PARTICIPANT INFORMATION SHEET AND CONSENT FORM
(MAD: Multiple Ascending Dose)

Short Title:	Phase 1 Single and Multiple Ascending Dose Study of LTG-001 in Healthy Participants
Protocol Number:	LTG-001-001
Sponsor:	Latigo Biotherapeutics, Inc. 1300 Rancho Conejo Boulevard, Suite 305 Thousand Oaks, California 91362 USA
Principal Investigator:	Dr Christopher Wynne
Institution Address:	Main unit: 264 Antigua Street, Christchurch, New Zealand Outpatient unit: Level 4 / 108 The Terrace, Wellington Central, Wellington 6011, New Zealand
Phone Number:	0800 862 278
Ethics Number:	2023 FULL 18297

This is the first time that LTG-001 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. This study will test an experimental drug, named LTG-001, that may potentially be used for the treatment of acute and chronic pain. LTG-001 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 the Multiple Ascending Dose (MAD) part of the study. This Participant Information Sheet 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 the document.

1 WHY ARE WE DOING THE STUDY?

1.1 Purpose

LTG-001 is being developed for the treatment of acute (short-term) and chronic (long-term) pain. One in five New Zealanders live with persistent pain, making it hard to sleep, work and enjoy life. Current pain therapies are limited and may increase risk of abuse of dependence. There is a large unmet need for new, more effective pain therapies to be available to people who need them.

LTG-001 works by inhibiting (blocking) a certain pathway in the cells which control certain pain sensing neurons. LTG-001 is a non-opioid, non-NSAID (non-steroidal anti-inflammatory) and non-narcotic based pain-relief. It is hoped that, by blocking this pathway in the cells, LTG-001 may be an effective treatment for acute or chronic pain while reducing the likelihood for abuse and dependence.

This study will investigate the effects of LTG-001 in healthy participants. You are being asked to take part in the MAD part of the study. Other parts of the study include investigating LTG-001 as a single ascending dose (SAD), comparing LTG-001 as a suspension to a tablet (Relative Bioavailability), LTG-001 given with or without food (Food Effect), and LTG-001 to assess pain tolerance (Cold Pressor Test). These other study parts have been completed.

The purpose of the MAD part of the study is to:

- Evaluate how safe and well tolerated LTG-001 is, in healthy participants.
- Measure levels of LTG-001 in the blood and urine over time, following multiple doses.

1.2 Study Design

Approximately 164 healthy participants will take part in this study, approximately 40 of those will take part in the MAD part. The study requires a Screening visit to determine eligibility, a 12-night stay at the New Zealand Clinical Research (NZCR) Christchurch research unit, and 1 scheduled follow up visit.

This is a randomised, blinded, placebo-controlled study:

Randomised means that the study medication you take (LTG-001 or placebo) will be assigned randomly (by chance).

Blinded means that neither you nor your study doctor will know whether you will be receiving LTG-001 or placebo. In an emergency, the study doctor can find out what you are receiving.

Placebo is a substance that looks like LTG-001 but contains no active medication.

5 dose groups (cohorts) are planned for the MAD part of the study. The group you are assigned to will depend on when you join the study. Details for the dosing groups are as follows:

Cohort	Dose of LTG-001 or Placebo	Frequency
1	75 mg	Two doses per day from Day 1 to Day 9, and morning dose on Day 10.
2	150 mg	
3	300 mg	
4	600 mg	One dose per day from Day 1 to Day 10
5	450 mg	Two doses per day from Day 1 to Day 9, and morning dose on Day 10.

Every person in the MAD part of the study will receive either 19 doses (cohorts 1, 2, 3 and 5) or 10 doses (cohort 4) of LTG-001 or placebo. If you participate in cohorts 1, 2, 3 or 5 you will receive two doses per day from Day 1 to Day 9 (one in the morning and one in the evening), and one dose on Day 10 (morning only). If you participate in cohort 4 you will receive one dose per day from Day 1 to 10, each morning. The dose will be given as a tablet(s), and will be given by mouth, with a glass of water. You will have to take several tablets to make up your dose of LTG-001.

In each dose group, 6 people will receive LTG-001 and 2 will receive placebo. Whether you receive active study drug or placebo will be assigned randomly (by chance). You will have a 6 out of 8 (75%) chance of receiving LTG-001.

