# A Phase 2a, Randomized, Double-blind, Placebo-controlled Trial to Evaluate the Antiviral Activity, Safety, and Pharmacokinetics of Repeated Oral Doses of JNJ-64281802 Against Dengue Serotype 3 Infection in a Dengue Human Challenge Model in Healthy Adult Participants

Informed Consent Form
Version date: June 25, 2024

NCT05048875

**WORKING COPYRESEARCH SUBJECT CONSENT FORM**

| | |
|---|---|
| **Title:** | A Phase 2a, Randomized, Double-blind, Placebo-controlled Trial to Evaluate the Antiviral Activity, Safety, and Pharmacokinetics of Repeated Oral Doses of JNJ-64281802 Against Dengue Serotype 3 Infection in a Dengue Human Challenge Model in Healthy Adult Participants |
| **Protocol No.:** | CIR 332<br>WCG IRB Protocol #20213557 |
| **Sponsor:** | Office of Clinical Research Policy and Regulatory Operations (OCRPRO)<br>National Institute of Allergy and Infectious Diseases (NIAID)<br>National Institutes of Health (NIH) |
| **Investigator:** | Anna Durbin, MD<br>Center for Immunization Research (CIR)<br>Johns Hopkins School of Public Health<br>855 North Wolfe Street, Suite 600<br>Baltimore, MD, 21205<br>United States |
| **Site:** | Center for Immunization Research<br>Johns Hopkins Bloomberg School of Public Health<br>301 Mason Lord Drive, Suite 4300<br>Baltimore, Maryland 21224<br>United States |
| **Study-Related Phone Number(s):** | Anna P. Durbin, MD<br>667-306-9772<br>410-340-6852 (24 hours) |

## RESEARCH CONSENT SUMMARY

You are being asked for your consent to take part in a research study. This document provides a concise summary of this research. It describes the key information that we believe most people need to decide whether to take part in this research. Later sections of this document will provide all relevant details.

## What should I know about this research?

- Someone will explain this research to you.
- Taking part in this research is voluntary. Whether you take part is up to you.
- If you don't take part, it won't be held against you.
- You can take part now and later drop out, and it won't be held against you
- If you don't understand, ask questions.
- Ask all the questions you want before you decide.

## How long will I be in this research?

Once enrolled, the study will last approximately 90 days with up to 60 days extra for the screening period for a total of up to 150 days.

## Why is this research being done?

You are being invited to volunteer for a research study about dengue virus (DENV). We want to study a medication to prevent dengue virus infection. We want to find out more information about the medication and see if the medication will prevent you from getting DENV infection. In the future, we hope the medication will be used in travelers to help prevent them from getting dengue virus. This study has completed the enrollment the first cohort of participants (30 total) who were randomized into groups receiving different dosages of the medication, or a placebo. The study is now enrolling its second cohort of participants (24 total) who will be randomized into 3 groups receiving different medication dosages and on 2 different schedules to gather additional information on how well the medication prevents the symptoms of dengue virus.

## What happens to me if I agree to take part in this research?

If you are eligible and invited to join, you will have one or more screening visits lasting approximately 2-3 hours.

The study will start with a 3 night overnight stay on Study Days -3, -2 and -1, leaving on the afternoon of Study Day 1. During the inpatient admission, you may receive either the study drug or a placebo. You will also be given a small amount of dengue virus (DENV) as a shot in the arm on Study Day 1.

In person visits will occur on: Study days 4, 6, 8, 11, 13, 15, 18, 21, 25, 29, 32, 36, 43, 57, 70, and 85. It is possible you may also have a study visit on Study days 27 and 34 if needed, based on your lab results. Depending on which group you are in, you will take the study medication (or placebo) during some of these outpatient visits. Between the visits, you will take the study medication (or placebo) at home if you are in a daily dosing group.

A detailed table showing in-person visits (Table 5: Summary of Procedure by Study Day) is provided later in the consent.

Outpatient visits last approximately 90-120 minutes. Study Day 15 or Study Day 21 (depending on which group you are in) will require you to stay the entire day, approximately 16 hours. The inpatient days (Study Days -3 to 1) are 100% inpatient – you cannot leave the unit on these days. For the outpatient study visits, you will need to come to the clinic at approximately the same time every day.

Some of the visits may include:

- A brief medical history and physical
- Vital signs, an ECG (a test to check your heart)
- Review of pregnancy prevention, pregnancy testing, bloodwork
- An alcohol breath test, a screen for drugs of abuse
- Dosing with the dengue prevention medication or placebo and a shot containing DENV
- Blood collection
- COVID 19 testing (will only be collected based on guidance from federal, state, local, and/or institutional health officials* or at the discretion of the clinician)

  *This guidance may be informed by the local COVID 19 infection rate, severity of infections, vaccination rates, and other factors.

## Could being in this research hurt me?

We do not know all the risks that may occur. The most important risks or discomforts that you may expect from taking part in this research include a temporary rash over the upper body, stomach, arms, and legs. The rash typically does not hurt, and it is not contagious. Risks also include the common symptoms that have been seen in people infected with DENV, including rash (as above), low-grade fever, headache, pain behind the eyes, joint aches, and muscle aches, with some people not reporting symptoms.

You may get bruising, pain, redness or swelling at the site of blood draw. You may get pain, redness, swelling, or itching at the site (in the arm) where you get the shot of dengue virus. You will likely have a peripheral intravenous (IV) line placed (a tube placed in the vein to draw blood from, usually in your arm/hand) during the inpatient stay. You may have pain, redness, swelling, infection, clotting or itching at the IV site.

**The risks to an unborn baby or fetus are unknown so you should not get pregnant or breastfeed during the study.** Because of this, we ask that persons of childbearing potential stay on effective birth control and depending on your type of birth control, you may also need to use barrier contraception (condoms) for the duration of the study. We ask that persons who are having sexual relationships in which their partner may become pregnant use a condom when engaging in sexual activity until at least 90 days after the last dose of study drug and must not

have plans to have a child during the study or within 90 days of the last study drug. Additionally, it is important to not breastfeed during the study or within 90 days of the last dose of the study drug because it is unknown whether the study drug may pass through breastmilk.

Study staff will discuss effective methods of contraception with persons of child-bearing potential and reminders to use the effective methods will continue throughout the study.

**No long-term medical care** or financial compensation for research-related injuries will be offered by the Johns Hopkins University, Johns Hopkins Hospital, the NIH, or the federal government.

## Will being in this research benefit me?

We do not know if getting the study medication will benefit you in any way.

## What other choices do I have besides taking part in this research?

Since this is not a treatment study there are no alternative treatments, but you may choose not to be in this study.

# DETAILED RESEARCH CONSENT

You are being invited to take part in a research study. A person who takes part in a research study is called a research subject, or research participant.

## What should I know about this research?

- Someone will explain this research to you.
- This form sums up that explanation.
- Taking part in this research is voluntary. Whether you take part is up to you.
- You can choose not to take part. There will be no penalty or loss of benefits to which you are otherwise entitled.
- You can agree to take part and later change your mind. There will be no penalty or loss of benefits to which you are otherwise entitled.
- If you don't understand, ask questions.
- Ask all the questions you want before you decide.
- You will receive an injection containing Dengue virus on the $4^{th}$ day.
- You will take the study medication or placebo in one of the two schedules below:
    - Twice daily for 2 days and then every day for 21 days or approximately 3 weeks (23 dosing days total)
    - Twice daily for 2 days and then once weekly for the following 2 weeks (5 dosing days total).

This consent form may contain words or information that you do not understand. Please ask the study doctor or the study staff to explain any words or information that you do not clearly understand. You may take home an unsigned copy of this consent form to review and to think about it or discuss it with family, friends, or healthcare provider before making your decision.

## Why is this research being done?

Dengue virus (DENV) is a disease which is spread to people by mosquitoes. Every year, about 100 million people get sick from dengue. This virus is found in warm places like the Caribbean, South America, Central America, Asia, Africa, and parts of Australia. Dengue virus is the leading cause of death in children in at least 8 tropical Asian countries. The virus is not found very often in the United States.

This virus can cause people to have rash, fever, joint pain, muscle aches, headaches, or loss of appetite. For most people who get dengue fever, the symptoms are mild or moderate and resolve on their own. The most severe form of the disease is very rare and is usually seen in children and infants; it is called dengue hemorrhagic fever (DHF) or dengue shock syndrome (DSS). Some of these people will have bleeding under the skin and inside the body or some will have very low blood pressure.

