PARTICIPANT INFORMATION SHEET AND CONSENT FORM

Short Title:	A Study to Evaluate L608 in Healthy Participants
Protocol Number:	PBI-L608-B12
Sponsor:	Pharmosa Biopharm Inc. 3F.-3, No.66, Sanchong Rd., Nangang Dist., Taipei City, Taiwan
Principal Investigator:	Dr. Chris Wynne
Institution Address:	New Zealand Clinical Research (NZCR) Christchurch: Main Building: 264 Antigua Street, Christchurch, New Zealand Satellite Site: Level 4/108 The Terrace, Wellington 6011, New Zealand
Phone Number:	Christchurch: 0800 862 278
Ethics Number:	**2024 FULL 20305**

This is the second time that L608 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 L608, that may potentially be used for the treatment of pulmonary arterial hypertension. L608 is an investigational product because it has not been approved by the New Zealand MedSafe or other drug regulatory authorities.

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 this document including the consent form.

1 WHY ARE WE DOING THE STUDY?

1.1 Purpose

L608 is being developed for the treatment of pulmonary arterial hypertension (PAH). PAH is a rare and progressive (gets worse over time) disorder where individuals have high blood pressure that affects arteries (blood vessels) in the lungs and in the heart. This slows the blood flow through the lungs and causes high blood pressure in the lungs, which puts pressure on the heart. The extra pressure on the heart causes the heart muscle to become weak and fail.

The current standard treatment for PAH only remains in the body for a short period of time, which means patients have to inhale (breathe in) treatment every 2 hours whilst awake. This limits the effectiveness as people often aren't consistent with the treatment and it impacts their quality of life. There are also many unpleasant side effects. Around 15 to 50 people have PAH for each 1 million adults globally, in New Zealand there are currently 75 people accessing PAH treatments.

L608 is an investigational inhalation suspension that should lead to a slower release of current standard of care (Iloprost). Iloprost will be given through a PN102 nebuliser, which is an investigational inhaler device currently not approved for use in New Zealand. Iloprost causes smaller blood vessels to open to improve blood flow. It is hoped that, by slowing the release of the medication, the patients will have to inhale the drug less often. It is hoped that this will optimise the drug exposure over a longer period of time and reduce some of the side effects caused by the current standard of care (Iloprost). This may improve the quality of life for patients with PAH.

The purpose of this study is to:

- Evaluate how safe and well tolerated L608 is after a single dose in healthy participants.
- Measure levels of L608 in the blood over time, following a single dose.
- Measure pulmonary (lung) function in response to a single dose of L608.

1.2 Study Design

Approximately 56 healthy volunteers will take part in this study. The study requires a 3-night stay at the New Zealand Clinical research (NZCR) unit and 2 scheduled clinic visits.

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

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

Blinded means that neither you nor your study doctor will know whether you will be receiving L608 or placebo. In an emergency, the study doctor can find out what you are receiving.

Every person in the study will receive a single dose of L608 or placebo (a substance that looks like L608 but contains no active medication). Each dose will be given using a nebuliser, which is a device that will deliver L608 or placebo as a mist so it can be inhaled (breathed) into the lungs.

7 dose groups (cohorts) are planned for 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 L608 or Placebo	Frequency
1	0.02 mg	Single dose via inhalation
2	0.03 mg	
3	0.04 mg	
4	0.06 mg	
5	0.08 mg	
6	0.10 mg	
7	0.11 mg	

In each dose group, two people will be dosed first (one will receive L608 and one will receive placebo). The rest of the group will be dosed only if there are no safety concerns after 24 hours of monitoring. In the rest of each dose group, 5 people will receive L608 and 1 will receive placebo. Whether you receive active study drug or placebo will be assigned randomly (by chance). If you are one of the two people in the group receiving the dose first, you will have a 1 out of 2 (50%) chance of receiving L608. If you are being dosed with the rest of the group, you will have a 5 out of 6 (83%) chance of receiving L608.

Dose groups will be enrolled in order. You will be told which dose group you will be in, and if you will be receiving the drug first. You will also be told if any changes are made to the planned dose for your group.

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 Pharmosa Biopharm Inc. and locally sponsored in New Zealand by Novotech (New Zealand) Limited, a Contract Research Organisation (CRO) which help 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.

New Zealand Clinical Research (NZCR) will receive a payment from Pharmosa Biopharm Inc. 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 B** Ethics Committee.

A description of this clinical study will be available on http://www.ClinicalTrials.gov. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

2 WHAT WOULD YOUR PARTICIPATION INVOLVE?

Participation in this study will last up to approximately 6 weeks, including a screening, dosing, 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 dose of L608 (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

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.

