of ARN-75039 under investigation is oral.

The goal of this study is to assess the safety and tolerability of single and multiple doses of ARN-75039 when administered by the oral route at escalating dose levels in healthy volunteers.

## **WHO IS BEING ASKED TO TAKE PART IN THIS STUDY?**

You have been asked to take part in this study because you are in general good health, are 18 to 55 years of age, have no history of heart or liver disease, no history of allergies, and have not participated in another research study for an experimental drug (or a medical device) within 30 days of the first dose of study drug.

### **Part 1- Single Ascending Dose (SAD) Cohorts (completed)**

In the Part 1 (SAD) study, 5 cohorts of 8 subjects were planned (40 volunteers, 30 ARN-75039 and 10 placebo [inactive substance that looks like the study drug]) with an additional optional cohort (up to 8 additional volunteers). Subjects in this part of the study received ARN-75039 after consuming a full breakfast.

A cohort of subjects in the SAD portion of the study were enrolled and received a second dose of ARN-75039 capsules in the fasted state (nothing to eat or drink, except water) following an appropriate washout period (at least 15 days) in order to assess food effect (including relative bioavailability).

Part 1 of the study has been completed.

### **Part 2- Multiple Ascending Dose (MAD) Cohorts (ongoing)**

In the Part 2 (MAD) study, up to 5 cohorts of 8 subjects (40 subjects, 30 ARN-75039 and 10 placebo) are planned. Subjects in the MAD part of the study receive ARN-75039 after consuming a full breakfast.

You are being asked to participate in Part 2 of the study.

## **HOW MUCH TIME IS REQUIRED TO TAKE PART IN THE STUDY?**

### **Multiple Ascending Dose (MAD) Cohorts**

If you decide to take part in the study, you will be asked to attend a screening visit. If you pass the screening visit, you will return to the clinic for a 12 day/11 night inpatient stay. When you have completed the inpatient period, you will be asked to return to the clinic for three follow up in person visits. The first in person follow up visit will be held on one day between days 15-19. The second in person follow-up visit will be held on one day between days 23-27. The third in person follow-up visit will be held on one day between days 37-41. By the end of this study, you will have spent 12 days and 11 nights in the clinic, with three additional in person one day follow-up visits.

The duration of your participation in the study from screening to final follow-up will be approximately 10 weeks.

## INFORMATION FOR FEMALE VOLUNTEERS

You should not screen for this study if:

- There is any possibility that you may become, or are pregnant,
- You have given birth in the last 3 months, or
- You are breast feeding.

You may screen for this study if:

- You have had a hysterectomy (uterus removed) or bilateral oophorectomy (ovaries removed), confirmed with documentation, or
- You are of post-menopausal age and have not had a menstrual period for 1 year, confirmed with hormone level at screening, or
- You are abstinent and consent to initiate immediate use of double barrier protection for the duration of the study should (hetero) sexual intercourse occur, or
- You are using an adequate method of contraception to avoid pregnancy from screening, throughout the study, until 28 days after the end-of-study visit.

Adequate methods of contraception include one of the following with use of condom for their male partners. Individuals of reproductive potential who are (hetero) sexually active must be willing to use effective contraception from Screening through 28 days after the End Of Study (EOS) visit.

- Diaphragm,
- Injectable contraception,
- Oral/patch contraceptives for a minimum of 6 weeks
- Contraceptive sponge,
- Implant,
- Intrauterine device (IUD) in use prior to enrollment, with use of condom for their male partners

The use of spermicide alone and condom alone are not acceptable methods of contraception.

Abstinence (not having sexual intercourse) may be an acceptable means of contraception as long as you consent to initiate immediate use of double barrier protection for the duration of the study should (hetero) sexual intercourse occur.

Except for continuous abstinence (no sexual intercourse with a male partner), no method of birth control can be considered 100% reliable in preventing pregnancy. Although the risk of becoming pregnant is low with many methods, unplanned pregnancies may occur with all birth control methods. Most occur because of improper or irregular use of the birth control method. If you are usually not sexually active but become sexually active, you must follow the advice documented above regarding contraceptive methods.

Do not donate ova (eggs) from the time of the first study drug administration and for at least 60 days after the last dose of study drug.

All females enrolled in this study will have a pregnancy test performed at screening, before admission periods (Day -1), Day 15 (Food Effect Cohort only), final visit, and/or early exit visits.

Please be aware that a pregnancy test may not be positive until 12 days after conception (fertilization of the egg by sperm). Therefore, if you do not follow the study birth control requirements and/or your birth control method has failed, you will not be able to count on a negative test to confirm that you are not pregnant.

If you know that you have not followed the study birth control requirements outlined above, then you must immediately inform us. You must not take any dose of the study drug if you have not followed these requirements.

If you are not sure about your birth control methods, please talk to the study doctor.

If you become pregnant during the study, you should stop taking the study drug immediately and contact the study doctor right away. If this happens, your pregnancy will be followed to its outcome (for example, until you have your baby). If you have a baby, the study doctor will follow up on the baby's health. Neither the study site nor the Sponsor will be responsible for the cost of any medical care related to the pregnancy, or for your child's care.

## **INFORMATION FOR MALE VOLUNTEERS**

The effect of the study drug on male sperm is unknown. In rare cases, drugs may damage sperm in ways that affect a child that is fathered. Affected sperm may be present in the semen for about 2 months. Therefore, it is recommended to avoid fathering a child for 90 days after the last dose of the study drug. In addition, do not donate sperm from the time of the first study drug administration and for at least 90 days after the last dose of study drug.

