INFORMED CONSENT TO TAKE PART IN A CLINICAL RESEARCH STUDY

TITLE:	A Randomized, Double Blind, Placebo-Controlled, Multiple Ascending Dose, Phase 1 Study of SLV213 in Healthy Volunteers
PROTOCOL NO.:	DMID 22-0027
PURPOSE:	COVID-19 infection
TYPE OF STUDY:	Phase 1 – Healthy Participants
SPONSOR:	Division of Microbiology and Infectious Diseases (DMID) National Institute of Allergy and Infectious Diseases (NIAID) National Institutes of Health (NIH) 5601 Fishers Lane, MSC 9806 Bethesda, Maryland 20892
STUDY DOCTOR:	Martin Kankam, MD, PhD, MPH, FAPCR
RESEARCH SITE ADDRESS:	Altasciences Clinical Kansas, Inc. 10103 and/or 10203 and/or 10183 Metcalf Avenue Overland Park, KS 66212
TELEPHONE NUMBER	913-696-1601 (24-hour number)

KEY INFORMATION

The following is a summary of the things you should know about this clinical research study:

- You are invited to take part in a clinical research study of the investigational drug SLV213. "Investigational" means that the drug is allowed to be evaluated in healthy persons like you in this study by the U.S. Food and Drug Administration (FDA), but not approved for use in people by prescription. Your participation is voluntary and your consent to participate is sought after you have read and understood information provided in this document and have your questions about the study answered before any study tests are done. If you consented and then change your mind, you may withdraw from the study and notify the study doctor.
- SLV213 is a compound that is being developed for the treatment of severe infection caused by the coronavirus SARS-CoV-2, which was the cause of COVID-19, and variants of that virus that still cause active infection. In this study, capsules (pills) of SLV213 containing the active drug, or placebo (pills containing only inactive ingredients) will be administered by mouth with water every 12 hours for 7 days.
- The purpose of this research study is to collect information about the safety of SLV213, that is, if any side-effects occur after taking it, and their type and how severe they are. Information will also be collected about the pharmacokinetics (PK) of SLV213 at the

doses to be used. (PK means the study of how the body absorbs, changes, and eliminates the active drug.)

- You will be assigned to one of 3 study treatment cohorts (groups), numbered 1 to 3. The cohorts will run one after the other in the order they are numbered, that is, Cohort 1 will be done before Cohort 2, and Cohort 2 before Cohort 3. The lowest dose, 400 mg every 12 hours, will be in Cohort 1, the median dose, 600 mg every 12 hours, will be in Cohort 2, and the highest dose, 800 mg every 12 hours, will be in Cohort 3.
- A total of 36 participants will take part in the study, 12 participants in each cohort, and 2/3 will take the active study drug and 1/3 will take the placebo. You will be assigned only in one cohort (group) randomly (like tossing a coin) to receive either the study drug (about 66% chance) or placebo (about 34% chance).
- If you decide to participate, you will be in the study for up to 56 days (from Screening Visit to Final Visit). There is a *Screening Period* of up to 27 days to determine if you meet the study requirements; a *Check-in Visit* on the day before dosing with the study drug is to start, to confirm you can take part in study and be admitted in the clinical trial unit (CTU) on the same day; an *Inpatient Treatment and Follow-up Period* of 9 days / 8 nights, with twice-daily dosing with the study drug or placebo assigned to your cohort every 12 hours for 7 days, and 2 days of follow up before discharge to evaluate the effects of the study drug; and an *Outpatient Follow-up Period* with 3 telephone calls by the study staff about 1, 2 and 3 weeks after receiving the last dose to evaluate delayed effects of the study drug.
- Screening evaluations will start after signing this form to document your willingness to take part in this study. We will collect demographic information about you (age, sex, race and ethnicity) and social habits (smoking, alcohol use, drug use, exercise) and complete standard medical evaluations (your medical history, history of medications you take, physical examination (PE), your vital signs (VS; blood pressure [BP], heart rate [HR], respiratory (breathing) rate [RR] and temperature [T]); blood and urine tests; and an electrocardiogram (ECG; a paper tracing of the heart signals). BP and HR will be measured while resting lying down and after standing. If you meet all screening study requirements, you will be asked to return to the clinic on the Check-in day to confirm you continue meeting the requirements to participate in the study. If you do, you will be admitted as inpatient in the CTU.
- On study Day 1 through Day 7, you will receive the study drug or placebo dose assigned to your cohort (group) every 12 hours, in the morning and evening every day. The study drug or placebo pills will be taken by mouth with water.
    - You will fast for various periods of time <u>before</u> receiving each dose depending on the study day. You will fast for at least 8 hours before receiving the morning dose on Day 1 and at least 8 hours before receiving the evening dose on Day 7. Before all the other doses you will fast for at least 2 hours.
    - You will also fast for various periods of time <u>after</u> receiving each dose depending on the study day. You will fast at least 4 hours after receiving the morning dose on Day 1 and at least 4 hours after receiving the evening dose on Day 7. After all the other doses you will fast for at least 1 hour.
    - You will be allowed to drink liquids during the periods of fasting except 1 hour before and 1 hour after each dose. Study staff will serve you meals after the end of fasting.

- The effects of the study drug on you will be assessed by your reports of symptoms and medical evaluations, ECGs, and blood tests.
- Blood plasma samples will also be collected from a vein in the arm before and after each dose, more frequently after the morning dose on Day 1 and the evening dose on Day 7, to measure the study drug concentration. The measurement will be used for PK analysis to study how your body handles the study drug. Additional blood serum samples will also be collected at the same timepoints as the PK samples for future research of the study drug if you consent to do so. These serum samples and any unused plasma PK samples will be stored for future research if you consent to do so.
- You will be discharged from the CTU 2 days after the last dose, on Day 9, and you will then be contacted by phone about every week, on Days 15, 21 and 28, to check how you feel and if you have any symptoms and take any new medications.
- You may be asked to return to the research site for evaluation of any new symptoms as needed after these phone contacts.
- You will be discharged from the study on Day 28 or later if there is a medical need for further follow up.
- Risks that could be caused by the study drugs are:
    - SLV213 was safe and well-tolerated in a previous study in healthy people who took a single dose of the study drug in the range of doses to be used in this study.

      The most common side effects thought to be related to the study drug were:

        - Headache
        - Change in taste
        - Change in the feces
        - One participant had a syncope (a transient [lasting for a short period of time] loss of consciousness with a drop in blood pressure when standing up) 30 minutes after taking a median dose, but not at later times, and in others who took two times and four times higher doses did not have the same symptoms.
    - Potential side effects are:
        - An allergic reaction. Symptoms include:
            - Rash
            - Wheezing and difficulty breathing
            - Dizziness and fainting
            - Swelling around the mouth, throat or eyes
            - A fast pulse
            - Sweating
        - Vomiting, especially in higher doses
        - Decreased food intake
        - Abnormal liver tests, that are transient
        - Increased heart rate with a drop in blood pressure when standing.

  - SLV213's potential to cause mutations and cancer needs further testing, and there are no long-term studies to evaluate this risk in animals and humans. However, this risk is considered low because the study drug will be administered for a short time in this study.
- Risks that could be caused by the study procedures are:
  - There may be side effects of inserting needles or a catheter (plastic tube) in the vein (IV) to collect blood, such as local pain, bruising, bleeding, phlebitis (inflammation or infection of the vein) or thrombophlebitis (clotting of blood in the vein) at the site of the IV catheter.
  - There may be side effects caused by the blood volume removed for testing, such as dizziness standing or feeling tired, or anemia (low blood counts). The amount of blood that will be drawn during the study is about 385 mL (13 ounces, about 1.6 cups). This is less than the volume when you donate blood, which is 500 mL (about 16.5 ounces, 2 cups).
  - There could be side effects from the ECG patches, such as a rash or minor irritation of the skin with itching. There could also be a need to shave a small area of the skin to place the patch.
- The CTU study staff will monitor your well-being during the study, evaluate you medically, and provide appropriate treatment as required. Precautions will be taken to minimize complications from blood draws or flushing the IV catheter.
- The study has no direct benefit for you. Knowledge gained in the study could be of future benefit to public health and to individuals with infections, who might benefit if the study drug is licensed.
- There are no alternatives to the research study. You are free to consent to participate in the study or not to participate or to withdraw after you consented initially. You will be compensated for the study days and procedures you complete. You will not be penalized if you withdraw from the study.
- Your personal health information will be protected. Your study medical record, laboratory test results and storage tubes containing your blood (plasma or serum) and urine specimens will be coded and will not identify you by name or provide any other personal information that can identify you.