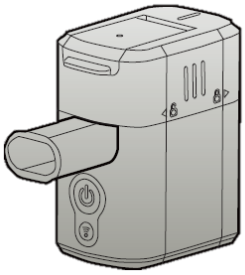
Vital Signs:
Vital signs include recordings of your pulse, blood pressure, oxygen saturation, breathing rate, and temperature.

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. Blood and urine samples will be collected:

- To monitor your safety (blood cells, clotting, chemistry, liver function, kidney function)
- To check whether you may be pregnant (for people of childbearing potential only)
- To confirm you are post-menopausal (for post-menopausal people only)
- To screen for recreational drugs such as cannabis, methamphetamine, and opiates
- To screen for specific infections (HIV, Hepatitis B and Hepatitis C)
- To measure the amount of L608 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.

Spirometry
Spirometry is a lung function test to assess how well your lungs work by measuring the amount and/or speed of air exhaled. You will be asked to blow into a device called a spirometer which measures how much air you can breathe out of your lungs. First, you breathe in fully and then seal your lips around the mouthpiece of the spirometer. You then blow out as fast and as far as you can until your lungs are empty. You will need to repeat this test a few times to ensure the measurements are accurate and consistent. You will be given time to recover between tests.



Inhaler use and training:
You will receive the medication through the PN102 nebuliser (an investigational inhaler device). At Screening, research staff will train you to be able to use the PN102 nebuliser.

Study Schedule

Period	Screening	In clinic Period				Follow-Up	
Study Day	**-28 to -2**	**-1**	**1**	**2**	**3**	**7**	**14 EOS [a]**
Questions about my health	X	X	X	X	X	X	X
Admission to the unit		X					
Discharge from the unit					X		
Physical Exam [b]	X	X			X	X	X
Vital Signs	X	X	X	X	X	X	X
ECG	X	X	X	X			X
BMI (Height & Weight)	X						
Administration training (inhalation device)		X					
Dose Administration			X				
Blood Sampling	X	X	X	X	X	X	X
Urine Sampling	X	X			X	X	X
Pregnancy Test [c]	X	X					X
Urine Drug and Alcohol screen	X	X					
Spirometry (lung function test)	X	X			X	X	X

[a] EOS = End of Study
[b] Physical examinations will be performed on other study days if needed
[c] Pregnancy test at Screening will be a blood test, Day -1 and 14 will be urine

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 – 65 years, inclusive.
✓	Have a BMI (Body Mass Index) between 18.5 kg/m^2 – 32.0 kg/m^2
✓	Weigh at least 50kg

You cannot take part in this study if you:	
✗	Are pregnant or breastfeeding
✗	Have taken any prescription medication (excluding contraceptives) or any other over-the-counter medication (including herbal products and vitamins) within 14 days prior to dosing.
✗	Have a history of a significant medical problem, heart or lung problems, mental health problems, severe allergy, unexplained bleeding, blood clotting issues, high blood pressure or unexplained fainting.
✗	Have a history of asthma, sleep apnoea, chronic obstructive pulmonary disease, pulmonary fibrosis, bronchiectasis, bronchospasm, and/or reactive airway.
✗	Have received blood products (e.g. transfusion) within 2 months prior to dosing or have donated/lost significant blood within 3 months prior to screening.
✗	Have smoked more than 100 cigarettes in your lifetime or have used any nicotine or tobacco containing products (including vaping products) within 3 months prior to screening.
✗	Have a history of drug or alcohol abuse within 1 year prior to admission.
✗	Have received a vaccination within 30 days prior to dosing, or within 14 days for influenza vaccines, or plan to receive a vaccination during study.
✗	Have received an investigation drug within 1 month prior to dosing, through till the end of study. This may be extended to 3 months for certain drugs, please check with the study team.

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. In certain cases, we are able to cater for dietary requirements, please discuss this with the study team before joining the study.

Restrictions:

- You will not be able to smoke or use any tobacco or nicotine containing products from 3 months prior to screening and through to the end of the study.
- You must not consume any caffeine, xanthine or poppy seed containing products (i.e., coffee, tea, chocolate, soda) for at least 48 hours prior to dosing, and whilst you are an inpatient.
- You must not consume any alcohol for at least 48 hours prior to dosing through to the end of the study.
- You must not consume any products containing grapefruit and/or pomelo within 10 days prior to dosing.
- You must not consume any prescription medication (excluding contraceptives) or any other over-the-counter medication (including herbal products and vitamins) within 14 days prior to dosing through to the end of the study.
    - Some medications cannot be consumed within 30 days prior to dosing. Your study doctor will let you know if this applies to you.
- You must be fasted (no food, only water) for at least 8 hours prior to dosing until 1 hour after the completion of dosing. Study staff will remind you prior to your dosing visit that you need to be fasted.
- You must refrain from strenuous exercise for at least 7 days prior to dosing through till the end of study.
- You must not donate blood 3 months prior to screening through till the end of study.
- You must not receive a vaccination 30 days prior to dosing and whilst on the study.
- You must not receive a tattoo or body piercing from dosing through till the end of study.
- You must not undergo any invasive procedures from dosing through till the end of 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, 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 pulmonary arterial hypertension.