Male subjects must use a condom in combination with any of the below means of contraception for their female partners from the time of the first study drug administration and for 90 days following the last dose of study drug.

- Surgically sterilized partner
- Partners that are at least 1 year post-menopausal, or
- Partners that are using one of the below methods:
  - Diaphragm,
  - Injectable contraception,
  - Oral/patch contraceptives for a minimum of 6 weeks
  - Contraceptive sponge,
  - Implant,
  - Intrauterine device (IUD) in use prior to enrollment

Abstinence may be an acceptable means of contraception as long as the individual consents to initiate immediate use of double barrier protection for the duration of the study should (hetero) sexual intercourse occur.

Periodic abstinence and withdrawal are not acceptable methods of contraception.

## **HOW WILL YOU KNOW IF YOU ARE ELIGIBLE TO TAKE PART?**

You will need to fast for at least 8 hours prior to your arrival at Spaulding Clinical Research, LLC. for your screening visit, meaning you should not eat any food and should only have water to drink.

At the beginning of the Screening visit, Informed Consent will be obtained.

**Before starting the study**, the following screening procedures will be performed:

- A complete medical history and physical examination (including waist measurement, height and weight measurements for Body Mass Index (BMI, a way to tell if your weight is proportional to your height).
- A complete questionnaire of your previous and current bowel habits and psychiatric symptoms (e.g., frequency and consistency of bowel movements – e.g., constipation/diarrhea/colitis) and history of mood disturbances, anxiety, and depression).
- Assessment of blood pressure, respiratory rate, heart rate, and oral temperature.
- A complete history of relevant allergies or drug sensitivities.
- An electrocardiogram (ECG, a painless recording of the electrical activity of your heart).
- A test to evaluate the speed food travels through your gut called “Colonic transit test (Sitzmarks®)”. During the test tiny "markers" are used to check the speed on how food is moving through your gut. A capsule will be administered to you after signing the informed consent form. You will be instructed to take that capsule with water 5 days before taking an X-ray of your abdomen.
- You will be asked if you have taken any medication recently.
- You will be asked if you have been feeling ill recently.
- Clinical laboratory tests (urine and blood samples), including screening for drugs, alcohol, and pregnancy tests (all female subjects), and testing for HIV, hepatitis B and C. Positive results of HIV or hepatitis tests will be reported to local health authorities as required by state law.

If you meet the “entry criteria” of the study, according to the study doctor, you will be tested again when you are admitted to Spaulding Clinical Research, LLC. You will have the entry criteria reviewed again to ensure that you still are eligible for the study.

This study involves the testing of an investigational drug developed by the sponsor. We ask subjects to keep information as confidential as possible. This would include but not limited to sharing details of the study, requirements for participation, information received on the risks and benefits of dosing with this study drug, and symptoms or reactions to study drug dosing while enrolled in the study, with persons other than the study staff, your family, and your healthcare provider. This would also include not disclosing such information on social media sites or webpages.

## **HOW WILL THE STUDY BE DONE?**

### **Multiple Ascending Dose (MAD) Cohorts**

Approximately 40 healthy adult subjects, both male and female will be enrolled in this study. The study will consist of one study treatment period, consisting of 12 days/ 11 nights and three outpatient visits. All subjects will be randomized (placed by chance) into a study treatment group. The dose regimens include twice daily (BID) oral dosing. The first dose will be administered in the morning after consuming a full meal. The second dose will be administered approximately 10 hours later after completing a full meal.

<b>Study Part</b>	<b>Cohort</b>	<b>Meal</b>	<b>Dose</b>	<b>Status</b>
2: MAD	7	Fed	Day 1: 36 and 24 mg doses Day 2: 24 mg BID Days 3-10: 12 mg BID	Completed
	8	Fed	Day 1: 75 and 50 mg doses Day 2: 50 mg BID Days 3-10: 25 mg BID	Completed
	9	Fed	Day 1: 150 and 100 mg doses	Completed

Study Part	Cohort	Meal	Dose	Status
			Day 2: 100 mg BID Days 3-10: 50 mg BID	
	10	Fed	Day 1: 240 and 160 mg doses Day 2: 160 mg BID Days 3-10: 80 mg BID	Completed
	11	Fed	Day 1: 360 and 240 mg doses Day 2: 240 mg BID Days 3-10: 120 mg BID	Planned

Once the study doctor determines that you are eligible to participate, you will be enrolled into one of the groups above for the first period. You will not be allowed to choose your group or the order in which you receive the dosing regimens. Because this is a double-blinded study, neither you nor the study doctor or study staff will know which study treatment you are receiving (ARN-75039 or placebo).

A placebo is a medically inactive substance which looks like the study drug.

You will go through the same tests and procedures described below for any of the study treatments you receive. The study doctor may recommend additional procedures, testing, or referrals if deemed necessary for safety purposes.

## WHAT TESTS AND PROCEDURES WILL BE USED IN THE STUDY?

### Multiple Ascending Dose (MAD) Cohorts

#### Day –1 Admission

Upon admission to Spaulding Clinical Research, LLC., you will be given an identity band to wear throughout your entire stay in the unit.

You will need to fast for at least 8 hours prior to your arrival, meaning you should not eat any food and should only have water to drink.

