

**Participant Information Sheet/Consent Form**

**Interventional Study - Adult providing own consent**

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| **Title** | A Phase II Randomised, Double-Blind, Placebo-Controlled Study of the Efficacy, Safety and Tolerability of Oral NP202 in Adults who have paroxysmal atrial fibrillation and a cardiac device |
| **Short Title** | NP202 for Atrial Fibrillation |
| **Principal Investigators** | Dr Bradley WilsmoreDr Austin May |
| **Location** | John Hunter Hospital, Newcastle |

1. **Introduction**

You are invited to take part in this research project. This is because you have paroxysmal atrial fibrillation and an implanted cardiac device (loop recorder, pacemaker or defibrillator). The research project is testing a new treatment for people who have paroxysmal atrial fibrillation. The new treatment is called Armaqor (Armaron NP202).

This Participant Information Sheet/Consent Form tells you about the research project. It explains the tests and treatments involved. Knowing what is involved will help you decide if you want to take part in the research.

Please read this information carefully. Ask questions about anything that you don’t understand or want to know more about. Before deciding whether or not to take part, you might want to talk about it with a relative or friend.

Participation in this research is voluntary. If you don’t wish to take part, you don’t have to. You will receive the best possible care whether or not you take part.

If you decide you want to take part in the research project, you will be asked to sign the consent section. By signing it you are telling us that you:

* Understand what you have read
* Consent to take part in the research project
* Consent to have the tests and treatments that are described
* Consent to the use of your personal and health information as described

You will be given a copy of this Participant Information and Consent Form to keep.

1. **What is the purpose of this research?**

NP202 is an experimental drug being developed by Armaron Bio Pty Ltd for potential use as a treatment for people with heart rhythm problems including paroxysmal atrial fibrillation.

NP202 works by modifying part of the heart muscle cells responsible for contraction and rhythm. This research will help us understand if NP202 affects the amount of atrial fibrillation in patients enrolled in the study. The amount of atrial fibrillation can be assessed during normal testing of a cardiac device.

NP202 has been tested in human healthy male volunteers. Thirty (30) volunteers received single doses up to 1,600mg, and 12 volunteers received 14 doses up to 1,000mg per day in a recently completed study. NP202 was well tolerated in that study.

NP202 is an experimental treatment. This means that it is not an approved treatment for paroxysmal atrial fibrillation in Australia, or anywhere in the world. NP202 has not been tested in females and this study is a first-in-human-females study.

This research is being conducted by Dr Bradley Wilsmore and Dr Austin May at the John Hunter Hospital, Newcastle. If you have questions or concerns at any time, please contact us on 02 4921 4720.

1. **What does participation in this research involve?**

Before you agree to the study, you will find detailed information below about the study drug.. You are encouraged to ask questions until you are sure that you fully understand the nature and requirements of the study.

If you agree to have some tests to see whether the study is suitable for you, you will be asked to sign a consent form.

You will be participating in a randomised controlled research project. Sometimes we do not know which treatment is best for treating a condition. To find out we need to compare different treatments. Controlled means that we put people into groups and give each group a different treatment. The results are compared to see if one is better. Randomised means that, to try to make sure the groups are the same, each participant is put into a group by chance (like flipping a coin).

We will allow sufficient time to review your blood tests results prior to treatment beginning. Early in the study, half the participants will receive NP202 1000mg, and half will receive placebo – you have a 1 in 2 chance of receiving NP202 initially. A placebo is a medication with no active ingredients. It looks like the real thing but is not. After completing 4 weeks with the initial allocation, all participants will swap to the opposite treatment – if you received the active treatment initially, you will be swapped to the placebo treatment to complete the study. If you received the placebo treatment initially, you will be swapped to the active treatment to complete the study.

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Enrol | 🡪🡪🡪 | 1 month | 🡪🡪🡪 | 2 month | 🡪🡪🡪 | 3 month | 🡪🡪🡪 | 4 month | 🡪🡪🡪 | 5 month |
|  | study drug 1 |  | no study drug |  | study drug 2 |  | no study drug |  | no study drug |  |

You will be participating in a double-blind study. This means that neither you nor your study doctor will know which treatment you are receiving. However, in certain circumstances your study doctor can find out which treatment you are receiving.

This research project has been designed to make sure the researchers interpret the results in a fair and appropriate way and avoids study doctors or participants jumping to conclusions.

The total period of your study involvement will be approximately 5 months. There are six scheduled follow up visits for patients enrolled in the study over a period of 5 months.

Enrolment Visit

After reading this information sheet, if you agree to participate in the study, you will be asked to sign the attached consent form. The following assessments will be performed:

* Your age, gender and ethnicity will be recorded.
* You will be asked about previous medical problems, your current health and any medications you are taking.
* You will undergo a physical examination. This will include a measurement of your height and weight.
* Your blood pressure, heart rate, breathing rate and body temperature will be measured.
* Your implanted device will be interrogated (download of stored data)
* You may have to have an echocardiogram to measure how efficiently your heart is working. An echocardiogram is like an ultrasound for your heart.
* You will take the first dose of study medication. Study medication is in capsules which you will take with a glass of water. You will continue to take study medication once a day for 30 days, followed by a break for 30 days, and then further study medication for 30 days.