This research will study an investigational drug called JNJ-64281802 (JNJ study drug) so we can find out if it works to prevent infection with DENV. We are also studying its safety and how it acts in people's bodies. To do this, we will give you the JNJ study drug (or a placebo – a dummy capsule with no medication) for 3 days before giving you a shot of a dengue virus called rDEN3Δ30 (referred to as DENV-3). You will continue to take the JNJ study drug until Study Day 21 (for the group assigned to a daily dosing schedule) or until Study Day 15 (for the groups assigned to a weekly dosing schedule). We want to find out if the JNJ study drug will keep you from having symptoms of dengue virus. We hope to find a medication we can safely give to people in the future to prevent dengue virus infection.

The use of JNJ study drug and DENV-3 in this research study is investigational. The word "investigational" means that the JNJ study drug and DENV-3 are not approved for this use by the Food and Drug Administration (FDA). The FDA is allowing the use of the JNJ study drug and DENV-3 in this study. This study has completed the enrollment of an initial cohort of 30 participants who were randomized to receive different dosages of the study drug (or placebo). It is now enrolling a second cohort of 24 participants who will receive different dosages of the study drug or placebo, and it will be administered on different dosing schedules (daily or weekly). This will provide additional information about how the study drug works and what dose may be best to prevent dengue virus. Table 1 provides an overview of number of participants for each cohort.

**Table 1: Overview of Cohorts, Groups, Number of Participants, and Dosing Schedule**

| ***Cohort*** | ***Group*** | ***# of Participants*** | ***Study Drug*** | ***Placebo*** | ***DENV-3 Challenge*** | ***Dosing Schedule*** |
|---|---|---|---|---|---|---|
| *Cohort 1* ***Complete*** | *Group 1a* | *4* | *2* | *2* | *4* | *Daily* |
| | *Group 1b* | *12* | *8* | *4* | *12* | |
| | *Group 2* | *14* | *12* | *2* | *14* | |
| *Cohort 2* ***Enrolling*** | *Group 3* | *8* | *6* | *2* | *8* | *Daily* |
| | *Group 4* | *8* | *6* | *2* | *8* | *Weekly* |
| | *Group 5* | *8* | *6* | *2* | *8* | *Weekly* |

During the study, we will check you for side effects and illness. We will check your blood for dengue virus and other markers. We will also study how your immune system responds to receiving a shot of DENV-3. To do this, we will measure disease fighting cells (antibodies) in your blood and collect different blood cells. It is hoped that this study will also help us learn more about signs and symptoms of DENV infection.

About 54 subjects will take part in this research. Thirty subjects were enrolled in Cohort 1 and have completed the study. You will be enrolled in Cohort 2.

Healthy adults 18-55 years old are eligible to screen for the study. Before entering the study, you will have blood tests, urine tests, and an ECG (heart test) to see if you are healthy. You will also have a blood test to check for previous exposure to diseases from mosquitos (Zika virus, dengue virus, West Nile virus, and St Louis Encephalitis). We want to study people who have never had this exposure. You will have testing to check for drugs of abuse (cocaine, alcohol, etc.). This visit is called the "screening visit" and may occur over multiple days. If you have multiple screening visits, some of the items may be repeated at multiple visits.

During one or more screening visits, you will have:

- A complete medical history
- A physical examination including height, weight, and body mass index (BMI)
- A review of inclusions/exclusion criteria
- Vital signs including your blood pressure, pulse, heart rate, and your body temperature
- An ECG (a test to check your heart)
- COVID 19 screening questions
- A nasopharyngeal (NP) or mid-turbinate swab to test for SARS-CoV 2, the virus that causes COVID 19 may be collected if determined necessary by the clinician or per guidelines. The swab may be obtained up to 72 hours in advance of the visit.
- Laboratory tests, may include:
    - A complete blood count (CBC)
    - A blood clotting test
    - Blood chemistries (including tests of your kidneys, liver, and muscle)

- Pregnancy test(s) and pregnancy prevention counseling.
  - *Pregnancy tests will be done before starting the JNJ drug (at screening and on Study Day -3 prior to receiving the study drug, as well as several times during the study)*
- FSH testing (a hormone test for some women who haven't had their period for 1 year and are menopausal)
- A urinalysis
- An alcohol breath test
- A urine drug test
- HIV test (a test for the virus that causes AIDS)
- Hepatitis B test (a test for a virus that hurts the liver)
- Hepatitis C test (a test for a virus that hurts the liver)
- Blood tests to see if you have ever had or been exposed to dengue virus and/or Zika virus, West Nile Virus, and/or St Louis encephalitis which come from mosquitoes
- There may be additional blood tests if the doctor feels it's needed

You will be told of any abnormal results that may require you to follow up with your personal doctor. Based on the results of these screening tests, you may be invited to join the study. There may be reasons why you cannot take part in this study.

If your tests show that you have HIV, the study doctor must notify the local health department. A separate HIV testing education form explains how positive results are reported to the local health department. Counseling will also be made available to you to discuss your positive HIV test and to receive information on how to get treatment for HIV if you do not have a regular doctor.

If your tests show that you have hepatitis B or hepatitis C virus, the study personnel must report it to the local health department. The health department will be notified according to their guidelines which includes disclosure of your health information. We will also provide information to you to follow up with a doctor if you do not have a regular doctor.

If your NP (nasopharyngeal) or mid-turbinate swab is positive for the COVID 19 virus, the study personnel must report it to the local health department. The local health department will be notified according to their guidelines which includes disclosure of your health information.

We encourage questions. If you have any questions or concerns, please talk to the research staff.

Persons who are pregnant, planning to become pregnant during the study or within 90 days (about 3 months) of the last dose of study drug, or who are breastfeeding will not be able to take part in the study because the effects of JNJ study drug and DENV-3 on the unborn fetus and infants are unknown.

Taking part in the study might harm your unborn child or breastfed baby. Animal studies have not indicated harmful effects on an unborn child but, because the effects of JNJ-64281802 on an

unborn human child or infant are not properly known, you cannot take part in this study if you are pregnant or breastfeeding a child. You must agree not to become pregnant while you are in this study. The effect of JNJ-64281802 on sperm is not known.

**All persons who can become pregnant, MUST agree to use highly effective birth control from the beginning of the study through the study and greater than or equal to 90 days (about 3 months) after the last dose of the study drug.** One of the following methods of birth control must be used for this study, see **Table 2** below. For persons who are taking hormonal birth control, you MUST also use barrier contraception (like condoms) with vaginal intercourse for at least 90 days from the last time you take the study drug (see table below). This is because the JNJ Study drug may decrease how well your birth control works. You must be willing to do this to be in this study. Discuss with the study provider what birth control you may use while in the study.

The only exceptions to the birth control requirements are persons who cannot become pregnant or who are postmenopausal (no period for 12 months + confirmed blood testing/medical records or no period for >24 consecutive months) and persons who are permanently sterile due surgery (see table below). We may confirm your method of birth control by collecting medical records.

A pregnancy test will be done during the screening visit(s), on the day you start the JNJ study drug, on the day of the DENV-3 shot, and at several visits throughout the study. If it's indicated, pregnancy testing will be done more frequently. This test must be negative for the staff to give you study medication(s).

**Table 2: Methods of Birth Control**

| CATEGORY | CONTRACEPTION |
|---|---|
| **People who can become pregnant** | **MUST USE ONE OF THE FOLLOWING METHODS**<br><br>• "Tubes tied" (Tubal ligation) or Tubal Coil<br>• Vasectomized partner (must be sole sexual partner, and absence of sperm must have been confirmed)<br>• IUD (copper)<br>• Females who exclusively have sex with females |
| **People who can become pregnant** | **WHO ARE TAKING ANY OF THESE:**<br><br>• Implantable progesterone-only hormonal contraception *(i.e. Nexplanon, Implanon, Jadelle, Norplant, etc.)*<br>• IUD (hormonal) |

| | |
|---|---|
| | • Intravaginal combined hormonal (Nuva-Ring)<br>• Birth Control Patch (hormonal)<br>• DepoProvera Shot (injectable)<br>• Combined oral contraception or "The Pill"<br>• Oral progesterone pills for contraception<br><br>**<u>MUST</u> ALSO USE:**<br><br>• Condoms |
| **CATEGORY** | **CONTRACEPTION** |
| **People who cannot become pregnant**<br><br>• **Postmenopausal**<br>  ○ No menses x 24 months<br>  ○ No menses for 12-24 months + confirmatory blood work (FSH level)<br>• **Permanently sterile greater than (3 months prior to study drug)**<br>  ○ Hysterectomy (uterus, tubes and ovaries removed)<br>  ○ Bilateral salpingectomy (both tubes removed)<br>  ○ Bilateral oophorectomy (both ovaries removed) | **DO NOT NEED ADDITIONAL CONTRACEPTION** |
| **People with male sex organs** | **Because the effects of the study drug(s) are unknown, we ask that people with male sex organs do the following from the first day of the study and for at least 90 days after the last dose of the study drug**<br><br>• Use a condom with sexual activity<br>• Have no plans to have a child during the study<br>• If you have had a vasectomy, you do not need to use a condom for birth control |

All people who can become pregnant must agree not to donate eggs (ova, oocytes) to help someone have a baby/or for yourself during the study and for greater than or equal to 90 days after last dose of study drug.