The following admission procedures will be performed:

- Medical history updates.
- Symptom-based physical examination including weight measurement, and waist measurement.
- Clinical laboratory tests (urine and blood samples), including screening for drugs, alcohol, and pregnancy tests (all female subjects).
- You will be asked for details of any medication taken since the screening or previous visit.
- You will be asked if you have been ill since the screening or previous visit.
- You will be asked if you complied with study restrictions.
- Rapid Antigen testing (COVID-19 Test).
- Ophthalmologic examination (dilated eye exam).
- An x-ray to evaluate the speed that food travels through your gut.
- Assessment of blood pressure, respiratory rate, heart rate, and oral temperature (includes triplicate measurements), also known as orthostatic vitals test (a test to see if your heart will beat faster than normal when you transition from sitting or lying down to standing up) will be completed.
- An electrocardiogram (ECG), (a painless recording of the electrical activity of your heart). In addition, a NASA 10-Minute Lean Test also known as an active stand test (a procedure that

measures heart rate and blood pressure to assess a person's response to standing up) will be completed. that causes your heart to beat faster than normal when you transition from sitting or lying down to standing up) testing will be completed.

- Meals (lunch, dinner, and a small snack).
- Inclusion/Exclusion assessment and preparation for randomization.

The results from these tests will help the study staff determine whether you are still eligible to enter the study. None of these tests are investigational and are commonly performed during routine medical care.

### **Study Treatment (Day 1-Day 11)**

- Adverse event assessment (check for side effects) and changes in concomitant medications (medicines you are currently taking).
- Randomization (assignment to a dose group) on Day 1 only.
- Symptom-based physical examination including weight measurement, and waist measurement.
- Assessment of blood pressure, respiratory rate, heart rate, and oral temperature (includes triplicate measurements taken on Day 2, 4, 6, 8 and 10).
- Weight measurement.
- Waist measurement (Day 5 and Day 10).
- ECG procedures using a Holter monitor (standard bedside ECG recording) on Days 1-10 starting predose and ending approximately 6 hours post morning and evening dose. Standard safety ECGs will be performed on Days 8 and 10.
- Ophthalmologic examination (dilated eye exam) (Day 10).
- Questionnaire of your current bowel habits (e.g., frequency of bowel movement - constipation/diarrhea), other called GI experiences (e.g., nausea, vomits, etc.), and psychiatric symptoms (mood disturbances, anxiety, or depression).
- Administration of study drug (twice daily on Days 1 through 10).
- Meals (breakfast, lunch, dinner, and a small snack).
- Clinical laboratory tests (urine and blood samples). Urine will be collected on Days -1, 2, 5 and 10.
- Blood samples will be collected on Day -1, 1, 2, 5, 8, and 10. Pharmacokinetic (PK) blood sampling (blood samples for determination of study drug levels) on Days 1, 2, 3, 8, 10 and 11.
- Pharmacokinetics looks at how your body:
  - Takes the study drug into your bloodstream.
  - Delivers the study drug through the blood.
  - Breaks down or processes the study drug.
  - Removes the study drug.
- You will be discharged from the unit following completion of the 24-hour PK sampling and all other procedures have been completed and reviewed on Day 11.

### **Study Treatment (Day 2 and Day 7)**

- Similar to the one you had during screening, a colonic transit test (Sitzmarks®) will be performed. During the test tiny "markers" are used to check the speed on how food is moving through your gut, and compare with the previous one.
  - Day 2:** a "markers capsule" will be administered to you with water between the 2 doses of study drug.
  - Day 7:** on this day, an X-ray image will be taken of your abdomen to see if any of the "markers" are left in your intestine or have been expelled.



**Follow-up Visit (Day 17)**

- Adverse event assessment (check for side effects) and changes in concomitant medications (medicines you are currently taking).
- Assessment of temperature, blood pressure, heart rate, respiratory rate, and oral temperature (includes triplicate measurements).
- Symptom-based physical examination (if needed).
- Weight measurement
- Waist measurement
- Clinical questionnaire of your current bowel habits (e.g., frequency of bowel movement - constipation/diarrhea), other called GI experiences (e.g., nausea, vomits, etc.) .), and psychiatric symptoms (mood disturbances, anxiety, or depression).
- Clinical laboratory tests (urine and blood samples).
- Pharmacokinetic (PK) blood sampling (blood samples for determination of study drug levels).

**Follow-up Visit (Day 25)**

- Assessment of temperature, blood pressure, heart rate, respiratory rate, and oral temperature (includes triplicate measurements).
- Symptom-based physical examination (if needed).
- Adverse event assessment (check for side effects) and changes in concomitant medications (medicines you are currently taking).
- Clinical questionnaire of your current bowel habits (e.g., frequency of bowel movement - constipation/diarrhea), other called GI experiences (e.g., nausea, vomits, etc.), and psychiatric symptoms (mood disturbances, anxiety, or depression).
- Clinical laboratory tests (urine and blood samples).

**Follow-up Visit/ End-of -study (EOS) (Day 39)**

- Adverse event assessment (check for side effects) and changes in concomitant medications (medicines you are currently taking).
- Assessment of temperature, blood pressure, heart rate, respiratory rate, and oral temperature (includes triplicate measurements).
- Symptom-based physical examination (if needed).
- Weight measurement
- Waist measurement
- Clinical questionnaire of your current bowel habits (e.g., frequency of bowel movement - constipation/diarrhea), other called GI experiences (e.g., nausea, vomits, etc.), and psychiatric symptoms (mood disturbances, anxiety, or depression).
- ECG procedures (standard bedside ECG recording).
- Pharmacokinetic (PK) blood sampling (blood samples for determination of study drug levels).
- Clinical laboratory tests (urine and blood samples) , and pregnancy test (all female subjects of child-bearing potential).

