PARTICIPANT INFORMATION SHEET AND CONSENT FORM (Part A: Single-Ascending Dose)

Short Title:	A Study to Evaluate ABI-6250 in Healthy Participants
Protocol Number:	ABI-6250-101
Sponsor:	Assembly Biosciences, Inc. Two Tower Place, 7th Floor, South San Fransisco, California, 94080, USA
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Phone Number:	0800 STUDIES (0800 788 3437)
Ethics Number:	**2024 FULL 21720**

This is the first time that ABI-6250 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 ABI-6250, that may potentially be used for the treatment of Chronic Hepatitis D virus infection (CHD). ABI-6250 is an investigational product because it has not been approved by the New Zealand MedSafe or other drug regulatory authorities.

There are multiple parts to this study, and you are being asked to take part in Part A. 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. You will also have the opportunity to join a remote/in-person group session where the study information will be discussed. There will then also be the opportunity for you to meet one-on-one with the study doctor to ask any questions you may have before deciding if you would like to take part in this study.

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

ABI-6250 is being developed for the treatment of CHD. CHD is caused by the Hepatitis D virus (HDV) and this infection leads to liver damage, which could include liver failure and liver cancer. It is the least common form of hepatitis and is rare in New Zealand, but it is the most severe form. Currently, there is no approved HDV treatment in New Zealand.

HDV relies on Hepatitis B virus (HBV) proteins for replication (to make copies of itself). This means people with CHD also have Chronic Hepatitis B virus (CHB) infection. HDV uses a human protein (sodium taurocholate cotransporting polypeptide – NTCP) to help enter liver cells. ABI-6250 is designed to bind to NTCP to stop the entry of HBV and HDV to liver cells. It is hoped that, by stopping the entry of these viruses into the liver cells, ABI-6250 may be an effective treatment for CHD.

This study will investigate the effects of single-ascending doses (SAD) of ABI-6250 in Part A and will also investigate the effects of multiple-ascending doses (MAD) of ABI-6250 in Part B of the study. You are being asked to take part in Part A of the study.

The purpose of Part A of this study is to:

- Evaluate how safe and well tolerated ABI-6250 is in healthy participants.
- Measure levels of ABI-6250 in the blood over time, following a single dose.
- Measure the body's response to a single dose of ABI-6250.
- Evaluate the effect of food (Food Effect) on the absorption and tolerability of ABI-6250 in healthy participants.

1.2 Study Design

Approximately 78 healthy participants will take part in this study. Part A will consist of up to 46 healthy participants. After the screening visit, the study requires a 5-night stay in the NZCR research unit and 3 scheduled clinic visits. If you are part of the food effect cohort, you will be required to complete two 5-night stays and 6 scheduled clinic visits in total.

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

For Cohorts (groups) **A1 to A6** you will be randomised and receive the drug blinded.

Randomised means that the study medication you take (ABI-6250 or placebo) will be assigned randomly (by chance).

Blinded means that neither you nor your study doctor will know whether you will be receiving ABI-6250 or placebo. In an emergency, the study doctor can find out what you are receiving.

Each person in Cohorts A1-A6 will receive a single dose of ABI-6250 or placebo (a substance that looks like ABI-6250 but contains no active medication). Each dose will be given by mouth, with a glass of water.

Up to 6 dose groups (cohorts) are planned for Part A of the study. The group you are assigned to will depend on when you join the study. Study staff will discuss which cohort you are in with you.

Details for the SAD dosing groups A1 to A5 are as follows:

Cohort	Dose of ABI-6250 or Placebo	Frequency
A1	25 mg	Single oral dose (tablet) on Day 1
A2	TBD*	
A3	TBD*	
A4	TBD*	
A5	TBD*	

TBD = To Be Determined

In each dose group (in Cohorts A1-A5) two people will be dosed first (one will receive ABI-6250, and one will receive placebo). The rest of the cohort will be dosed only if there are no safety concerns after 24 hours of monitoring. In the rest of each cohort, 5 people will receive ABI-6250 and 1 will receive placebo. Whether you receive active investigational medicine (ABI-6250) or placebo will be assigned randomly (by chance). You will have a 6 out of 8 (75 %) chance of receiving ABI-6250. All doses will be given while you are fasted (no food only water).