If you become pregnant during the study, tell the staff right away. The study drug will be stopped, but we may ask you to continue to come in for regular study visits and/or ask you to

agree to let us keep checking on you until the end of your pregnancy. We may ask you to return for one or more visits (or call you on the phone) even if the study ends prior to your delivery.

If you do not have your own doctor to care for you during your pregnancy, we can refer you to an obstetrician (OB) to care for you.

We will ask you to sign a medical information release form so that we can learn about your pregnancy and, if applicable, your baby's health at birth.

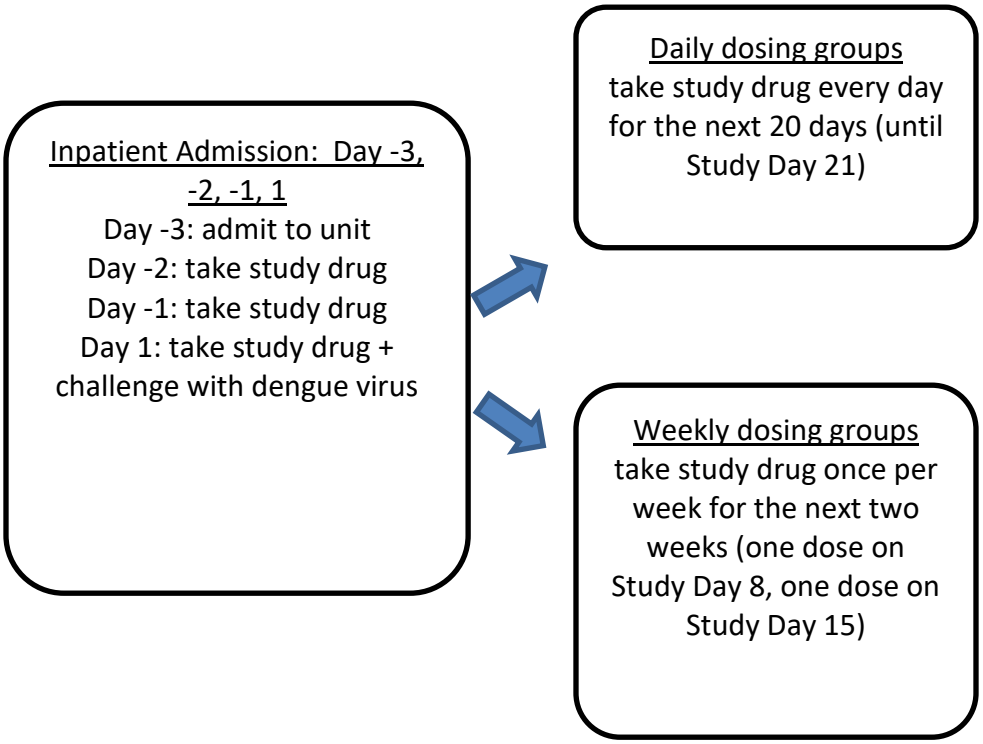
During the study and for greater than or equal to 90 days after last study drug, people must wear a condom when having sex (where sperm could be passed to a partner). People must not donate sperm during the study and for greater than or equal to 90 days after the last study drug**.**

## How long will I be in this research?

Once enrolled, this research will last approximately 90 days with up to an additional 60 days for the screening period.

## What happens to me if I agree to take part in this research?

If you are eligible and you are invited to enroll in this study, you will be asked to participate in all of the scheduled study visits where you will be taking a non-FDA approved medication "JNJ 64281802" for a total of **25 doses over 23 days (or 7 doses over 17 days depending on which group you are in).** On the 3rd day of taking the medication, you will be given a shot of Dengue virus. You will continue taking the medication for a specified number of days after the shot. Depending on which group you are in, you may take the medication on a daily basis or on a weekly basis. See the picture below to summarize:




Additionally, you will be asked to follow specific rules regarding your diet and lifestyle. If you have any questions, please discuss them with the research staff.

You may be asked COVID 19 screening questions each day you are seen in person, depending on local and CDC guidance*. If you have symptoms that may be due to COVID 19, we may test you for COVID 19 before we see you in the clinic. Below you will find a detailed list of visit days in the chronological order they happen.

Admitted to In-Patient Unit (Study Day -3):

The CIR's inpatient isolation unit is located on the Johns Hopkins Bayview Medical Campus in the 301 building. The isolation unit is a ***smoke-free*** dorm-like setting where you will live and eat with other participants.

Order of events:

- Arrive at CIR at scheduled time
- Alcohol breath test (per PI/provider discretion), COVID 19 test (will only be collected based on guidance from federal, state, local, and/or institutional health officials* or at the discretion of the clinician)

  **This guidance may be informed by the local COVID 19 infection rate, severity of infections, vaccination rates, and other factors.*

- Personal items checklist, vital signs, review of medical history and current medications
- Other study procedures as required

It is important that you know:

- Visitors are not allowed.
- You will be asked to stay on the unit 24 hours per day so you will not be able to come and go from the unit.
- You will stay on the unit for three nights, Day -3, -2 and -1, and will be sent home on Study Day 1.

See the table below for a visual representation of the schedule while you are on the inpatient unit.

**Table 3: Inpatient Schedule**

| Study Day | Meals | Study Drug | Dengue Challenge | Blood Draw | Physical Exam | Vital Signs |
|---|---|---|---|---|---|---|
| -3 | Unrestricted | | | | |  |
| -2, -1 | Standard breakfast 30 minutes before study drug<br><br>Lunch/dinner/snacks etc. are unrestricted |  | |  |  |  |
| 1 | Standard breakfast 30 minutes before study drug<br><br>Lunch/dinner/snacks etc. are unrestricted |  |  |  |  |  |

Frequent blood draw day with food and water restrictions (Study Day -2):

On the first day that you will receive the study drug (Day -2), there will be approximately 8 blood draws at scheduled times over 24 hours. This is done because it provides information about how the drug is acting in your body. To reduce the number of times that we need to stick you to draw blood, an IV may be inserted on Day -3 or Day -2. We will be able to collect blood samples through the IV. A blood sample will be collected before you take the JNJ study drug, and your blood will also be drawn at 1, 2, 4, 8, 12, 16, and 24 hours after taking the study drug.

To make sure that the IV stays working, we will need to flush it regularly with a saline (saltwater) solution.

Approximate schedule of activities:

- Wake up, ECG, vital signs, pregnancy test (if applicable), blood draw
- Standard breakfast will be provided (medication must be taken within 30 minutes of breakfast)
- Take study drug within 30 minutes of breakfast
- Several blood draws over the next 24 hours (drawn via IV to avoid repeated sticks). For example, one possible schedule may be:
    - Breakfast 8:30am
    - Take study drug 9:00am
    - Blood draw 10:00am
    - Blood draw 11:00am
    - Lunch
    - Blood draw 1:00pm
    - Snack (if desired)
    - Blood draw 5:00pm
    - Dinner
    - Blood draw 9:00pm followed by second dose of study drug
    - Blood draw 1:00am
    - Blood draw (following day) 9:00am

    Once your first blood draw has been taken (either through an IV or with a stick), you will get the first dose of JNJ study drug or placebo (a dummy capsule that looks the same as the study drug but has no medication in it). You will receive a dose of the study drug or placebo. Whether you get study drug or placebo, or what dose of study drug you get will be randomly assigned (like flipping a coin). You cannot choose what you will receive. Neither you nor the research staff will know if you are receiving study drug or placebo. However, you will know what group of the study you are in, see Table 1. You will not be notified whether you received study drug or placebo unless you request to do so in writing. If you request to be notified, this information may be shared with you once all participants in the study have completed their last study visit and the data is complete. This may be a long time after you place the request. This information is available to the study doctor at any time in an emergency.