## Information Obtained During the Study

### **Multiple Ascending Dose (MAD) Cohorts**

#### **Blood Sampling**

Blood samples will be collected for measurement of levels of ARN-75039 **in every study treatment cohort** at the following times:

- PK assessments should be performed on Day 1 and Day 10 pre-dose, 30 minutes, then 1, 2, 4, 6, 8, 10 (before second dose), 12, 14, and 24 hours after the initial morning dose. (The 24-hour PK assessment can be combined with pre-dose for the following dose day, where applicable, 24 hour/ pre-dose  $\pm$ 30 min) A pre-dose sample and a sample 6 hours after dosing will be collected on Days 2 and 8 (only for the initial daily dose). A pre-dose sample will be collected on Day 3 prior to the initial morning dose. (Subjects will be discharged on Day 11 after collection of the 24-hour post-dose PK sample.) PK assessments should be performed on Days 17, and 39 at approximately the same time as the dose of study drug was administered.

You will have numerous blood samples drawn during the entire study for study drug levels or safety assessments as shown above. The blood samples may be taken by individual needle sticks into one of your arm veins, or, if necessary, at study staff discretion, by an indwelling catheter (a thin plastic tube placed in a vein in your arm). Additional blood samples may be obtained throughout the study based on the study doctor's recommendations. The total amount of blood taken for the entire study will not exceed 500 mL (approximately 20 mL for screening, will not exceed 390 mL for the determination of ARN-75039 concentration, and approximately 90 mL for clinical laboratory tests) or about 2.1 cup for the entire study.

#### **Urine Sampling**

- You will have urine samples collected at screening, Day -1 (Check In), Days 1, 2, 8, 10, 17, 25 and 39. These will be used to screen for either alcohol or drugs, and for routine safety analysis. Additional urine samples including urine drug screen may be obtained for safety reasons throughout the study based on the study doctor's recommendations.

#### **ECG Measurements**

- Safety ECG measurements using a Holter monitor or a bedside ECG machine will occur at your screening visit, Days -1 (Check In), 1, 8, 10, and 39. There will be periods of time where you will need to lie very still to get precise readings of your heart's rhythm. You may be required to lay still for approximately 15 minutes. On Days 1-10, you may be required to be connected to the portable ECG monitor starting predose until at least 6 hours post morning and evening dose.

Some individuals may develop redness, irritation, skin breakdown, or discoloration of the skin at the site of ECG electrodes placed on the chest/body. This may develop due to sensitivity to the electrodes or to our skin preparation procedure. In order to get the quality results, we need, it is necessary for us lightly scrub the skin with an abrasive pad to remove any skin impedance such as oil, dead skin cells and lotions. We may trace each electrode site with a permanent marker to assure electrodes are placed in the same place on the body for each ECG event to maintain quality and consistent results. This tracing may occur as often as once a day during confinement.

You may receive additional Rapid Antigen testing (COVID-19 Test) throughout the study based on study doctor's recommendations.

## WHAT ARE YOUR RESTRICTIONS DURING THE STUDY?

You will need to avoid the following while taking part in this study, and most importantly from the time of your screening visit until you check in:

Must be willing and able to comply with measures to avoid photosensitivity (skin sensitivity to the ultraviolet (UV) rays from sunlight and other light sources) reactions (for example, avoidance of outdoor sun exposure and tanning; consistent use of long sleeve shirts, long pants, hats, and sunglasses; consistent use of SPF 75 or greater sunscreen when outdoors) from Day 1 through Day 8 in Part 1 and through Day 25 in Part 2.

<b>Restricted Item:</b>	<b>Duration:</b>
Alcohol	72 hours prior to first dose and throughout the duration of the study
Exercise	48 hours prior to Day -1 through the last PK sample collection time point
Caffeine or other xanthines (for example, coffee, tea, cola or chocolate)	72 hours prior to first dose and throughout the duration of the study
Grapefruit/grapefruit juice/Seville oranges	72 hours prior to first dose and throughout the duration of the study
Prescription medication	7 days prior to first dose and throughout the duration of the study
Over the counter medication	7 days prior to first dose and throughout the duration of the study
Vitamins and herbal medications (including cannabis)	7 days prior to first dose and throughout the duration of the study
Nicotine containing products	Smoking greater than 20 cigarettes, cigars, cigarillos or E-cigarettes per week in the 3 months prior to study drug administration through the end-of-study visit.
Investigational Product	30 days or 5 half-lives prior to dose
Blood products	No blood product donation within 30 days before Screening through the last PK sample collection time point.
Avoidance of outdoor sun exposure and tanning	Consistent use of long sleeve shirts, long pants, hats, and sunglasses and consistent use of SPF 75 or greater sunscreen when outdoors from Day 1 through Day 8 in Part 1 and through Day 25 in Part 2.
<b>Required Item:</b>	
Contraception	Females: Post-menopausal, surgically sterile, or using effective contraception from screening until 28 days after the final follow-up visit.
	Males: From first study drug administration through 90 days after the last dose of study drug.

You will receive a diet that does not contain any alcohol or caffeine. You may be required to eat at a reasonable pace (within 30 minutes). Your meals may be monitored to determine the percentage of food you have consumed.

All doses of study drug will be administered orally with 240 mL of water, or the smallest additional amount of water needed to swallow all the capsules.

