QSC200932

PARTICIPANT INFORMATION SHEET AND INFORMED CONSENT FORM

(DNDi-0690-01)

TITLE: A study in healthy volunteers to look at how the test medicine DNDI-0690 is taken up and broken down by the body and to look at the safety and tolerability of the test medicine

***(*A Phase I, Double-blind, Randomised, Single Centre, Parallel-group, Single-dose, Dose-escalation, Placebo-controlled Study of the Safety, Tolerability and Pharmacokinetics of DNDI-0690 after Oral Dosing in Healthy Subjects)**

We're inviting you to take part in a research study. This study is for research purposes only and you will receive no medical benefit by taking part.

- Before you decide to volunteer it is important for you to understand why we're doing the research and what it involves.
- Please take time to read the following information carefully. Talk to your friends, relatives and whoever you feel is appropriate about the study if you want to.
- When you visit the unit one of our team will go through this information sheet with you to help you decide if you would like to take part or not.
- Please ask us if there is anything that is not clear or if you would like more information. Feel free to ask any questions at any time.
- It's entirely up to you if you want to take part in the study. Take your time to decide whether or not you wish to take part.

We've split this information sheet into 3 Sections.

- Section A will tell you about the purpose of the study and what will happen to you if you decide to take part.
- Section B will give you information on confidentiality, what will happen to the samples that you give, what to do if you have a problem and any contact details you may need.
- Section C contains the Informed Consent Form which you must sign if you would like to take part in the study. This is a form to confirm that you have read and understood all of the information that we have given to you and that you want to take part in the research study.

Quotient Sciences Recruitment Department Contact:

0330 303 1000

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Section A

1 Why Are We Doing This Study?

DNDi (the sponsor) is developing a new medicine to treat leishmaniasis which is a tropical disease with a strong link to poverty. Leishmaniasis is spread by the bite of certain types of sand-flies. Cases have been recorded in 101 countries around the world and there are 350 million people at risk of getting the disease. Symptoms of the disease can range from skin ulcers, fever, and weight loss and can be fatal if left untreated.

Treatments that are currently available for Leishmaniasis are limited, can be toxic and require a stay in hospital lasting several weeks. They are also not easy to administer. For example, some treatments need to be given by an infusion into the vein, others require several injections per day in the muscles. DNDi is conducting this study to develop a safer, short-term treatment that can be given easily by mouth without the requirement for long stays in hospital.

We will be looking at how the test medicine is taken up and broken down by the body. We will also look at the safety and tolerability of the test medicine and we may look at how food affects the way the test medicine is taken up and broken down by the body.

This study will involve a total of 8 groups of volunteers, Groups 1 to 6 have now completed the study. The first volunteers included in this study (Groups 1 to 6) were the first humans to receive this test medicine.

You will take part in Group 7 or Group 8.

2 Why Am I Being Asked To Take Part?

You have been invited to be screened to take part in this study because the information we have about you on file seems to match the requirements for the study. We need to perform a medical check to make sure that you can take part (detailed in Section 3.1).

To be able to take part in this study, you must:

- Be a healthy male or be a healthy female who is no longer able to have children (considered as non-childbearing potential);
- Be between 18 and 55 years of age for males, between 18 and 60 years of age for females;
- Not consume more than 21 alcohol units per week for males and 14 alcohol units per week for females (1 Unit = ½ pint beer or a 25 mL shot of 40% spirit, 1.5 to 2 units = 125 mL glass of wine, depending on type);
- Not have a history of drug or alcohol abuse;
- Not have donated blood or lost a lot of blood (e.g. through surgery or an accident) in the last 3 months or last more than 100 mL of blood (about half a cup) in the last 30 days;
- Not donate blood during the 3 months after the follow up visit
- Follow the contraception requirements of the study with your partner, as detailed in Section 12.3;
- Not have previously received the test medicine DNDI-0690;

- Not have taken part in a clinical trial in which you received another test medicine in the last 3 months;
- Not have smoked or used nicotine containing produces or e-cigarettes within the last 12 months;
- Not drink more than 6 cups of coffee or equivalent caffeine per day;
- Not have had any surgery in the past 12 weeks prior to admission (except appendectomy [removal of the appendix]);
- Not have had a febrile (high fever) or infectious illness for at least 7 days before first dosing;
- Not have had a severe allergic reaction to anything;
- Not be an employee, or an immediate relative of an employee, of either Quotient Sciences or the sponsor company DNDi;
- Not have any holidays planned for the time that the study is happening (timing details can be obtained from the recruitment department);
- Be capable of understanding and following the requirements of the study;
- Be willing to eat a high fat breakfast which includes bacon (this will only apply to you if you are male and take part in group 7 of the study);
- Not have had your gall bladder removed or have a history of gall stones (only if you are male and take part in group 7 of the study).

3 What Will Happen to Me Before, During And After The Study?

The study will involve up to 4 visits to the Quotient Sciences unit, as follows:

Visit	Fasting Required on Arrival
Screening Up to 28 days before dosing	Yes
↓	
Study Visit (Day -1 to Day 4) 4 overnight stays	Yes
↓	
Discharge From the Clinical Unit 3 days after you are dosed	N/A
↓	
Follow up visit 7 to 10 days after dosing	Yes

The total time you will be involved in this study is expected to be 6 weeks from the screening visit until the follow up visit.

3.1 Screening Visit(s)

You will attend Quotient Sciences for a medical assessment to check you meet the criteria to take part in the study, this is known as “screening”.

You should arrive at your screening visit having not eaten or drunk anything other than water for at least 8 hours.

The screening visit will be either 1 longer visit of up to 4 hours or 2 shorter visits of up to 2 hours to check if you are suitable for the study. At this visit you will be introduced to the study as a group with other volunteers and then you will also have the opportunity to ask any questions 1 to 1 with a study doctor.

A study doctor or nurse will explain the study and then, ask you to sign an informed consent form. This informed consent form is Section C of this information sheet. You will sign this form to say that you understand what will happen to you, what you will have to do during the study and that you are happy to take part.