Cohorts **A6 and A7** are the food effect cohorts. **Only one** of these two cohorts will be conducted.

Food Effect means that the researchers are comparing what happens when ABI-6250 is given after a high fat breakfast (fed) vs. on an empty stomach (fasted). For the fed dosing, **you need to be able eat ALL of a high calorie breakfast (approx. 800-1000 calories) within a 30-minute window prior to dosing.**

As a member of Cohort A1-A5 you may be asked to complete a second dosing period as part of Cohort A6 (Food Effect Cohort). Study staff will discuss this option with you.

Cohort A7 will be crossover which means that in one dosing period you will be fasted and in the other dosing period you will be fed.

Details for the SAD Food Effect dosing groups A6 and A7 are as follows:

Cohort	Period 1 (1 dose on Day 1)	Period 2 (Will occur at least 10 days after Period 1 Day 1. 1 dose on Day 1)
A6	ABI-6250 or Placebo (this will be as part of Cohort A1-A5 – that is described above) **Fasted**	ABI-6250 or Placebo **Fed**
A7	ABI-6250 **Fasted or Fed**	ABI-6250 **Fasted or Fed**

The dose level (of ABI-6250 or placebo) for the food effect cohorts, A6 and A7, is still to be determined. For these cohorts you will take part in two dosing periods total, **each dose period will be separated by at least 10 days.**

For Cohort A6, you will have already completed your first dosing period as part of Cohort A1-A5. You will then be asked to join Cohort A6 in a period 2 dosing, where you will receive the same investigational medicine (ABI-6250 or placebo) you had in period 1 but this time after a high calorie breakfast. If Cohort A6 takes place, then Cohort A7 will not be completed.

For Cohort A7, every participant will receive two doses of ABI-6250. In the first period you will receive the dose fasted or fed (after a high calorie breakfast) and the second period will be under conditions opposite of Period 1. Each dose will be given by mouth, with a glass of water. You will have a 6 out of 6 (100%) chance of receiving ABI-6250 if you are enrolled in this cohort.

You will be told which cohort you will be in and your dose level. You will also be told if any changes are made to the planned dose for your group or if you are invited to take part in a second dosing period.

Blood samples and other tests to measure investigational medicine 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 Assembly Biosciences Inc. and locally sponsored in New Zealand by PPD, part of Thermo Fisher Scientific, a Contract Research Organisation (CRO) which will 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 Assembly Biosciences 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 **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 6 weeks, including a screening, dosing (in-patient), and follow-up period (out-patient). If you are part of the food effect cohort, your participation will be approximately 7 weeks. 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 ABI-6250 (or placebo) is called Day 1 and all other days are counted back or forward from this. If you are part of a food effect cohort (A6 or A7), Day 1 will be when you receive each dose.

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

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

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

Electrocardiogram (ECG) and Holter Monitoring:
An ECG measures the electrical activity of your heart, using 12 wires attached to your chest and limbs with sticky pads.
If you are in **Cohorts A1-A5**, you will wear a Holter monitor (a machine that periodically records the heart rhythms) starting approx. 1 hour before you receive investigational medicine and for 24 hours after you receive the study medication on Day 1. 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 investigational medicine 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, fats, liver function, kidney function)
- To check whether you may be pregnant (for people of childbearing potential only)
- To check whether you are post-menopausal (for people of childbearing potential over the age of 54)
- To screen for recreational drugs such as cannabis, methamphetamine, and opiates
- To screen for specific infections (HIV, Hepatitis A, Hepatitis B, Hepatitis C)
- To measure the amount of ABI-6250 in the blood (pharmacokinetics)
- To measure the body's response to ABI-6250 (pharmacodynamics)
- To check the DNA sequence of your NTCP gene (no additional genes will be analysed). **This will involve genetic testing**. Genetics is the study of genes (factors inherited from our parents and how they work). You can think of genetic information as a large instruction book that your body reads to understand how it should be built and function. All humans have the same instruction book in their

body, but some words or letters may be different from one person to the other. Some of those differences have no effect on your health but others can influence how medicines to treat a disease will work.
This test looks at variations in your NTCP gene to assess if there is an impact on the body's response after ABI-6250 dosing.
If you do not wish to have this type of genetic testing done, you cannot take part in the study.

On Day 1, you will have frequent bloods taken.

