PARTICIPANT INFORMATION SHEET AND CONSENT FORM

Short Title:	A Study to Evaluate DR-01 in Healthy Participants
Protocol Number:	DR-01-HV-001
Sponsor:	Dren Bio, Inc. 384 Foster City Blvd, Foster City, CA 94404, United States of America
Principal Investigator:	Dr Rohit Katial
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Phone Number:	0800 STUDIES (0800 788 3437)
Ethics Number:	**2024 FULL 21752**

This is the third clinical trial where DR-01 will be studied in humans, but it is the first time where DR-01 will be given as an injection in healthy volunteers.
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 DR-01, that may potentially be used for the treatment of autoimmune conditions and blood cancers. DR-01 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

DR-01 is being developed for the treatment of autoimmune disorders (e.g. alopecia areata and vitiligo) and blood cancers (e.g. large granular lymphocytic leukaemia (LGLL) and cytotoxic lymphomas) that are associated with CD94. CD94 is a protein (receptor) found in the surface of cytotoxic immune cells (NK cells and some T cells) that detect and eliminate infected, foreign, or harmful cells in the body. Overactivation of these cytotoxic cells can lead to impaired immune system function with conditions such as alopecia and vitiligo, and excessive replication of these cytotoxic cells can lead to blood cancers like LGLL and cytotoxic lymphoma. Currently, treatment options for those conditions inadequately control disease and have less than favourable side effects.

DR-01 (the investigational medicine) is a monoclonal antibody (a medicine that mimics the body's natural antibodies, which protect your body from unknown substances) that works by binding to CD94 and activating an immune process of reducing these cytotoxic immune cells (e.g. NK cells and some T cells) in the body without impacting other cells in the immune system. It is hoped that, by targeting CD94 and reducing the number of cytotoxic immune cells, DR-01 may be an effective treatment for disorders associated with these immune cells.

Currently, DR-01 is being studied with people with autoimmune conditions and blood cancers using an intravenous (IV) dose. This study will investigate DR-01 being administered as an injection dose.

The purpose of this study is to:

- Evaluate how safe and well tolerated DR-01 is after a single dose in healthy volunteers.
- Measure levels of DR-01 in the blood over time, following a single dose.
- Measure the body's response to a single dose of DR-01.
- Assess the body's immune response to DR-01.

1.2 Study Design

Up to 36 healthy volunteers will take part in this study. The study requires a screening visit, and 1 overnight stay and 11 scheduled follow up clinic visits after completing Day 1 (the treatment day) at New Zealand Clinical Research.

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 DR-01 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 DR-01 or placebo (a substance that looks like DR-01 but contains no active medication).

Each dose will be given as a subcutaneous (SC) injection which means it will be administered under the skin on the abdomen. You will be given one or two injections to achieve the dose.

3 dose groups (cohorts) are planned for the study and each cohort will consist of 8 people. 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 DR-01 or Placebo	Frequency
1	80 mg	1 dose on Day 1 via SC injection
2	240 mg	
3	450 mg	

In each dose group two people will be dosed first (one will receive DR-01 and one will receive placebo). The rest of the group will be dosed only if there are no safety concerns after 48 hours of monitoring. In the rest of each dose group, 5 people will receive DR-01 and 1 will receive placebo. Whether you receive DR-01 or placebo, it will be assigned randomly (by chance). You will have a 3 out of 4 (75 %) chance of receiving DR-01.

There may be an additional approximately 12 people (expansion cohort) enrolled in a dose group at the discretion of the Sponsor. You will be told if you are enrolled in the expansion cohort.

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

Blood samples and other tests to measure DR-01 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 Dren Bio, Inc., and locally sponsored in New Zealand by Novotech (New Zealand), a Contract Research Organisation (CRO) which help conduct and monitor the study in New Zealand.

Dren Bio, Inc. may benefit financially from this research study if, for example, the study assists Dren Bio, Inc. to obtain approval for a new drug. By taking part in this research study, you agree that samples of your blood or tissue (or data generated from analysis of these materials) will be provided to Dren Bio, Inc.

New Zealand Clinical Research (NZCR) will receive a payment from Dren Bio, 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 Southern Ethics Committee.

A description of this clinical study will be available on https://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 13 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 DR-01 (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

Collection of Your Information and Questions About Your Health:
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 and Injection Site Assessment:
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. Your injection site will also be assessed at 2 hours and 6 hours post dose on Day 1, on Day 2, and Day 3. You will be asked to rate the pain and itchiness of the injection site using a visual analogue scale. Study staff will explain this further to you during those days that this is assessed.