After this, a study doctor will ask you questions about any medications you have taken, your surgical and medical history.

To confirm your surgical and medical history, we will need a medical report from your GP (General Practitioner). If you are a new volunteer or the medical report we have for you is older than 12 months, we will request a new medical report from your GP.

This medical report will include, but is not limited to:

- Medical and surgical problems you have had in the past or ongoing
- Any allergies you have
- Any medicines you have been given
- Any operations or procedures (e.g. X-rays) you have had
- Your reproductive status/contraception

This report might be a full print out of your records held by the GP so might include everything recorded in your medical history. If you tell us of any visits to the GP or hospital or something is noted in your medical history that we think might be important, we will ask your GP for further details.

Tests will be done as listed in the table in Section 3.10. If the study is delayed for more than 28 days after your screening visits, the tests described in the table in Section 3.10 might have to be repeated. If required, we will contact you to arrange an extra visit.

In cases where medical tests may be abnormal, for safety reasons we might have to perform extra tests to confirm or clarify the test result. Any extra tests will be discussed with you before we carry them out and your GP will be informed of any significant abnormal blood results during screening.

The screening procedures could possibly find underlying health conditions that you didn’t know you had. If this happens, anything we find will be discussed with you and your study doctor will arrange appropriate treatment and/or, with your permission, we will refer you to your GP.

If we find an unexpected problem during your medical check it could affect private healthcare or life insurance in the future.

Once you have had your medical check and all results and reports returned, the study doctor will decide if you are suitable to take part in the study. You will be contacted by the Recruitment Department to confirm that you should attend for admission to the study visit (see section 3.2).

3.2 Admission

If you are suitable and are accepted into the study, you should arrive at the clinical unit for admission at 08:00 am on the day before dosing. There are many factors which affect how the study is organised, so sometimes we have to change the dates at short notice. If this happens we will discuss the new dates with you.

You should arrive having not eaten or drunk anything other than water for at least 8 hours.

On arrival to the clinical unit we will need to do a bag search to check for any items that are not permitted in the unit during the study, such as medicines, cigarettes, nicotine substitutes, food and drinks.

We will carry out some extra tests at admission to make sure that you are still suitable to take part in the study. These tests are listed in the table in Section 3.10. We will ask for an update on your surgical and medical history. If there are any problems with these tests carried out on admission, the study doctor may decide that you are not suitable to be dosed.

3.2.1 Reserve Volunteers

We need to have extra volunteers on standby just in case of non-attendance, exclusion or last-minute withdrawal. All volunteers who are invited will be admitted to the clinical unit on the day before dosing. Reserve volunteers are generally selected on a first-enrolled basis but may be selected for other logistical reasons for example, availability and willingness to participate in other groups or studies. We can't promise you a place on the study.

You should not come to the research unit until a member of the Recruitment Department has spoken to you and confirmed that you should attend.

Most of the time, reserve volunteers only need to stay overnight until dosing is completed. **However, if you are a reserve volunteer you must make sure you are available** for the whole time the study is happening in case we need you to take part.

Reserve volunteers are reimbursed for their time and inconvenience (see Section 11.1.1).

In every case, the final decision on "included" and "reserve" volunteers will be made by the study doctor at Quotient Sciences.

3.3 Study Visit(s)

If you are accepted into the study, you will attend the unit for 1 study visit where you will be dosed once with either the test medicine or matching placebo (dummy medicine). You will be dosed with the test medicine or placebo either after a minimum of a 10 hours fast (no food or drink other than water, for at least 10 hours before dosing) or after eating a high fat breakfast (Group 7 only). On the day of admission (Day-1) you will be provided with meals at standard times.

If you are a male, you will be included in group 7, meaning you will receive the test medicine fed.

If you are a female, you will be included in group 8, meaning you will receive the medicine fasted.

Fasted dosing (groups 1 to 6 and group 8): If you are to receive the test medicine or placebo fasted you will be given a light snack before bedtime and you will not be allowed to eat or drink anything other than water for a minimum 10 hours before dosing until 4 hours after dosing.

Fed dosing (group 7 only): If you are to receive the test medicine after a high fat breakfast you will be given a light snack before bedtime and will not be allowed to eat or drink anything other than water for at least 10 hours. You will then be asked to eat a high fat breakfast which will consist of the following:

- 1 Fried egg
- 2 Strips of bacon
- 2 Slices of sliced bread with butter
- 1 Hash brown
- A glass of whole milk (240 mL)

You will be asked to eat this breakfast within 25 minutes. Controlled meals eaten before dosing must be eaten on the ward so that clinical staff can keep track of how much you eat and how long it takes.

You must only agree to take part in this study if you agree to eat all of this breakfast.

Lunch will be provided to all study volunteers at approximately 4 hours post-dose, a snack at approximately 10 hours post-dose and an evening meal at approximately 14 hours post-dose. On the following days, meals will be provided at appropriate times.

On the morning of Day1 (day after admission), you will be asked to swallow the test medicine or placebo (dummy medicine) as one or more capsules. This will be given with 240 mL of water. Following dosing you will need to stay on site for at least 72 hours (3 days) for more study procedures (see table in Section 3.10).

You will not be allowed to drink water for 1 hour before the planned dosing time, until 1 hour after the dose other than the water given to you with the test medicine. We need to monitor everything you drink once you arrive in the clinical unit. When you require a drink during your stay in the clinical unit, you must ask a member of the clinical team who will be available at all times to provide drinks. It is important that we monitor all liquids you consume so you must always request drinks from the clinical team and must not drink any other liquids that the clinical team have not provided.

You must eat the food we give you, and nothing else.

The study doctor can withdraw you from the study at any time. You can be withdrawn because of safety reasons or if you fail to follow the study instructions or restrictions. If you are withdrawn, we will continue to follow-up with you for safety reasons.

