PARTICIPANT INFORMATION SHEET AND CONSENT FORM
(Part C: Multiple Dosing - Cold Pressor Test)

Short Title:	Phase 1 Single and Multiple Ascending Dose Study of LTG-305 in Healthy Participants
Protocol Number:	LTG-305-001
Sponsor:	Latigo Biotherapeutics, Inc. 1300 Rancho Conejo Boulevard, Suite 305, Thousand Oaks, California 91362 U.S.A
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Ethics Number:	2024 FULL 20202

This is the first time that LTG-305 will be studied in humans.
You will not get any health benefit from the drug used in this study; but there are risks of you having a drug reaction, injury, or illness.

You are invited to take part in a clinical research study (also referred to as "research project"). This study will test an experimental drug, named LTG-305, that may potentially be used for the treatment of acute or chronic pain. LTG-305 is an investigational product because it has not been approved by the New Zealand MedSafe or other drug regulatory authorities.

There are multiple parts to this study, and you are being asked to take part in Part C (Multiple Dosing – Cold Pressor Test). Part C (Multiple Dosing) is described in more detail in later sections of this Participant Information Sheet, which will help you decide if you'd like to take part. It sets out why we are doing the study, what your participation would involve, what the benefits and risks to you might be, and what would happen after the study ends. We will go through this information with you and answer any questions you may have. We expect this will take about 30-60 minutes. You do not have to decide today whether or not you will participate in this study. Before you decide you may want to talk about the study with other people, such as family, whānau, friends, or healthcare providers. Feel free to do this.

Whether or not you take part is your choice. If you don't want to take part, you don't have to give a reason. If you do want to take part now, but change your mind later, you can pull out of the study at any time.

If you agree to take part in this study, you will be asked to sign the Consent Form on the last page of this document. You will be given a copy of both the Participant Information Sheet and the Consent Form to keep.

Please make sure you have read and understood all the pages of this document including the consent form.

1 WHY ARE WE DOING THE STUDY?

1.1 Purpose

LTG-305 is being developed for the treatment of acute (short term) and chronic (long term) pain. In New Zealand, almost 1 in 6 people reported to experience chronic pain which affects their quality of life. Current therapies comprising of nonsteroidal anti-inflammatory agents (NSAIDs), anti-depressants, anti-epileptics and opioids have limited effects in reducing chronic pain and have a great risk of abuse or dependence.

LTG-305 works by inhibiting (blocking) channels (pathways) in the brain which are associated with controlling pain sensory neurons (brain cells) in the nervous system. LTG-305 is a non-opioid, non-NSAID and non-narcotic form of pain relief. It is hoped that, by blocking these pathways in the brain, LTG-305 may be an effective treatment for acute or chronic pain while reducing the negative side effects associated with current pain therapies like abuse and dependence.

This study will investigate the effects of LTG-305 in healthy participants. You are being asked to to take Part in Part C (Multiple Dosing), where you will be asked to submerge your hand in cold water to assess pain tolerance after multiple doses of LTG-305. Other parts of the study include investigating LTG-305 as a single ascending dose (SAD [Part A]), multiple ascending doses (MAD [Part B]) of LTG-305 and single dosing with the Cold Pressor Test (Part C – Single Dosing) in healthy participants.

The purpose of Part C (Multiple Dosing) is to:

- Evaluate how the body responds to pain using a cold pressor test in biologically male participants, after receiving multiple doses of LTG-305
- Measure levels of LTG-305 in the blood over time, following multiple doses.

1.2 Study Design

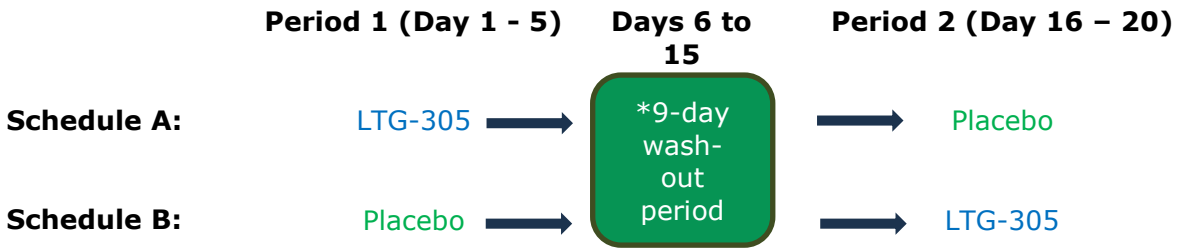
Approximately 220 healthy participants will take part in this study, up to 60 of those will take part in Part C (Multiple Dosing). This part of the study requires two 5-night stays (10-nights total) at the New Zealand Clinical Research (NZCR) research unit and 1 safety follow up phone call.

This is a randomised, placebo-controlled, cross-over study.

Randomised means that the order of study medication you take (LTG-305 and placebo) will be assigned randomly (by chance). Placebo is a substance that looks like LTG-305 but contains no active medication. Cross-over means that all participants in this part of the study will receive both LTG-305 and placebo, but the order you receive these is randomly assigned. The dose level will be determined by the results of the previous study groups. You will be told what dose you will receive.