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

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

Blood and Urine Samples:
At 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) or to or to confirm post-menopausal status (for people who are post-menopausal).
- To measure the number of specific immune cells (e.g. white blood cells).
- To screen for recreational drugs such as cannabis, methamphetamine, and opiates
- To screen for specific infections (HIV, Hepatitis B, Hepatitis C, Tuberculosis, Cytomegalovirus, Epstein-Barr virus, Herpes simplex virus)

- To measure the amount of DR-01 in the blood (pharmacokinetics)
- To see whether you develop antibodies to DR-01. Antibodies are proteins that recognise foreign substances in the body, so that the immune system can fight them off. If a person develops antibodies against a drug, the antibodies can sometimes stop the drug from working or cause reactions if the drug is given again.
- To measure the effect of DR-01 on specific immune system cells and proteins.

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.

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

Pre-treatment medications:
Prior to your dose of DR-01 or placebo, you may be provided with medications that help to control fever and reduce the potential for a reaction. These pre-medications may include paracetamol and antihistamines (such as loratadine), and prednisone (a steroid medication). **You will be informed if you will need to take the pre-medications prior to dosing.**

Study Schedule

Period	Screening	Dosing		Follow-Up										
Study Day	**-35 to -2**	**-1**	**1**	**2**	**3**	**5**	**6**	**8**	**11**	**15**	**22**	**29**	**43**	**57 EOS [a]**
Admission to the unit		X												
Discharge from the unit			X[b]											
Clinic Visit	X	Overnight stay		X	X	X	X	X	X	X	X	X	X	X
Physical Exam and Injection Site Assessment	X		X [c]	X [c]	X [c]	X [c]	X [c]	X [c]	X [c]	X [c]	X [c]	X [c]	X [c]	X
Vital Signs	X		X	X	X	X		X	X	X	X	X	X	X
ECG	X		X	X										X
BMI (Height & Weight)	X		X[d]											
DR-01 or Placebo Administration			X											
Blood Sampling	X	X [f]	X	X	X	X	X	X	X	X	X	X	X	X
Urine Testing	X		X							X		X		X
Urine Drug Screen	X	X [f]												
Alcohol Breath Test		X [f]												
COVID-19 Test	X													
Pre-treatment medications			X[e]											
Collection of Your Information and Questions about Your Health	X													

[a] EOS = End of Study

[b] You will be discharged from the clinic after the 6 hours post-dose assessments are completed.

[c] A full physical examination will be done on screening and EOS visit. A symptom directed physical examination may be done on the rest of the scheduled visits. On Days 1, 2 and 3 your injection site will be evaluated by the study staff. You will be asked to rate the pain and itchiness of the injection site using a visual analogue scale.
[d] Weight will be measured on Day 1.
[e] On Day 1, Participants may receive pre-treatment medications prior to their dose of DR-01 or placebo. Participants will be informed prior to this occurring.
[f] These tests may be done on Day 1 to confirm your eligibility.

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 18.0 kg/m^2 – 35.0 kg/m^2
✓	Weigh between 40kg – 120 kg (inclusive)

You cannot take part in this study if you:	
✗	Are pregnant, breastfeeding or intending to become pregnant while in the study.
✗	Have taken any prescription medication (excluding contraceptives), over the counter medication such as vitamins, herbal supplements, antihistamines within 7 days prior to dosing. Paracetamol and occasional use of ibuprofen is allowed to be taken whilst in the study.
✗	Have history of cancer 5 years prior to screening. There are some exceptions, please discuss this with study staff.
✗	Had a serious infection that needed hospitalisation or IV antimicrobial treatment 28 days prior to screening.
✗	Have a current chronic infection or recurrent viral infection. If you are unsure, please speak with the study doctor.
✗	Current positive test at screening for HIV, or Hepatitis B or C infection, or Tuberculosis, COVID-19.
✗	Have a history of a significant medical problem, mental health problem or severe allergy (e.g. anaphylaxis).
✗	Have donated more than 500mL of blood within 3 months prior to screening.
✗	Have a positive drug of abuse test and alcohol breath test at screening.
✗	Have a history of drug or alcohol abuse and heavy nicotine usage i.e. includes vaping (defined as more than 1 pack of cigarettes a day or the equivalent of nicotine in vaping; more than 7 units of alcohol per week for females and 14 units of alcohol per week for males).
✗	Have participated in a clinical trial in the last 3 months (for a biologic therapies) or 1 month (for non-biologic therapies) prior to screening. Or have been exposed to 4 investigational medicines within 12 months prior to dosing.