For the first 2 days of the study (Day -2 and Day -1) you will receive a higher “loading” dose of study drug. For the remaining days where you get JNJ study drug (Day 1 through Day 15 or 21, depending on which group you are in) you will get a lower “maintenance” dose. During the remaining time you will take 2 capsules daily. At certain times during the study, you will only be able to drink a small amount of water to take the drug. A summary of amount of study drug and number of capsules you will receive is provided below in Table 4.

**Table 4: Loading and Maintenance Dosing for JNJ-64281802 for Cohort 2**

| | ***Loading*** | | ***Maintenance*** | |
|---|---|---|---|---|
| | ***Dose (mg)*** | ***# of Capsules*** | ***Dose (mg)*** | ***# of Capsules*** |
| ***Group 3*** | *800 mg twice daily* | *4 capsules twice daily* | *250 mg* | *2 capsules daily* |
| ***Group 4*** | *450 mg twice daily* | *3 capsules twice daily* | *1200 mg* | *6 capsules weekly* |
| ***Group 5*** | *250 mg twice daily* | *2 capsules twice daily* | *500 mg* | *4 capsules weekly* |

*Participants receiving placebo will be administered the same number of capsules that are identical in appearance to those with study drug.*

*Day -2 and -1 After taking Study Drug:*

Staff will monitor you for any signs of illness throughout the day. You will receive education on the signs and symptoms of dengue virus as well as information about how and when to contact study staff. You will sleep there again that night.

*Challenge Shot Day & Discharge Day (Study Day 1)*

*On Study Day* 1 you will stay on the inpatient unit until early afternoon. The study staff will check your vital signs, give you a physical exam (including an EKG to check your heart), ask you questions about how you are feeling, draw blood, and remove your IV. You will also receive your next dose of study drug. Approximately 1 hour later, you will be challenged with dengue virus (via injection). You will be monitored for at least 30 minutes to check if you have any side effects. You will then be released and can go home.

Persons of childbearing potential: We will confirm and discuss your chosen birth control method for the study as well as ways to prevent pregnancy. For persons of childbearing potential, we will do a pregnancy test. We will make sure the test is negative before we give you the shot. If the pregnancy test is positive, we will not give you the shot. Persons who are having sexual relationships in which their partner may become pregnant: We will discuss pregnancy prevention.

The dengue virus shot will be given as a shot in your upper arm. After receiving the shot, you will be asked to stay for at least 30 minutes to check if you feel sick and to assess the injection site and to recheck your temperature. While you wait, you will receive education regarding the signs and symptoms of potential side effects, and how and when to contact study staff.

We will give you a thermometer and provide training on how to use it. We will ask you to record your temperatures twice per day from Day 1 through Day 29 and more frequently if think you have a fever. If you are having your temperature checked in the clinic that reading can be used

for one of the two daily temperatures. A table showing the study procedures is shown below (Table 4):

**Table 4: Summary of Clinic Procedures by Study Day**

| |  |  |  |  |  |  |  |  |
|---|---|---|---|---|---|---|---|---|
| Study Day | Inpatient Night | In Person Visit | JNJ Study Drug – **Weekly** Dose Given at Clinic | JNJ Study Drug – **Daily** Dose Given at Clinic | DENV-3 Shot | Blood Draw | Pregnancy Test | Record Temperature |
| **-3** | **X** | | | | | | | **X** |
| **-2** | **X** | | **X** | **X** | | **X** | **X** | **X** |
| **-1** | **X** | | **X** | **X** | | **X** | | **X** |
| **1** | | **X** | **X** | **X** | **X** | **X** | **X** | **X** |
| **4** | | **X** | | **X** | | **X** | | **X** |
| **6** | | **X** | | **X** | | **X** | | **X** |
| **8** | | **X** | **X** | **X** | | **X** | | **X** |
| **11** | | **X** | | **X** | | **X** | | **X** |
| **13** | | **X** | | **X** | | **X** | | **X** |
| **15** | | **X** | **X** | **X** | | **X** | | **X** |
| **18** | | **X** | | **X** | | **X** | | **X** |
| **21** | | **X** | | **X** | | **X** | **X** | **X** |
| **25** | | **X** | | | | **X** | | **X** |
| **27** | | **X*** | | | | **X*** | | **X** |
| **29** | | **X** | | | | **X** | **X** | **X** |
| **32** | | **X** | | | | **X** | | |
| **34** | | **X*** | | | | **X*** | | |
| **36** | | **X** | | | | **X** | | |
| **43** | | **X** | | | | **X** | | |
| **57** | | **X** | | | | **X** | | |
| **70** | | **X** | | | | **X** | | |
| **85** | | **X** | | | | **X** | **X** | |

* Visits on Day 27 and 34 may be required based on lab results from Days 25 and 32.

<u>Dosing Visits Day 2 through Day 15 or 21 (depending on which group you are in)</u>

The clinic visits will last about 90 – 120 minutes. If you are assigned to the daily dosing group, on the days you are not scheduled to return to the clinic you will need to take the study drug at home following the guidelines given and keep a log. On the days you are scheduled to take the medication and ALSO have a clinic visit, you will take the study drug during your clinic visit. The study drug must be taken between 6am and noon each day (or each week, depending which

group you are in) at approximately the same time, and **we ask that you arrive to the clinic around the same time every scheduled visit**. Your clinic visits will be scheduled electronically using an online application that will be explained to you. Every day you are scheduled to take the study drug, whether at home or in the clinic, we will ask **you to eat a standard breakfast within 30 minutes of taking the medication**. At each clinic visit study staff will perform some or all of the following:

- Give you JNJ study drug or placebo (dummy capsule without medication)
- Monitor you for 30 minutes if needed
- Ask you COVID 19 screening questions (may be completed prior to visit)
- Ask you questions about how you are feeling
- Record your last food and water intake
- Review dietary and lifestyle restrictions
- Review pregnancy prevention counseling
- Perform a pregnancy test on eligible volunteers
- Review your temperatures
- Review whether you have experienced any signs or symptoms of DENV
- Draw your blood
- Give you a physical examination
- Check your vitals (blood pressure, pulse, temperature)
- Collect a NP or mid-turbinate nasal swab and test for COVID 19 (may be collected up to 72 hours in advance).
- Perform an ECG (a test to check your heart)

<u>Long outpatient visit/Last day of Taking Study Drug Day 15 or 21 (depending on your assigned group)</u>

You will be asked to arrive early and stay late on Study Day 15 or 21 (depending on your group). The visit will be approximately 12 hours. This will be the last day you will receive the JNJ study drug. You will have your blood drawn every few hours therefore an IV may be inserted on that morning. A blood sample will be collected prior to study drug administration, and additional blood draws will occur 1, 2, 4, 8, and 12 hours, following the final dose of study drug. To make sure that the IV is still working, we will need to flush it regularly with a saline (saltwater) solution.

In addition to collecting a blood sample, we will perform the following procedures before administering the study drug:

- Collect vital signs
- Perform a physical exam
- Do an ECG (a test to check your heart)
- Assess for signs and symptoms of dengue virus

During this visit we will ask you to follow the same food restrictions (standard breakfast 30 minutes prior to study drug administration).

There will be 8 or 10 follow up visits after you finish taking the study drug depending on your group assignment (Daily dose group- 8 follow up visits after the last medication dose on Day 21; Weekly dose groups- 10 follow up visits after the last medication dose on Day 15).

Routine Follow up Visits: Day 18 through Day 85 (weekly dosing group) or Day 25 through Day 85 (daily dosing group)

You will come in for follow ups on the following study days depending on your assigned group:

Daily dosing groups:

- Routine Follow ups with medication dosing: Day 4, 6, 8, 11, 13, 15, 18
- Full-day Follow up: Day 21 (about 12 hours)
- Routine Follow ups: Day 25, 29, 32, 36, 43, 57, 70, 85 *You may require additional follow ups on Day 27 and/or Day 34 depending on lab results from Day 25 and/or Day 32, respectively.