INTRODUCTION

You are being asked to be a volunteer in a clinical research study. You cannot be in this study if you are in another research study or have been in another study within the past month. Before you agree to be a part of this study, it is very important that you read and understand the study plan and in what ways you will need to cooperate. This consent form may have words in it that you do not understand. You may ask the study doctor or the study staff to explain any words or information that you do not understand. If you sign and date this form, it means you want to be in this study.

This form describes the reason for the study, and the way the study will be done. It also describes the benefits, risks, discomforts, and warnings about the study. This form will also explain how

your medical information will be used, and who may see it. It describes your rights as a volunteer in the study.

The study staff will ask you many questions. Your answers must be completely truthful. Your health history and any changes in the way you feel during the study are very important. You must tell the study staff about any changes in your health or the way you feel. If you are not truthful, you may harm yourself by being in this study. By signing this consent form, you understand that you must provide truthful answers for your safety.

Altasciences Clinical Kansas, Inc., the research site, is being paid by the Division of Microbiology and Infectious Diseases (DMID) of the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health (NIH). DMID is also referred to as the "study sponsor" in this document.

BACKGROUND AND PURPOSE

The study doctor, DMID, and the study drug company, Selva Therapeutics, Inc, are conducting this research study of SLV213, an investigational drug that is being developed as a potential treatment of infections caused by coronaviruses related to the viruses that caused COVID-19. This research study is the first one where the effects of SLV213 taken every 12 hours for 7 days will be studied to determine the safety, tolerability, and PK of the study drug.

SLV213 capsules contain K777, a synthetic antibiotic that can block enzymes called Cathepsin L that are present in human cells and are used by the coronavirus to facilitate its entry into the cells that results in the infection. (Enzymes are specialized proteins that perform multiple functions in cells). SLV213 is considered investigational in this study because it is not a licensed/approved drug and will be used in total daily doses that are higher and the duration of study treatment is longer than the doses and duration of study treatment previously used in people.

SLV213 is evaluated in healthy persons before it is tested in people with infections in order to understand the safety profile and the PK of the study drug. It is expected that the study drug will be effective in infections for which the number of existing effective oral treatments are limited and, if given early after infection it could decrease the need for hospitalization or the development of severe disease.

INFORMATION ABOUT THE STUDY

This study will be done at one research site (described as clinical trial unit [CTU] in this document) in the U.S. Study participants will be adults between 18 to 65 years of age who are in good health, do not take certain medications, and, for women, who are not pregnant or breastfeeding. There will be a total of approximately 36 male and female participants in this study, assigned in 3 cohorts (groups) of 12 participants each. In each group, 8 participants will take active study drug (SLV213), and 4 participants will take placebo (inactive ingredients) randomly (like tossing a coin), with the chances being 66% to receive active study drug and 34% to receive placebo. The study drug doses will be taken in the form of capsules by mouth with water every 12 hours, morning, and evening, for 7 days. If you are eligible to take part in the study, you will take the same dose and the same number of capsules each time, according to the group you will be placed in after you consent to take part in the study and meet the study

requirements. Each dose of SLV213 (the active study drug) for each group are: 400 mg (Group 1), 600 mg (Group 2) and 800 mg (Group 3).

The study drug doses, the number of capsules taken in each cohort, and the duration of study treatment are shown in the following table:

Cohort Number	Study Drug	Study Drug Dose	Daily Study Treatments / Frequency	Duration
1	SLV213 or placebo	400 mg SLV213 Or placebo	4x100 mg capsules study drug or 4 capsules placebo By mouth every 12 hours	7 days
2	SLV213 or placebo	600 mg SLV213 Or placebo	6x100 mg capsules study drug or 6 capsules placebo By mouth every 12 hours	7 days
3	SLV213 or placebo	800 mg SLV213 Or placebo	8x100 mg capsules study drug or 8 capsules placebo By mouth every 12 hours	7 days

Additional participants may also be admitted to the CTU before dosing and may serve as back-up study participants. You may be selected to participate in this research study as either a regular study participant or as a back-up study participant. If you were selected as a back-up but did not receive a study treatment, you could be placed in a future group if you are still interested in taking part in the study. If you are placed in a future cohort, you may have to repeat screening assessments.

The study will take up to 56 days to complete and is made up of the following periods: a *Screening Period* up to 27 days (Day -28 to Day -2), with a single visit during which you will have screening evaluations and tests; a *Check-in Visit* (Day -1), during which you will have screening tests repeated to confirm your eligibility. If you still qualify, you will be admitted into the CTU, where you will stay overnight, and enrolled into the study; an *Inpatient Study Treatment and Follow-up Period* lasting 9 days/8 nights, with eligibility reviewed before the study treatment is administered on Day 1, twice daily doses, 12 hours apart, of the study drug or placebo from Day 1 to Day 7 and a follow-up of 2 days after the last dose (Days 8 and 9), with discharge from the CTU on Day 9; and an *Outpatient Follow-up Period* of up to 21 days after the last study treatment, that is conducted through the phone with study staff on Day 15 (±2 days), Day 21 (±2 days) and Day 28 (±2 days) and, if needed, visits to the CTU for medical evaluation after the phone calls.

The schedule for screening, check-in / enrollment, study treatment, and outpatient follow-up periods is shown in the table below:

Screening Period		**Inpatient Study Treatment and Follow-up**		**Outpatient Follow Up**
Screening	**Check-in/ Enrollment**	**Dosing**	**Follow-up**	
Day -28 to Day -2	Day -1	Day 1 to Day 7	Days 8 and 9 Day 9 (discharge)	Days 15, 21, and 28 (±2 days each) - Day 28 (final visit)

Screening Visit: This visit can be completed in a single visit, anytime from 28 to 2 days before receiving study drug or placebo. During this visit, you will be informed about the study, have your questions answered and, if you decide to participate in the study, as shown by signing and dating this consent form, you can immediately start having screening assessments. These will include medical evaluations (medical and medication history, vital signs [BP, HR, RR, and T] and physical examination [PE]), and ECG. BP and HR will be measured while resting lying down and after standing. If you pass these assessments, you will have standard clinical laboratory blood tests (blood counts, chemistries, coagulation tests) and urine tests, a pregnancy test if you are female, a test to confirm if you are post-menopausal if you're female, tests for HIV and Hepatitis B and C, and urine tests for detecting illegal drugs, alcohol, and cotinine (nicotine products). We will contact you in a few days to let you know if you passed the screen tests or not or if we want you to return to the CTU to repeat any lab tests. If you passed the screen tests you will be given an appointment for the second visit. You should come in the CTU for the second visit prepared to be admitted on the same day if you continue meeting the requirements to participate in the study.

Check-in Visit (Day -1): This visit is the day before receiving study drug or placebo. During this visit your medical information will be reviewed, VS will be taken with BP and HR measured while resting lying down and after standing, a PE will be done, and standard clinical lab blood and urine lab tests, a pregnancy test if you are female, and urine tests for detecting illegal drugs, alcohol, and cotinine (nicotine products) will be done. You will stay in the CTU waiting for the results of the tests. If the test results are acceptable, you will be admitted into the CTU, where you will stay overnight, and enrolled into the study.