You will be randomised to either **Schedule A** or **Schedule B** to receive one dose daily from Day 1 to Day 5 (Dosing Period 1), and one dose assignment daily from Day 16 to Day 20 (Dosing Period 2). You will not be told which study schedule you will be on. Each dose will be given by mouth, with a glass of water after you have been fasting (no food or drink other than water) overnight.

You will be assigned to either Schedule A or Schedule B:



** 9-day washout period is approximate. The washout period may be shorter or longer by 1 day depending on the date you enter the study. You will be told how long the washout period will be.*

Before and after receiving your dose of LTG-305 (or placebo), you will have your pain tolerance assessed using cold pressor tests (which will be further explained in section 2).

Up to 3 dose levels may be explored in up to 3 dose groups (cohorts) of 20 participants each. Dose levels will be determined by results from previous dose groups. You will be told which dose level you will receive. On Day 6 and Day 21 you will be discharged in the morning.

Blood samples and other tests to measure study drug levels and effects on the body will be collected at specific time points during the study, your safety will be monitored, and any changes in your health will be recorded.

1.3 Nature and Sources of Funding of the Study

This research project is being conducted and funded by Latigo Biotherapeutics, Inc. ("Latigo") and locally sponsored in New Zealand by PPD, part of Thermo Fisher Scientific, a Contract Research Organisation (CRO) which help conduct and monitor the study in New Zealand.

By taking part in this research project, you agree that data generated from your assessments throughout the study, will be provided to the Sponsor. The knowledge gained from this data may lead to new discoveries, which would assist them in obtaining approval for a new drug and benefit the sponsor financially. There would be no financial benefit to you from these discoveries.

New Zealand Clinical Research (NZCR) will receive a payment from Latigo for undertaking this research project.

No member of the research team will receive a personal financial benefit from your involvement in this research project (other than their ordinary wages).

1.4 Approval by Ethics Committee.

This study has been reviewed by an independent group of people called a Health and Disability Ethics Committee (HDEC). The ethical aspects of this research project have been approved by the Northern A Ethics Committee.

A description of this clinical study will be available on http://www.ClinicalTrials.gov. 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.

2 WHAT WOULD YOUR PARTICIPATION INVOLVE?

Participation in this study will last up to approximately 8 weeks (51 days), including a screening, in-clinic treatment, and follow-up period. If you wish to participate in this study, you will be asked to sign this consent form before any study assessments can be performed.

The details of the study and tests performed are discussed and shown below. During the screening period, assessments will be done to check whether the study is suitable for you. The day you have your first dose of LTG-305, or placebo is called Day 1 and all other days are counted back or forward from this.

The results of the screening assessments will determine whether or not you can take part in the study. However, even if all your results are normal, you may not be guaranteed a place. We may screen more participants than we need and so you may be asked to be a reserve. This will mean you will be asked to come to the clinic and undergo the tests and procedures until the point that we have enrolled enough eligible participants. You will then be discharged and where possible we will try to include you in a later group.

On Day 1 and Day 16, you will admit to the NZCR unit and remain at the clinic for 5 nights and stay until approximately 24 hours after your final dose before being discharged the following day (after your last cold pressor test).

2.1 Tests and Procedures

Collection of Your Information
At your Screening visit, the study staff will record your demographic information, such as your name, age, sex, race/ethnicity, address and phone number. The study doctors will also ask you questions about your health, including medical history, medications you are taking, social history (including smoking, alcohol and drug use), and contraception.

Physical Examination:
During the study, the doctor will perform a physical examination to check your health. Your height and weight will also be measured to calculate that your Body Mass Index (BMI) is within range for the study.

Electrocardiogram (ECG):
An ECG measures the electrical activity of your heart, using 12 wires attached to your chest and limbs with sticky pads.

Vital Signs:
Vital signs include recordings of your pulse, blood pressure, breathing rate, and temperature.

Blood and Urine Samples:
At screening, blood samples are taken by direct vein puncture. On the Day 1, 5, 16 and 20, a cannula (thin plastic tube) will be inserted into a vein in your arm to take blood samples. If your cannula stops working, direct vein punctures will be used. On these days, you will have blood samples taken frequently. Blood and urine samples will be collected:

- To monitor your safety (blood cells, clotting, chemistry, fats, liver function, kidney function)
- To screen for recreational drugs such as cannabis, methamphetamine, and opiates. You will also be tested for nicotine.
- To screen for specific infections (HIV, Hepatitis B & Hepatitis C)
- To measure the amount of LTG-305 in the blood (pharmacokinetics)

Alcohol Breath Testing
You will be screened for the presence of alcohol via a breathalyser. You will blow into the mouthpiece for a few seconds to measure the presence of alcohol on your breath.

COVID-19 testing – During the study, you will be required to have COVID-19 testing done at Screening, Day 1 and Day 16. You will be informed of these tests by study staff.

Cold Pressor Test (CPT)
You will complete CPT's to assess the pain tolerance difference between LTG-305 and placebo. You will place your non-dominant hand in a warm water bath (approximately 35°C), you will then transfer your hand into a separate cold-water bath (approximately 1°C) and keep it in there for as long as tolerable. You will have this test done three times on the day of Screening, and then two times pre-dose on Day 1 and Day 16- and 6-times post-dose on Day 1, 5, 16 and Day 20. You will be asked to rate your pain on a scale from 0 to 10 using the Numeric Pain Rating Scale (NPRS).