Weekly dosing group:

- Routine Follow ups: Day 4, 6, 8, 11, 13 (medication dosing on Days 8 and 15)
- Full-Day Follow up: Day 15 (about 12 hours)
- Routine Follow ups: Day 18, 21, 25, 29, 32, 36, 43, 57, 70, 85 *You may require additional follow ups on Day 27 and/or Day 34 depending on lab results from Day 25 and/or Day 32, respectively.

The routine follow-up visits will take approximately 60-90 minutes. If you become sick during the study, we may ask you to follow up more frequently either in person or on the telephone. At each visit we will perform some or all of the following:

- Ask you questions about how you are feeling and review your medical history
- Review dietary and lifestyle restrictions
- Review pregnancy prevention counseling and perform a pregnancy test on eligible persons of childbearing potential
- Review your temperatures
- Review if you have experienced any signs or symptoms of DENV
- Draw your blood
- Give you a physical examination
- Check your vitals (blood pressure, pulse, temperature)
- Check your height/weight
- Perform an ECG (a test to check your heart)

- Ask COVID 19 screening questions (may be completed prior to visit)
- Collect and test NP or mid-turbinate nasal swabs for COVID 19 (may be collected up to 72 hours in advance).

Dengue Memory Enhancement Card

On the day you receive the shot of dengue virus (Day 1) you will be given a Dengue Memory Enhancement Card.

You will use the Dengue Memory Enhancement Card (DMEC) to record your temperature twice a day from Day 1 until Day 29 using the thermometer you were provided on Study Day 1. On days that you have an in-person visit, you do not have to record your own temperature for one of the measurements, we will do this for you.

When taking your own temperature, we ask you do the following:

- Please wait 15 minutes after eating, drinking, and smoking before taking your temperature.
- If your temperature reaches 100.4°F or greater, you will be asked to repeat it after 20 minutes.
- Do not eat, drink, or smoke while waiting to recheck your temperature.
- If it is still 100.4°F or greater repeat it 1 hour after your first temperature.
- Call the study clinician if your temperature is 100.4°F or greater at any time.
- Bring your DMEC with you to each visit to review your temperatures with study staff.
- Do not take fever reducing medications (i.e., acetaminophen [TYLENOL]) for 6 hours before checking your temperature.

You will be allowed to keep the thermometer at the end of the study.

Phone Calls

Study staff may contact you by phone in between scheduled clinic visits to follow up on any symptoms you report and ensure you are safe.

Blood Sample Collection

You will have blood drawn at most study visits. Each time we will take less than 6 tablespoons of blood for a total of approximately 610 mL over the duration of the study (from Study Day -2 through Study Day 85). While you are in the study, we will not take more blood than what the Red Cross recommends.

The blood we draw at your visits will be tested to:

- Check on your health after receiving the JNJ study drug or placebo, and the dengue shot
- Look for dengue virus in your blood
- See if your body has made antibodies (germ fighters) against the dengue virus
- See how much JNJ study drug is in your body
- Test markers on your white blood cells and genes and look for proteins in your blood that may be important for your body to fight dengue infection

Some or all of your samples may also be kept and used indefinitely. This will allow for future scientific research, as new discoveries are made. The sponsor or the JNJ Development Team will ensure that your samples are kept secure.

The samples of biological material taken are deemed to be a "donation" and you should be aware that, in principle, you will not receive any financial benefit (royalties) associated with the development of new therapies derived from the use of your donation of biological material and which may be of commercial value.

***You cannot enroll in this study if you do not consent for your unused samples to be used for future research***. If you change your mind at any time about allowing your samples to be used for future research, call or write the study research staff. Your samples will then no longer be made available for future research and your unused samples will be destroyed. This will not affect your access to the care, medicine, and equipment you would otherwise be getting. This can be done at any time and for any reason. The results obtained from your samples before you withdraw your consent remain the property of the study sponsor.

As technology advances, there may be new ways to access and trace information back to you (or your close biological relatives) that we cannot predict. The sponsor will use reasonable measures within its control to safeguard your information. Even though no one would be able to know just from looking at your genetic data that the information belongs to you, there is a potential risk to you and to your family. This is because your genetic information is unique to you. Therefore, there is a chance that someone could trace the information back to you or your close biological relatives. This could happen if you (or your biological relatives) had DNA testing done another time that could be matched against your results from this study. The risk of this happening is small but could grow in the future.

To protect your privacy, your samples will be labeled with your study number and participant number. No personal identifiers are used (such as name, initials, social security number). The scientists doing the research will not know your identity.

Your samples may be sent to other third partners and to regulatory authorities.

Photographs

As part of this research, we would like your permission to take photographs of your skin or of the injection site to help answer the research question. We will not use the photographs for advertising or non-study related purposes. You should know that:

- You can still enroll in this study even if you do not consent to having pictures taken.
- You may ask us to stop taking photographs at any time.
- If you agree to allow us to take photographs of your skin and then change your mind, just ask us to destroy the image(s). If we have already removed identifiers from the image(s), we may not be able to do this.
- Your face or any other identifying marks will not be in the picture.

Unscheduled Admission to the Inpatient Unit

During the study if you have a high fever and are sick with other dengue-like symptoms, the study doctor may ask you to go to the ER or to come to stay on the inpatient unit to be watched more closely. If you are asked to stay on the inpatient unit for an unscheduled visit because you are sick, some or all the following procedures may be performed:

- Physical exam
- Collection of vital signs
- Assessment for dengue virus signs or symptoms
- Blood collection for testing
- If it is between Study Day -2 and 15 or 21 (depending on the group you are in) you may still be administered the JNJ study drug. In this case, we would ask that you continue to follow certain food and water restrictions.
- Additional tests may be ordered to determine the cause of your illness.

If the study doctor determines that you should be admitted to the inpatient unit, the stay will last approximately 3-9 days (or longer if necessary), depending on your symptoms. You will be discharged once you no longer have a fever and any symptoms you had are subsiding. Following discharge, you will continue with regularly scheduled visits.

In addition:

- A study doctor (provider) can be reached 24 hours a day during the study.
- If you become ill during the study, additional tests (for example blood tests, nasal wash, or x-rays) may be done. You will not be charged for these tests. Any risks associated with these tests will be explained to you before they are performed. You may refuse to have these tests done if you do not want them.
- We will contact you to remind you of study visits and to check on you if you miss a study visit. We may contact you by one or more of the following means:

- Telephone call
- Text message
- Electronic media (Twitter, Facebook, etc.)
- Email message
- Card mailed by US Postal Service
- Ask one of the people you provided as a contact to remind you to come to the clinic.

## What are my responsibilities if I take part in this research?

If you take part in this research, you will be responsible to:

- Follow our facility's guidelines on masking and other COVID 19 related policies.
- Tell the staff if you become sick or feel ill. We may ask you to come to the clinic so that we can check on you.
- Contact the staff or study doctor before taking medication or receiving any vaccines – excluding the COVID 19 vaccine. This includes medicines that you buy without a prescription like herbal or over-the- counter medicines, such as Advil; and medicines that affect the immune system, such as prednisone. Additional information about specific medications is provided below.
- Do not donate any blood products during the study and for 6 months after the last dose of study drug. Do not donate greater than 1 unit of blood within 30 days or greater than 1 unit of plasma within 7 days before the first dose of study drug.
- Tell the staff if you receive any blood products through the study and for 90 days following the last dose of JNJ study drug.
- Do not join another clinical study. You may not receive any other experimental drugs or vaccines while you are in this study and for 90 days after the last dose of JNJ study drug. The only exceptions to this are participation in COVID 19 vaccine trials and/or receipt of the COVID 19 vaccine under EUA authorization; you may receive the COVID 19 vaccine at any time.
- Do not participate in any unusual strenuous exercise in the 4 days prior to starting dosing with JNJ study drug and for 30 days after the last dose of JNJ study drug.
- Do not travel to any region where dengue virus is usually found. If you need to travel unexpectedly discuss this with study staff.
- Limit alcohol consumption to an absolute minimum.
- Do not consume grapefruit or grapefruit juice from 7 days before the first dose of JNJ study drug through Study Day 85.
- Do not consume large amounts of caffeine for 48 hours before the first dose of JNJ study drug through Study Day 85. Limit amount to less than 5 cups of coffee/tea, 8 cups of cola, or equivalent.
- Do not use drugs of abuse for at least 3 weeks following the last dose of JNJ study drug. These drugs include but are not limited to amphetamines, barbiturates, benzodiazepines, cocaine, methadone, opiates, and PCP.