Inpatient Study Treatment and Follow-up Period: Eligibility for starting dosing will be confirmed in the morning on Day 1, followed by baseline VS measurements and BP and HR measured while resting lying down and at 1 and 3 minutes after standing, and ECG. An intravenous catheter will be inserted in one of your forearm veins for withdrawing blood before and after receiving the study treatment. During the *Dosing Period* (Days 1 to 7), you will receive the study drug or placebo by mouth with water twice daily, 12 hours apart (in the morning and evening). You will fast, meaning you will not have any solid food, for various periods of time before and after dosing depending on the study day but you will be able to drink liquids except 1 hour before and 1 hour after each dose. You will have medical observations, collection of blood (plasma) for PK analysis (measurement of the study drug concentration in plasma to evaluate how your body handles the study drug) and, if you consented, additional blood (serum) for future research. You will stay in the CTU during the *Inpatient Follow-up Period* of 2 days after the last dose of the study drug or

placebo (Days 8 and 9), to complete medical observations and will be discharged from the CTU on Day 9.

Outpatient Follow-up Period: After you are discharged, study staff will contact you by phone three times about a week apart to ask how you are doing and if you had experienced any illness or seen a doctor or had any new symptoms since the last time and taken any medications. You will complete the study on Day 28 if the study doctor determines that your medical assessment is stable and there is no need for further follow up. If there is a medical concern, you may be asked to return to the CTU to follow up on any abnormal lab tests or other findings as necessary until they are no longer present, or they are not clinically significant in the judgement of the study doctor.

Details of medical assessments and study procedures on each study visit from screening to the end of the study are described below. (See WHAT WILL HAPPEN DURING THE STUDY?).

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.

MEDICAL MONITORING

The study staff will monitor you for side effects during your stay in the CTU and provide medical care as needed if you have any medical problems. Guidelines have been created to evaluate the safety of the study drug. If you have any side effects, we will evaluate your symptoms and treat you as indicated according to standard medical practices.

WHAT WILL HAPPEN DURING THE STUDY?

SCREENING PERIOD (Day -28 to Day -1)

SCREENING VISIT (Day -28 to Day -2):

During this visit, you will be informed about the study, have your questions answered and, if you decide you want to participate in the study, show your intent by signing and dating this consent form.

After signing this consent and before you begin the study, your demographic information (age, gender, race, ethnicity) will be recorded and you will have the following screening tests done to determine if you are in good health and qualify to continue participation in the study:

- Complete medical history and medication review.
- Review of contraception (birth control) methods you are practicing.
- Vital signs (VS; blood pressure [BP], heart rate [HR], breathing rate [RR} and oral temperature [T]) measured lying down. BP and HR will also be measured at 1 and 3 minutes after standing.
- Height and weight measured, and Body Mass Index (BMI) calculated.
- Complete Physical Examination.

- A 12-lead ECG (standard recording) - This will require attachment of electrodes from the ECG machine to your chest, arms, and legs. Male participants may have to have their chest hair shaved for the ECG. Female participants may not be allowed to wear a bra during ECG-related procedures.
- Blood and urine collected for clinical laboratory tests (blood counts, chemistries, coagulation tests and urinalysis). (You will be asked to not eat or drink anything other than water for at least 4 hours before blood collection.)
- Urine tests for alcohol, drug screen for illegal drugs, and cotinine test (for detecting nicotine products). (The tests for alcohol and illegal drugs must be negative to qualify.)
- A serum pregnancy test if female. (The test must be negative to qualify.)
- Blood collected for measurement of follicle-stimulating hormone if post-menopausal female.
- A blood test for HIV, the virus that causes AIDS, and blood tests for Hepatitis B and Hepatitis C Viruses. (Test results must be negative to qualify.)
    - Note that it may take weeks or months after being infected with HIV for the test to be positive. If you have a positive HIV or Hepatitis B and C test, you cannot be in the study. If these tests are positive, you will be notified by study staff at the CTU and given information on how to follow up for further medical care. As required by law, positive test results for HIV and Hepatitis must be reported by the CTU to the State Department of Health. If you have any questions about what information is required to be reported, please ask the study staff. If the CTU becomes aware during your participation in this study that there is any change in the HIV or Hepatitis test results, you will be withdrawn from the study. Your test results are private (confidential); however, this cannot be guaranteed. For example, it is possible for a court of law to get health or study records without your permission. The study doctor may be required to report these results to the local health authorities.

You will be told of the results of medical tests and whether you can continue participating in the study.

- *If you do not meet the study requirements*, you will be discharged from the study.
    - You will be told why you were not selected for the study.
    - If there is a medical condition or abnormal laboratory test that needs further medical attention, you will be counselled to follow up with your primary doctor or contact community physicians or clinics where you can go for testing and follow up.
    - You may sign a release form to allow the CTU to release medical tests to you or send them to your own doctor or clinic.
- *If your medical tests confirm your eligibility* to participate in the research study, the study staff will ask you to return to the CTU on Day -1 to complete the inpatient screening tests to confirm your eligibility to participate in the study.
    - You will be told to come prepared to stay for the inpatient study treatment if you pass the tests.

- You will be counselled to avoid pregnancy, use appropriate contraception (both male and female), and avoid prohibited medications, tobacco and other nicotine products, alcohol, and marijuana and illegal drugs.
- You should avoid strenuous physical activity.

CHECK-IN VISIT (Day -1) (1 day before the study treatment period)

On this day, you will have medical evaluations and blood and urine clinical lab tests, a urine pregnancy test (if you are a female), urine tests for alcohol, illicit drugs and cotinine, and a test for COVID-19 (collected through a nasal swab) to confirm that you continue meeting the requirements for admission and receiving the study drugs. All urine tests for alcohol, illicit drugs, and cotinine (for nicotine products) and the COVID-19 test should be negative to qualify. The study doctor will review the results of your tests to see if you still qualify.

- *If you do not meet the study requirements*, you will be discharged on this day. You will be told why you were not selected for the study. If there is a medical condition or abnormal laboratory test that needs further medical attention, you will be counselled to follow up with your primary doctor or contact community physicians or clinics where you can go for testing and follow up. You may sign a release form to allow the CTU to release medical tests to you or send them to your own doctor or clinic.
- *If you meet the study requirements*, you will be admitted to the CTU.

After you are admitted, you will complete an orientation of the inpatient facility, and asked to read the House Rules that describe what you are expected to follow while you stay in this facility and participate in the study.

- You will be told what study treatment cohort (group) you were assigned to and review the procedures that will be performed during the Inpatient Study Treatment period. You will not be told if you are going to receive active study drug or placebo.
- You will be counseled to avoid excessive exercise.
- You will be encouraged to drink plenty of fluids to keep well hydrated.
- You will receive dinner and snacks in the Research Site.
- You will eat dinner, but you will not be allowed to eat anything for about 8 hours before your first dose the following morning. During that time, you will be allowed to drink water or other liquids offered by the CTU up until 1 hour before dosing the next morning.

INPATIENT STUDY TREATMENT AND FOLLOW-UP PERIOD (Days 1 to 9)

You will receive the study drug orally (by mouth) every 12 hours daily in the morning and evening on Days 1 to 7 and stay followed as inpatient until Day 9. Food and liquids will be restricted for various periods of time before and after each dose during Days 1 to 7 as described below. The following procedures will be done during this period:

DAY 1 (In-patient Study Treatment):

Before the Morning Dose:

- You will not eat any food at least 8 hours before taking the first dose of the study drug (dosing) on the morning of Day 1. That means that you will not eat breakfast before dosing. You will be allowed to drink water or other liquids offered by the CTU staff during that time up until 1 hour before taking the morning dose.
- If you have new symptoms since admission, your medical history will be updated, and you may have a physical exam to evaluate them. Any medications you took will be reviewed. The results of the above will be reviewed to see if you still qualify to receive the study drug.
- You will have an IV catheter placed in a vein in your forearm to draw blood.
- You will have your vital signs (VS) checked about 30 min before dosing starts while lying down. BP and HR will also be measured at 1 and 3 minutes after standing.
- You will have a blood PK sample (blood sample to measure the concentration of the study drug, 6 mL) and a research sample if you consented (3.5 mL) drawn about 30 minutes before dosing starts.
- You will be randomized (like throwing a dice) to receive active study drug (SLV213) or placebo (an inactive compound) before the morning dose on Day 1. You will not be told if you are going to receive active study drug or placebo. You will receive the same dose of the active study drug or placebo on all study treatment days.