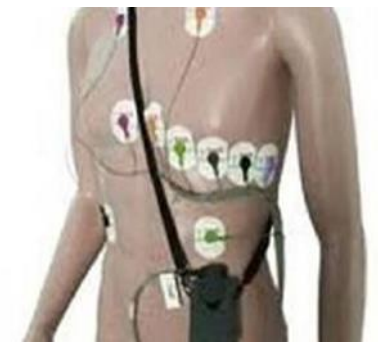
3.4 ECG Monitoring

During your time in the clinic we will monitor the electrical rhythm and electrical activity of your heart using an electrocardiogram (ECG). You will have small sticky pads attached to your shoulders, chest and ankles. These pads are used to detect electrical signals produced by your heart as it beats. The signals are recorded by a machine and will be looked at by a doctor. We will conduct the ECG monitoring on approximately 13 occasions during the study, although we may need to repeat this monitoring if required.

3.5 Holter Monitoring

From approximately 1 hour before dosing with the test medicine until 24 hours after dosing you will be asked to wear a Holter monitor.

The Holter monitor records your heart rhythm in a similar way to an ECG. Leads will be attached to your chest, shoulders and hips via electrodes attached to small sticky pads. The Holter device itself is a small box, about the size of a compact camera, which sits in a pouch either on a belt around your waist or on a strap over your shoulder (see Picture 1 below). You will not be able to shower while the Holter is attached to you.



Picture 1: The Holter device when attached

At specified timepoints throughout the recording period you will be asked to rest quietly. You will also not be allowed to use electrical devices such as mobile phones and laptops during these Holter extraction periods. This is to ensure the data that will be extracted at certain timepoints are of optimal good quality. The data collected are stored on a data card that sits inside the device.

3.6 Urine Collections

At your study visit, we will need to collect all of your urine in a jug or pot from dosing until you are discharged from the clinical unit.

This means that the toilets will be locked at all times and you will need to ask a member of the clinical team to give you access to the toilet. It is very important that we collect all samples that you produce, so please ensure that you do not urinate in the shower or miss any collections.

3.7 Blood Samples

We will collect blood samples (for measurement of the test medicine and for safety assessments) at regular intervals for up to 72 hours after dosing.

Each blood sample that we take from you will be approximately 6 mL (this is just over 1 teaspoon).

In total, we will collect approximately 17 samples from you, throughout the study. Additional blood samples can be taken if some tests are required to be repeated or you require further monitoring for safety reasons.

The total amount of blood taken from you during the whole study, including the screening visit and follow-up will not exceed 550 mL in a 4-week period. This maximum amount is about 20% more than the volume taken during a single blood donation (the amount taken during a single blood donation is about 470 mL, which is just under a pint). We prefer to take blood samples using a cannula (plastic tube) placed in a vein in your arm which stays there until we have finished taking samples. This is so that we don't have to keep using needles on days when multiple blood samples are needed. When a single sample is taken within a day (for screening visit for example), the sampling will be done with a needle.

No blood samples for genetic testing will be taken in this study.

3.8 Discharge From the Clinical Unit

We will perform some tests before you leave the clinical unit for your safety. These tests are listed in the table in Section 3.10. If we have any concerns about your safety, we may ask you to stay for extra safety tests.

3.9 Follow Up Visit

Once you have finished the study, or if you withdraw from the study, you must attend a follow up visit. This will take place 7 to 10 days after you dose with the test medicine. It will last about 30 minutes. A date and time will be arranged with you. At the follow up visit the following tests will be done:

- heart monitoring using an ECG machine test;
- blood tests for safety; urine tests for safety;
- urine test for pregnancy (females only)
- your blood pressure and pulse rate will be checked;

If any results are outside the specified range or if you tell us that you feel unwell, you may be asked to return to the site for repeat tests. If the results remain outside the specified range, we may refer you to your GP for your ongoing care.

3.10 Summary of Study Tests

Whilst at the clinical unit, you will have the following tests.

Test	Screening	On Admission (Day-1)	Day 1 Dosing Day	Day 2	Day 3	Discharge from the Clinical Unit (Day 4)
A discussion about your medical history	✓	✓				
Weight	✓	✓				✓
Height	✓					
Breath test for alcohol and smoking	✓	✓				
Urine test for drugs of abuse	✓	✓				
Blood and urine tests for safety*	✓	✓		✓	✓	✓
Blood test to confirm post-menopausal status (females only)	✓					
Blood test for pregnancy (females only)	✓	✓				
Blood test for Troponin I (a protein found in the blood which can indicate heart or muscle damage)		✓	✓	✓	✓	
Blood test to measure the amount of test medicine (and its breakdown products) in the blood			✓	✓	✓	✓
Urine test to measure the amount of test medicine and to look at biomarkers in the urine			✓	✓	✓	✓
Heart monitoring using ECG**	✓	✓	✓	✓	✓	✓
Blood pressure and pulse rate	✓	✓	✓	✓	✓	✓
Tympanic temperature (measured in the ear)	✓	✓				
Physical examination	✓	✓		✓		✓
Holter monitoring			✓			

*** Urine and blood tests for safety will be taken to ensure you are eligible to take part, and to monitor your health and wellbeing throughout the study**

****An ECG (electrocardiogram) is used to measure the electrical activity of your heart. A number of leads will be connected to small sticky pads placed across your chest shoulder and ankles**

3.11 Your Study Design Explained

You will be 1 of up to 64 healthy volunteers involved in this study. There will be up to 8 groups (also called cohorts); each group will contain 8 volunteers. All volunteers in each group will be either all males or all females. Groups 1-7 will be male only and Group 8 will be female only. You will only participate in one of the groups.

This is a Single Ascending Dose (SAD) study, which means that each volunteer will have one dose of the test medicine or placebo on one occasion. The dose level of the test medicine that is given to volunteers will change for each group.

This study uses a placebo which is a “dummy test medicine”. It looks like the test medicine but contains no active medicine. This is a double-blind study, which means that you will not know if you are receiving the test medicine or placebo and your study staff will not know either. Only some of the researchers will know and your study doctor will not know. Blinding the study means that the results will not be affected by subjects or study staff knowing if you have taken the test medicine or placebo.