In the event that an assessment is not performed on the day outlined within the Study Schedule below, the assessment may be performed at your next study visit.

Table 1: Study Schedule

Period	Screening	Dosing Period #1[1]					Washout period	Dosing Period #2[1]					Follow-Up Phone Call
Study Day	**-28 to -1**	**1**	**2**	**3, 4**	**5**	**6**	**6 to 15**	**16**	**17**	**18, 19**	**20**	**21**	**24**
Admission to the unit		X						X					
Discharge from the unit						X						X	
Phone Call[5]													X
Physical Exam[2]	X											X	
Vital Signs	X	X	X	X	X			X	X	X	X	X	
ECG	X				X			X			X		
BMI (Height & Weight)[3]	X											X	
LTG-305 or placebo Dose Administration		X	X	X	X			X	X	X	X		
Blood Sampling[4]	X	X	X		X	X		X	X		X	X	
Urine Testing	X												
COVID-19 Testing	X	X						X					
Urine Drug Test and Alcohol Breath Test	X	X						X					
Cold Pressor Tests	X	X	X		X	X		X	X		X	X	
Questions about your health and medication	X	X	X	X	X	X	X	X	X	X	X	X	X

[1] You will admit to the clinic in the morning of Day 1, 5, 16 and Day 20.
[2] A full physical examination is done at Screening, a symptom-directed physical exam is done at all other time points.
[3] Height is only taken at Screening.
[4] Blood samples will be taken frequently on Day 1, Day 5, Day 16 and Day 20.
[5] During the safety phone call, the study nurse will ask you questions about your health

2.1 Who Can Take Part in this Study?

To take part in this study you must:	
✓	Be able to give informed consent and follow the study procedures.
✓	Be a biological male aged 18 – 55 years, inclusive.
✓	Have a BMI (Body Mass Index) between 18.0 kg/m^2 – 32.0 kg/m^2, inclusive
✓	Be in good health

You cannot take part in this study if you:	
✗	Have a history of a significant medical problem, mental health problem or severe allergy.
✗	Have taken any prescription medication within at least 14 days prior to Day 1; have used over-the-counter medications, herbal medications, or vitamin supplements within at least 7 days prior to Day 1; have used antibiotics or systemic steroids (e.g. prednisone) within at least 28 days prior to Day 1; or have received a vaccination within 14 days prior to Day 1.
✗	Are unable to take oral medications or has a medical condition which may impact gastrointestinal absorption.
✗	Have received an investigational medication or device or participated in a drug study within at least 28 days prior to Day 1 or participated in a clinical study with a monoclonal antibody or biologic medication within at least 180 days (6 months) prior to Day 1.
✗	Have a history of alcohol abuse, and/or have used any illicit drugs (e.g. cocaine, PCP, ecstasy etc.) within 6 months of Screening, or have had any past/current history of dependence on recreational drugs (e.g. marijuana) or used them within at least 28 days prior to Day 1. You must pass a drug test at your Screening visit, Day 1 and Day 8.
✗	Have donated more than 500mL of blood within 3 months prior to Day 1
✗	Have used any nicotine or nicotine containing products (including vaping products) within 14 days prior to Day 1.
✗	Have any pain conditions, including but not limited to chronic pain conditions, any current pain condition requiring pain relief during the study, any opioid use within the last 1 year prior to screening.
✗	Have any hand/arm/skin conditions including but not limited to eczema/psoriasis/dermatitis affecting hand or arm, peripheral vascular disease, sickle cell disease, skin grafts, injuries to the hand or arm, neurological or musculoskeletal conditions affecting hand or arm, and/or Raynaud's disease.
✗	Significant tattoo coverage on the hand/arm that will be utilised in the CPT.

If you think that any of the above applies to you, or you have one of the conditions described, please discuss these with your study doctor for more thorough assessment to see if you can take part in this study or not. Additionally, there are other criteria that you will need to meet in order to be eligible for the study, but the study doctor will discuss this with you at your screening visit. There may be reasons for excluding you that we may not able to divulge as it may impact the integrity of the study.

2.2 Study Instructions

It is important that you follow the instructions you are given and attend all scheduled clinic visits. It is also possible that the study doctor may schedule extra visits or tests for you, if considered necessary. In the event that an assessment is not performed on the day outlined within the Schedule of Activities within this document, the assessment may be performed at your next study visit.

You will be given a Participant Identification Card if you participate in this study, stating the name of the study and the study doctor's contact information. This card should be carried with you at all times so that you can contact the study doctor at any time and so you can show it to any other doctor, dentist, or pharmacist that you might visit while in this study.

At each visit, the study staff will ask you questions about your health and the medications you are currently taking. You should always report any changes in your health, unusual feelings, or symptoms to the study staff. It is also important that you do not start, stop, or make changes to any of the medications you are currently taking without first discussing this with your study doctor.

During your inpatient stay with us, we will provide you with all your meals. Meals play an important role in clinical trials due to their relationship with metabolism of the investigational medicine (the way that the drug is processed and broken down by the body). By signing this document, you are agreeing that you will be compliant with all meal requirements on this study. In certain cases, we are able to cater for dietary requirements, please discuss this with the study team before joining the study.

As the medication may cause short term cognitive impairment (as described in section 3.3 "Possible Risks and Disadvantages?"), you are asked not to operate any motor vehicles until the day after your dose. The study staff can organise transport for you home after you discharge on dosing days if you require it, at no cost to you.