Morning Dose:

- You will receive the study drug or placebo by mouth with at least 240 mL (8 fluid ounces, about 1 cup) of water (See the table on page 5 about the number of pills you will take depending on the group you are assigned to).

After the Morning Dose:

- **You should report any side effects that you may experience after each dose and any other time until the end of the study.** You will also be observed for side-effects.
- You will have a physical exam done as needed for evaluation of new symptoms after dosing starts until the end of the study.
  - You will have Vital Signs measured about 2 hours after the morning dose lying down. BP and HR will also be measured at 1 and 3 minutes after standing.
- Any medication that you take will be recorded to the end of the study.
- You will not eat solid food at least 4 hours after you take the morning dose, but you will be able to drink water or other liquids offered by the CTU staff starting 1 hour after the dose.
- You will have blood samples drawn for plasma PK (6 mL each) and future research if you consented (3.5 mL each) at 30 min, and 1, 2, 4, 6, 8 and 12 hours after the morning dose (Day 1 only).
- You will have the blood drawing IV line checked periodically by the study staff to make sure it works and flushed or removed and replaced if needed. Let the study staff know if you experience any discomfort or other symptoms at the site of the IV line.

- You will start drinking fluids 1 hour after you took the study treatment,
- You may be served a meal 4 hours after the first dose. Let the study staff know if you have any nausea and you cannot eat.
- You will be counseled to avoid excessive exercise until the study end.

Before the Evening Dose:

- You will not eat any food at least 2 hours before taking the evening dose. You will be allowed to drink water or other liquids offered by the CTU study staff up until 1 hour before taking the evening dose. The study staff will serve food.
- If you have new symptoms, you will have a physical exam and any medications you took will be reviewed.
  - Your vital signs measured within 30 min before the evening dose lying down. BP and HR will also be measured at 1 and 3 minutes after standing.
- You will have the IV line for drawing blood checked to make sure it works and flushed or removed and replaced if needed.
- You will have blood collected for plasma PK (6 mL) and future research if you consented (3.5 mL) about 30 minutes before the evening dose (This is the same sample as the one collected 12 hours after the morning dose).

Evening Dose:

- You will receive the study drug or placebo by mouth with at least 240 mL (8 fluid ounces, about 1 cup) of water (See the table on Page 5).

After the Evening Dose:

- **You should report any side effects that you may experience after each dose and at any other time until the end of the study.** You will also be observed for side-effects.
- You may have a physical exam done as needed for evaluation of new symptoms.
- Any medication that you take will be recorded.
- You will not eat solid food at least 1 hour after you take the second dose, but you will be able to drink water or other liquids offered to you by the CTU study staff starting 1 hour after the dose.
- You will have your vital signs measured lying down. BP and HR will also be measured at 1 and 3 minutes after standing.
- You will have the blood drawing IV line checked periodically by the study staff to make sure it works and flushed or removed and replaced if needed. Let the study staff know if you experience any discomfort or other symptoms at the site of the IV catheter.
- You may be served a meal 1 hour after the evening dose. Let the study staff know if you have any nausea and you cannot eat.
- **Since you will receive the study drug or placebo doses at about the same time every day on Days 2-7, the CTU study staff will arrange to have your meals served at times that allow you to have your food and water or other liquids, while at the same time keeping in place the restriction for food and fluid intake before and after each dose on each future dosing day.**

DAY 2 to DAY 6 (In-patient Study Treatment):

You will continue taking 2 doses of study drug or placebo twice a day, one in the morning and one in the evening, about 12 hours apart.

You will not eat any food for about 2 hours before and 1 hour after each dose on each one of Days 2 to 6. Let the study staff know if you have any nausea and you cannot eat.

You will be able to drink water or other liquids offered by the CTU staff at all times except 1 hour before and 1 hour after each dose.

Before Dosing:

- You should report any side effects that you may experience.
- Any medication that you take will be recorded to the end of the study.
- Your blood draw IV line will be checked periodically to make sure it works and flushed or removed and replaced if needed.
- Your vital signs will be measured within 30 min before dosing lying down. BP and HR will also be measured at 1 and 3 minutes after standing.
- You will have blood samples collected for clinical lab tests (blood counts, chemistries, and coagulation tests) on Days 2, 4 and 6 (before the morning dose). You will be required to fast at least 4 hours prior to blood collection.
- You will have urine collected on Day 4 (before the morning dose).
- You will have an ECG on Day 4 (before the morning dose).
- You will have blood drawn for plasma PK (6 mL) and for future research if consented (3.5 mL) within 30 minutes before the morning dose (this is the same as the blood sample drawn 12 hours after the previous evening dose) and 30 minutes before the evening dose every day of Days 2 to 6.

Dosing:

- You will take the study drug or placebo with at least 240 mL (8 fluid ounces, about 1 cup) of water.

After Dosing:

- **You should report any side effects that you may experience after each dose and any other time on each day.**
- You will be observed for side-effects after taking each dose.
- You may have a physical exam for evaluation of your symptoms.
- Any medication that you take will be recorded.
- You will have Vital Signs measured about 2 hours after each dose lying down. BP and HR will also be measured at 1 and 3 minutes after standing.
- You will have blood drawn for plasma PK (6 mL) and for future research if consented (3.5 mL) 12 hours after each dose on Days 2 to 6.

DAY 7 (In-patient Study Treatment):

Before the Morning Dose:

- You will not eat any food at least 2 hours or drink any water or other fluids at least 1 hour before the morning dose. Let the study staff know if you have any nausea and you cannot eat.
- You should report any side effects that you may experience.
- Any medication that you take will be recorded.
- Your blood draw IV line will be examined checked periodically to make sure it works and flushed or removed and replaced if needed.
- Your vital signs will be measured within 30 min before dosing lying down. BP and HR will also be measured at 1 and 3 minutes after standing.
- You will have blood drawn for plasma PK (6 mL) and for future research if consented (3.5 mL) within 30 minutes before the morning dose (this is the same as the blood sample drawn 12 hours after the evening dose on Day 6).

Morning Dose:

- You will take the study drug or placebo with at least 240 mL (8 fluid ounces, about 1 cup) of water.

After the Morning Dose:

- You should report any side effects that you may experience.
- You will have a physical exam done as needed for evaluation of new symptoms.
- You will have Vital Signs measured about 2 hours after the morning dose lying down. BP and HR will also be measured at 1 and 3 minutes after standing.
- Any medication that you take will be recorded.
- You will not eat solid food at least 1 hour after the morning dose, but you will be able to drink water or other fluids offered by the CTU study staff starting 1 hour after the dose. Let the study staff know if you have any nausea and you cannot eat.
- You will have blood samples drawn for plasma PK (6 mL) and future research if you consented (3.5 mL) at 12 hours after the morning dose.
- You will have the blood drawing IV line checked periodically to make sure it works and flushed or removed and replaced if needed. Let the study staff know if you experience any discomfort or other symptoms at the site of the IV line.
- You will be counseled to avoid excessive exercise until the study end.

Before the Evening Dose:

- You will not eat any food at least 8 hours or drink any fluids at least 1 hour before the evening dose.
- You should report any side effects that you may experience.
- Any medication that you take will be recorded.

- Your blood draw IV line will be checked periodically to make sure it works and flushed or removed and replaced if needed.
- Your vital signs will be measured within 30 min before dosing lying down. BP and HR will also be measured at 1 and 3 minutes after standing.
- You will have blood drawn for plasma PK (6 mL) and for future research if you consented (3.5 mL) within 30 minutes before the evening dose (this is the same sample as blood drawn 12 hours after the morning dose).

Evening Dose:

- You will take the study drug or placebo with at least 240 mL (8 fluid ounces, about 1 cup) of water.