In each cohort of 8 volunteers, 6 will receive the test medicine and 2 will receive the placebo. Within each cohort 2 volunteers will be dosed 24 hours ahead of the other 6, one with the test medicine and one with placebo, this is called the “sentinel cohort”. If you are in a sentinel cohort you have a 1 in 2 (50%) chance of receiving the test medicine. If you are part of the remaining 6 volunteers, 5 will receive the test medicine and 1 will receive the placebo, you will have a 5 in 6 chance of receiving the test medicine.

This is a first-in-human study which means this will be the first time this test medicine has been given to humans.

The starting dose given to the first group of volunteers will be 10 mg of the test medicine. A committee will be in charge of evaluating if it is safe to increase the dose or not (in next group) and the study doctor will be part of that committee. The dose of test medicine will only be increased if the study doctor decides it is safe to do so.

4 Do I Have To Take Part?

It is entirely up to you if you take part or not. If you decide not to take part this will not affect whether we include you in future studies at Quotient Sciences.

5 What Happens If I Change My mind?

Even if you decide to take part in the study, you can withdraw from the study at any time without giving a reason, but you are strongly advised to attend a follow-up visit for your own benefit and to ensure your safety. This will not affect the standard of care you will receive or the benefits to which you are otherwise entitled. You should only volunteer if you have time to complete the whole study.

6 Can I Be Taken Off The Study?

The study doctor can withdraw you from the study at any time (from screening to final visit). You can be withdrawn because of safety reasons or if you fail to follow the study instructions or restrictions which you have agreed to.

The Sponsor can also decide to stop the trial at any time. If you’ve received the test medicine, we will ensure you receive the appropriate follow up care.

7 What If New Information Becomes Available?

Sometimes we may be given new information during the study about the test medicine being studied after you have given consent or during the study. If this happens your study doctor will tell you about it and discuss with you if you want to continue in the study. Your study doctor might also decide you should not continue in the study. If you and the doctor are happy for you to continue in the study, you will be asked to sign an updated informed consent form.

8 Will There Be Any Side Effects?

The first volunteers included in this study (Groups 1 to 6) were the first humans to receive this test medicine.

There have been very few side effects seen in this study so far. A total of 48 volunteers having taken part in this study (groups 1 to 6), the side effects seen in these volunteers that are possibly related to the test medicine are:

- Diarrhoea - seen in 1 volunteer
- Excess flatulence - seen in 1 volunteer
- Headache - seen in 1 volunteer

The test medicine has been investigated in animal studies and has not shown any major safety concerns. In a study with monkeys who were given the test medicine changes to liver function were noted and based on these results, it is thought that some changes to liver function could be anticipated. For this reason, we will monitor the liver function of participants in this trial.

In the study involving monkeys the test medicine has been shown to possibly be harmful to the kidneys which was seen after 28 days of dosing. In this study you will only receive one dose of the test medicine, and the dose you will receive has been calculated to be lower than the doses found to have harmful side effects in animals. Therefore, it is very unlikely any harm to your kidneys will occur. As a precaution, blood and urine samples will be collected to test for biomarkers which will indicate if there has been any damage to the kidneys. We will also exclude any volunteers whose kidney function results do not meet acceptable criteria for this study.

Similarly, toxicity on the heart was found in some animals. For that reason, we will monitor your heart closely, with ECG monitoring at regular intervals throughout the study. We will also look at biomarkers in your blood (biomarkers indicate specific processes in the body) specific for heart injury.

We will also analyse blood samples to look at other functions of your body in order to monitor the safety of the test medicine.

In two separate studies where male monkeys were given the test medicine every day for 7 days and 28 days respectively, effects on the testes were noted. Seven weeks after the end of the 28-day dosing study some effects were still observable and so the monkeys were not classed as recovered. This means if you are a male volunteer, the test medicine could have an effect on your fertility (your ability to make a woman pregnant). These effects were seen in male monkeys given the test medicine over 7 and 28 days at daily doses which were at least 5 times higher than the highest dose being planned for this study. The effects of the test medicine in pregnant women is unknown, this is why only females that are no longer able to have children (non-child bearing potential) are included in this study.

In this study, you will be receiving a much lower dose than the doses given to animals. The starting dose will be 10 mg. If you are in a later dosing group the dose you will receive will be decided following evaluation of the safety assessments and data from the previously dosed group(s). The maximum dose allowed to be given in this study will result in a maximum blood level of the test medicine that is approximately 1.3 times lower than in the monkeys seen with side effects relating to the testes.

You should notify the study staff immediately if you experience any side effects during the study.

All drugs have the potential to cause severe isolated reactions, which may be life-threatening. As with any drugs there is a risk that a rare or previously unknown side effect will occur. The clinical unit is fully equipped to care for you if you should suffer a severe reaction. Additionally, the unit is very close to the Queen's Medical Centre, a large hospital in Nottingham and you can be taken here within 10 minutes in the case of an emergency.

9 What Are The Possible Disadvantages And Risks Of Taking Part?

- **Blood sampling** - During the study you will have frequent blood samples taken. This is a standard procedure which is unlikely to cause you any problems but can sometimes cause pain and discomfort. When using needles and cannulas there is a risk of bruising, reddening and swelling of the vein, but this normally clears up with no further trouble. There is also a risk of light headedness and fainting and a very rare chance of clot formation, nerve damage and/or infection at the site where blood is taken.
- **ECG/Holter monitoring -** You may have minor discomfort, like removing a plaster, when the electrodes taped to your chest to measure your heart's electrical signals are removed. A reaction to the electrode tape may cause redness or swelling of your skin.
- **Test medicine -** The dosage form used for delivery of the test medicine in the study is new and is still being tested to evaluate the levels of test medicine in the blood after the dosage form is swallowed and to see if the test medicine is safe to use.
- **Potential risk to fertility** - In studies carried out in male monkeys, effects on the testes were noted that did not fully recover 7 weeks after dosing, therefore there could be possible effects on a male's fertility (the ability to make a woman pregnant). These effects were seen in monkeys given the test medicine at daily doses which were at least 5 times more than the maximum dose being planned for this study. The effects of the test medicine in pregnant women is unknown, this is why only females

that are no longer able to have children (non-child bearing potential) are included in this study.