	If you are unsure, please speak to the study doctor for clarification.
✗	Have received any live or live-attenuated vaccines (e.g. MMR vaccine, chicken pox vaccine, etc.) within 28 days prior to dosing or during the study. COVID-19 and flu vaccines are allowed in the study.

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. You should also tell your study doctor about any changes to these conditions during your participation in the research study. 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.

Restrictions:

- You will not be able to smoke or use any nicotine containing products during your stay in the unit. For the remainder of the study, you should maintain your usual smoking habits.
- You must limit your alcohol intake to no more than 7 standard units of alcohol per week for females and no more than 14 standard units of alcohol per week for males whilst you are enrolled in the study.
- Whilst on the study, you should also maintain your usual caffeine intake is acceptable.
- You must refrain from strenuous exercise for at least 48 hours prior to all clinic visits.
- You will not be able to take any prescription medication (excluding contraceptives), over the counter medication such as vitamins, herbal supplements, antihistamines from dosing until the end of the study. If you are unsure, please speak with the study doctor for clarification.
- You will not be able to receive any live or live-attenuated vaccines (e.g. MMR vaccine, chicken pox vaccine, etc.) from dosing until the end of the study.

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

3 WHAT ARE THE POSSIBLE BENEFITS, 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 autoimmune conditions or blood cancers. The results from this study may also lead to new commercial products or tests.

3.2 Reimbursement and Costs

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

You will be reimbursed the sum of $3,100 (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.

You will be reimbursed separately 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).

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 DR-01 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 DR-01?

This is the third clinical trial where DR-01 is being tested in humans and as such there is limited human experience available to identify all of the risks of DR-01.

As of 18 Oct 2024, 56 participants have been treated with DR-01 at dose levels ranging from 0.3 mg/kg through 10 mg/kg. The safety data from these participants show DR-01 is safe and generally well tolerated. The most common side effect related to DR-01 was infusion-related reaction (IRR), a reaction to the study drug during or shortly after the first administration of DR-01. All IRRs resolved shortly after stopping the infusion and/or administration of medications to treat the IRR. This study will administer DR-01 subcutaneously instead of intravenously, to reduce the likelihood of a reaction to the study drug.

Other side effects that were possibly related to DR-01, and that occurred more than twice, included general complaints that are common in clinical trials, such as headache, nausea, and constipation.

Of the 56 participants exposed to DR-01, 4 participants experienced serious reactions that were at least possibly related to DR-01: 2 participants experienced serious IRRs, 1 participant experienced a serious fever, and 1 participant experienced cytokine release syndrome [CRS] (the body's immune system overreacts to an infection or a treatment and releases cytokines (proteins that are responsible for inflammation) excessively which drives further inflammation) which was reported as related to DR-01 but also consisted of symptoms that the participant experiences at baseline (i.e., rapidly progressing lymphoma, with tumour-related fevers and hypotension before starting on trial).

Based on the drug type of DR-01, the following side effects may also be expected:

- There is a chance that you may have a reaction to the study drug during the injection, also known as an injection-site reaction (ISR). An ISR may happen at any time and up to 48 hours afterward. If an ISR occurs, you may experience pain, itching, thickening and/or redness around the injection site. Photographs may be taken of the injection sites if you experience an ISR. There is a chance that you will have a body-wide reaction to the drug. If this occurs, you may also experience fever, chills, and sweating. You will be monitored closely for any injection reactions. ISRs will be managed by applying a cold compress to the area, such as an ice pack, to help to reduce swelling and take an antihistamine to reduce the body’s reaction to the injection.
- DR-01 may cause a low amount of white blood cells. If the white blood cells are low, there is risk for infection. This could be a new infection or could be activating a virus that you were infected with in the past, like hepatitis. Your doctor will evaluate you for this and may give you antiviral medicine to prevent an infection, if needed.

There is a risk that you could develop antibodies against DR-01. Developing antibodies to DR-01 could neutralise the effect of the drug, which means it may not work if you used it for treatment purposes in the future. It could also cause an allergic reaction if you have future doses of DR-01.

As with other drugs, DR-01 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. No identifying features e.g., eyes, birthmarks, tattoos, injuries, scars, anatomic anomalies, etc. will be included in the photographs.

Because DR-01 has limited exposure 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 DR-01 You will be monitored closely for them and treated if they occur.