- In order to avoid a false positive drug test, we ask you to avoid foods containing poppy seeds or other codeine-containing substance for 72 hours before screening visits.
- Do not donate sperm or eggs throughout the study and for 90 days after the last dose of JNJ study drug.
- Follow the restrictions on food and water intake throughout the study.
- Persons who are of childbearing potential must use a reliable form of birth control (as discussed above in ***Table 2: Methods of Birth Control***).
- If you become pregnant during the study, tell the staff right away.
- Agree to protect yourself from mosquito bites as described in the information and mosquito repellent we provided you.

Medications unrelated to the study

To avoid interactions with the JNJ study drug there are some additional rules regarding medications we will ask you to follow if you are enrolled in this study. In general, we ask that you discontinue current medications and refrain from using medications during this study. If there is a medical condition that requires the use of medications, we encourage you to seek appropriate care and take physician prescribed medications and contact the study staff as soon as possible if you start any new medication.

- Do not use any immunosuppressive corticosteroids (except topical and nasal) or other immunosuppressive drugs in the 28 days prior to taking JNJ study drug and for 28 days following the last dose of study drug.
- Do not use any anticoagulant medication for the 7 days prior to inoculation with DENV-3 and for 28 days following the shot.
- There are many more medication restrictions, please discuss any and all medication use with study staff.
- While Tylenol (acetaminophen) and Advil (ibuprofen) may be used during the study, the amount you can take is limited. Please discuss this with study staff.
- Post-menopausal participants may continue stable hormone replacement therapy. However, hormone therapy could be affected by the study drug so discuss this with study staff.
- Hormonal birth control should be continued, additional contraceptive methods should be used concurrently because the JNJ study drug may decrease the effectiveness of hormonal birth control.
- Do not get any live vaccines within the 28 days before you start taking the JNJ study drug and the 28 days after you stop taking the study drug.
- Do not get any killed (inactivated) vaccines within the 14 days before you start taking the JNJ study drug and 14 days after you stop taking the study drug. Depending on the time of year, we may offer you a flu vaccine prior to starting the study.
- Do not get any vaccines against DENV or Zika virus until 90 days after the last dose of JNJ study drug.

- The only vaccine that is allowed is the COVID 19 vaccine and/or COVID 19 booster, which is allowed at any time during the study. Please inform the study staff of when you are planning to receive this vaccine.
- We will ask you to tell us if you do get a licensed or EUA vaccine anytime during the study.
- If you test positive for COVID 19 during the course of the study, we will ask you to follow CDC recommended quarantine guidelines – we will conduct your visits by the telephone or at a research space specifically for COVID 19 positive participants for the time you are in quarantine.

These rules and restrictions have been designed to protect your own safety during the study and to ensure that we will be able to collect reliable data about the JNJ study drug and the DENV-3 agent.

## Could being in this research hurt me?

This research will study an experimental live DENV and an investigational dengue prevention medication called JNJ-64281802. We do not know all the risks that may occur. We do know some risks that have been discovered in people infected with DENV. The effects of the JNJ drug and DENV on the unborn fetus are unknown. ***You should not become pregnant or breast-feed during this study***.

**Potential Risks Due to JNJ-64281802**

All drugs can cause side effects. Problems that are not expected may arise and they may be life-threatening. If you have any side effects or problems during your participation in this study, you should let your study doctor know right away.

In the laboratory, JNJ-64281802 is a potent antiviral (small-molecule) with activity against all 4 dengue serotypes.

JNJ-64281802 has been tested carefully and extensively in laboratory animals (rats and dogs) according to regulatory guidelines and it is considered generally safe and well tolerated in animals.

Clinical Studies: during study 64281802DNG1001, when tested for the first time in healthy participants, JNJ-64281802 was generally well tolerated with some side effects. Two Grade 2 (mild to moderate) events of rash occurred in the multiple ascending dose part that were considered very likely related to JNJ 64281802 by the investigator.

Based on these limited data from the first-in-human study DNG1001, rash is considered a potential risk. Careful clinical monitoring of rash events will be performed in all planned clinical studies for JNJ-64281802.

Other study subjects have experienced headache and fatigue.

You may be asked to swallow up to 6 capsules of the JNJ study drug. This may cause some discomfort.

There may be risks with the use of JNJ-64281802 that are not yet known. Sometimes during a study, the sponsor may learn new information about the study drug and the risks. It is possible that this new information might make you change your mind about being in the study. If new information is discovered, your study doctor will tell you about it right away.

**Birth Control and Pregnancy During the Study**

The effects on an unborn child or infant are not known. Participants will be asked to use effective birth control and/or barrier contraception and refrain from breastfeeding.

Women who are not able to get pregnant:

Defined as premenarchal, post-menopausal, and/or permanently sterile, can participate without specific measures.

If you are a woman who is able to get pregnant:

Taking part in the study might harm your unborn child or breastfed baby. Animal studies have not indicated harmful effects on embryo-fetal development. Because the effects of JNJ-64281802 on an unborn human child or infant are not properly known, you cannot take part in this study if you are pregnant or breastfeeding a child. You must agree not to become pregnant while you are in this study.

If you are sexually active and able to get pregnant you must use birth control during the study and for 90 days after your last dose of study drug. Birth control methods that can be used while in this study include intrauterine device (IUD), tubal closure, male partner who does not produce sperm (for example, surgical vasectomy), and complete abstinence from heterosexual intercourse. When relying on any hormonal contraceptive, an additional barrier-based contraceptive method must be used. The type of birth control you use must be discussed with the study doctor before you begin the study. The study doctor must approve the method you use before you can enter the study.

You must not donate eggs during the study and for 90 days after your last dose of study drug.

If you are a man:

Taking the medicinal product during the study could lead to an unknown risk for an embryo or fetus and the effect of JNJ-64281802 on sperm is unknown. If your female sexual partner does

not use an IUD or have closure of her tubes or if she relies on hormonal contraception, you must also use a condom (with or without spermicidal) when you have intercourse, from when you start taking the study drug until 90 days after your last dose. This is done to prevent pregnancy. You must also not donate sperm during the study and for 90 days after your last dose of study drug.

If you have had a vasectomy, you do not need to use a condom for birth control.

**Potential risks due to infection with DENV-3**

Common risks from the DENV infection:

- You may have a fever, feel tired or have low energy, headache, pain behind the eyes, bruising, bleeding, muscle aches or joint aches.
- You may get a skin rash. This rash may be itchy.
- You may get a low white blood cell count, but it is expected to be normal within a few days.
- You may have an elevation in your liver function test (indicating stress on your liver), which typically resolves within 1 week.
- You could have an allergic reaction (a rash, hives, or trouble breathing) right after the shot.

  Some allergic reactions can be life-threatening. We will watch you for at least 30 minutes after you receive the shot to check for signs of an allergic reaction and will treat you immediately for any sign of an allergic reaction.

- Transmission by Mosquitoes. You should protect yourself from mosquito bites. The best way to protect yourself from bites is:
  - Wear long sleeved shirts and long pants
  - Use a mosquito spray or cream that contains a chemical called DEET (20 - 30% DEET) for at least 2 weeks after you receive the shot. We will provide you with insect repellent.
  - Stay in places that have screens on the windows
  - In addition, on the day you receive the shot you will be given a card that tells you in detail how to avoid being bitten by mosquitoes.

**Delayed Risks from Inoculation with DENV**

- Because you will receive a small amount of DENV, your risk of developing Dengue Hemorrhagic Fever (DHF) or Dengue Shock Syndrome (DSS) following a second infection with DENV may be increased if you travel to an area where dengue occurs. Subjects who develop DHF/DSS can become very sick and should be treated in a hospital. It is not known whether this is a true risk or how long this risk might last after the shot, but it may be for the rest of your life. The countries

currently reporting dengue are listed in the Background section of this consent. This list may change over time. An up-to-date map can be found on the Centers for Disease Control website http://www.healthmap.org/dengue/index.php. You can also find out if dengue virus is present in the specific country you plan to travel to by contacting Dr. Durbin at 410-340-6852 or by contacting the local health department in the country where you plan to travel.

- If, in the future, you must travel to a place where dengue viruses are active, you should protect yourself from mosquito bites.
- There is a vaccine for dengue, but it is approved only for people who have already had dengue and who are 9 – 16 years of age. If a licensed vaccine against all 4 DENV types becomes available in the future, you should talk with your doctor about whether or not you should receive such a vaccination before traveling to a dengue-endemic region.