3.2 Reimbursement and Costs

All tests required to be done for this study will be paid for by Pharmosa Biopharm Inc. and there will be no cost for you to participate in this study.

You will be reimbursed the sum of $3,000 (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 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 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).

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 L608 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.

Many side effects go away shortly after treatment ends. However, sometimes side effects can be serious, long lasting or permanent. Your study doctor will discuss the best way of managing any side effects with you.

If a side effect is serious enough to be life-threatening, seek medical assistance immediately by calling 111 and inform your study doctor as soon as possible.

What are the Risks or Side Effects of L608?

This is the second time that L608 is being tested in humans. As this drug is new, it is unknown what all of the possible side effects may be and there may be unknown risks.

As of 16 April 2024, L608 has been given as a single dose to 32 healthy participants at 0.005mg, 0.01mg, 0.015mg and 0.02mg in another ongoing study (PBI L608p1). The highest dose level (0.02mg) is equal to the lowest dose level planned to be given in this study. Of the 32 participants, 20 participants who received either L608 or placebo experienced side effects as listed below.

- 3 or more participants out of 32 experienced these side effects:
  - Cough – 5 participants
  - Dry throat – 3 participants
- 2 participants out of 32 experienced these side effects:
  - Chest discomfort
  - Dizziness
  - Headache
  - Throat irritation
- 1 participant out of 32 experienced these side effects:
  - Tightening of your airways, which can make it hard to catch your breath (bronchospasm)
  - Chest pain
  - Shortness of breath
  - Bruising
  - Blocked nose (nasal congestion)
  - Nausea
  - Low blood pressure (hypotension)
  - Rash
  - Inflammation of the inside of your nose and sinuses (rhinitis)
  - Feeling sleepy
  - Throat pain
  - Involuntary shaking of your body (tremor)

Apart from 2 participants with moderate blocked nose and throat irritation, all the other side effects were mild. Majority of the participants recovered on their own (i.e. without any medical intervention). It is important to note that treatment allocations in the PBI L608p1 study remains blinded as the study is still ongoing, so we do not know if the above side effects were experienced by participants who received placebo or L608.

As L608 is a similar drug to the current standard of care Iloprost, the risks for Iloprost are listed below:

Very common (Occurring in more than 10% of patients)	Common (Occurring in 1 to 10% of patients)	Frequency Unknown
Bleeding in the throat and nose	Tachycardia (Fast heart rate)	Thrombocytopenia (low platelets in the blood –

		difficulty with blood clotting)
Headache	Hypotension (Low blood pressure)	Allergic reaction
Vasodilation (widening of blood vessels)	Dizziness	Bronchospasm/Wheezing
Chest pain/tightness	Heart palpitations	Altered taste
Cough	Difficulty breathing	Stuffy nose
Nausea	Fainting	
Pain in jaw/trismus	Diarrhoea	
Peripheral edema (Leg swelling caused by fluid in leg tissues)	Rash	
Difficulty falling asleep or staying asleep	Back pain	
Flushing (red face)	Throat irritation or pain	
Blurred vision	Vomiting	
	Mouth and tongue irritation including pain	

As with other drugs, L608 may cause an immune reaction or allergic reaction. Symptoms may include rash, flushing, itching, sneezing or runny nose, abdominal pain, diarrhoea, 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.

Please talk to the study staff if you experience any side effects from the study drug. You will be closely monitored throughout the study to ensure your safety.

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 lightheaded 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.

Spirometry:
Spirometry is a simple test that is not painful. You may feel a bit short of breath or lightheaded afterwards. Spirometry is quite a safe test but blowing out hard can increase the pressure in your chest, tummy, and eyes.

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 may receive the COVID-19 vaccination, but not within 30 days prior to dosing through to the end of the study.

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

3.4 Contraception

Reproductive Risks for Sexually Active Participants of Child-Bearing Potential

The effects of L608 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 at least Screening through until at least 3 months after your dose of study drug:

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., 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 pill or progestogen-only 'mini-pill')

You / your partner **must also use a male condom** form of contraception, from Screening through until 3 months after your dose.

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

Total abstinence from heterosexual intercourse during the entire period of risk associated with the study drug (from Screening until at least 3 months after your dose) is considered an acceptable form of contraception if this is in line with your preferred and usual lifestyle.