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:
Adhesive electrodes (patches) will be attached to your skin on select locations of your body (arms, legs, and chest). The areas where the electrodes will be placed may be cleaned and some areas may need to be shaved. Minor skin irritation may occur where the electrodes are placed. The test is usually painless and takes less than a minute to perform. After the test, the electrodes are removed.

Pre-medications:
Pre-medications may be given prior to the administration of DR-01 (or placebo) to reduce the potential for a reaction to the investigational medicine. These pre-medications may include paracetamol and antihistamines (such as loratadine), and prednisone (a steroid medication). **You will be informed if you will need to take the pre-medications prior to dosing.**

Common paracetamol side effects: include stomach cramps, nausea, headache and rash. Rare but serious side effects of paracetamol include severe skin and allergic reactions.

Antihistamines (e.g., diphenhydramine or equivalent): Side effects include constipation, dizziness, drowsiness, excitement (most often in children), headache, increased chest congestion, loss of appetite, muscle weakness, nausea, nervousness, and vomiting. More serious side effects include vision problems and painful urination or difficulty urinating.

Corticosteroid (e.g., methylprednisolone or equivalent): These common side effects of prednisolone happen in more than 1 in 100 people: weight gain, indigestion, problems sleeping (insomnia), feeling restless, sweating a lot, and mild mood change.

Covid Test:
Nasal swabs from COVID testing may cause discomfort or minor nose bleeding.

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 DR-01 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. Please note that if you had a tubal ligation/bilateral tubal ligation or non-documented hysterectomy; you are considered to be of childbearing potential.

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 60 days before dosing (Day 1) and until at least 30 days after your dose:

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®). Please note that you must have this in place at least 90 days prior screening.
- Sterilisation (e.g., vasectomy, documented 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 and your partner must also use a barrier form of contraception, if you have started using an oral contraceptive pill (combined hormonal pill or progestogen-only 'mini-pill') within 60 days prior to screening until at least 30 days after your dose. 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 and in combination 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 at least 90 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, from dosing until at least 90 days after your dose of investigational medicine.

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 DR-01 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 above for participants of child-bearing potential, from at least screening before your dose of investigational medicine through until at least 90 days after your dose. Please note that if you do not have a documented vasectomy then you must comply with the contraception requirements needed for the study.

You and your partner must also use a barrier method of contraception, from your dose of investigational medicine through until 90 days after your dose. 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 contraception.

Total abstinence from heterosexual intercourse during the entire period of risk associated with the investigational medicine (from screening until at least 90 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, from dosing until at least screening after your 90 days dose of the investigational medicine.

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

As this research study is for the principal benefit of its commercial sponsor Dren Bio, 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, Dren Bio, Inc., has satisfied the Southern 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, 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 Awanui Laboratories/LabPlus for testing and disposed after 3 months by internationally accepted means.

All other study samples (pharmacokinetics, immunogenicity etc) taken in this research study are mandatory and will only be used for the purposes of this study. They will be sent to central laboratories (LabConnect Aust Pty Ltd) in Victoria, Australia; (ICON, plc) Whitesboro, USA; (Dren Bio) California, USA and (CellCarta Pty Ltd) New South Wales, Australia for testing and disposed after 15 years by internationally accepted standards.

Samples taken from you during this study will be used only for the purposes described in this consent form. The maximum amount of blood collected from each participant during the study will be up to approximately 513 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, Tuberculosis as well as a COVID-19. 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, Tuberculosis then the study doctors will provide initial counselling and medical advice and will assist in arranging any follow up tests that you require. HIV, Acute (newly diagnosed) Hepatitis B/C, Tuberculosis and COVID-19 are all 'notifiable diseases', which means that it is required by law to notify government health authorities of any new cases.

5.1 Are There Any Cultural Considerations?

You may hold 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, **kaitiakitanga** (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 come and 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., COVID-19, Hepatitis B/C) • The study doctor may share your information with other people, in the rare event of a serious threat to public health or safety, or to the life or health of you or another person OR if the information is required in certain legal situations
De-identified (coded) Information – *this information is only labelled with your unique study ID*		
• 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 [no features such as eyes, birthmarks, tattoos, injuries, scars, anatomic anomalies, etc. will be included], if required (as above)	• **Electronic**: will be stored-on a secure platform and will be retained indefinitely. Storage will comply with local and/or international data security guidelines. • Electronic de-identified photographs will be stored securely for at least 15 years, then destroyed.	• 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.