You may eat only meals and snacks that are provided to you during periods of your stay. On certain study days you may be required to get up very early (between 4 and 6 am) in order to complete study events. This will only be done when absolutely necessary, and while it is important that you have sufficient rest during the study, sometimes an early start to the day is unavoidable.

### **ARE THERE RISKS TO YOU IF YOU ARE IN THIS STUDY?**

Please be advised that non-pharmacological treatments (such as heating pack, stretches, hydration, etc.) are our first line of therapy for mild adverse events. Our study doctor will be notified if a concomitant medication may be needed to treat an Adverse Event (side effect). Following the study plan guidelines, the study doctor will assess your AE and develop a treatment plan.

Risks are possible side effects of the study drug and those of taking blood and other medical procedures:

#### **For ARN-75039 (study drug):**

- Gastrointestinal effects- abdominal pain, oral paresthesia (mouth numbness), diminished sense of taste, nausea, vomiting, diarrhea
- General effects- Photophobia (eyes sensitive to lights), somnolence (sleepiness), muscle aches, tachycardia (fast heart rate)
- There is the chance for sunburn or your skin feeling sensitive after being in the sun or using a tanning bed while you are taking ARN-75039. During the study, you should not sunbathe or use tanning beds. You should wear long sleeve shirts, long pants, hats, and sunglasses. You should use sunscreen of SPF 75 or higher when outdoors while you are in the study.

**It is possible that you could experience a potentially serious irregularity in your heart rhythm during the study. For this reason, we will be monitoring your heart rhythm closely throughout the entire study, and we will have immediate medical care available for you if any problems occur.**

**An intravenous catheter (a thin plastic tube placed in a vein in your arm) may be placed at the study doctor's discretion to quickly deliver rescue medications in the event of an emergency situation.**

Problems or side effects that are not now known could also occur. You will be given any new information that may affect your willingness to start or continue in the study.

If you have a side effect of the study drug, such as a skin rash or other visible injury, it might be useful to take a picture of the affected area to send to the sponsor. If the condition is on your face, all reasonable attempts will be made to disguise your facial features and hide your identity. It is possible that your face may be recognizable. By signing this consent, you authorize the study doctor or study staff to take such a picture and provide it to the sponsor.

**Additional Risks**

As with any drug, it is possible that you could experience an allergic reaction to the study drug used in this study. Symptoms of any allergic reaction can include:

- Rash
- Hives
- Itching
- Difficulty breathing
- Closing of the throat
- Swelling of the lips, tongue or face
- Rarely, death.

**If you think you are having a severe allergic reaction, while outside the study center call 9-1-1 and seek medical attention immediately.**

It is very important that you tell the study doctor and the study staff about any side effects that you might experience.

You may experience side effects or discomforts that are not listed on this form. Tell your study doctor or study staff immediately if you have any problems. Your safety will be closely monitored during the course of the study.

**For Blood Draws**

- Fainting
- Redness
- Pain
- Bruising
- Rarely, there may be a small blood clot or infection at the site of the needle puncture

**Intravenous catheter (IV)**

- Redness
- Pain
- Infection
- Bruising
- Damage to blood vessels
- Bleeding from the site of insertion
- Swelling in the area
- Allergic reaction to the adhesive tape that secures the IV in place
- Rarely, there may be a small blood clots at the site of the needle puncture

In instances where a nurse, a doctor, or a technician, sustains an exposure to your blood, tissue or body fluids by needle stick, cut or splash to mucosa or damaged skin, it may be necessary to test your blood, tissue, or body fluid sample for certain viral infections including Hepatitis B and C and HIV on the sample already available. This is to enable that person to receive appropriate counseling, monitoring and treatment if necessary. In this instance the study investigator or designee will offer you the information relevant to your health and advise you on the next steps. Confidentiality of your data will be respected at all times according to the state law.

**For Blood Pressure Monitoring**

The blood pressure cuff may also cause discomfort, irritation, or bruising to the upper arm.

**Fasting**

Fasting could cause dizziness, headaches, stomach discomfort or fainting.

**For ECG Monitoring (using a Holter monitor while staying at Spaulding Clinical Research)**

You will be given a small portable heart monitor to wear. The monitor is connected by wires that are stuck to your chest, using tape or stickers. To attach the monitor wires, a small section of your chest might have to be shaved. You must return the monitor to the study staff. It is possible to be sensitive to the adhesives used on the electrodes that are applied to your chest when having an ECG performed. If this is the case, you could develop a temporary redness, irritation, skin breakdown, or discoloration of the skin where the electrodes were applied.

**HIV, Hepatitis, and Tuberculosis Testing**

The risks of HIV testing include psychological and social risks. A positive test can lead to restrictions in freedom of travel to some countries and possible prejudices in job employment, insurance eligibility, housing and other forms of discrimination. Positive HIV, hepatitis, and tuberculosis test results must be reported to health authorities under state law.

**Sitzmarks® Testing**

Even though it may be rare, some people may have bad side effects when taking the capsule. These may include:

Signs of an allergic reaction, like rash; hives; itching; red, swollen, blistered, or peeling skin with or without fever; wheezing; tightness in the chest or throat; trouble breathing, swallowing, or talking; unusual hoarseness; or swelling of the mouth, face, lips, tongue, or throat.

Severe constipation or stomach pain. These may be signs of a severe gut problem.

**Reproductive Risks**

The effects of the study drug on human pregnancy and the unborn child (fetus) are unknown. Therefore, it is very important that you do everything within your power not to become pregnant within 28 days of the EOS visit if female, or father a child during this study and for 90 days following the last dose if male. Please ensure that you follow the study birth control requirements outlined in the sections regarding information for male and female subjects above.