- **Loss of sleep -** During the study we may have to perform some tests early in the morning or during the night, which we will have to wake you up for. You may be on a ward with up to 20 other people which could mean that your sleep is interrupted.
- **Private medical insurance -** If you have private medical insurance you should check with the company if taking part in the study is considered a 'material fact' that should be reported to the insurance company before agreeing to take part in this study. You will need to do this to ensure that taking part in the study will not affect your medical insurance. **If we find an unexpected problem during your medical check, it could affect private healthcare or life insurance in the future.**

10 What Are The Possible Benefits Of Taking Part?

You will get no medical benefit from the test medicine, however development of a treatment for Leishmaniasis may benefit the population as a whole.

11 What Expenses and Payments Will I Receive?

11.1 Inconvenience Allowance For Completing The Study

You will be given an inconvenience allowance of £1044 plus travel allowance for taking part in the whole study (as compensation for your time, inconvenience and lifestyle restrictions).

This allowance may be reduced if;

- you do not complete the study for non-medical reasons
- you do not follow the requirements and restrictions of the study;
- you do not follow the rules of the clinic (please refer to your copy of the House Rules);

The allowance will not be increased if study days are delayed.

This allowance may be reduced if you do not complete the study for medical reasons unrelated to your participation in this study. If you do not complete the study as a result of side effects caused by the test medicine, you will be reimbursed in full.

11.1.1 Inconvenience Allowance For Reserve Volunteers

If you are a reserve volunteer, you will receive up to £340 plus travel allowance if you are not required for dosing.

11.1.2 Inconvenience Allowance For Volunteers Not Eligible At Screening

If you attend a screening visit but we can't offer you a place on this study, you will receive a screening fee of up to £80 plus travel expenses. If you are offered a place, this is included within the study/reserve expenses listed above.

11.2 If You Are In Receipt Of Any Benefits

If you are in receipt of any benefits, you should seek further advice from your benefits provider as to whether the payment that you receive from taking part in this study will affect your eligibility for those benefits.

There may be circumstances when we are required by law to disclose such payments to the relevant authorities when requested.

11.3 If You Are A UK Taxpayer

Depending on your personal circumstances, part of this payment may be classed as income by HMRC. Participants are reminded that they are responsible for their own tax affairs.

If you test positive for drugs of abuse (illegal use of drugs) or alcohol at any time during this study, you will NOT be entitled to receive your inconvenience allowance or travel expenses and we reserve the right to remove you from the volunteer panel.

12 What Restrictions Will I Have to Follow?

12.1 General Requirements

You must follow the restrictions we give you before and during the study. This is for your safety and to ensure the data we collect from you during the study is accurate:

- You should be able to attend all study days and return visits and stay for the whole length of time;
- You should tell us about any special dietary requirements (e.g. vegetarian, vegan, dislike of certain foods) before you volunteer;
- If you are taking a medicine prescribed by your GP, you must not stop taking this in order to participate in this study;
- You should follow the contraception requirements of the study with your partner, (if you are a male volunteer) as detailed in Section 12.3;
- If you are female please wear appropriate clothing such as trousers and a top, as a physical examination or ECG may require removal of an all-in-one outfit, such as a dress;
- You can only participate to one trial at a time;
- After discharge from this trial, you will not be allowed to participate in any other trial for 3 months.

12.2 Summary Of Study Restrictions

Restricted Item / Activity	How Long For	Why?
Prescription or over the counter medication and dietary supplements, herbal medicines (such as St John's Wort)	28 days before dosing until discharge from the study (after the follow up visit 7-10 after dosing). (4g/day paracetamol is allowed within 7 days before dosing with the test medicine)	Other medicines might interfere with the test medicine
Food containing poppy seeds (ie poppy seed topped bread)	48 hours before screening and admission until discharge from the study (after the follow up visit 7-10 after dosing).	This could show a positive result on our drugs of abuse test as it is very sensitive
Food containing grapefruit and cranberry	72 hours before admission until discharge from the study (after the follow up visit 7-10 after dosing).	A chemical in these fruits can slow down how long it takes your body to break down and remove the test medicine
Unaccustomed and strenuous exercise	72 hours before screening and admission until discharge from the study (after the follow up visit 7-10 after dosing).	This could result in an abnormal blood test
Alcohol	24 hours before screening and 48 hours admission until discharge from the study (after the follow up visit 7-10 after dosing).	Alcohol might interfere with the test medicine and can also cause other side effects
Smoking (or smoking substitutes e.g. nicotine patch or use of electronic cigarettes)	12 months before screening until discharge from the study (after the follow up visit 7-10 after dosing).	Smoke contains chemicals that can slow down how long it takes your body to break down and remove the test medicine
Caffeine or xanthines or products containing these (e.g. chocolate, tea, coffee, carbonated drinks)	24 hours before admission until discharge from the study (after the follow up visit 7-10 after dosing).	These chemicals can affect how long it takes for your body to break down and remove the test medicine

12.3 Contraception Requirements

There is no information about the effect of the test medicine on an unborn child and therefore, may involve risk to the baby as it grows during pregnancy.

Male Volunteers

All men who are sexually active (even if vasectomised) with a female partner of child bearing potential must use a condom from the time of informed consent until 90 day after study discharge (after the final follow up visit 7-10 days after dosing).

Condoms must be used even if your partner is not of childbearing potential (e.g. if they are sterilised, post-menopausal, already pregnant or not female) you are still required to use condoms to prevent exposure of your partner to the test medicine for 1 week after study discharge (after the final follow up visit 7-10 days after dosing).

Male volunteers should not donate sperm from the time of informed consent until 90 days after study discharge (after the final follow up visit 7-10 days after dosing).