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. Your coded information will be entered into electronic case report forms and sent through a secure server to the sponsor. Coded study information will be kept by the sponsor in

secure, cloud-based storage indefinitely. All 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.

Ownership Rights

Information from this study may lead to discoveries and inventions or the development of a commercial product. The rights to these will belong to Dren Bio, Inc. You and your family will not receive any financial benefits or compensation, nor have any rights in any developments, inventions, or other discoveries that might come from this information.

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

- The drug being shown to not be safe
- If the study doctor decides it is in the best interest of your health and welfare to stop.
- 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 Rohit Katial, Principal Investigator
Phone: (09) 373 3474 or 0800STUDIES (08007883437)
Email: serenity.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 Ira Tātai Whakaheke (Māori Governance Rōpu)

Mobile: 021 0203 1167
Phone: 09 486 8320 ext 43204
Email: helen.wihongi@TeWhatuOra.govt.nz

Waikato:

Te Puna Oranga Māori Health Service, Te Whatu Ora (Health New Zealand) - Waikato

Phone: (07) 8343644
Email: research@waikatodhb.health.nz

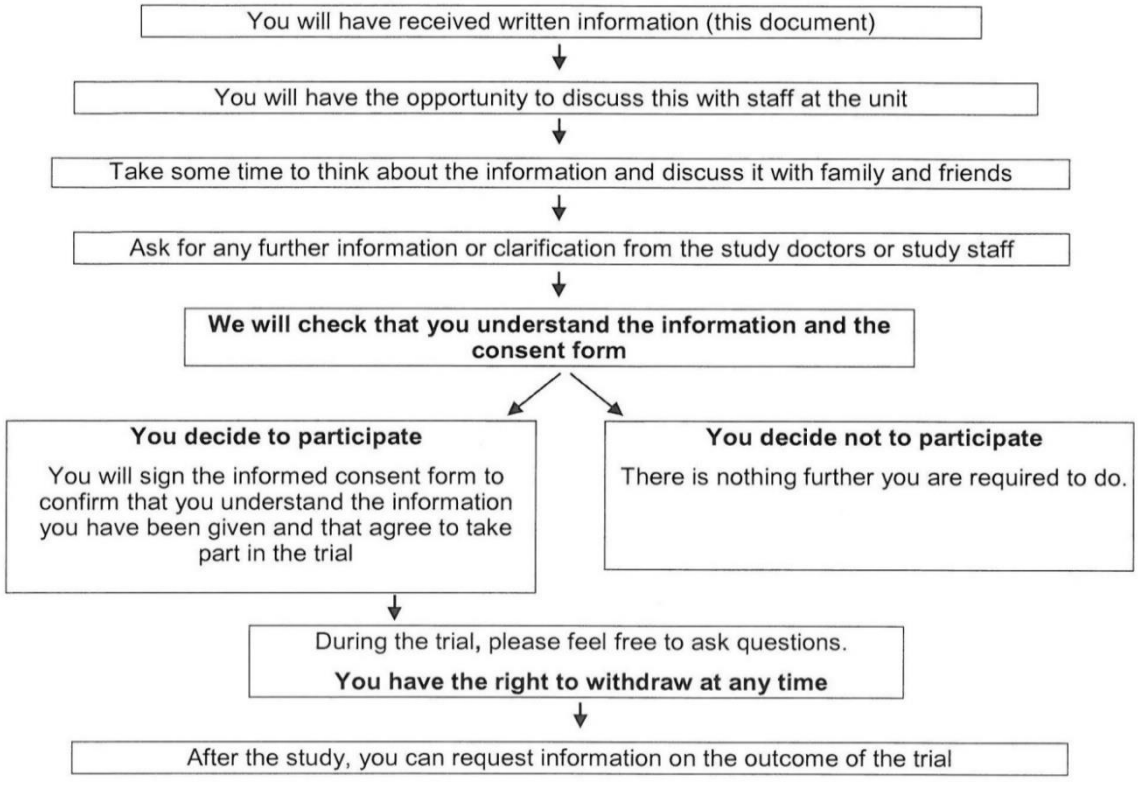
You can also contact the health and disability ethics committee (HDEC) that approved this study on:

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

Short Title: A Study to Evaluate DR-01 in Healthy Participants

Protocol Number: DR-01-HV-001

Principal Investigator: Dr Rohit Katial

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

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

_____ (full name)

_____ (signature)

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

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

_____ (full name)

_____ (signature)

_____ (project role)

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