After the Evening Dose:

- **You should report any side effects that you may experience.** You will also be observed for side-effects.
- You may have a physical exam done as needed for evaluation of new symptoms after dosing starts until the end of the study.
- Any medication that you take will be recorded to the end of the study.
- You will not eat solid food at least 4 hours after you take the evening dose, but you will be able to drink water or fluids offered by the CTU staff starting 1 hour after the dose. Let the study staff know if you have any nausea and you cannot eat.
- You will have your vital signs measured about 2 hours after the evening dose lying down. BP and HR will also be measured at 1 and 3 minutes after standing.
- You will have blood samples drawn for plasma PK (6 mL each) and future research if you consented (3.5 mL each) at 30 min, and 1, 2, and 4 hours after the evening dose.
- You will have the blood drawing IV line checked periodically to make sure it works and flushed or removed and replaced if needed. Let the study staff know if you experience any discomfort or other symptoms at the site of the IV catheter.
- The study staff will let you know if they will flush the blood draw line to keep it open so that it can be used on the following day or removed and replaced.
- You may start drinking water or other liquids offered by the staff 1 hour after the evening dose.
- You will be served a meal 4 hours after the evening dose. Let the study staff know if you have any nausea and you cannot eat.

Since you will have to fast for at least 4 hours after the evening dose, the CTU study staff will arrange to have your evening meal late in the evening.

DAY 8 (Inpatient Follow-up):

- **You should report any side effects that you may experience.**
- You will have vital signs measured lying down. BP and HR will also be measured at 1 and 3 minutes after standing.

- You will have blood and urine samples collected for clinical laboratory tests. You will be required to fast at least 4 hours prior to blood collection.
- You will have an ECG.
- You will have blood sample drawn 4 times on Day 8 for plasma PK (6 mL each) and for future research (3.5 mL each) at 6, 8, 12 and 24 hours after the evening dose on Day 7.
- You may have a physical examination for evaluation of your symptoms.
- Any medication that you take will be recorded.
- You will be served all three meals today at regular hours and drink water and fluids offered by the staff.

Day 9 (Inpatient Follow-Up / Discharge):

- You will be asked about any new symptoms you developed since the day before
- You will be asked about any medications you took.
- You will have vital signs measured lying down. BP and HR will also be measured at 1 and 3 minutes after standing.
- You will have a complete physical examination.
- You will have blood drawn 2 times on Day 9 for plasma PK (6 mL each) and for future research (3.5 mL each) at 36 and 48 hours after the evening dose on Day 7.
- You will then have the IV blood draw catheter removed and the blood draw site inspected.
- You should report any discomfort you have at the blood draw site.
- If you are female, you will be counseled to continue contraception and avoid pregnancy for 30 days after the last dose of study drug.
- If you are male, you will be counseled you and your female partner to use appropriate contraception and you should also avoid sperm donation for 30 days after the last dose of study drug.
- You should avoid excessive exercise.
- You will be provided contact information and instructions to report to the Research Site (CTU) any side effects or new symptoms you experience and any medication that you take that after your discharge.
- You will review with the CTU study staff your contact information and be told you will be expecting telephone calls to ask you about how you are doing and medications you are taking.
- You will be discharged in the evening of Day 9.

OUTPATIENT FOLLOW UP
(DAYS 15 (±2 days), 21 (±2 days) and 28 (±2 days) - Day 28 is Final Visit):

- **You should report to or visit the CTU if you have any side effects or an illness after your discharge from the CTU on Day 9.**
- CTU study staff will contact you by phone about every week for three weeks after your discharge from the clinic to ask how you are doing, if you had any side-effects or visited your physician or the ER since the last visit or call, and if you used any medications after your discharge.

- You may be asked to return to the CTU for a clinical exam and any tests, as needed, to evaluate any new symptoms or follow up any previous symptoms or abnormal labs.
- You will be counseled to avoid any prohibited medications until the end of the study.
- You will be counseled to avoid pregnancy and continue contraception for 30 days after the last dose.
- If you are male, you will be counseled to avoid donating sperm for 30 days after last dose.
- You should avoid excessive exercise. until after the last call from the clinic on Day 28.
- The study staff will let you know on Day 28 if you have completed the study or need to return to the clinic for follow up of any on-going side effects.

UNSCHEDULED VISITS (Out-patient follow up)

You may be asked to report to the research site for an unscheduled visit if the study staff feel it is necessary for your safety. This may occur if you experienced any side effects that require further evaluation after any of the scheduled out-patients visits on Days 15, 21 and 28, and at any time after your discharge from the inpatient stay on Day 9 if you have any ongoing side effects. During those visits, you will be asked about the medical history of the event and have VS measured (lying down and BP and HR at 1 and 3 minutes after standing) and a focused physical examination as needed, and clinical laboratory tests, ECG, and other tests as indicated. You will be told if further follow up is needed.

EARLY TERMINATION:

If you choose to withdraw from the study or are terminated by the study doctor before you complete the study, you will not receive any more doses of study drug or placebo. However, you will be asked to consent to remain in the study to complete safety and PK blood collections following the last study dose you received.

If you do not consent to remain in the study, the following activities could be completed depending on your clinical status:

- You will be asked to provide information on the side-effects you may experience.
- You will be asked to document medications you take.
- You may have the Vital Signs measured lying down. BP and HR will also be measured at 1 and 3 minutes after standing.
- You will have a physical examination.
- You will have a 12-lead ECG if needed.
- You will have blood drawn and/or urine collected for clinical laboratory tests if needed.
- You may have blood drawn for plasma PK (6 mL) and for future research (3.5 mL each) if needed.
- The study staff will give you information and tell you if you need to return for follow up for another visit.

The study staff may also request to have procedures performed that are not listed above to ensure your safety throughout the study.

ADDITIONAL DRUG AND ALCOHOL SCREENS

Random urine drug and alcohol screens may be repeated at any time during the study if the study staff suspects alcohol or drug use. If you test positive for drug or alcohol use at any time after the first dose of study drug, you may be discontinued from the study.

CONTROLLED SEARCH

Designated study staff reserves the right to do a controlled search by having you put on a gown in order to have your clothes and person checked for disallowed items that may have been brought into the research site. This search involves removing all undergarments as well as putting on a gown so that there is no place the disallowed items could be kept.

At each admission into the research site, a search of your clothing, like pockets, and bags will occur. You will not be required to remove your clothing or undergarments, but study staff may ask you to turn your pockets inside out or check areas of clothing that could conceal restricted items. Study staff will also perform a bag check and confiscate any items not permitted to be brought into the research site. These belongings will be returned to you at discharge from the research site.

BLOOD SAMPLES

Blood samples will be drawn by single needle-sticks or through an IV catheter, as determined by the study staff. An IV catheter is a small plastic tube inserted into your arm vein by a needle. The needle is removed, but the tube temporarily remains in your vein. This tube allows the removal of blood without having to stick you each time. It will be removed every 3-4 days or sooner if not required for frequent blood collection or not working well or if you have local pain or vein irritation.

Blood will be collected for the following tests during the study:

1. For clinical laboratory tests (blood counts, chemistries, and coagulation tests) to evaluate the effects of the study drug on your body organs. If you complete the study, the total volume of blood collected for this purpose will be about 100 mL, (about 3.3 ounces, a bit less than 7 tablespoons). Additional blood samples may be drawn during the study, if the study staff considers it necessary for monitoring your health. Blood samples left after all routine clinical laboratory testing is done will be discarded by the clinical safety laboratory.

2. For plasma PK tests to measure the concentration of SLV213, the investigational drug, and study how your body handles the study drug after each dose (how fast it enters your circulation after taking it by mouth, how high is the peak concentration and how long it last, and how long the drug stays in your body). The total volume of blood collected for this purpose will be about 180 mL (6 ounces, about ¾ of a cup). Plasma samples left over after testing, will be stored for future research at the sponsor's (NIAID) storage area if you consent (give your permission to do so).

3. For serum for future research with SLV213, to see if it has an effect on other body systems that are not evaluated during this study, such as the immune system, which is the system that protects against infections. The total volume of blood collected for this

purpose is about 105 mL (about 3.5 oz, a bit less than half a cup.). These samples will also be collected and stored if you give permission to do so.

If all of these samples above are collected, the total volume of blood drawn from you will be about will be about 384.7 mL (a bit less than 13 oz or around 1.6 cups). For comparison, a standard blood donation at a blood collection center, once in a 56-day period, is about 500 mL (a bit under 17 ounces or a bit over 2 cups).