**Risks from blood drawing**

- Drawing blood may cause pain, bruising where the needle enters the body, a lump called a hematoma, or infection at the place where blood is taken. To ease the discomfort, a topical anesthetic cream may be used during blood draw at the phlebotomist's (with your consent) discretion.
- In rare cases, blood drawing can cause you to feel lightheaded or result in fainting.
- Bleeding may occur from the site of blood draw.

**Risks from Peripheral Intravenous Access (IV)**

- Risks from putting in an IV include pain, bruising where the IV enters the body, a lump called a hematoma, or infection at the place where IV is placed.
- In rare cases, putting in an IV can cause you to feel lightheaded or result in fainting.
- Bleeding may occur from the site where the IV was placed.
- There are several very rare, but serious risks from an IV. These include that air could enter your blood stream through the IV, that the IV could be placed into an artery, or that it could be placed outside of your vein. Because we are only using the IV to draw blood and will not give you any medications through the IV, these risks are smaller.

**Risks of getting a subcutaneous (under your skin) shot with DENV-3**

- You may experience pain, swelling, bruising, redness or itching at the place in the upper arm where you receive the shot.
- You may develop an infection at the place where the shot is given.
- In rare cases, receiving a shot can cause you to feel lightheaded or result in fainting.
- Bleeding may occur from the site of the shot.

**Risk of Nasopharyngeal (NP) or mid-turbinate nasal swab**

- NP or mid-turbinate nasal swab may be uncomfortable. It may cause sneezing, runny nose, and/or watering of the eyes.

**Other Risks**

- You may be assigned as an alternate if there are an excess of potential participants. If this is the case, you will be admitted for 1 night (Day -3) and be sent home the following day if not ultimately enrolled. You will be compensated for your time (see compensation section).
- We will ask you to wait to get routine licensed vaccines like the covid shot, flu shot or nasal spray flu vaccine from before 14 days prior (killed vaccine) or 28 days prior (live vaccine) to the first dose of JNJ study drug until at least 14 after the last dose (killed vaccine) and 28 days after the last dose (live vaccine) of study drug, respectively. This may put you at more risk for illness such as the flu or covid.
- There may be psychological or social risks that result from taking part in the study, such as concern about being tested for HIV. Disclosure of a positive test may result in discrimination by friends, family, employers, insurance companies, and others.
- Risks occasionally associated with the use of topical anesthetic cream include temporary skin discoloration, skin irritation, rash, hives, and rarely, dizziness or drowsiness.
- Risks of ECG test are minimal and include that it may be uncomfortable due to placement and removal of electrode patches as well as cause possible skin irritation.

There may be other side effects and risks that we don't know about yet. If we learn about any new side effects or risks while you are in the study, we will tell you and you can decide if you want to continue in the study.

**Interviews or questionnaires**

You may get tired or bored when we are asking you questions about your medical history, reproductive history, or pregnancy prevention information. Some questions may make you feel embarrassed or uncomfortable. Let us know if you feel distressed. You do not have to answer any question you do not want to answer.

**Personal Privacy**

Research staff will work to protect your personal privacy throughout the study. Sensitive questions regarding your medical history, reproductive history, and pregnancy prevention will be asked in a private area. All forms where personal information is recorded will be kept securely stored at the study site in a locked area. Please discuss any concerns you have about protecting your personal privacy with research staff.

**Identifiable private information**

There is a risk that information about you may become known to people outside this study. We will protect your information to reduce the chance of this happening. We assign you a study ID number upon screening to minimize use of identifying information on forms, documents, and specimens.

All study-related information will be stored securely at the study site in a locked area with limited access. All laboratory specimens, reports, study data collection, and administrative forms will be identified by coded number to maintain your confidentiality. All local databases will be secured with password-protected access systems.

## Will it cost me money to take part in this research?

There will be no costs to you for being in this study. Ask your study doctor (provider) to discuss the costs of treating possible side effects. Otherwise, you might have unexpected expenses from being in this study.

## Will being in this research benefit me?

There are no direct benefits to you for participating in this study. We hope that the information we gather from this study will lead to a drug that will prevent people from getting dengue.

## What other choices do I have besides taking part in this research?

This research is not designed to diagnose, treat, or prevent any disease. Your alternative is to not take part in the research.

If you do not join, your care at Johns Hopkins will not be affected.

If you do not join, your employment/education at Johns Hopkins will not be affected.

## What happens to the information collected for this research?

As a part of this study, the researchers may ask to see your health care records from your other health care providers.

### What information is being collected, used, or shared?

To do this research, we will need to collect, use, and share your private health information. By signing this document, you agree that your health care providers (including both Johns Hopkins Medicine and others) may release your private health information to us, and that we may use any and all of your information that the study team believes it needs to conduct the study. Your

private information may include things learned from the procedures described in this consent form, as well as information from your medical record (which may include information such as HIV status, drug, alcohol or STD treatment, genetic test results, or mental health treatment). Prior to contacting your health care provider to release your health information we will discuss with you what specific records we will be asking for and why we need them.

**Who will see, use or share the information?**

Your private information and your medical record will be shared with individuals and organizations that conduct or watch over this research, including:

- The research sponsor
- People who work with the research sponsor
- Government agencies, such as the Food and Drug Administration
- WCG IRB, the Institutional Review Board (IRB) that reviewed this research

The people who may request, receive, or use your private health information include the researchers and their staff. Additionally, we may share your information with other people at Johns Hopkins, for example if needed for your clinical care or study oversight. To improve coordination of your research and clinical care, some information about the study you join will be included in your electronic medical record. By signing this form, you give permission to the research team to share your information with others outside of Johns Hopkins. This may include the sponsor of the study and its agents or contractors, outside providers, study data and safety monitors, government agencies, other sites in the study, data managers, the Janssen Drug Development Team, and other agents and contractors used by the study team. We try to make sure that everyone who sees your information keeps it confidential, but we cannot guarantee that your information will not be shared with others. If your information is disclosed by your health care providers or the research team to others, federal and state confidentiality laws may no longer protect it.

## What happens to the information collected for this research?

All medical records which identify you, and related health information, will be maintained and updated in a password-protected locator database or in your study chart which will be in a double locked room.

Information from this study will be given to the sponsor. The sponsor is the organization responsible for financing and overseeing this study. The sponsors of this study are the National Institutes of Health (NIH), National Institute of Allergy and Infectious Diseases (NIAID), Office of Clinical Research Policy and Regulatory Operations (OCRPRO). "Sponsor" includes any persons or companies that are contracted by the sponsor to have access to the research information during and after the study. Information about side effects of the study drugs will also

be given to the US Food and Drug Administration (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, including photographs, and the consent form signed by you *will be* looked at and/or copied for research or regulatory purposes by the sponsor, and *may be* looked at and/or copied for research or regulatory purposes by:

- The FDA
- Department of Health and Human Services (DHHS) agencies
- Governmental agencies to whom certain diseases must be reported
- Governmental agencies in other countries
- Johns Hopkins University
- The Johns Hopkins University Bloomberg School of Public Health
- WCG IRB
- Janssen Pharmaceuticals

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.

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.

Data or specimens collected in this research might be deidentified and used for future research or distributed to another investigator for future research without your consent.

**Confidentiality**: The National Institutes of Health has given us a **Certificate of Confidentiality** for this study. This Certificate does not mean that the government approves or disapproves of this study. This Certificate adds special protection for research information that identifies you. It allows us, in some circumstances, to refuse to give out study information about you without your consent when it is sought in a legal action. Still, we may disclose identifying information about you if, for example, you need medical help. We may also give out information about you if the government audits us. The research team will also give information to local or state authorities:

- if they suspect abuse or neglect of a child or dependent adult;
- if certain communicable diseases are present; and
- if the team learns that you plan to harm someone. In this case, the team also may warn the person who is at risk.

**Do you have to sign this Authorization?**

You do not have to sign this Authorization, but if you do not, you may not join the study.

**How long will your information be used or shared?**

Your Authorization for the collection, use, and sharing of your information does not expire. Additionally, you agree that your information may be used for similar or related future research studies.

**What if you change your mind?**

You may change your mind and cancel this Authorization at any time. If you cancel, you must contact the Principal Investigator in writing to let them know by using the contact information provided in this consent form. Your cancellation will not affect information already collected in the study, or information that has already been shared with others before you cancelled your authorization.

We may publish the results of this research. However, we will keep your name and other identifying information confidential.