If you are sexually active with a female partner that has the potential to become pregnant, you must use a condom and your female partner must use an additional effective method of contraception (from the list below) from the time of informed consent until 90 days after study discharge (after the final follow up visit 7-10 days after dosing).

If your partner is already pregnant, you must use a condom from the time of dosing until 1 week after study discharge (after the final follow up visit 7-10 days after dosing).

The Following Methods Are Considered Effective:

- Combined (oestrogen and progestogen-containing) hormonal contraception that stops the woman's eggs being released: These contraceptives may be given:
  - orally
  - into the vagina
  - patch
- Progestogen-only hormonal contraception. These contraceptives may be given:
  - orally
  - by injection / implant
  - as an intrauterine hormone-releasing system (IUS)
- Implantable intrauterine device (IUD)
- Surgical sterilisation (for example, documented bilateral tubal occlusion, hysterectomy for female volunteers or female partners; vasectomy for male volunteers or male partners)

Alternatively, if you do not normally have sex (abstinence), this will be acceptable, but only if this is what you normally do. Periodic abstinence (not having sex occasionally) and withdrawal are not acceptable methods of contraception.

Female Volunteers of Non Childbearing Potential

Female volunteers who are of non-childbearing potential do not need to use any methods of contraception. A woman is considered of childbearing potential unless post-menopausal or permanently sterile. Post-menopausal is when a woman has been through the menopause. This means she has stopped having periods for at least 12 months and is no longer able to have children. Permanent sterilisation methods include:.

- Hysterectomy (surgical procedure to remove the womb)
- Bilateral salpingectomy (removal of both fallopian tubes)
- Bilateral oophorectomy (removal of both ovaries)
- Bilateral tubal ligation (Surgical procedure that involves blocking both fallopian tubes to prevent eggs reaching the womb)
- Bilateral tubal occlusion (A Procedure that involves creating a barrier in both fallopian tubes to prevent eggs from reaching the womb)

All Volunteers

If you or partner becomes pregnant in the time between you taking the test medicine until 1 week following study discharge, you must inform the study doctor immediately. For the sake of safety, it is important for the sponsor and the study doctor to follow-up on the pregnancy and the child until he/she is 2 years of age to ensure that the test medicine does not have any effect on your child.

Please note that you must discuss these contraception requirements with your partner.

You can ask advice from your study doctor or your GP on the best contraception for you and your partner.

13 HIV and Hepatitis B and C Testing

During the screening visit you will be tested for HIV and Hepatitis B and C.

13.1 HIV (Human Immunodeficiency Virus)

HIV is the virus which causes AIDS (Acquired Immune Deficiency Syndrome). It is a serious disease which decreases the body's resistance to infections and other illnesses.

13.2 Hepatitis B and C

Hepatitis B and C are viral infections that cause inflammation of the liver. They are serious diseases that both may lead to long term liver damage and eventually liver failure. These might also result in the development of liver cancer.

13.3 How are HIV and Hepatitis B and C Transmitted?

HIV and Hepatitis B and C are almost always transmitted from infected blood or other infected body fluids (e.g. semen, vaginal secretions, breast milk). The most common way of passing these on are through sexual intercourse or through contact with blood.

We need to test your blood for these viruses to ensure that you are healthy and also to protect our staff, as they will be handling your blood samples. If you think that you are at risk of infection with HIV or Hepatitis B or C, you should discuss this matter with your own GP or by visiting the Genito-Urinary Medicine (GUM) clinic in Nottingham (located at Nottingham City Hospital; Tel: 0115 969 1169) or a clinic nearer to you.

13.3.1 How Will I Be Tested?

You will be asked to give your consent for a HIV and Hepatitis B and C test to be carried out. A sample of blood will be taken from your arm during your screening visit, which will be tested for all these viruses.

13.3.2 I've Never had Hepatitis. Why Do I Need To Be Tested For Hepatitis B or C?

The initial infection with Hepatitis B or C virus may cause only a very mild illness or even no illness at all. Some people may acquire the Hepatitis B infection from their mothers before birth and so never realise that they have been infected. Even if the initial infection was very mild, people can still become long term carriers of the virus. Infection can be difficult to detect without a blood test as carriers may appear to be perfectly fit and well for many years, although some of them may develop severe liver disease eventually.

13.3.3 What If I've Had a Hepatitis B Vaccine?

We will still need to check for infection as the vaccine is not always 100% effective. If you have had the vaccine, this won't interfere with the results of the test for infection.

13.3.4 Who Will Know The Result Of The HIV And Hepatitis Tests?

Your test results will be reviewed by the study team. Your results will be filed with your study notes and handled in a confidential manner. Your own GP will only be told if a result is positive. By signing the informed consent form (Section C), you are giving us your permission to notify your GP but we would try to let you know first, before doing this. Only if we were unsuccessful in contacting you for follow up, would we notify your GP without speaking to you first. In this case, all correspondence with your GP will be strictly confidential.

13.3.5 What Happens If I Do Not Give Consent For The Test?

The test forms part of the study requirements therefore if you do not want to have the sample taken or you are not willing to provide consent this would mean you will not be eligible to proceed onto the study.

13.3.6 What Happens If A Result Is Positive?

If you have a positive result, you cannot take part in this study. This is for your own safety and wellbeing as well as to minimise the risk to our staff of possible infection when handling your blood. You will be informed of the result by a study doctor. The study doctor will refer you to a GUM clinic or your GP as appropriate.

By signing the informed consent form (Section C), you are giving us your permission to notify your GP or your local GUM clinic, depending on your preference.

A negative HIV test does not necessarily mean that you are not infected, as a test may not reveal the presence of infection for 3 months after exposure.

14 What Happens When The Study Stops?

There will be no continued provision for your care after the trial as this is a healthy volunteer study. If you are interested in understanding whether you received active or placebo then we will be able to tell you, but only after the data has been processed, which may take some time. Please contact the recruitment department for further information.