Restrictions:

- You will not be able to smoke, vape or use any nicotine containing products for at least 14 days prior to Day 1 until your last study visit.
- You must not consume any caffeine or xanthine containing products (i.e., coffee, tea, chocolate, soda) for at least 48 hours prior to Day 1 until your last study visit.
- You must not consume any alcohol for at least 48 hours prior to Day 1 until you last study visit.
- You must not consume any food or drink containing grapefruit or Seville oranges from at least 14 days prior to Day 1 until your last visit.
- You must be fasted (no food, only water) for at least 10 hours prior to each of your doses and for 2 hours after taking your dose on Days 1-5 and Days 16-20.
- You must refrain from strenuous exercise for at least 48 hours prior to Day 1 until your last study visit.
- You must not donate blood or plasma during the study.

You must not bring in prohibited items, including food, drinks, vapes,/cigarettes, alcohol and prohibited medication. By signing this consent form, you agree to have your bags checked at admission. Any prohibited items will be removed and returned to you on discharge from the unit.

3 WHAT ARE THE POSSIBLE BENEFITS, COSTS AND RISKS TO YOU PARTICIPATING?

3.1 Benefits

This study is not designed to provide you with any therapeutic benefits. The information from this study might help to develop better treatments in the future for acute and chronic pain.

3.2 Reimbursement and Costs

All tests required to be done for this study will be paid for by Latigo, and there will be no cost for you to participate in this study. You will still have to pay for the costs of your regular medical care that are not a part of this study.

You will be reimbursed the sum of $6,600 (before tax), following the final study visit. However, the timing of reimbursement is flexible and can be adjusted to suit your needs – please discuss this with study staff if you have any concerns regarding your reimbursement. **We are required to deduct withholding tax at the applicable rate you have declared in the IR330C form**. You will be responsible for any other tax obligations (e.g., ACC). If you are GST registered, it may be possible for you to submit a GST invoice. Contact paymentforms@nzcr.co.nz if you would like to discuss this further.

The payment will be made after you complete the study, to cover your time and inconvenience. If you are receiving a benefit or allowance, your usual payments may be affected. Your tax statement will state that you were paid from your dosing day through to your final study visit.

To be able to participate in the clinical study you must be eligible to work in NZ (e.g. as a NZ resident, NZ citizen, or with the appropriate work visa) for the entire duration of the study. If you are no longer eligible to work in NZ during the study, you will be withdrawn from the study and your reimbursement will be a pro-rata of the total amount.

You will be reimbursed for travel and parking (if you use personal transport) or you can use uber or taxi for your study visits, which can be arranged and paid for by NZCR if you live in the metropolitan area. Please discuss arranging study transport with the site study staff. If you live outside this area, we will discuss your travel costs individually. Full reimbursement requires completion of all visits according to study requirements. If you are withdrawn from the study for medical reasons, having received trial medication, you will receive reimbursement in full.

If you leave the study at your own choice or are released from the study for non-medical reasons, you will receive a partial reimbursement (a pro-rata reimbursement) according to how far you contributed to the study.

In order to meet dosing requirements, additional (reserve) participants may be admitted to the unit. If you are invited to attend the study as a reserve, you will be asked to admit to the unit on Day 1 until everyone is eligible (**day reserve**). If you are a reserve, and you are not required to be dosed, you will be reimbursed for your time and inconvenience (day reserve = $250).

If you complete the screening visit assessments and are found not eligible for the study, you will not receive any reimbursement.

3.3 Possible Risks and Disadvantages?

Medications often cause side effects. You may have none, some or all the effects listed below, and they may be mild, moderate, or severe. There may also be unknown side effects from taking LTG-305 alone or with other drugs you may be taking. If you have any of these side effects, or are worried about them, talk with your study doctor. Your study doctor will also be looking out for side effects.

What are the Risks or Side Effects of LTG-305?

This is the first time that LTG-305 is being tested in humans.

40 participants who received single doses of placebo or LTG-305 ranging from 40 mg to 720 mg has been performed already in the study. However, as this was a blinded study we do not know who received LTG-305 vs who received placebo. The following mild side effects that were noted included:

- Common cold in 3 participants

- Headache in 2 participants
- 1 participant each: dizziness, near-fainting, tingling sensation, acne, itching rectal bleeding, vaginal bleeding and sore throat

As 40 participants is a small number, the human experience available to identify all the risks of LTG-305 is still considered limited.

Animal studies have been done with LTG-305 to try and predict what type of side effects might occur in people. However, animal studies do not always predict human responses to drugs. Among side effects that could occur, some could be life-threatening. The doses planned for this study in people are much lower than any of the doses given to animals. The study in people will begin with low doses of LTG-305 that will be gradually increased if the drug is well tolerated.

When LTG-305 was given to animals at doses 120 times higher than the equivalent starting dose planned for people, no adverse (harmful) side effects were seen. The effects seen in animals at this dose were considered to be mild and reversible, and included small changes in blood tests (red and white blood cells, cholesterol, blood fats, and clotting factors), liver, heart rate, ECG values and blood pressure.