We protect your information from disclosure to others to the extent required by law. We cannot promise complete secrecy.

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.

Data or specimens collected in this research might be deidentified and used for future research or distributed to another investigator for future research without your consent.

## Source of funding for the study/conflict of interest:

A conflict of interest occurs when a researcher or the University has a financial or other interest that might affect the researcher's judgment when conducting a research study. The NIAID/NIH pays for the funding of this study under contract No. 75N93019D00031. Dr. Durbin is a faculty member at Johns Hopkins University.

## Who can answer my questions about this research?

If you have any questions concerning your participation in this study or if at any time you feel you have experienced a research-related injury or a reaction to the study vaccine, or if you have questions, concerns or complaints about the research, contact:

| | |
|---|---|
| Dr. Anna P. Durbin: | 410-614-4736 (office)<br>410-340-6852 (cell phone). |

This research is being overseen by WCG IRB. An IRB is a group of people who perform independent review of research studies. You may talk to them at 855-818-2289 or clientcare@wcgclinical.com if:

- You have questions, concerns, or complaints that are not being answered by the research team.
- You are not getting answers from the research team.
- You cannot reach the research team.
- You want to talk to someone else about the research.
- You have questions about your rights as a research subject.

## What if I am injured because of taking part in this research?

If you need short term medical care because you got sick from DENV or the JNJ Study drug, the study will pay for the care. However, no long-term medical care or financial compensation for research-related injuries will be offered by the Johns Hopkins University, Johns Hopkins Hospital, the NIH, or the federal government.

A study doctor will be available at all times while you are in the study to check on you and treat you for any short-term medical care resulting from your taking part in this research study. The services at the Johns Hopkins Hospital or the Johns Hopkins Bayview Medical Center will be available to you in case of any such injury. This short-term medical care will be paid for through our contract with the NIH. Short-term medical care will be given at a facility determined by JHU and NIH. No long-term medical care or financial compensation for research-related injuries will be offered by the Johns Hopkins University, Johns Hopkins Hospital, the NIH, or the federal government. At your request, your insurance company will be billed for payment of any such long-term treatment or hospitalization. It is up to you to check with your insurance company before you start this study to find out what your insurance company will pay for.

## Can I be removed from this research without my approval?

You may be removed from the study (withdrawn) at any time by the study doctor or the sponsor without your consent if:

- Staying in the study would be harmful.
- You need treatment not allowed in the study.
- You have a side effect that requires stopping the research
- You become pregnant.
- The study is cancelled.
- The study staff or the study sponsor decides to discontinue your participation for any reason

- You do not follow instructions from the staff or do not keep appointments
- The Data and Safety Monitoring Board (a scientific review board that monitors clinical research studies) recommends the study should be stopped
- The FDA or the WCG IRB recommends the study should be stopped
- If new information becomes available regarding the safety of the challenge virus
- You do not consent to continue in the study after being told of changes in the research that may affect you
- There may be other reasons to take you out of the study that we do not know at this time.

If you are taken out of the study early, Johns Hopkins may use or give out your health information that it has already collected if the information is needed for this study or any follow-up activities.

We will tell you about any new information that may affect your health, welfare, or choice to stay in this research.

## What happens if I agree to be in this research, but I change my mind later?

- Your participation in this study is voluntary.
- You can agree to be in the study now and change your mind later.
- If you wish to stop, please tell us right away.
- You may leave the study at any time.
- Leaving this study early will not stop you from getting regular medical care.
- Leaving this study early will not affect your employment/education.

If you leave the study early, Johns Hopkins may use or share your health information that it has already collected if the information is needed for this study or any follow-up activities.

If you decide to withdraw from the study soon after you get the shot, the study doctor may ask permission to follow you briefly for safety reasons. We may ask you to let us check on you or return for a follow-up and/or final study visit.

Your decision to withdraw or to not take part will not result in any penalty or loss of benefits to which you are entitled. If you decide to leave the study, the samples that have been collected will be used as described in this consent form. If you do not wish us to use these samples after you leave the study, you may request that we destroy them and they will be destroyed. You should ask the study doctor listed below any questions you may have about this research study. You may ask questions in the future if you do not understand something that is being done.

We will tell you about any new information that may affect your health, welfare, or choice to stay in this research.

## Will I be paid for taking part in this research?

For taking part in this research, you may be paid up to a total of $3850.00. Your compensation will be broken down as follows:

- You will receive a voucher for parking or public transportation tokens, as needed, for the days that you screen or have study visits.
- You will be paid $200 for screening only if you are enrolled in the study.
- You will be paid $300 for each inpatient night and full day visit (Study Days -3, -2 and 1)
- You will be paid $250 on the day you receive the shot (Day 1).
- If you are an alternate, you will be admitted on Study Day -3 and stay on the inpatient unit overnight. If you are not given the JNJ-Study Drug or placebo, you will be paid $200 for your time and sent home on Study Day -2.
- You will be paid $125 for each of the 15 standard (60-90 minute) follow-up clinic visits. You will only be paid for the visits that you complete. If you are required to follow up on Day 27 and/or Day 32, you will be reimbursed at that same rate for those visits. (bringing the maximum potential compensation to $4100 if Day 27 and Day 34 are indicated based on lab results).
- You will be paid $250 for the full-day visit (Day 15 or Day 21 depending on which group you are in)
- You will receive $75 for returning a completed diary card (Dengue Memory Enhancement Card.)
- If you are late for a visit or do not complete all required procedures during a study visit, your payment may be reduced for that study visit.
- If you complete all study visits and procedures on time and adhere to the code of conduct, you will be paid a $300 bonus. You may only receive a portion of the bonus if not all study visits are completed on time, if you do not complete study procedures, or if you do not follow inpatient policies and the lifestyle requirements.
- If you choose to withdraw (dropout) before the study is completed, you will only receive payment for the number of visits that you have completed.

Payment will be distributed by check or other payment method such as ClinCard® (similar to a Visa card). An ***approximate*** schedule of when payments will be distributed will be provided to you separately.

You may be required to provide your social security number or tax identification number to be paid for taking part in this study. Federal tax law requires that you report your research payments when you file your taxes. If your total payments from Johns Hopkins exceed $600 per year, Johns Hopkins will report these payments to the Internal Revenue Service, and you will receive a 1099-MISC form from us.

## Addendum:

You will complete your study enrollment and responsibilities as a research volunteer after completion of your last study visit (Day 85). You are **not** required to participate in any further study activities beyond Day 85.

However, you have been contacted by the study team to complete voluntary add-on study visit(s) to collect additional information and a blood sample. The FDA has asked us to collect a blood sample after study Day 120 to check to see if your body has made any antibodies to dengue. This visit and blood draw are voluntary.

You will be compensated up to $150 per visit for any additional outpatient visits that you complete after your study enrollment period ends.

You **can** decline to participate in any add-on study visit(s). If you choose to decline, it will **not** affect your ability to enroll in future studies at the Center for Immunization Research.

**Do not sign this consent form unless you have had a chance to ask questions and have received satisfactory answers to all your questions. If you agree to participate in this study, you will receive a signed and dated copy of this consent form for your records.**

## STATEMENT OF CONSENT:

I have read the information in this consent form. All my questions about the study and my participation in it have been answered. I freely consent to participate in this research study.

I authorize the release of my medical records, including photos and the results of HIV and hepatitis testing, for research or regulatory purposes to the sponsor, the FDA, DHHS agencies, governmental agencies in other countries, and WCG IRB.

By signing this consent form, I have not given up any of my legal rights.

_____
Printed Name of Subject

## CONSENT SIGNATURE:

| | | |
|---|---|---|
| _____ | _____ | _____ |
| Signature of Adult Subject Capable of Consent | Time | Date |

## Attestation Statement

I confirm that the research study was thoroughly explained to the subject. I reviewed the consent form with the subject and answered the subject's questions. The subject appeared to have understood the information and was able to answer the following questions correctly:

1. What is the purpose of this study?
2. If you decide to be in the study, what will you be asked to do?
3. What is the possible benefit of participating in this study?
4. What are the possible risks of participating in this study?
5. If you decide not to participate in this study, what options do you have?
6. Will participating in this study cost you anything? If so, what will you have to pay for?
7. Do you have to be in this study?
8. If you decide to be in the study, can you leave the study when you want to?

| Printed Name of Person Conducting the Informed Consent Discussion | Position | |
|---|---|---|
| Signature of the Person Conducting the Informed Consent Discussion | Time | Date |