Section B

15 What If There Is A Problem?

15.1 If You Feel Unwell

When you are discharged from the clinical unit after you have been given the test medicine, you will be given a trial participation card which will have a 24-hour phone number that you can use to contact the study doctor.

Please carry this card with you and if you feel unwell at any time after discharge please contact the unit in the first instance. If you prefer to visit your GP, please take your trial participation card with you and inform your GP that you have recently taken part in a study at Quotient Sciences. If in the unlikely event that you need to attend the A&E Department of your nearest hospital, please ensure your Trial Participation Card is with you.

15.2 Complaints

If you have any **medical queries** in relation to this study after you have been discharged from the clinical unit, **you should contact 0330 303 1000** and ask to speak to the study doctor. For any out of hours queries see your trial participation card.

If you have any concerns about the way you have been dealt with, please contact the Recruitment Department, Quotient Sciences, Mere Way, Ruddington Fields, Nottingham, NG11 6JS (see Page 1 for contact telephone number).

15.3 Harm

If your health or wellbeing is affected as a result of taking part in the study the Sponsor will provide compensation to you in accordance with the Association of the British Pharmaceutical Industry "Guidelines for Phase I Clinical Trials 2018 Edition".

The sponsor will pay compensation for any injury resulting from participation in the trial, without the need to prove fault on the part of the sponsor or anyone else connected with the trial.

Any payment would be without legal commitment (please ask if you wish for more information on this). We would not be bound by these guidelines to pay compensation where the injury resulted from a drug or procedure outside the trial protocol or where you did not follow the restrictions in the protocol. Quotient have appropriate insurance to cover incidents outside of the Protocol which may cause harm.

The amount of compensation shall be calculated by reference to the amount of damages that would commonly have been awarded for similar injuries by an English court had liability been admitted. The amount of compensation will be reduced if you are partly responsible for the injury or if you have been compensated under another insurance policy.

You and the Sponsor shall refer to an independent person any dispute or disagreement about the compensation undertaking. If you and the Sponsor cannot agree on the identity of an independent person, the President of the Royal College of Physicians, London will be invited to appoint an independent person with the power to consult an advocate of not less than 10 years standing on any issue of law including the amount of damages to be paid.

The contractual commitment to compensate you shall follow the laws in England and, subject to the provisions above, the English courts shall have sole jurisdiction over any dispute that may arise out of it.

If you would like an explanation of these legal terms, please feel free to ask.

If you want to contact us regarding a **study-related injury**, please **contact the Recruitment Department on 0330 303 1000**.

For more information on insurance and compensation in the event of injury in Phase I clinical trials, please see the Association for the British Pharmaceutical Industry (APBI) guidelines that can be found online using the following link:

http://www.abpi.org.uk/about-us/resources/publications-library/clinical-trials-insurance

16 How will my personal information be handled?

16.1 What happens to my personal information?

Your personal information will be used to help the Sponsor and Quotient to conduct the study and understand more about the study drug.

16.2 What personal information is collected about me for the study?

The study doctor and other study staff will collect your personal information. This may include:

- your name, address and telephone number, along with your passport or national insurance number;
- your age, gender, ethnic and racial background;
- life style information; health and medical history;
- your study treatments and response to study treatments; and
- data resulting from testing your biological samples.

16.3 Who has access to my personal information?

All your personal information collected for this study will be stored in the study medical records at the Quotient site.

Sponsor staff, review boards and ethics committees (that approve and monitor studies), and others may check the study records. This is done to make sure that the study is being run properly.

Regulatory agencies, such as the US Food and Drug Administration (FDA), European Medicine Agency (EMA), Medicines and Healthcare products Regulatory Agency (MHRA) or others, review and approve new medicines. These agencies will be granted direct access to your information. This is so they can verify clinical trial procedures and/or data.

Each of these people or organisations will be under an obligation to keep your personal information confidential.

16.4 How is my personal information protected?

Your personal information will be given a numbered code (such as 123456). Once it is coded, linking it to you is only possible through a code list. The code list is kept secure and confidential by the Quotient study site. Information that directly identifies you will not leave the study site or be sent to the Sponsor with the study results. Only pseudonymized data will be recorded electronically, meaning that these data will not allow to identify you.

16.5 How long will my personal information be used?

Your personal information will be used for only as long is needed for the study and may be retained for longer, where required by law. The Sponsor must retain data from clinical trials for up to 25 years.

16.6 Will my data be transferred?

If your data is transferred, we will always ensure appropriate measures will be taken to protect your personal information. Along with coding your personal information as detailed above we also make sure we have contracts and other protections in place before we share your personal information. These measures comply with data protection and privacy laws.

Personal information may be transferred to trusted persons in other countries. Data protection and privacy laws may not be as strong in these countries as the laws in your home country. When personal information is transferred, the Sponsor makes sure that appropriate and suitable safeguards are used.

We may transfer your coded personal information to:

- the Sponsor who is based in Switzerland;
- companies which are part of the Quotient group to help us complete the study, some of which are in the USA;
- laboratories or clinical facilities which help us to conduct analysis on samples you give us as part of the study; and
- couriers or transport companies to enable us to deliver the samples to external laboratories.
- Any regulatory authority from EU, United States or countries where leishmaniasis is present (endemic) for the purpose of registering the future medicine.
- Coded Data may be posted on publicly available database for the purpose of publishing results of the trial in scientific journals.

We also need to log your involvement in the study on the UK national database called The Overvolunteering Prevention System (TOPS). This information will be available to other clinical units and contains the following information:

- your National Insurance number (if you're a UK citizen); or
- your passport number and country of origin (if you're not a UK citizen); and
- the date of your last dose of study medicine (but only if you go on to take part in a study).
- For your own safety your GP will be told if any of the test results from your blood or urine samples are significantly abnormal or if you become unwell as a result of taking part in the study.

16.7 What right do I have to access my personal information?

At any time, you may ask the study doctor to see your personal information. In certain circumstances, you may request:

- to learn more about what is done to your personal information;
- a copy of your personal information; and
- to correct and/or delete your personal information (subject to certain conditions).