As with other drugs, LTG-305 may cause an immune reaction or allergic reaction. Symptoms may include rash, flushing, itching, sneezing or runny nose, abdominal pain, diarrhea, swelling of face, tongue or throat, dizziness, lightheaded or fainting, trouble breathing, irregular or racing heart rate, and seizures. If you have a skin reaction or other adverse event, the study doctor may take a photograph to document the event.
Life-threatening or fatal allergic reactions can occur. However, severe reactions are very rare. If you have a severe allergic reaction after leaving the study site, seek treatment immediately by dialing 111 or going to an Emergency Department.

What are the Risks or Side Effects of Study Procedures?

Blood Sample Collection & Cannulas:
Risks include bruises, swelling with itching, and slight bleeding. The area may become inflamed. In rare cases, it may result in a blood clot, an infection or nerve damage. As needles can cause pain, you may feel light-headed or faint.

ECG Tests:
Sometimes the sticky pads used to attach the ECG leads can cause skin irritation (redness / itchiness).

Physical Examination:
During this examination you may be asked to remove some items of clothing so a full examination can be done. You can request a chaperone to be with you at the time of the physical examination, please ask one of our research nurses.

Cold Pressor Test (CPT):
The cold pressor test can cause pain of mild to moderate intensity. You can remove your arm from the water at any time and any discomfort dissipates quickly after removal of your arm from the water bath.

3.4 Contraception

Reproductive Risks for Sperm in Sexually Active Participants

The effects of LTG-305 if passed on through semen are unknown, but there is a risk it may cause birth defects or foetal deaths. **You are responsible for informing your sexual partner of these possible risks.**

If you are sexually active and have any partner who is of child-bearing potential (meaning a partner who may become pregnant) it is very important that you use contraception during this study. You and your partner must use one of the methods of contraception listed below, from your first dose of the study medication through until at least 3 months after your last dose of the study medication:

A highly effective method (less than 1 pregnancy per 100 people using the method for one year) e.g.

- Implant contraceptive (e.g., Jadelle®)
- Intra-uterine device (IUD) containing either copper or levonorgestrel (e.g., Mirena®)
- Sterilization (e.g., vasectomy, bilateral tubal ligation ('clipping or tying tubes') or hysterectomy)

OR an effective method (5 - 10 pregnancies per 100 people using the method for one year) e.g.

- Injectable contraceptive (e.g., Depo Provera)
- Oral Contraceptive Pill (combined hormonal contraceptive pill or progestogen-only 'mini-pill')

You must also use a male condom if you have a biologically female partner (**this includes a biologically female partner who is postmenopausal, permanently sterile or already pregnant**), from your first dose of investigational medicine through until 3 months after your dose.

Please note that barrier methods alone are not highly effective methods of contraception.

If a pregnancy occurs, you must report this to the study doctor as soon as possible. Your partner will be asked to give consent for their information and their infant's information to be collected for monitoring purposes.

You must also agree not to donate sperm, from admission (Day 1) until at least 3 months after your last dose of the study medication.

4 WHAT WOULD HAPPEN IF YOU WERE INJURED IN THE STUDY?

As this research project is for the principal benefit of its commercial sponsor Latigo, if you are injured as a result of taking part in this study you **won't** be eligible for compensation from Accident Compensation Corporation (ACC).

However, Latigo has satisfied the Northern A Health and Disability Ethics Committee that approved this study that it has up-to-date insurance for providing participants with compensation if they are injured as a result of taking part in this study.

New Zealand ethical guidelines for intervention studies require compensation for injury to be at least ACC equivalent. Compensation should be appropriate to the nature, severity and persistence of your injury and should be no less than would be awarded for similar injuries by New Zealand's ACC scheme.

Some sponsors voluntarily commit to providing compensation in accordance with guidelines that they have agreed between themselves, called the Medicines New Zealand Guidelines (Industry Guidelines). These are often referred to for information on compensation for commercial clinical trials. There are some important points to know about the Industry Guidelines:

- On their own they are not legally enforceable and may not provide ACC equivalent compensation.
- There are limitations on when compensation is available, for example compensation may be available for more serious, enduring injuries, and not for temporary pain or discomfort or less serious or curable complaints.
- Unlike ACC, the guidelines do not provide compensation on a no-fault basis:
  - The Sponsor may not accept the compensation claim if:
  - Your injury was caused by the investigators, or;
  - There was a deviation from the proposed research plan, or;
  - Your injury was caused solely by you.

An initial decision whether to compensate you would be made the by the sponsor and/or its insurers.

If they decide not to compensate you, you may be able to take action through the Courts for compensation, but it could be expensive and lengthy, and you might require legal representation. You would need to be able to show that your injury was caused by participation in the trial.

You are strongly advised to read the Industry Guidelines and ask questions if you are unsure about what they mean for you:

If you have private health or life insurance, you may wish to check with your insurer that taking part in this study won't affect your cover.

5 WHAT WILL HAPPEN TO MY TEST SAMPLES?

Blood and urine samples will be collected throughout the study. These samples will be used for various tests. Some of the samples will be used for regular routine blood counts and blood chemistry, to monitor your general health. All these routine samples will be sent to Canterbury Health Laboratories for testing and destroyed after 3 months by internationally accepted means.

All other study samples (pharmacokinetics, etc) will be sent to a central laboratory, Aligex Biolabs in Adelaide, Australia for testing and destroyed within 15 years by internationally accepted means.