If you become pregnant during the course of the study, you will be withdrawn from the study immediately. Neither Spaulding Clinical Research, LLC. Nor the sponsor will be responsible for the cost of any obstetric or related care, or for your child's care. Female subjects are agreeing, by signing and dating this form, that information about your pregnancy and birth of your child may be collected. The information collected will include your health and the health of your unborn child during pregnancy, pregnancy outcome (miscarriage, termination, live birth, etc.), and the health of the baby after it is born (up to 6 weeks after delivery).

Partners of male subjects who become pregnant will be asked to sign a separate consent form to allow collection of the information listed above. Your information will be kept confidential in accordance with state and HIPAA law.

**NEW FINDINGS**

Your study doctor will tell you of any information learned during the course of the study that might cause you to change your mind about taking part in the study. You may contact the study doctor at any time after your participation ends to find out if any new information about this study has become available.

## **WHAT IS THE ALTERNATIVE TO BEING IN THE STUDY?**

Since this is a study involving healthy volunteers, your alternative is not to take part.

## **WILL YOU BENEFIT FROM TAKING PART IN THE STUDY?**

You will not receive direct medical benefit from receiving the study drug. You may benefit by having your medical history recorded, undergoing a physical examination, and having blood and urine tests as they apply to this research project.

Just by taking part in this research study, you may be helping future patients by providing important information about the study drug and by contributing to medical knowledge.

## **WHO IS PAYING FOR THIS STUDY?**

A pharmaceutical company called Arisan Therapeutics, Inc. is the sponsor of the study. Arisan Therapeutics, Inc. is a company that creates and makes medicines and other health products. The Department of Defense (DoD) is funding the study.

Arisan Therapeutics, Inc. pays the study doctor to run this study.  
The study drug and all tests, procedures and visits required by the study are provided at no cost to you.  
The sponsor, Arisan Therapeutics, Inc., pays for them.

Information about this study is confidential. This information belongs to Arisan Therapeutics, Inc. We ask that you keep it private. You can discuss this information in private with your personal doctor or family to talk about your healthcare or to decide about taking part in this study.

## **WILL YOU BE PAID FOR BEING IN THIS STUDY?**

Compensation for screening is as follows:

- \$100.00 for the initial screening visit if you qualify and take part in a study. \$100.00 for the initial screening visit for your time and inconvenience if you do not qualify for a study.
- \$100.00 if you complete the return visit for Sitzmarks<sup>®</sup> capsule administration.
- \$100.00 if you complete the X-ray of your abdomen prior to enrollment in the study.
- If the results of the drug and alcohol tests are positive, or if you attempt to falsify your drug screen you will not receive any compensation.
- If you screen for the study, qualify and are enrolled, your screening, return visit, and X-ray payment will be included in your first stipend payment. If you are not accepted into the study your screening payment, return visit (if applicable), and x-ray payment (if applicable) will be processed and mailed within 7 calendar days of study enrollment.

Compensation for this study is as follows:

### **Part 2 (Multiple Ascending Dose)**

For subjects that complete the entire study (Day -1 to the final follow up visit), you will receive up to \$8,655.00. This payment will be made in 5 separate payments as follows:

- \$5460.00 will be paid after all check out procedures have been completed at the end of Day 11 (\$455.00 for each day that you were in-house).

- \$420.00 will be paid after all procedures have been completed at the end of the Day 17 outpatient visit.
- \$420.00 will be paid after completion of the Day 25 outpatient visit.
- \$420.00 will be paid after all procedures have been completed at the end of the Day 39 outpatient visit.
- The remaining \$1685.00 will be paid after the follow-up visit, and any additional follow-up procedures are completed, and all results are reviewed. Once follow-up procedures have been completed and accepted by the study doctor, your final payment will be processed and mailed within 14 calendar days.

If you withdraw from the study early, you will only be paid for the visits you completed.

**NOTE:** You may be required to return to the clinic for repeat blood test or other assessment (ECG, physical, vital signs) in between periods or after the final check out. This is considered part of the study and no additional compensation is available. Your final payment will not be released until all follow-up procedures have been completed and accepted by the study doctor. Once follow up procedures have been completed and accepted by the study doctor, your final payment will be processed and mailed within 14 calendar days.

**NOTE:** If you meet eligibility criteria you may be asked to be an alternate subject. Alternate subjects are eligible subjects that are in addition to the number of subjects in the event an enrolled subject drops out before their dose can take place or in the event it is not safe for a subject to move forward with dosing. If you are selected as an alternate subject who has to stay the night in the clinic and you agree to participate as an alternate subject, you may receive up to \$250 if you are not needed to dose. If you are selected as an alternate subject and you do not have to stay the night, you may receive up to \$150. If you are needed to replace a subject, you will be paid as stated for participating in and completing the study. If you agree to be an alternate subject, you will have all of the predose procedures as the enrolled subjects so that if you are needed, you will be ready to participate. If you are not needed, you will be discharged shortly after completion of the dosing round.

No deductions for any state or federal withholding or any other similar taxes will be made, and you are solely responsible for reporting such payments on your state and federal income tax returns.

If you need to stay at Spaulding Clinical Research, LLC. For a longer period of time for safety reasons, you will be compensated at a rate proportional to the entire compensation for the study.

If you are dismissed from the study for medical reasons OR if the study is temporarily or permanently halted, your compensation will be proportional to the time you spend in the study.