Dose groups will be enrolled in order. You will be told which dose group you will be in. You will also be told if any changes are made to the planned dose for your group as these dosing levels may be adjusted based on the SAD and Relative Bioavailability parts of the study.

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” or “Sponsor”) and locally sponsored in New Zealand by PPD, part of Thermo Fisher Scientific, a Contract Research Organisation (CRO) which helps conduct and monitor the study in New Zealand.

By taking part in this research study, 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.

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 Central 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 43 days, including a screening, dosing, assessment, 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-001 (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.

2.1 Tests and Procedures

Documentation of Medical History:
At your Screening visit and during the study, the doctor will ask you questions about your health, medication history and social history (e.g. smoking history, alcohol use). The doctors will also ask demographic questions and record your details.

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) and Holter Monitoring:

- An ECG measures the electrical activity of your heart, using 12 wires attached to your chest and limbs with sticky pads. On Day 1 and Day 10, you will have several ECG measurements taken.
- You will wear a Holter monitor, a machine that continuously records the heart rhythms, starting approx. 1 hour before you receive study drug and for 48 hours after you receive the study drug on Days 1 and 10. You will carry the Holter monitor in a pocket or pouch worn around your neck or waist. You will not be able to shower during this time.

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

Blood and Urine Samples:
At clinic visits, blood samples are taken by direct vein puncture. On the day you receive your study drug dose, 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 Day 1 and Day 10, 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 check whether you may be pregnant (for people of childbearing potential only) or to confirm post-menopausal status (for people who are post-menopausal)
- 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-001 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:
At your Screening visit and the day you check-in to the clinic (Day -1), you will have a rapid-antigen test (RAT) done to confirm that you do not have a current COVID-19 infection. The test will be done by taking a swab up your nostril. You may have COVID-19 testing done at other times throughout the study, based on NZCR site policy. You will be told if or when you will need COVID-19 testing done at other times. It is acknowledged that the head is tapu by Māori. Please let study staff know if you have any cultural concerns regarding the nasal swabbing.

Study Schedule

Period	Screening	Dosing												Follow-Up Visit
Study Day	**-28 to -2**	**-1**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**17**
Admission to the unit		X													
Discharge from the unit														X	
Clinic Visit	X	Clinic overnight stay (12-nights)													X
Physical Exam[1]	X	X												X	
Vital Signs	X	X	X	X	X	X	X	X	X	X	X	X		X	
ECG[2]	X	X	X	X	X	X	X	X	X	X	X	X		X	
Holter Monitoring[3]			X	X	X							X	X	X	
BMI (Height & Weight)[4]	X	X												X	
Dose of LTG-001 or placebo[5]			X	X	X	X	X	X	X	X	X	X			
Blood Sampling[2]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

[1] A full physical examination is done at Screening, a symptom-directed physical exam is done at all other time points.
[2] ECGs and blood samples will be done/taken several times on Day 1 and Day 10
[3] You will wear the Holter monitor continuously from 1 hour prior to dosing until 48-hours after your dose on Day 1 and Day 10
[4] Height is only taken at Screening.
[5] Two doses per day (one dose on day 10) will be given in cohorts 1, 2 ,3 and 5, one dose per day will be given in cohort 4.

Urine Testing	X	X	X						X			X[6]		X	
COVID-19 Testing	X	X													
Urine Drug Test and Alcohol Breath Test	X	X													

[6] You will be asked to provide a urine sample prior to dosing and in addition urine will be collected for 12 hours (cohorts 1, 2, 3 and 5) or 24 hours (cohort 4) after dosing on Day 10.

2.2 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 aged 18 – 55 years (inclusive) at the time of signing the informed consent form.
✓	Have a BMI (Body Mass Index) between 18.0 kg/m^2 – 32.0 kg/m^2
✓	Be in good health

You cannot take part in this study if you:	
✗	Are pregnant or breastfeeding
✗	Have a history of a significant medical problem, mental health problem or severe allergy.
✗	Have taken any prescription medication (excluding contraceptives) 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 to 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 and Admission on Day -1.
✗	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.

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.

2.3 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.

When you are an inpatient with us, we will provide you with all of your meals. Meals play an important role in clinical trials due to their relationship with metabolism of the study drug (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.