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.

Full Fat Breakfast (Food effect groups A6 and A7 <u>only</u>)
If you are in the **food effect** dosing groups (Cohort A6 or A7), you will be asked to eat **all** of a high fat, high calorie breakfast prior to receiving one of your doses. You will be instructed to eat the meal within a 30-minute period. An example of a high fat breakfast may include two eggs fried in butter, two strips of bacon, two slices of toast with butter, 113g of hash browns, and 237 mL of whole milk.

Study Schedule 1 (Cohort A1-A5 and Cohort A7 Period 1)

Period	Screening	In Patient [a]						Follow-Up		
Study Day	**-28 to -2**	**-1**	**1**	**2**	**3**	**4**	**5**	**7**	**9**	**11 (EOS) [b]**
Questions about my health	X	X	X	X	X	X	X	X	X	X
Admission to the unit		X								
Discharge from the unit							X			
Physical Exam [c]	X	X					X			X
Vital Signs	X	X	X	X	X	X	X	X	X	X
ECG	X	X	X	X	X	X	X			X
Holter monitoring			X	X						
BMI (Height [d] & Weight)	X	X								X
Dose Administration			X [e]							
Blood Sampling	X	X	X	X	X	X	X	X	X	X
Urine Sampling	X	X	X			X				X
Pregnancy Test [f]	X	X								X
Urine drug and alcohol breath test	X	X								

[a] Cohort A7: This is the schedule for your period 1 dosing
[b] EOS = End of Study (If you are not in Cohort A7).
[c] Symptom directed physical exams can occur at other visits as needed
[d] Height will only be collected at screening
[e] Cohorts A1 – A5 will be fasted (no food) prior to dosing. Cohort A7 may be fasted or fed (dose given after a high fat breakfast), staff will discuss this with you.
[f] Pregnancy tests only for people of childbearing potential. Urine pregnancy tests will be performed on Day -1 or 1 (predose) and Day 11. A blood pregnancy test will be performed at Screening and if the urine pregnancy test is positive.

Study Schedule 2 (Cohorts A6 and A7 Period 2 only)

Period	In Patient (Period 2) [b]						Follow-Up		
Study Day	**-1**	**1**	**2**	**3**	**4**	**5**	**7**	**9**	**11 EOS [c]**
Questions about my health	X	X	X	X	X	X	X	X	X
Admission to the unit	X								
Discharge from the unit						X			
Physical Exam [a]	X					X			X
Vital Signs	X	X	X	X	X	X	X	X	X
ECG	X	X	X	X	X	X			X
BMI (Weight)	X								X
Dose Administration		X [d]							
Blood Sampling	X	X	X	X	X	X	X	X	X
Urine Sampling	X					X			X
Pregnancy test [e]	X								X
Urine drug and alcohol breath test	X								

[a] Symptom directed physical exams can occur at other visits as needed
[b] Period 2 will be at least 10 days after Period 1 Day 1 dosing.
[c] EOS = End of Study
[d] You will either need to be fasted, or fed. Study staff will discuss this with you.
[e] A urine pregnancy test (only for subjects of childbearing potential) will be measured on Day -1 or 1 (predose) and Day 11. If the urine test is positive, a blood test for pregnancy will also be performed.

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 – 60 years, inclusive.
✓	Have a BMI (Body Mass Index) between 18.0 kg/m^2 – 32.0 kg/m^2

You cannot take part in this study if you:	
✗	Are pregnant or breastfeeding, or plan to become pregnant between now and the end of study.
✗	Have taken any herbal/dietary supplements, over-the-counter medications, or prescription medications (except contraception and paracetamol) within 14 days prior to your Day 1 dosing, through the end of the study.
✗	Have a history of drug or alcohol abuse within 3 years prior to screening.
✗	Have a history of a significant medical problem, mental health problem or severe allergy, including Gilbert's Syndrome.
✗	Have donated or lost more than 500mL of blood within 60 days prior to screening, or donated plasma within 7 days prior to Screening, or plans to donate blood or plasma through end of study.
✗	Have used any nicotine or nicotine containing products (including vaping products) within 90 days prior to Day 1 dosing or are unwilling to abstain from tobacco and nicotine-containing products through end of study.
✗	Have had cancer in the last 5 years, with exceptions – please ask the study doctor
✗	Have received an investigational agent within the last 30 days prior to dosing. Please inform your study doctor of all recent use of investigational agents.
✗	Have an illness (such as the flu, common cold or COVID-19) within 5 days prior to receiving your dose of investigational medicine

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 investigational medicine (the way that the drug is processed and broken down by the body). By signing this document, you are agreeing that you will be compliant with all meal requirements on this study. In certain cases, we are able to cater for dietary requirements (this will not be possible for the food effect cohort), please discuss this with the study team before joining the study.