For more information about collected samples for future research see section see below on page (See section on Blood Specimens for Future Research Testing below).

YOUR ROLE IN THIS STUDY

Taking part in a research study can be an inconvenience to your daily life. Please consider the study time commitments and responsibilities as a research participant when you are deciding to participate. Your responsibilities as a participant include the following:

- You cannot participate in this study if you have participated in a prior study within the past 30 days.
- We ask you to provide accurate responses to questions about your past medical and surgical history (illnesses and surgeries you had including abnormal lab tests, X-rays, and other procedures), medications you are taking, medications you are allergic to and your family history. Failure to respond accurately may result in side-effects that may be harmful after you receive the study drug(s).
- You must read, and agree to follow, the House Rules at the Research Site if you want to take part in this study. House Rules discuss proper behavior at the Research Site and are important to ensure your safety and make sure the study results are accurate. Failure to follow these rules may result in reduced compensation or involuntary discharge from this study.
- You must report any side effects and medical problems to the study staff.
- You must give true and complete answers to any questions.
- You must be able to comply with the study procedures and visit schedule.
- You must follow all instructions from the study staff.
- You must inform the study staff if you decide to discontinue your participation in the study. If you decide to discontinue your participation in the study, you may be asked to consent to stay in the study and complete any remaining procedures for the most recent study treatment period. If you do not consent to complete any remaining procedures, you will be asked to complete the early termination visit procedures as described in this consent form.
- You must agree to use an effective method of contraception, as defined later in this consent form, throughout the study and for 30 days after the last dose. If you are male, you must agree not to donate sperm for 30 days after dosing and, if you are sexually active, you and partner to use safe contraception.
- You must not do any strenuous activity for 2 days before the dosing starts and at any time during the study until discharge on Day 9.

- Refrain from consumption of red wine, Seville oranges, grapefruit, or grapefruit juice, [pomelos, exotic citrus fruits, grapefruit hybrids, or fruit juices] from 7 days before the start of the study until discharge on Day 9.
- Refrain from alcohol use 7 days before starting dosing and for the duration of the trial.
- You must not use marijuana or other illegal drugs during the study.
- You will be recommended to avoid using nicotine products from a week before starting dosing. Smoking is prohibited during the in-patient period of the study following Check-in (Day -1) to discharge from the CTU (Day 9)
- You must not participate in another research study at any time during this study or continue participating in another study and have blood draws. This includes studies of a drug, biologic (such as vaccine or proteins), device, or blood product.

PROHIBITED MEDICATIONS, VACCINATIONS, and BLOOD DONATIONS

Additional restrictions to ensure the health and safety of study participants are listed below:

- Please report all prescription medications, including contraceptive hormones (pills, patches, or injections and intrauterine devices containing hormones), and non-prescription medications, herbs, vitamins, or nutritional supplements you are taking at the time of Screening and on check-in (Day -1). Their use without the knowledge of the site physician may cause an interaction with the study drug and increase your risk of having a severe side-effect.
- You must not take any prescription medications within 14 days before check-in on Day -1 (a day before the start of study drug treatments) or during the study. Certain drugs should be avoided for a longer period before taking the study drug.
- If you are female, you must not use contraceptives containing hormones (pills, patched, injections, or intrauterine devices containing hormone) during the study. (See below Information about Birth Control).
- If you are male, you must not use condoms containing spermicides during the study. (See below Information about Birth Control).
- You must not take any over the counter (OTC), non-prescription medications, herbs, vitamins, or nutritional supplements including St. John's wort from at least about 14 days before dosing) and for the duration of the study.
- Report any symptoms that you may experience. The study doctor may allow the use of acetaminophen up to 1,000 mg a day for 1-3 days as needed for any common pains and aches (headache, muscle pains), or medication for other common disturbances if approved by the study doctor(s).
- You must not donate any blood or blood products (red cells, white cells, platelets, plasma) during the course of this study. Tell the study doctor if you donated any blood or blood products within 3 months before dosing. If you did, we could delay your screening.
- You must not receive any blood or blood products during this study unless it is medically necessary.

RISKS OF THE INVESTIGATIONAL DRUGS

Observed Risks with SLV213:
There were no identified risks associated with SLV213 in a completed study in 40 healthy participants who were given single doses by mouth ranging from 50 mg to 800 mg. The most common complaints that were mild and transient and seen at all doses were:

- Headache
- Change in taste
- Change in the feces (stool)

There was no evidence of injury to the liver or the heart at any dose. The most severe event was orthostatic hypotension with syncope (passing out while standing up because of a drop in blood pressure) in one participant 30 min after a dose of 200 mg. The participant recovered without consequences and the event did not happen at later timepoints in the same participant or in others who took higher doses of 400 mg and 800 mg. Overall, the drug was well tolerated, there were no serious adverse events or reactions.

Potential Risks with SLV213:
SLV213 has the potential to cause:

- An allergic reaction, like all chemicals. Symptoms include:
  - Rash
  - Wheezing and difficulty breathing
  - Dizziness and fainting
  - Swelling around the mouth, throat or eyes
  - A fast pulse
  - Sweating
- Vomiting, especially at high doses
- Decreased food intake
- Abnormal liver tests, that are transient
- Increased heart rate with a drop in blood pressure when standing and may result in syncope (transient loss of consciousness).

Further testing is needed to understand the potential for SLV213 to alter the function of the liver, kidneys, brain and heart. Long-term studies in animals and humans are not available.

Potential Drug Interactions:
There are no clinical data on drug interactions with the SLV213. However, based on the knowledge about the metabolism of the study drug, medications strongly metabolized by CYP3A4 and CYP2D6 or are strong inducers or strong inhibitors of these two enzymes should be avoided from 14 days before the first dose to the end of the study to prevent any adverse effects after administration of SLV13. There is a very long list of substances that are in this category, and except for grapefruit juice and St. John's wort, the remaining are drugs available by prescription, which are prohibited for use in this clinical trial. **You are reminded to report what prescription**

or non-prescription medications and supplements you take, and we will let you know if the drug is permitted or prohibited.

Use During Pregnancy and Lactation:
The effects of the study drugs on the pregnant mother and the fetus have not been studied Therefore, you should not participate in the study if you are pregnant or plan to become pregnant during the study or if you are currently breastfeeding.

Overdose:
There is no specific antidote in case of overdose. The same measures as recommended for other drugs (treatment cessation, adequate hydration, and kidney dialysis) will be provided as medically necessary.

Drug Abuse and Dependency:
No clinical experience available.

BLOOD SAMPLE RISKS
There may be side effects of drawing blood from a vein with a needle and/or IV catheter placement. Local pain, bruising, bleeding, redness, swelling, or induration (palpable hard area) might occur at the site of the needle stick where blood is drawn. Infection at the blood draw site is possible but unlikely as aseptic technique will be used. There is a possibility of dizziness or fainting while your blood is being drawn. Precautions will be taken to minimize the above side effects. There is a small risk your blood counts will decrease slightly during the course of the study, but not expected to cause anemia (low blood counts that cause symptoms and need treatment). Any symptoms that may occur are usually reversible with good nutrition and drinking fluids.

ECG RISKS
ECG patches may cause a skin reaction such as redness or itching. You may also experience localized skin discomforts and/or hair loss associated with the placement of ECG patches.

UNKNOWN RISKS
You may have side effects or discomforts that are not listed in this form. Some side effects may not be known yet. New ones could happen to you. Tell the study staff right away if you have any problems.

INFORMATION ABOUT BIRTH CONTROL

Females:
The effects of study drug(s) on the unborn child are not known at this time. Therefore, it is important that women who are pregnant, may become pregnant or who are breastfeeding NOT participate in this study. If you are a woman who can get pregnant, you must use an acceptable form of birth control that is very effective in preventing pregnancy for at least one month before screening. You must also agree to continue using acceptable contraception until dosing and for at least 30 days after dosing, and to avoid becoming pregnant during this study.