Restrictions:

- You will not be able to smoke, vape or use any nicotine containing products for at least 14 days prior to Day 1, and during the study.
- 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, and during the study.
- You must not consume any alcohol for at least 48 hours prior to Day 1, and during the study.
- You must not consume any food or drink containing grapefruit or Seville oranges from at least 14 days prior to admission (Day -1), and during the study.
- You must be fasted (no food, only water) for at least 10 hours prior to your dosing and for 4 hours after taking the dose on your morning dose on Day 1 and Day 10. For morning doses on all other days, and for all evening doses, you must be fasted for 2 hours prior to your dosing and 1 hour after taking the dose.
- You must refrain from strenuous exercise for at least 48 hours prior to Day 1, and during the study.
- You must not donate blood or plasma during the study.

At admission, you will have your bag checked for prohibited items (e.g., drinks or foods). Any prohibited items will be removed and returned to you on discharge from the unit.

3 WHAT ARE THE POSSIBLE BENEFITS 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 be reimbursed the sum of $6,600 (before tax) following the final study visit**. 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 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 for your study visits if you live in the metropolitan area. 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 of 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 either; admit to the unit on Day -1 just for the day (**day reserve**) or admit to the unit on Day -1 and stay overnight (**night 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 = $150 or night reserve = $350).

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 or some side effects, and they may be mild, moderate, or severe. There may also be unknown side effects from taking LTG-001. 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-001?

This is the first time that LTG-001 is being tested in humans and as such there is no human experience available to identify all of the risks of LTG-001.

Animal studies have been done with LTG-001 to try and predict what type of side effects might occur in people. However, animal studies do not always predict human responses to drugs. At high doses in animals, there were some changes in blood tests, which included amounts of red and white blood cells, cholesterol, blood fats, blood clotting factors, and liver tests. Some changes in heart function and blood pressure were also noted. The doses planned for this study in people are much lower than any of the doses given to animals. There were no adverse (harmful) side effects seen in animals when LTG-001 was given at doses 200-times higher than the planned starting dose in people. The study has a limit to prevent you from being exposed to a level of LTG-001 that was associated with adverse (harmful) side effects in animals.

The study will begin with low doses of LTG-001 that will be gradually increased if the drug is well tolerated.

As mentioned above, animal studies do not always predict human response to drugs. LTG-001 may cause side effects, some could be life-threatening.

In other studies with medications that work in a similar way to LTG-001, participants experienced no serious adverse events related to the drug and the medication was well-tolerated. All other side effects were considered mild to moderate. The most common side effects were headaches, nausea, constipation, dizziness, and vomiting.

As an example, like other drugs, LTG-001 may cause an 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. These reactions can be life-threatening / fatal.

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 and Holter Monitoring:
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.

COVID-19

There is the potential that while you are on the study you will want to receive the COVID-19 vaccination and/or booster vaccination if you have not received this already. You cannot have the COVID-19 vaccine within 14 days prior to Day 1 and until you complete the study.

Additionally, COVID-19 testing will be done during the study if required. You will be informed when this will be performed.

3.4 Contraception

Reproductive Risks for Sexually Active Participants of Child-Bearing Potential

The effects of LTG-001 in pregnancy and breastfeeding are unknown, but there is a risk it may cause birth defects or foetal deaths, and/or be passed on in breast milk. If you are pregnant or breastfeeding, you cannot take part in this study.

If you are sexually active and of child-bearing potential (able to become pregnant), it is very important that you do not become pregnant during this study. A person of child-bearing potential is any pre-menopausal person who may become pregnant. If you are unsure if this applies to you, please check with the study doctor before you start the study medication. **You must use one of the methods of contraception listed below**, from your first dose of the study drug until your final study visit:

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®)
- Sterilisation (e.g., bilateral tubal ligation (‘clipping or tying tubes’), or vasectomy if performed within 6 months and confirmed if successful of male partner)

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 pill or progestogen-only ‘mini-pill’ which inhibits ovulation)

Your partner must also use a male condom from your first dose of study drug through until your final study visit.

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

If you are unsure which method of birth control you are using (or want to start using) and whether it is acceptable for this study, please ask the study doctor for more information.

You must also agree to not donate eggs, from admission (Day -1) until your final study visit.

If you do become pregnant during the study, you must tell the study doctor as soon as possible. If you do become pregnant you will be asked to sign a separate consent form, to allow the Sponsor to collect information about your pregnancy and the outcome of your pregnancy.

Reproductive Risks for Sperm in Sexually Active Participants

The effects of LTG-001 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 a male condom, from your first dose of the study drug until at least 3 months after your last dose of the study drug.