Restrictions:

- You must not smoke or use any nicotine containing products within 90 days prior to Day 1 and through until the end of the study.
- You must not consume any caffeine containing products (i.e., coffee, tea, chocolate, soda) for at least 48 hours prior to Day 1 dosing, through until the end of the study.
- You must not consume any alcohol for at least 48 hours prior to Day 1, and through until the end of the study.
- You must not use illicit drugs (including marijuana) from screening through until the end of the study.
- You must not consume grapefruit, pomelo or Seville oranges (and their juices) for 7 days prior to Day 1 dosing, and through until the end of the study.
- For Cohort A1-A5 and A7 (**fasted** dosing period), you must be fasted (no food, only water) for at least 8 hours prior to your screening visit, Day -1, Day 4, and Day 11. You also must be fasted 10 hours prior to your dose of study drug on Day 1 and for 4 hours after dosing. Study staff will remind you prior to each visit that you need to be fasted.
- For the Cohort A6 and A7 **fed** dosing period, you must be fasted for at least 8 hours prior to your screening visit, Day -1, Day 4 and Day 11. You must be fasted 10 hours prior to your dose of study drug until 30 minutes before dosing when you will receive a high-fat, high-calorie test meal. After your dose you will fast for 4 hours. Study staff will remind you prior to each visit that you need to be fasted.
- You must not engage in strenuous exercise (weightlifting or more than 30 minutes of cardio) beyond what you are used to from Day 1 through until the end of the study.
- You should keep away from excessive sun light/ultraviolet (UV) light from Day 1 through 7 days after your last dose.
- You should not take any herbal/dietary supplements (i.e. vitamins, St. John's Wort, ginkgo biloba, garlic supplements), over the counter (except paracetamol up to 4g/day) or prescription medications for at least 14 days before Day 1 dosing and through until the end of the study.
- You must not donate blood or plasma until your last study visit.

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 CHD.

3.2 Reimbursement and Costs

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

For those who take part in Cohort **A1-A5** you will be reimbursed the sum of $3,000 (before tax), following the final study visit**.** For those that take part in Cohort **A6 or A7** (and undergo 2 dosing periods) you will be reimbursed $5,000 total (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 receive reimbursement as part of this study you must be eligible to work in NZ (e.g. as a NZ resident, NZ citizen, or with the appropriate work visa) for the entire duration of the study. If you are no longer eligible to work in NZ during the study, you will be withdrawn from the study and your reimbursement will be a pro-rata of the total amount.

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.

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.

You will also 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. Travel reimbursement will occur throughout the study as needed. Please discuss arranging study transport with the site study staff. If you live outside this area, we will discuss your travel costs individually.

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, some or all the effects listed below, and they may be mild, moderate, or severe. There may also be unknown side effects from taking ABI-6250 alone or with other drugs you may be taking. If you have any of these side effects, or are worried about them, talk with your study doctor. Your study doctor will also be looking out for side effects.

What are the Risks or Side Effects of ABI-6250?

This is the first time that ABI-6250 is being tested in humans and as such there is no human experience available to identify all of the risks of ABI-6250.

Animal studies have been done with ABI-6250 to try and predict what type of side effects might occur in people. However, animal studies do not always predict human responses to drugs. When ABI-6250 was given to animals at doses higher than the doses that will be given in this study, no adverse (harmful) side effects were seen. No harmful drug-related events to the central nervous (brain and spinal cord) system, respiratory (breathing) system, or circulatory (heart) system were observed in the animal studies. Overall, ABI-6250 was well-tolerated for 28 days of daily dosing. There were no drug-related harmful findings at dose levels tested, which were higher than the daily doses that will be given to participants in the study. There were changes in body weight, food consumption, some laboratory tests, and the liver in some animal studies. These changes were considered non-harmful and returned to normal after ABI-6250 was discontinued.