The following are acceptable forms of birth control for this study:

- Intrauterine devices (IUD) without hormones.
- Surgery to prevent pregnancy in females (such as bilateral tubal ligation, salpingectomy [removal of the tubes], oophorectomy [removal of the ovaries], or hysterectomy [removal of the uterus], or Essure® placement with a history of documented radiological confirmation test at least 90 days after the procedure).
- If in a monogamous relationship and the male partner uses a barrier method without spermicide)
- Being in a monogamous relationship with a partner who has had vasectomy for 180 days or more before your planned study treatment with study drug.

True abstinence (meaning 100% of the time without sexual intercourse with vaginal penetration).

Tell the study staff if you use any other forms of birth control.

If at any time during this study you think you may be pregnant, you are requested to contact the CTU study doctor, **Martin Kankam, MD,** at **913-696-1601** (24 hours).

Males:
The effect of study drug(s) on the unborn child is unknown at this time. The effect of the study drug on the male reproductive system is unknown. Therefore, you must agree to use an acceptable form of birth control from dosing with study drug through at least 30 days after the last dose. Acceptable birth control means not having sex (abstinence) or having a vasectomy. If you are sexually active, you should agree to use a condom without spermicide throughout this study and for at least 30 days after dosing. **Tell the study staff if you use any other form of birth control**.

You should also not donate sperm for 30 days after the last dose.

It is also recommended that you make certain that your female partner is also using an acceptable form of birth control if you have not had a vasectomy and are using a condom. If you think that your partner may be pregnant at any time during this study to 30 days after dosing, you are requested to contact the CTU study doctor, **Martin Kankam, MD, at 913-696-1601 (24 hours)**.

REPORTING PREGNANCY
If you are a female capable of becoming pregnant, you should report to the study staff if you miss your period and suspect you are pregnant or if you become pregnant during the 30 days after dosing. With your permission, you will continue to be followed for safety during this study. You are requested to provide pregnancy outcome to the study staff upon delivery or pregnancy termination.

If you are a male capable of causing pregnancy and your female partner becomes pregnant during the 30 days after dosing, we ask you to inform study staff of the pregnancy and provide pregnancy outcome upon delivery or pregnancy termination.

INFORMATION ON USE OF ALCOHOL, MARIJUANA OR ILLEGAL DRUGS
You are not allowed to use alcohol, marijuana, or illegal drugs (such as cocaine, etc.) because they may cause you serious harm and are strictly forbidden while you are in this study. You will

be tested for drugs and alcohol at Screening and on Check-in (Day -1). If you are found to be in possession of or using marijuana or other illegal drugs at the CTU, then Altasciences Clinical Kansas, Inc. is obligated to report the use of marijuana or other illegal drugs to the appropriate legal authorities.

INFORMATION ON ACTIVITIES TO AVOID

You should avoid excessive exercise from 48 hours before dosing until the discharge from the research site on Day 9.

NEW INFORMATION ABOUT STUDY DRUG(S)

The study doctor or study staff will discuss with you any important new information, findings, or changes to the way the research will be performed that may affect your decision to remain in this study. If this happens, you will be asked to decide if you want to keep taking part in this study. You may be given an additional informed consent and will be asked to agree in writing that you were told about these new findings.

BENEFITS TO THE STUDY PARTICIPANT

The goal of this research study is to provide scientific information. You will not receive any medical benefits. This study may help doctors and scientists learn things about the study drug that will help others.

ALTERNATE THERAPY

This is a clinical research study. It is not treatment or therapy. The other choice is to not participate in this study.

PAYMENT FOR PARTICIPATION

If, after screening, you are enrolled in the study and complete all the study visits, you will receive a total of up to $5,250.00 at the completion of your participation in the study to help cover the costs of your participation and compensate you for your time. If after enrollment your participation is ended early, or if you withdraw for any reason, the amount you will be paid will be prorated and the payment made when your participation in the study ends. This means that you will receive payment only for the portion of the study that you completed and only after your participation in the study has been completed. Payment will be prorated as follows:

Visit 1	Screening	$200.00
Visit 2	Day -1 Admit	$375.00
Visits 3-9	Days 1 to Day 7 In-house study treatments	$3,375.00
Visit 10	Day 8 In-house follow-up	
Visit 11	Day 9 Discharge	
Visit 12	Day 15 Follow-Up telephone call	$85.00
Visit 13	Day 21 Follow-Up telephone call	$85.00
Visit 14	Day 28 Follow-Up telephone call/ End of Study	$85.00
Completion Amount		$1,045.00
Total		$5,250.00

Visit 1 will be compensated in the amount of $200.00 at the completion of the visit.

Visits 2 through 11 (9 overnight stays) will be compensated in the amount of $3,750.00 ($375.00 per overnight stay) at discharge on Visit 11.

Visit 12, 13, and 14 will be compensated in the amount of $85.00 for each visit completed by telephone. Compensation will be issued in the form of a check, pre-loaded MasterCard, or cash. The form of compensation will be determined by the study staff.

For any outpatient visit that occurs on a weekend, the associated compensation will be paid on the next business day.

Unscheduled visits may be compensated up to $50.00 as determined by the study staff.

All visits must be completed within the scheduled timeframe in order to receive the end of study completion amount of $1,045.00 on Visit 14. Failure to complete all visits within the allowable timeframe will make you ineligible to receive the completion amount.

Money may be deducted from your study compensation if you do not follow the in-house rules or other reasonable instructions given by the study staff. For example, if illegal substances are brought into the CTU or you are found to be using an illegal substance while in house, up to half of your previously earned amount may be deducted and you may be withdrawn from the study as determined by the study staff.

If you withdraw or are withdrawn from the study early, you will only be compensated for the visits that you complete.

The remainder of your earned in-house stipend will be compensated to you on the originally scheduled study day/date of discharge from the in-house portion of the study.

You may be required to report the compensation received for this study to the Internal Revenue Service (IRS) as taxable income. According to the IRS guidelines, you will be responsible for paying taxes on any compensation that you receive from your study participation. Altasciences Clinical Kansas, Inc. will send you a 1099-form for this purpose. Altasciences Clinical Kansas, Inc. will also report to the IRS any compensation that you receive that total $600.00 or more for the calendar year. You must tell Altasciences Clinical Kansas, Inc. of your new mailing address if you move after your participation in a study. This is to make sure you receive your 1099 for your year-end tax reporting.

COMPENSATION FOR INJURY

- In the event you experience an adverse reaction (side-effect), illness or injury during this study, you should immediately seek treatment. It is important that you tell the CTU study doctor, **Martin Kankam, MD**, if you have experienced one of these events. You must contact the study staff at **(913) 696-1601** as soon as you are able. You may obtain medical care in the same way as you would ordinarily receive any other medical treatment. Immediate necessary care, emergency treatment, and professional services will be available to research participants just as they are to the community generally. No long-

term medical care or financial compensation for research-related injuries will be provided by the NIH or the Federal Government.

- Medical care will be given to you at no cost if you are injured because of being in this study.
- While you are in this study, you may be injured because of your personal conduct or during activities, which are not part of this study. There are no plans to pay you for these types of injuries.

PREP ACT DECLARATION

A Declaration under the Public Readiness and Emergency Preparedness Act (PREP Act) was issued by the Secretary of the United States Department of Health and Human Services on March 10, 2020. This Declaration limits the legal rights of a participant in clinical studies utilizing COVID-19 countermeasures, such as the study SLV213, used in this study. Because this study is covered by the PREP Act Declaration, covered persons, such as the manufacturers, study sponsor, researchers, healthcare providers and others have liability immunity (that is, they cannot be sued by you or your family under the laws of the United States).

If you believe that you may have been harmed as a result of this study, certain claims for serious injury or death caused by the countermeasure may be eligible for compensation through the Countermeasures Injury Compensation Program (CICP). This is a program set up by the Health Resources and Services Administration (HRSA) of the United States Government. Information about this program can be found at https://www.hrsa.gov/cicp/about/index.html or by calling 1-855-266-2427. If you are eligible for this program, you must file a claim within one year of the administration or use of the covered countermeasure. A factsheet on CICP and how to file a Request for Benefits Package to the CICP Summary, will be provided to you.

COSTS TO YOU

There is no cost to you to participate in this study. You do not have to pay for any study-related medicines, procedures, or study treatment at the Research Site during this study.