If you are dismissed from the study because you have not complied with the instructions of the study staff, no compensation is available. Non-compliance includes, but is not limited to, improper conduct, taking alcohol and/or any drugs (including recreational drugs), tampering with the study drug, or consuming any foods/beverages not allowed in the study.

You must follow the inpatient clinic rules of conduct while you are taking part in this study. If you do not follow the rules, a deduction may be taken from your total stipend. You may not be able to take part in future studies at Spaulding Clinical Research. These rules will be reviewed with you at your first inpatient visit.



By signing this consent, you expressly agree that you are an Independent Contractor for Spaulding Clinical Research, LLC. As an Independent Contractor, you will receive a 1099 form from Spaulding Clinical Research, LLC. The 1099 form shall document and report all payments and/or study stipends you received as an Independent Contractor for Spaulding Clinical Research, LLC. In addition, because you are an Independent Contractor and will be receiving payments and/or study stipends, those earnings are subject to wage garnishment. If Spaulding Clinical receives an Earnings Garnishment Notice (or similar) from a State or Federal legal entity, we will adhere to that garnishment.

## **COMPENSATION FOR INJURY**

It is important that you follow carefully all the instructions given by the study doctor and his/her study staff regarding this study.

If you become ill or are physically injured as a result of participation in this study, please contact the study doctor right away at the telephone number listed on page one of this consent form. He/she will treat you or refer you for treatment.

The reasonable costs of such treatment beyond that provided by your insurance will be covered by the sponsor, Arisan Therapeutics, Inc. Arisan Therapeutics, Inc. will provide payment for medical expenses for injuries:

- If you received reasonable medical care
- If you followed instructions
- If the injury is related to the study drug, in the opinion of the study doctor, or to properly performed study procedures that are not part of your usual medical care,
- That are not the result of the natural course of any underlying disease and/or pre-existing disease process present prior to the proper administration of ARN-75039.

In no way does signing this consent form waive your legal rights nor does it relieve the study doctors, sponsor or involved institutions from their legal and professional responsibilities.

NOTE: The DoD will not provide for medical care for research-related injury.

## **PROTECTING THE PRIVACY OF YOUR HEALTH DATA**

Unless required by law, your name will not be disclosed outside the research clinic. Your name will be available only to the following people or agencies: the study doctor and study staff; and authorized representatives of the study doctor; ethics committees, health authority inspectors, such as the US Food & Drug Administration (FDA) and the European Medicines Agency; representatives of the DoD; Arisan Therapeutics, Inc. study monitors and auditors; and authorized Clinical Research Organization representatives. The above mentioned individuals will use the personal information collected as part of this study, including your medical records ("Study Information") to check that the study is conducted correctly and to ensure the accuracy of the study information. These people are all obligated to maintain confidentiality by the nature of their work, or are bound by confidentiality agreements. If required, the study doctor may contact your personal doctor to collect additional medical information and your past medical history.

The study doctor may only share your study information with people whom you have permitted to see it. However, once your study information is shared as authorized, it may no longer be protected by Federal law and may be re-disclosed without your permission. 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 researchers and others to protect your privacy.

While participating in this study, the study doctor will replace your name with a special code that identifies you. This code, along with your study information, will be used by the study sponsor, Arisan Therapeutics, Inc., and their representatives, for the study purposes mentioned above and to help establish whether the study drug is safe and effective. Arisan Therapeutics, Inc. may share your coded information, as necessary, with Arisan Therapeutics, Inc. affiliates who work within the scope of this consent; people and companies who work with Arisan Therapeutics, Inc. and who work within the scope of this consent; Ethics committees and Regulatory agencies such as the US Food & Drug Administration (FDA), the National Health Authorities, and the European Medicines Agency, and the DoD.

Study Information, your study code, and samples collected as part of this study will be included in Arisan Therapeutics, Inc.'s secure electronic trial systems. These systems may be managed and monitored by companies who work with Arisan Therapeutics, Inc.

You should be aware that some countries may not offer the same level of privacy protection as you are used to in the country where you live or where this study is conducted. However, Arisan Therapeutics, Inc. will keep any information it receives to the same standard of confidentiality as far as permitted by applicable local law. Arisan Therapeutics, Inc. has also entered into agreements with third parties working for Arisan Therapeutics, Inc. to secure adequate protection of your data and samples.

The Study Information will be kept confidential within the limits of the law and used only for research purposes mentioned above. If the results of this study are published or presented in a meeting, you will not be named, and nobody will be able to tell that you were in the study from the publication or presentation.

Your participation in this study is voluntary and you may cancel this consent at any time and without any reason. If you do so, your participation in the study will end and the study staff will stop collecting information from you; however, you will be asked to come back to the study site for an end of study visit. Your samples will then be destroyed. However, Arisan Therapeutics, Inc. will continue to retain and use any research results that have already been collected to verify the scientific integrity of the study. If you wish to leave the study inform your study doctor.

You have the right to review your Study Information and medical records and request changes to the Study Information if it is not correct. However, please note that during the study, access to Study Information may be limited if it weakens the integrity of the research. You may have access to the Study Information held by the study doctor at the end of the study.

If you have any questions about the collection and use of information about you, or would like to exercise rights that you may have regarding this information, you should ask your study doctor.