You/your partner must also use one of the contraception options listed above for participants of child-bearing potential, from your first dose of study drug through until at least 3 months after your last 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 drug.

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

As this research study 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 Central 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 310 mL. 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 a member of the Māori advisory board for Pegasus health spanning Christchurch and Selwyn. NZCR also have open dialogue with the Director of Māori Health Research for Te Whatu Ora Waitematā and Te Toka Tumai Auckland.

If you need cultural support, please let us know and we will arrange this for you. For additional cultural support or tikanga advise, 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, he/ she 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. Your name, 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 • Study questionnaires • Photographs of any skin reactions (if required)	• **Paper**: stored securely under restricted access at NZCR. Following study completion paper forms are transferred to a secure site and stored for 25 years, then destroyed • **Electronic**: stored on secure NZCR servers	• NZCR staff • Your GP / usual doctor • Local laboratory staff to process and report your screening and safety tests • Sponsor 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 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) • 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 • De-identified photographs, if required (as above)	• **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-001 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. If you have already dosed in the study, your study doctor will request you to attend a early discontinuation safety follow up visit.

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: leaf@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:

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

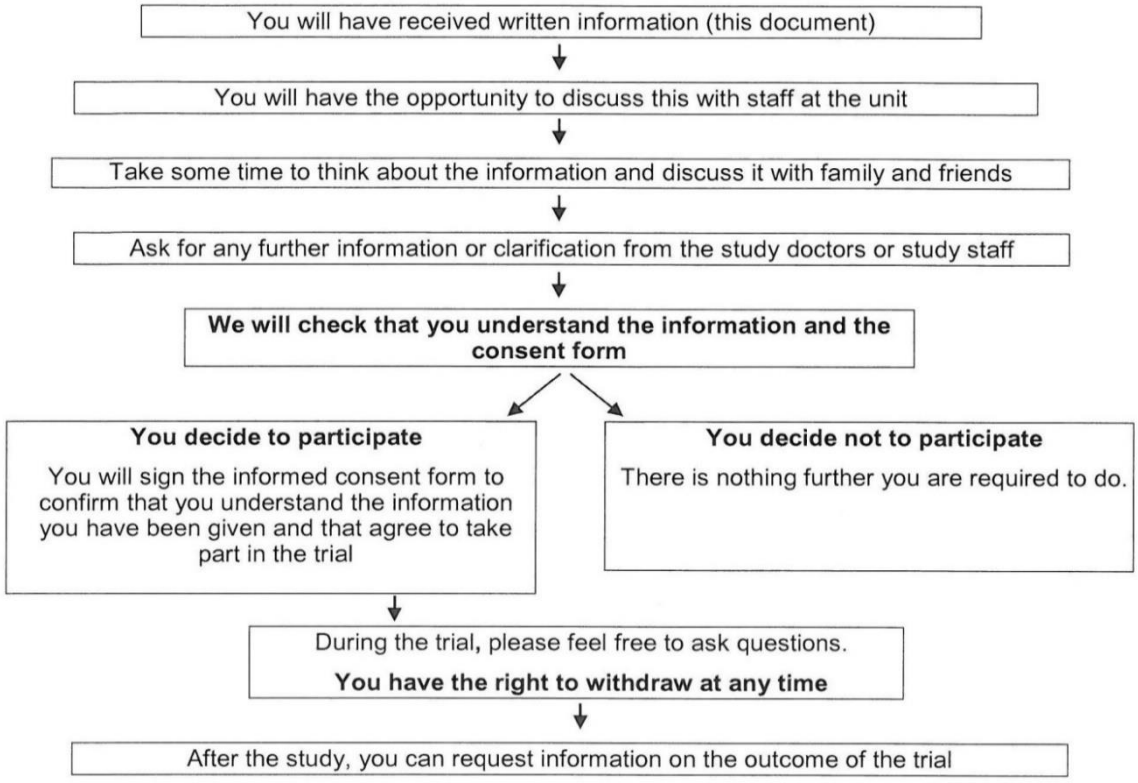
You can also contact the health and disability ethics committee (HDEC) that approved this study on:

Email: hdecs@health.govt.nz

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
(MAD: MULTIPLE ASCENDING DOSE)

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

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

Declaration by participant:

- I have read or have had read to me in my first language, and I understand the Participant Information Sheet.
- 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 study 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 blood and/or urine 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 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: _____