The maximum amount of blood collected from each participant during the study will be up to approximately 160 mL. Additional safety samples may be taken if needed. For comparison, a standard blood donation at a blood collection centre, is about 470 mL. Samples collected by NZCR will be identified by your study number, year of birth, initials, and sex, to allow study doctors to quickly respond to any abnormal results. Before the results of these tests are sent to the Sponsor, your identifiable information will be removed and replaced with a code.

The proposed blood tests include a screening test for HIV and for viral Hepatitis B and C, as well as a COVID-19 test. Signing the consent form means that you agree to have this testing performed. It is important to understand that a positive screening test does not necessarily mean you have the disease. Should you receive a positive screening result for HIV or either Hepatitis B or C, then the study doctors will provide initial counselling and medical advice and will assist in arranging any follow up tests that you require. HIV, Acute (newly diagnosed) Hepatitis B/C, and COVID-19 are all 'notifiable diseases', which means that it is required by law to notify government health authorities of any new cases.

5.1 Are There Any Cultural Considerations?

You may hold beliefs about sacred and shared values about your tissue samples and/or data originating from this tissue. The cultural issues associated with sending your tissue samples and data overseas and/or storing your tissue and data should be discussed with your family/whānau as appropriate. If you wish to know more about the study, we can arrange for an Investigator to come and talk to you and your whānau. NZCR are committed to preserving and upholding mauri through karakia and the handling of samples. You are invited to perform a karakia at the time of sample collection, please inform staff if you would like any assistance. However, due to your samples being sent to countries outside of New Zealand, a karakia will not be able to be performed at the time of your sample disposal.

Personal and health information is a tāonga and will be treated accordingly. The following data sovereignty principles are in place to ensure that the data generated from this research is protected and may benefit Māori now and into the future. The principles included are whakapapa, whanaungatanga, rangatiratanga, kotahitanga, manaakitanga and kaitiakitanga. Clinical trials are often driven by Sponsor companies overseas and involve very few Māori as participants.

Consideration of Tikanga and Tiriti obligations are highly valued at NZCR, whereby staff attend Tiriti and Tikanga workshops to acknowledge and understand Māori cultural values and principles. NZCR also maintain contact with the Office of the Chief Advisor Tikanga across Te Whatu Ora Waitemata and Te Toka Tumai Auckland and Te Puna Oranga Māori Research Review Committee for consultation of Māori

health services. NZCR also have open dialogue with the chair of the Māori Governance Rōpu for Ira Tātai Whakaheke.

Before deciding whether to participate in this study or not, it may be appropriate to discuss your participation with your whanau/family/Kaumatua/hapu/Iwi and consider both the potential risks and benefits that may be involved. If you need cultural support, please let us know and we will arrange this for you. For additional cultural support or tikanga advice, please contact your local Māori support contact listed at the end of this document.

6 WHAT ARE THE RIGHTS OF PARTICIPANTS IN THE STUDY?

6.1 Participation is Voluntary

Participation in any research project is voluntary. If you do not wish to take part, you do not have to. If you decide to take part and later change your mind, you are free to withdraw from the project at any stage. This will not affect, your relationship with NZCR.

If you do decide to take part, you will be given this Participant Information and Consent Form to sign and you will be given a copy to keep.

6.2 New Information

Sometimes during the course of a research project, new information becomes available about the medication that is being studied. If this happens, your study doctor will tell you about it and discuss with you whether you want to continue in the research project. If you decide to withdraw, your study doctor will make arrangements for your regular health care to continue. If you decide to continue in the research project, you may be asked to sign an updated consent form.

Also, on receiving new information, your study doctor might consider it to be in your best interests to withdraw you from the research project. If this happens, they will explain the reasons and arrange for your regular health care to continue.

6.3 Privacy and Confidentiality and Right to Access Information Collected During the Study

What will Happen to my Information?

During this study, the study doctors, researchers, nurses and other NZCR staff will record information about you and your study participation. This includes the results of any study assessments. Information such as your name, sex, age, race/ethnicity, address and phone number will be on the demographics page for the study so we can identify you correctly at visits and contact you. This information may be used to obtain health records (detailed below) but is not supplied to anyone overseas.

If needed, **information from your hospital records and your usual doctor (GP) may also be collected**, and your GP will be notified about your participation in the study. You cannot take part in this study if you do not consent to the collection of this information.

Type of information	Where is it stored?	Who can access it?

Identifiable Information – *this information can be traced back to you*		
• Information collected from you • Laboratory results • Photographs of any skin reactions (if applicable)	• **Paper**: stored securely under restricted access at NZCR. Following study completion paper forms are transferred to a secure site and stored for 15 years, then destroyed • **Electronic**: stored on secure NZCR servers (in New Zealand and Australia)	• NZCR staff • Your GP / usual doctor • Local laboratory staff to process and report your screening and safety tests • Sponsor/CRO monitors to ensure the study is run properly and data is collected accurately • Representatives from the Sponsor if you make a compensation claim as a result of study-related injury. Identifiable information is required to assess your claim • Ethics committee, regulatory authorities, and sponsor/CRO representatives if the study or site is audited • Medical Officer of Health for positive test results for a notifiable disease (i.e., COVID-19, Hepatitis B/C, HIV) • The study doctor may share your information with other people, in the rare event of a serious threat to public health or safety, or to the life or health of you or another person OR if the information is required in certain legal situations
De-identified (coded) Information – *this information is only labelled with your unique study ID*		
• Study assessment results are uploaded into the study database to be analysed	• **Electronic**: will be stored-on a secure platform and will be retained indefinitely. Storage will comply with local and/or international data security guidelines.	• The Sponsor, for the purposes of this study. • People and companies working with or for the Sponsor, for the purposes of this study. • Regulatory or other governmental agencies worldwide.
Anonymised Information – *this information cannot be traced back to you (code removed)*		
• All de-identified information for which the code has been removed	• **Electronic**: stored on a secure sponsor-managed database	• Access not restricted