## **WHOM TO CONTACT ABOUT THIS STUDY?**

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns or complaints about the study such as:

- Whom to contact in the case of a research-related injury or illness;
- Payment or compensation for being in the study, if any;
- Your responsibilities as a research subject;

- Eligibility to participate in the study;
- The study doctor's or study site's decision to withdraw you from participation;
- Results of tests and/or procedures;

**Please contact the study doctor 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, contact:

- By **mail**:  
Study Subject Adviser  
Advarra IRB  
6100 Merriweather Dr., Suite 600  
Columbia, MD 21044
- or call **toll free**: 877-992-4724
- or by **email** [adviser@advarra.com](mailto:adviser@advarra.com)

Please reference the following number when contacting the Study Subject Adviser: Pro00067292.

**IS YOUR PARTICIPATION VOLUNTARY?**

Yes, your participation in this study is strictly voluntary. You may refuse to take part in it, or you may stop participating at any time, even after signing this informed consent. There will be no penalty or loss of benefits to which you are otherwise entitled. However, if you decide to leave the study before it ends, the study doctor will need to see you before you are released from the study.

The study doctor, sponsor, or the FDA may also decide to remove you from the study at any time without your consent. The study doctor may choose to take you out of the study because of unexpected or serious side effects, or for other scientific, technical, or safety considerations.

Examples why you may be taken out of the study are:

- Staying in the study would be harmful
- You need treatment not allowed in this study
- You failed to follow instructions
- You become pregnant
- The study is cancelled
- Your study treatment arm is stopped

If your participation ends for any reason, you will return to the study for the following study procedures:

- Physical examination.
- Pregnancy test (if necessary).
- Body weight and body temperature.
- Blood pressure and pulse rate.
- Safety ECG procedures (standard bedside ECG recording).
- Blood draws for hematology, chemistry, lipid panel, albumin, globulin, and insulin.
- Blood draws for PK.

- Ophthalmologic examination (Dilated eye exam).
- Urine will be collected for urinalysis.
- Adverse events and concomitant medications.

If you should decide to leave the study you should tell the study doctor or study staff. They will make sure that proper procedures are followed and a final visit is made for your safety.

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.

**STATEMENT OF CONSENT**

I have read this form and its contents were explained to me. I agree to be in this research study for the purposes listed above. All of my questions were answered to my satisfaction. I will receive a signed and dated copy of this form for my records. I am not giving up any of my legal rights by signing this form.

I agree to have photograph(s) to document adverse event(s) as applicable for this trial. By signing this consent, I authorize the study doctor or study staff to take such a picture and provide it to the sponsor.

\_\_\_\_\_  
Signature of Research Subject

\_\_\_\_/\_\_\_\_/\_\_\_\_  
Date

\_\_\_\_\_  
Printed Name of Research Subject

\_\_\_\_\_  
Time (24hr)

**STATEMENT OF PERSON OBTAINING INFORMED CONSENT**

I have carefully explained to the subject the nature and purpose of the above study. There has been an opportunity for the subject to ask questions about this research study. I have been available to answer any questions that the subject has about this study.

\_\_\_\_\_  
Initials of Person Obtaining Informed Consent

\_\_\_\_/\_\_\_\_/\_\_\_\_  
Date

**HEALTH INSURANCE PORTABILITY AND ACCOUNTABILITY ACT (HIPAA)  
AUTHORIZATION AGREEMENT  
Permission to Review, Use and Release Information about You**

If you decide to be in this study, the study doctor and study staff will use and share health data about you to conduct the study. Health data may include:

- Your name.
- Address.
- Phone number.
- Date of birth.
- Medical history.
- Information from your study visits, including all test results.

Health data may come from your study records or from existing records kept by your doctor or other health care workers.

For this study, the study staff may share health data about you with authorized users (in compliance with guideline standards of the Office of Human Research Oversight (OHRO)). Authorized users may include:

- Representatives of Arisan Therapeutics, Inc.
- Representatives of Spaulding Clinical Research, LLC.
- Representatives of Advarra IRB (a Research Ethics Review Board that reviews this study).
- The Food and Drug Administration (FDA) and other US governmental agencies, and the DoD.
- Government agencies to whom certain diseases (like HIV, hepatitis, and STIs) must be reported.
- Governmental agencies of other countries.
- Labs working with the sponsor on this study.
- Other authorized users.

The sponsor and those working for the sponsor may use the health data 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.

Once your health data has been shared with authorized users, it may no longer be protected by federal privacy laws.

Your permission to use and share health data about you will not end unless required by state law. If state law applies, your permission to use and share health data about you will end in 50 years unless you revoke it (take it back) sooner.

You may take back your permission to use and share health data about you at any time by writing to the study doctor. If you do this, you will not be able to stay in this study. No new health data that identifies you will be gathered after your written request is received. However, health data about you that has already been gathered may still be used and given to others as described in this form.

Your right to access your health data 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 health data.

If you decide not to sign this form, you will not be able to take part in the study.

## STATEMENT OF AUTHORIZATION

I have read this form and its contents were explained. My questions have been answered. I voluntarily agree to allow study staff to collect, use and share my health data as specified in this form. I will receive a signed and dated copy of this form for my records. I am not giving up any of my legal rights by signing this form.

\_\_\_\_\_  
Signature of Research Subject

\_\_\_\_/\_\_\_\_/\_\_\_\_  
Date

\_\_\_\_\_  
Printed Name of Research Subject

## STATEMENT OF PERSON OBTAINING AUTHORIZATION

I have carefully explained to the subject the nature and purpose of this form. I have been available to answer any questions that the subject has about this form.

\_\_\_\_\_  
Initials of Person Obtaining Authorization

\_\_\_\_/\_\_\_\_/\_\_\_\_  
Date