SOURCE OF FUNDING

This research study is being funded by NIAID/NIH, which has a contract with a company named DVC to do studies like this one. Altasciences Clinical Kansas, Inc. is a partner of Altasciences, Inc. a subcontractor of DVC, to conduct this research study under the direction of Martin Kankam, MD.

VOLUNTARY PARTICIPATION IN THIS STUDY

Your participation in this study is voluntary. You will be starting this study of your own free will and without any kind of pressure. You may quit this study any time you wish. If you withdraw from this study, you will not be penalized. You will not lose any benefits to which you were otherwise entitled.

If you have health problems, you will get medical attention. You may be withdrawn from this study by the study staff and/or the sponsor of this study, without your consent, if it is in your best medical interest. It is possible that the study staff and/or sponsor may think you can stay in this study. You must decide what you want to do.

The study staff may stop your participation in this study at any time without your consent for any of the following reasons:

- If you don't follow the study staff's instructions;
- If something serious happens to you which may require treatment;
- If the study staff decides it is in the best interest of your health, and welfare to discontinue further participation; and
- If you do not later consent to any future changes that may be made in the study plan.

The sponsor may stop this study for other reasons not known now.

The FDA or the Institutional Review Board (IRB, see below) may also terminate this study if there are safety concerns.

IF YOU WITHDRAW FROM THE STUDY

If you do not complete this study for any reason, you will be asked to undergo a physical exam, vital signs measurement, 12-lead ECG, blood and urine laboratory tests, and tests for the measurement of study drug concentration in your blood if early termination occurs within 24 hours of dosing. This is needed to identify any changes that may have occurred after you began to take the study drug and to protect your safety, health, and welfare.

If you received any amount of the study drug but withdraw from the trial within 24 hours after dosing, you will be encouraged to continue follow-up (with your consent) for safety assessments. We may also ask you to provide PK blood and urine sample(s) to complete scheduled collection if you had received study drug on the day you withdrew from the study.

BLOOD SPECIMENS FOR FUTURE RESEARCH TESTING

We would like to ask your permission to store any **residual (left-over) blood (plasma)** collected for testing the study product concentration (plasma PK). With your consent, we will store **leftover blood for additional research** that is not part of this study, also known as **secondary research**. The samples will be stored in a NIAID/DMID repository and may be shared with the company or other researchers for purposes to develop diagnostics or further research for treatment of COVID-19, such as to evaluate the metabolism and other effects of SLV213. No genetic testing will be done with the blood. You may choose not to store leftover blood, or change your mind later and withdraw your consent, which means all your samples at the end of the study will be destroyed. You may continue in the main study even if you do not agree or withdraw consent for storing leftover samples. There is no benefit to you, however, society may benefit from additional research. The risks of leftover samples used for other research is a possible loss of privacy. Your samples will be coded or linked to your data (for example, results from this study); however, no information that identifies you will be released to the company or researchers. Please initial and date your choice below in the box to the left of the YES or NO answers.

	YES You may store my unused blood samples in coded tubes for an indefinite period of time. The link to my personal identifying information will not be sent to other researchers or the company that receives the samples.
(Initials) (Date)	
	NO You may not store my unused blood samples for secondary research. Destroy all unused samples at the end of the study.
(Initials) (Date)	

With your consent, we would also like to collect and store **extra blood (serum) for additional research** that is not part of this study, also known as **secondary research**. The extra blood will be drawn when study blood is drawn, for a total volume of 90 mL (6 tablespoons). The samples will be stored in a NIAID/DMID repository and may be shared with the company or other researchers for purposes to develop diagnostics or further research for treatment of COVID-19, for example to evaluate the metabolism and other effects of SLV213. No genetic testing will be done with the blood. You may choose not to provide the extra blood or change your mind later and withdrawn from the collection of extra blood samples. You may continue in the main study even if you do not agree now or withdraw consent later for extra samples. There is no benefit to you, however, society may benefit from additional research. The risks of extra samples are similar to risks for drawing blood for this study. Your samples will be coded or linked to your data (for example, results from this study); however, no information that identifies you will be released to the company or researchers. Please initial and date your decision below in the box to the left of the YES or NO answers.

	YES. You may collect, store for unlimited period of time, and use additional serum samples for secondary (other) research.
(Initials) (Date)	
	NO. Do not collect, store, and use additional serum samples for secondary (other) research.
(Initials) (Date)	

CERTIFICATE OF CONFIDENTIALITY

To help us protect your privacy, we have a Certificate of Confidentiality from NIH. The study staff can use this certificate to legally refuse to give information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if there is a court subpoena. The study staff will use the certificate to resist any demands for information that would identify you, except for reporting of communicable diseases, such as Hepatitis Virus and HIV infections, to state and local health departments, or for reporting possession or use of marijuana or other illegal drugs while at the CTU to the appropriate legal authorities.

A Certificate of Confidentiality does not prevent disclosure of your information to the NIH, FDA, or federal funding agency. Information from this study will be given to DMID and Selva Therapeutics, Inc, the pharmaceutical organization developing SLV213 and other drugs for the treatment of infectious diseases. Any persons or companies, which are contracted by the sponsor for conducting this study, measuring study drug level in blood samples, monitoring the execution of this study, and analyzing the data, will have access to the research information during and after this study. The information will also be given to the FDA. It may be given to governmental agencies in other countries where the study drug may be considered for approval.

Medical records which identify you and the consent form signed by you will be looked at and/or copied for research or regulatory purposes by:

- The sponsor
- An agent for the sponsor
- An agent for the study doctor
- The FDA
- Department of Health and Human Services (DHHS) agencies
- The Institutional Review Board, Advarra IRB.

Absolute confidentiality cannot be guaranteed because of the need to give information to these parties. The results of this research study may be presented at meetings or in publications. Your identity will not be disclosed in those presentations.

- Altasciences Clinical Kansas, Inc. will handle the medical information obtained in this study with the strictest confidence. It will be protected as required by laws and/or regulations. It will not be made publicly available.
- If the results of this study are published, you will not be identified by name.
- Your identity will not be disclosed to anyone else, unless required by law.

By signing this consent, you authorize Altasciences Clinical Kansas, Inc. to verify your study participation history with other businesses that conduct clinical research studies.

A Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If you give your consent to release information to a medical care provider, an insurer, or other person to receive research information, then the researchers will not withhold that information.

PRIMARY CARE PHYSICIAN NOTIFICATION

We would like your permission to contact the doctor you see regularly to let them know that you are taking part in this study. It is important for all your doctors to know that you may be taking an experimental drug. Your doctor will want to know and think about all the drugs you are taking before giving you any new ones. While you are in the study, the study doctor will ask about your symptoms. If you have symptoms after the study ends, your other doctor may want to contact the study personnel.

If you agree, your primary care physician (regular doctor) will be informed of your participation in the study. Indicate your choice below by initialing only one (1) section below.

_____ (Initials Date)	I do not have a primary care physician.
_____ (Initials Date)	I do not want my primary care physician notified.
_____ (Initials Date)	I would like my primary care physician notified and below is my physician's contact information. Physician's Name: _____ Address: _____ _____ Phone No.: _____

PERSONS TO CONTACT FOR QUESTIONS, CONCERNS, OR COMPLAINTS

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 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 participants. If you have any questions about your rights as a research participant, and/or concerns or complaints regarding this research study, 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

Please reference the following number when contacting the Study Subject Adviser: Pro00073286.

CONSENT

I have read all information in this document, and all my questions have been answered to my satisfaction. I voluntarily consent to participate in this study. I will be given a signed and dated copy of this consent form and have been told the description of the study drug, and the name, address, and phone number of the study physician. My signature gives my consent to participate. By signing and dating this form, I have not given up any of my legal rights as a research participant.

Print Participant Name	Date
Participant's Signature	
Person Obtaining Informed Consent Printed Name	
Person Obtaining Informed Consent Signature	Date
Study Doctor's Signature*	Date

*The study doctor's signature evidences only that the study doctor has reviewed the consent form and the signatures of the participant and person obtaining consent, for compliance.