Future Research Using Your Information

Your coded information may be used for future research related to LTG-305 or acute and chronic pain.

This future research may be conducted overseas. You will not be told when future research is undertaken using your information. Your information may be shared widely with other researchers or companies. Your information may also be added to information from other studies, to form much larger sets of data.

You will not get reports or other information about any research that is done using your information.

Your information may be used indefinitely for future research unless you withdraw your consent. However, it may be extremely difficult or impossible to access your information or withdraw consent for its use once your information has been shared for future research.

Security and Storage of Your Information
During the study, your information will be stored on paper forms at NZCR and electronically on secure servers. When the study has finished, paper forms will be transferred to a secure site and stored for at least 15 years, then destroyed. De-identified information in electronic form will remain on a secure platform and will be retained indefinitely. Storage will comply with local and/or international data security guidelines.

Risks
Although efforts will be made to protect your privacy, absolute confidentiality of your information cannot be guaranteed. Even with coded and anonymised information, there is no guarantee that you cannot be identified. While the risk is currently very small, the chance that someone might access and misuse your information (for example, by making it harder for you to get or keep a job or health insurance) might increase in the future as people find new ways of tracing information.

Your coded information is being sent overseas. Other countries may have lower levels of data protection than New Zealand. There may be no New Zealand representation on overseas organisations which make decisions about the use of your information. There is a risk that overseas researchers may work with information in a way that is not culturally appropriate for New Zealanders.

Rights to Access Your Information and Results
You have the right to request access to your information held by the research team. You also have the right to request that any information you disagree with is corrected.

Please ask if you would like to access your screening and safety tests during the study. You may access other study-specific information before the study is over, but this could result in you being withdrawn from the study to protect the study's scientific integrity.

If you have any questions about the collection and use of information about you, you should ask a study doctor.

7 WHAT WILL HAPPEN AFTER THE STUDY ENDS, OR IF I WANT TO PULL OUT?

7.1 If You Decide to Withdraw

You may withdraw your consent for the collection and use of your information at any time, by informing your Study Doctor. Please notify a member of the research team before you withdraw. This notice will allow that person or the research supervisor to discuss any health risks or special requirements linked to withdrawing, such as follow up visits.

If you withdraw your consent, your study participation will end, and the study team will stop collecting information from you. Information collected up until your withdrawal from the study will continue to be used and included in the study. This is to protect the quality of the study.

7.2 Why the Study Might be Unexpectedly Stopped

This research project may be stopped unexpectedly for a variety of reasons. These may include reasons such as:

- Unacceptable side effects and safety issues
- Poor recruitment
- Poor study conduct

7.3 Results

When the research project ends the study data must be analysed, so the results of the study may not be available until about a year after the research finishes. The study doctors and/or Sponsor may decide to discuss or publish the results of the study. This may include publication in journals, presentation at conferences or other professional forums. In any publication, information will be provided in such a way that you cannot be identified. Results of the study will be provided to you. If you do not wish to receive a summary of the study results when they become available, then please inform NZCR staff.

8 WHO DO I CONTACT FOR MORE INFORMATION OR IF I HAVE CONCERNS?

If you have any questions, concerns, or complaints about the study at any stage, you can contact:

Dr Christopher Wynne, Principal Investigator
Phone: 0800 862 278
Email: petal.christchurch@nzcr.co.nz

If you want to talk to someone who isn't involved with the study, you can contact an independent health and disability advocate on:

Phone: 0800 555 050
Fax: 0800 2 SUPPORT (0800 2787 7678)
Email: advocacy@advocacy.org.nz
Website: https://www.advocacy.org.nz/

Māori cultural support is available through:

Christchurch:

Dr. Matea Gillies
Mobile: 027 4105 025
Email: gillies-lamb@xtra.co.nz

Wellington:

Glen Alexander
Mobile: 022 4993 099
Email: glen.alexander1968@gmail.com

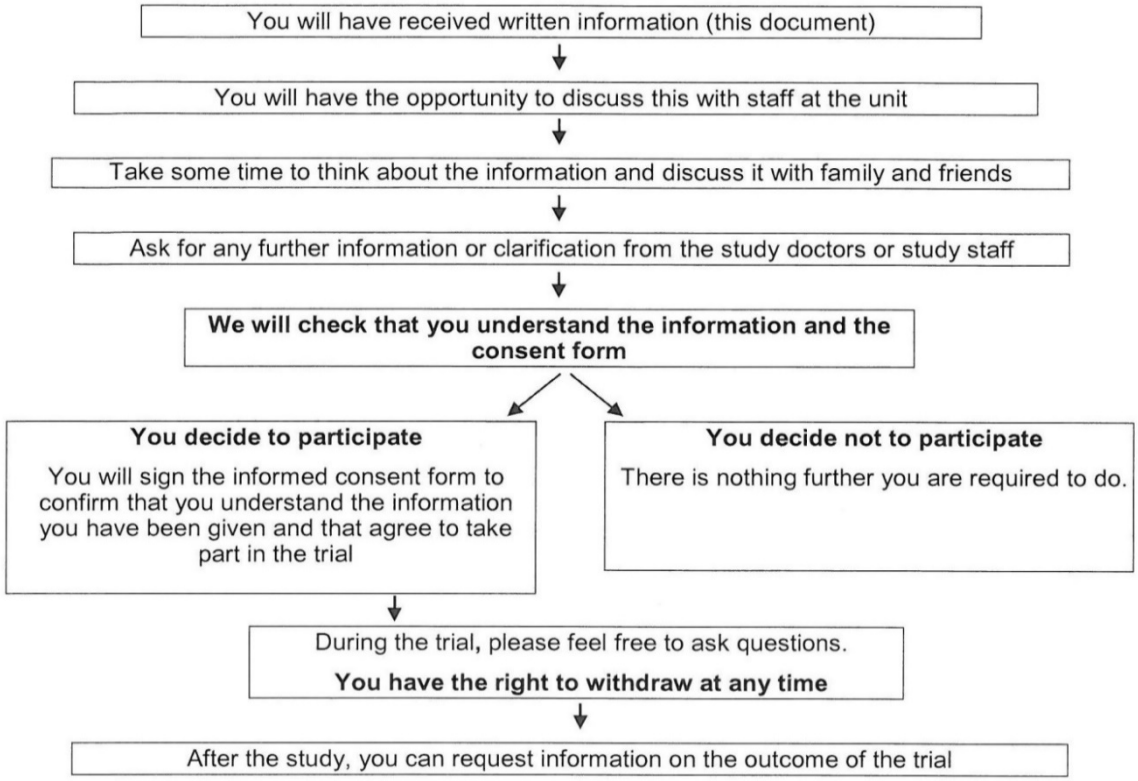
You can also contact the health and disability ethics committee (HDEC) that approved this study on:

Email: hdecs@health.govt.nz
Phone: 0800 400 569 (Ministry of Health general enquiries)

9 WHAT ABOUT ANY OTHER QUESTIONS I MAY HAVE?

10 DO I HAVE TO DECIDE STRAIGHT AWAY?

No, you do not have to decide straight away. You should take some time to consider whether or not to participate, we will be in touch in a week or so to discuss your decision**.** The following steps are useful in helping you reach a decision.



CONSENT FORM
(MULTIPLE DOSING - COLD PRESSOR TEST)

Short Title:	Phase 1 Single and Multiple Ascending Dose Study of LTG-305 in Healthy Participants
Protocol Number:	LTG-305-001
Principal Investigator:	Dr Christopher Wynne

***Please let study staff know if you require an interpreter*.**

Declaration by participant:

- I have read the Participant Information Sheet or have had it read to me in a language I understand, and I fully comprehend what it says.
- I have been given sufficient time to consider whether or not to participate in this study.
- I have had the opportunity to use a legal representative, whanau/ family support or a friend to help me ask questions and understand the study.
- I am satisfied with the answers I have been given regarding the study and I have a copy of this consent form and information sheet.
- I understand that taking part in this study is voluntary (my choice) and that I may withdraw from the study at any time without this affecting my medical care.
- I consent to the research staff collecting and processing my information, including information about my health (including information collected from my GP and other Health Providers).
- If I decide to withdraw from the study, I agree that the information collected about me up to the point when I withdraw may continue to be processed.
- I understand that there may be risks associated with the medication in the event of myself or my partner becoming pregnant. I undertake to inform my partner of the risks and to take responsibility for the prevention of pregnancy.
- I agree to my tissue samples being sent overseas, and I am aware that these samples will be disposed of using established guidelines for discarding biohazard waste.
- I agree to an approved parties including Sponsor or CRO representatives for monitoring and auditing, auditor appointed by the New Zealand Health and Disability Ethic Committees, or any relevant regulatory authority or their approved representative reviewing my relevant medical records for the sole purpose of checking the accuracy of the information recorded for the study.
- I understand that my participation in this study is confidential and that no material, which could identify me personally, will be used in any reports on this study.
- I understand the compensation provisions in case of injury during the study.
- I know who to contact if I have any questions about the study in general.
- I understand my responsibilities as a study participant.
- I understand that I will receive a summary of the study results and if I do not wish to receive this, I will inform site staff.
- I consent to my GP or current provider being informed about my participation in the study and of any significant abnormal results obtained during the study.

Statement by Participant I hereby consent to take part in this study. I understand that I will receive a signed copy of this consent form for my records.

_____ (full name)

_____ (signature)

__ __ / __ __ __ / __ __ __ __ (Date DD/MMM/YYYY) Time:_____

Statement by Consenter (Investigator/designee) I have discussed this study with the above-named participant. The participant appeared to fully understand the information provided about the study.

_____ (full name)

_____ (signature)

_____ (project role)

__ __ / __ __ __ / __ __ __ __ (Date DD/MMM/YYYY) Time: _____