You may also:

- object to what is done to your personal information;
- complain to your local data protection authority (the Information Commissioner's Office in the UK), if your privacy rights are violated; and
- claim compensation for damages or distress incurred or suffered from unlawful use of your personal information, through the courts.

16.8 What if I withdraw my consent?

At any time, you can withdraw your consent for the use of your personal information. If you withdraw consent for use of your personal information for this study, then you will leave the study. This will not affect your medical care.

If you withdraw consent for use of your personal information for the study, the Sponsor may still use your personal information if it needs to do so for legal reasons or if necessary for certain scientific research purposes related to this study and permitted by law.

16.9 Who owns the study results?

The Sponsor will be the owner of the study results. The Sponsor plans to use the results, and may get patents, or sell the product in the future, or make profits in other ways. You will not be paid for any part of this.

16.10 Who should you contact with questions?

For questions or requests regarding how your personal information is handled, or if you require additional information, please contact Quotient's Data Protection Officer, Michael Astle via email: DPO@quotientsciences.com.

16.11 What is a data controller?

A data controller collects and processes personal information. It determines why and how it is processed.

DNDi (the sponsor) is the data controller for this study. The Sponsor's Data Privacy Officer can be contacted at dataprivacy@dndi.org.

In order to retain your anonymity, please contact the Quotient Data Protection Officer in the first instance.

17 What Will Happen To The Samples I Give?

All samples (for example, urine, blood) will be collected on the ward by a trained member of the clinical team. These samples are processed in a secure laboratory in the UK or the EU.

Blood and other samples will only be used for the purpose of this study and will be destroyed once they are no longer required.
Blood and urine samples for safety analysis are identified by the study number, sample type, date of sample, date of birth, initials, gender and your volunteer panel number

Blood and urine samples for analysis of the amount of test medicine in your body are identified by the study number and subject number, initials, date of sample and time point of blood draw.

If you withdraw your consent for participation in the study, we will need to use the data collected up to your withdrawal. Any samples (e.g. blood/urine) already sent off site for analysis are identified as described above. These samples may still be analysed and reported unless you ask for them to be destroyed following your withdrawal.

18 What Will Happen To The Results Of The Research Study?

The results of the study will be analysed and given to the sponsor company in the form of a report that is usually prepared by Quotient Sciences.

Anonymised data from this study may be used to support future development of the test medicine. You cannot be identified from anonymised data. Study data could be kept for 25 years or longer after completion or discontinuation of the study. The study data must also be kept for a minimum of 2 years following the discontinuation of drug development, or if all marketing authorisations planned for the test medicine are in place.

19 Who Has Approved The Study?

The study has been reviewed and approved by a recognised Ethics Committee in the UK.

The clinical study has also been reviewed and approved by the Medicine and Healthcare products Regulatory Agency (MHRA), the government appointed agency for United Kingdom. The MHRA are also responsible for evaluating Quotient Sciences's unit and granting the unit approval to carry out clinical study activity.

20 Contact Details For Further Information

If you want any further information on clinical research please see the UK Clinical Research Collaboration (UKCRC) booklet called 'Understanding Clinical Trials' (http://www.ukcrc.org/wp-content/uploads/2014/03/iCT_Booklet.pdf).

If you require any further information or advice on whether to participate in this study you should contact the Recruitment Department at Quotient Sciences, the contact telephone number for this can be found on Page 1.

If you are unhappy with anything on the study, please follow the complaints advice in Section 15.2.

You will be provided with a signed and dated copy of this information and consent form.

Thank you for considering taking part in this study.

Volunteer Number | | | | | | |

Volunteer initials: | | | |

Section C

INFORMED CONSENT FORM (QSC200932, SPONSOR STUDY NUMBER DNDi-0690-01) **Initials**

1. I confirm that I have read and understood the information in this document for the above study. I have had the opportunity to consider the information and ask questions. Any questions I have asked have been answered to my satisfaction. ☐
2. I understand that my participation is voluntary, and I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected. ☐
3. I understand that relevant sections of my medical notes and data collected during the study may be looked at as described in Section 16. ☐
4. I agree to my personal information being used in the manner and for the purposes set out in this document. This information may include my initials and date of birth and my full name and/or address. In particular, I understand and agree that information about me that is a result of me taking part in the study will be processed by Quotient Sciences Limited and its group companies and data that does not identify me may be used to support future research. Quotient will: ☐
   - Analyse my clinical data during and after the trial, to assess the test medicine and to produce reports;
   - Send coded data which cannot readily be linked back to myself, to the Sponsor outside of the EEA where data protection laws are not as comprehensive as in the European Union, for central analysis. Such data may be seen by government regulatory authorities outside of the EEA;
   - Hold my data on file and provide to government regulatory authorities in accordance with the government's requirements for clinical trials.
5. I understand that my GP is required to send a report of my medical history but may send a full print out which will be used by the study team to assess my eligibility for the study. ☐
6. I understand it is important to tell Quotient Sciences about all medical problems for which I needed to see a GP or nurse, and all medicines I have taken since the date of the last report from my GP. ☐
7. I understand that samples will be screened for HIV and Hepatitis B and C and the implications of a positive result. ☐
8. I consent to provide blood and urine samples for this trial and understand what will happen to the samples I provide and the data they generate. ☐
9. I agree to follow all study restrictions as outlined in section 12.2 and the contraception requirements as outlined in Section 12.3. ☐
10. I agree to take part in the above-mentioned study. ☐

		Time	Date
_____	_____	☐☐.☐☐ (24 h clock)	☐☐ ☐☐☐ ☐☐☐☐ Day Month Year
Full Name of Volunteer	Signature		

		Date
_____	_____	☐☐ ☐☐☐ ☐☐☐☐ Day Month Year
Name of Physician / Nurse Giving Information	Signature	

This information and consent form cannot be reproduced without the permission of Quotient Sciences. If you require extra copies to discuss with family, friends or your GP, please contact the recruitment department on 0330 303 1000.