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 for at least 3 months after your dose of study drug.

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 L608 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 contraception options listed below, from at least Screening through until at least 3 months after your dose of study drug:

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 / your partner **must also use a male condom** method of contraception, from Screening through until 3 months after your dose.

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

Total abstinence from heterosexual intercourse during the entire period of risk associated with the study drug (from Screening until at least 3 months after your dose) is considered an acceptable form of contraception if this is in line with your preferred and usual lifestyle.

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 for at least 3 months after your dose of 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 Pharmosa Biopharm Inc., 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, Pharmosa Biopharm Inc. has satisfied the **Northern B** 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 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 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 or Awanui Laboratories for testing and destroyed after 3 months by internationally accepted means.

All other study samples (pharmacokinetics) will be sent to a central laboratory (Novotech Laboratories) in Taipei, Taiwan for testing and destroyed within 1 year by internationally accepted means.

The maximum amount of blood collected from each participant during the study will be up to approximately 260 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. 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 and Acute (newly diagnosed) Hepatitis B/C 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 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 healthcare 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 healthcare 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, phone number, race and ethnicity 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	• **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	• 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

	• **Electronic**: stored on secure NZCR servers	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., HIV, 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	• **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 L608 or pulmonary arterial hypertension.

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 for approximately 7 years. 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. Chris Wynne, Principal Investigator
Phone: 0800 862 278
Email: dawn.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

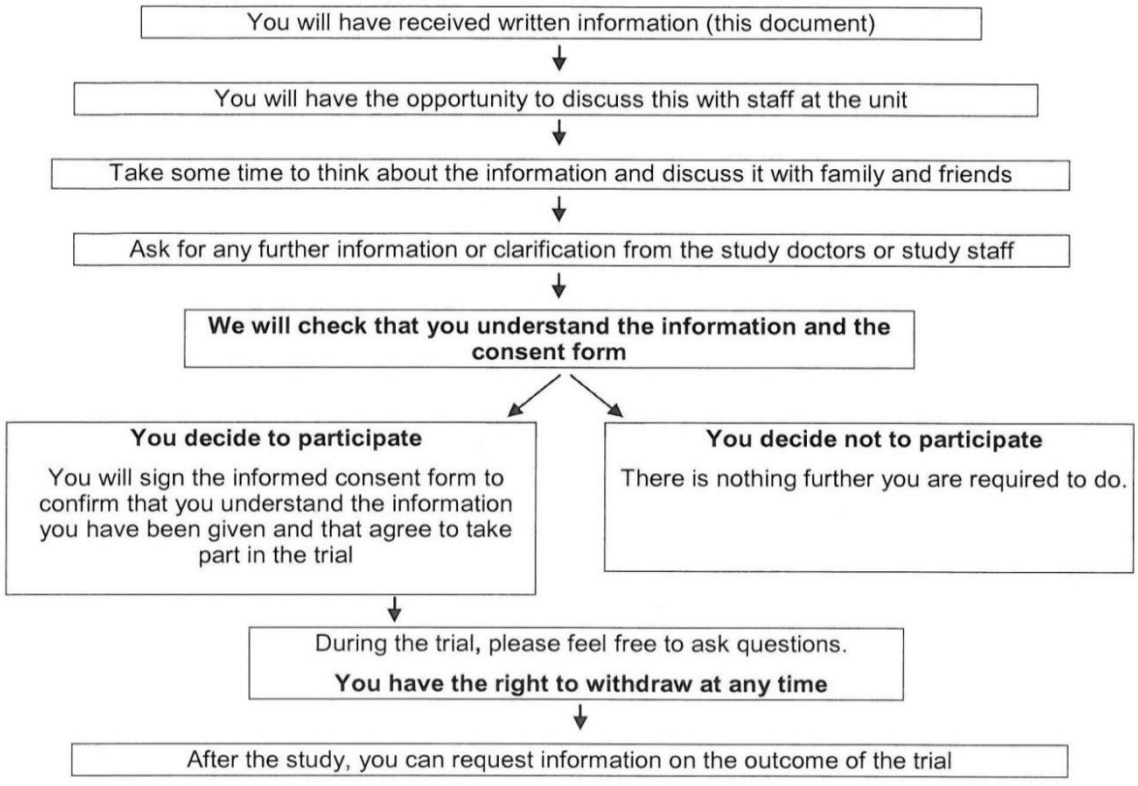
You can also contact the health and disability ethics committee (HDEC) that approved this study on:

Email: hdecs@health.govt.nz

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

Short Title: A Study to Evaluate L608 in Healthy Participants

Protocol Number: PBI-L608-B12

Principal Investigator: Dr. Chris 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 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:_____