It is currently not possible to know whether taking ABI-6250 may cause cancer or birth defects in humans. Whether or not what was observed in animal studies will be seen in humans is unknown. What happens in animals does not always predict what will happen in humans who receive ABI-6250, but you should know about this information to help you decide if you want to participate in this study. If you feel you may be experiencing any side effects or new signs or symptoms during the study, or you are worried about them, talk with your study doctor, who will be looking out for side effects throughout your study participation.

The doses planned for this study in people are lower than any of the doses given to animals. The study will begin with low doses of ABI-6250 that will be gradually increased if the drug is well tolerated. The maximum dose level that any participant may receive is limited, as is the maximum increase in ABI-6250 dose level between groups of participants.

Some medications may not be safe when taken with ABI-6250. You should contact the study doctor before starting any new medications or supplements (including vitamins or herbal medicines).

As with other drugs, ABI-6250 may cause an immune reaction or allergic reaction. Symptoms may include rash, flushing, itching, sneezing or runny nose, abdominal pain, diarrhea, swelling of face, tongue or throat, dizziness, lightheaded or fainting, trouble breathing, irregular or racing heart rate, and seizures. These reactions can be life-threatening / fatal. If you have a skin reaction or other adverse event, the study doctor may take a photograph to document the event.

Because ABI-6250 has never been tested in humans, there is always a risk of some unexpected serious, life-threatening side effects occurring following the administration of a new experimental treatment. It is unknown whether some unexpected serious or life-threatening side effect could occur with ABI-6250. You will be monitored closely for them and treated if they occur.

If new findings develop during the course of this study that might suggest a chance for significant side effects when taking ABI-6250, or that might affect your continued willingness to participate, your study doctor will inform you as soon as possible.

Please talk to your study doctor if you have any questions or would like more details on possible side effects.

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 (Holter monitoring is not performed in Cohorts A6 or A7):
Sometimes the sticky pads used to attach the 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.

3.4 Contraception

Reproductive Risks for Sexually Active Participants of Child-Bearing Potential

The effects of ABI-6250 in pregnancy and breastfeeding are unknown, it is not known if the investigational medicine 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 your last study visit:

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

- Intra-uterine device (IUD) containing either copper or levonorgestrel (e.g., Mirena®)
- Sterilisation (e.g., vasectomy of sole male partner at least 6 months prior to dose, bilateral tubal ligation ('clipping or tying tubes' or hysterectomy)

Hormonal methods of contraception, other than the Mirena®, are not acceptable forms of contraception for this study.

You and your partner are also encouraged to use a barrier form of contraception, from your dose of investigational medicine through until your last study visit. Barrier methods of contraception include:

- Condoms (external or internal) – not to be used together due to increased risk of breakage
- Diaphragm ('cap')

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 investigational medicine (from screening until your last study visit) 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, from screening through until the end of the study.

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 an optional separate consent form, which would 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 ABI-6250 if passed on through semen are unknown, it is not known if the investigational medicine 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 may use one of the contraception options listed above for participants of child-bearing potential or the methods listed above, from at least screening through until your 90 days after your last study visit.

A hormonal method of contraception (e.g., pill, implant, injection) is also acceptable for your partner. This method of contraception must inhibit ovulation.

You and your partner must also use a condom (external or internal) from screening through until at least 90 days after your last study visit.

Please note that barrier methods alone are not effective methods of contraception unless you have had a vasectomy at least 6 months prior to your dose of investigational medicine.

Total abstinence from heterosexual intercourse during the entire period of risk associated with the investigational medicine (from screening until your 90 days after your last study visit) 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 (this is optional).

You must also agree not to donate sperm, from screening until at least 90 days after your last study visit.

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

As this research study is for the principal benefit of its commercial sponsor Assembly Biosciences 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, Assembly Biosciences Inc., 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.

The sponsor has voluntarily committed to provide 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:
https://www.medicinesnz.co.nz/fileadmin/user_upload/2015__Medicines_New_Zealand_Compensation_Guidelines__FINAL.pdf

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 LabPlus for testing and destroyed after 3 months by internationally accepted means.

All other study samples (pharmacokinetics, pharmacodynamics, bile acid and NTCP pharmacogenetic testing) will be sent to one of the following central laboratories: Aliri Bioanalysis (Utah, USA), GeneWiz (New Jersey, USA), PPD Global Central Labs (Kentucky, USA) and Robert Bosch Gesellschaft für Medizinische Forschung mbH (Stuttgart, Germany) for testing. These samples may then be stored at a central laboratory Azenta (Indianapolis) in USA for up to 5 years after the study is completed and will be destroyed by internationally accepted means.

The maximum amount of blood collected from each participant during the study will be up to approximately 165 mL for 1 dosing period (Cohort A1-A5, and Cohort A7 period 1) and approximately an additional 75 mL will be collected if you take part in a second dosing period (Cohort A6 and Cohort A7 period 2). Additionally, approximately 2 mL will be drawn and discarded before each blood draw if using a cannula. 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 Hepatitis A, 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, Acute (newly diagnosed) and Hepatitis A/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 sacred and shared values about your tissue samples and/or data originating from this tissue. In line with this we include data sovereignty principles in our practices and in our data management plan. These principles are in place to ensure that the data generated from this research is protected (**whanaungatanga** – our obligations) and may benefit Māori now and into the future. More information on data can be found in Section 6.3 including what happens to your data, **karitiakitanga** (guardianship) and how this impacts **whakapapa** (risks and benefits for whānau). NZCR also honour **Kotahitanga** (collective beliefs) and ensure that participants are not discriminated based on beliefs.

If you wish to perform karakia at the time of sample collection, please let the study staff know. 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.

If you would like to take part in this study you may want to talk to your whānau/kaumatua about it as the study will impact on your whakapapa (that is any tissue and data we gather from you will include information about your whanau, hapū and iwi whakapapa). If you are involved in any hapū and iwi events and have access to people who understand the impact of this research on your whakapapa you may be able to contact them.

There are other ways of accessing cultural support if you need it. There is a contact at the end of this form that you can ring if needed.

Cultural support is different from wanting to know about the study. In this case we can arrange for an investigator to talk to you and your whānau.

New Zealand Clinical Research is committed to meeting their Tiriti obligations and organise tikanga and Tiriti training for staff every two years.

6 WHAT ARE THE RIGHTS OF PARTICIPANTS IN THE STUDY?

6.1 Participation is Voluntary

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

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

6.2 New Information

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

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

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

What will Happen to my Information?

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

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

Type of information	Where is it stored?	Who can access it?
Identifiable Information – *this information can be traced back to you*		
• Information collected from you • Laboratory results • Photographs if required for any adverse events e.g. skin reactions.	• **Paper**: stored securely under restricted access at NZCR. Following study completion paper forms are transferred to a secure site and stored for 15 years, then destroyed • **Electronic**: stored on secure NZCR servers (in New Zealand and Australia)	• NZCR staff • Your GP / usual doctor • Local laboratory staff to process and report your screening and safety tests • Sponsor/CRO monitors to ensure the study is run properly and data is collected accurately • Representatives from the Sponsor if you make a compensation claim as a result of study-related injury. Identifiable information is required to assess your claim • Ethics committee, regulatory authorities, and sponsor/CRO representatives if the study or site is audited • Medical Officer of Health for positive test results for a notifiable disease (i.e., HIV, Hepatitis A/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*		

• De-identified information about you (sex, race/ethnicity and age/year of birth) • 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 (except photographs which will be stored for 15 years). 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 ABI-6250 or CHD.

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 or withdraw from participating in the study at any time, by informing your Study Doctor. You will not be able to participate in the study after withdrawing your consent for the collection and use of your information.

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. You will be asked to complete a Premature Termination visit to check your health and any possible side effects.

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
- The study doctor feels this study is not in your best interest
- You need a medication that is not allowed by the study
- A regulatory agency or EC stops the study

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:

Prof. Edward Gane, Principal Investigator
Phone: (09) 373 3474 or 0800STUDIES (08007883437)
Email: hummingbird.auckland@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:

Auckland:

The Co-Chair of the Māori Governance Rōpu for Ira Tātai Whakaheke

Mobile: 021 0203 1167
Email: helen.wihongi@TeWhatuOra.govt.nz

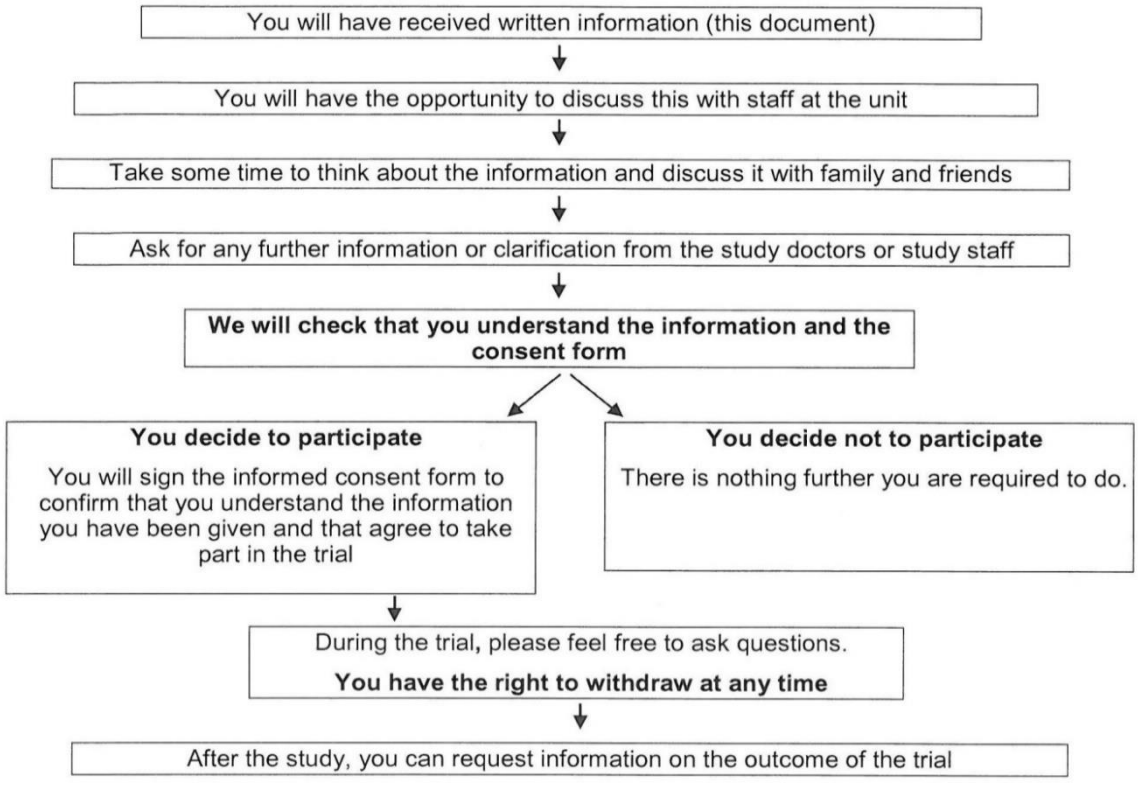
You can also contact the health and disability ethics committee (HDEC) that approved this study on:

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

9 WHAT ABOUT ANY OTHER QUESTIONS I MAY HAVE?

10 DO I HAVE TO DECIDE STRAIGHT AWAY?

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



CONSENT FORM
(PART A)

Short Title: A study to Evaluate ABI-6250 in Healthy Participants

Protocol Number: ABI-6250-101

Principal Investigator: Prof. Edward Gane

***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 and coded information being sent overseas, and I am aware that the tissue samples will be disposed of using established guidelines for discarding biohazard waste.
- I agree to an approved parties including Sponsor or CRO representatives for monitoring and auditing, auditor appointed by the New Zealand Health and Disability Ethic Committees, or any relevant regulatory authority or their approved representative reviewing my relevant medical records for the sole purpose of checking the accuracy of the information recorded for the study.
- I understand that my participation in this study is confidential and that no material, which could identify me personally, will be used in any reports on this study.
- I understand the compensation provisions in case of injury during the study.
- I know who to contact if I have any questions about the study in general.
- I understand my responsibilities as a study participant.
- I understand that I will receive a summary of the study results and if I do not wish to receive this, I will inform site staff.
- I consent to my GP or current provider being informed about my participation in the study and of any significant abnormal results obtained during the study.

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

_____ (full name)

_____ (signature)

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

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

_____ (full name)

_____ (signature)

_____ (project role)

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