Further Visits

You will return to the clinic after enrolment at 1 month, 2 months, 3 months, 4 months and 5 months. At each visit, the following will be measured:

* You will be asked about any changes in your health and any changes to medications you are taking.
* Your weight, blood pressure, heart rate, breathing rate and body temperature will be measured.
* Your implanted device will be interrogated (download of stored data)
* At the 2 month visit you will be given a new bottle of medication.

The Conduct of this study will be monitored by the Research Ethics and Governance Office of Hunter New England Health.

There are no additional costs associated with participating in this research project, nor will you be paid. All medication, tests and medical care required as part of the research project will be provided to you free of charge.

You may be reimbursed for any reasonable travel, parking, meals and other expenses associated with the research project visit.

If you decide to participate in this research project, the study doctor will inform your local doctor.

1. **Other relevant information about the research project**

Overall, approximately 20-50 participants will take part in this study at the John Hunter Hospital.

1. **Do I have to take part in this research project?**

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.

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.

Your decision whether to take part or not to take part, or to take part and then withdraw, will not affect your routine treatment, your relationship with those treating you or your relationship with the John Hunter Hospital.

1. **What are the alternatives to participation?**

You do not have to take part in this research project to receive treatment at this hospital. You will still receive standard heart medications, for example a blood thinner, if you do not participate, as the study medication is being given in addition to these. Your option for participation includes choosing not to participate. Your study doctor will discuss these options with you before you decide whether or not to take part in this research project.

1. **What are the possible benefits of taking part?**

We cannot guarantee or promise that you will receive any benefits from this research; however, possible benefits may include improvements in your heart function, or more frequent follow up.

1. **What are the possible risks and disadvantages of taking part?**

Medical treatments often cause side effects. You may have none, some or all of the effects listed below, and they may be mild, moderate or severe. 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.

In studies of NP202 conducted in animals, the following effects occurred:

* A dark yellow discolouration of your urine;
* Gastrointestinal effects (discomfort, soft or loose stool);
* Slight enlargement of the liver;
* Slight changes in clinical laboratory parameters (changes in number of red, white and other blood cell types, haemoglobin levels, electrolyte levels, or blood clotting).

These effects were at a much higher dose of NP202 than is being given in this study.

None of the above side effects were seen in the human healthy male volunteer study; however, it is possible that you may have some of them. NP202 has not been tested in females and this study is a first-in-human-females study.

In the healthy volunteer study, 10 of the 12 participants (83%) taking multiple doses of NP202 reported a yellow or green discolouration of their semen. Samples were taken and tested for sperm count, motility (movement) and morphology (shape). There were some minor changes (both improvement and worsening) however, these were not thought to be related to NP202 but rather to natural variation. This has been reported in other drugs which are similar to NP202.

There were very few other effects reported and NP202 was generally well tolerated. There may be side effects that the researchers do not expect or do not know about and that may be serious. Tell your doctor immediately about any new or unusual symptoms that you get.

Many side effects go away shortly after treatment ends. However, sometimes side effects can be serious, long lasting or permanent. If a severe side effect or reaction occurs, your doctor may need to stop your participation in the study.

The treatment of the side effects will depend on the symptoms.

If participation in this research project uncovers a medical condition of which you are unaware, the study doctors will treat or refer you to the appropriate person for follow up. They will also discuss whether you can continue in the study.

Risks of procedures

The effects of NP202 on the unborn child and on the newborn baby are not known. Because of this, it is important that research project participants are not pregnant or breast-feeding and do not become pregnant during the course of the research project and for 3 months afterwards. You must not participate in the research if you are pregnant or trying to become pregnant, or breast-feeding. If you are female and child-bearing is a possibility, you will be required to undergo a pregnancy test prior to commencing the research project. If you are male, you should not father a child or donate sperm for at least 3 months after the last dose of study medication.

Both male and female participants are strongly advised to use effective contraception during the course of the research and for a period of 3 months after completion of the research project. You should discuss methods of effective contraception with your study doctor.

For female participants: If you do become pregnant whilst participating in the research project, you should advise your study doctor immediately. Your study doctor will withdraw you from the research project and advise on further medical attention should this be necessary. You must not continue in the research if you become pregnant.

For male participants: You should advise your study doctor if you father a child while participating in the research project. Your study doctor will advise on medical attention for your partner should this be necessary.

1. **What if new information arises during this research project?**

Sometimes during the course of a research project, new information becomes available about the treatment 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 will be asked to sign an updated consent form.

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

1. **Can I have other treatments during this research project?**

Whilst you are participating in this research project, you should continue to take your usual medications. It is important to tell your study doctor and the study staff about any treatments or medications you may be taking, including over-the-counter medications, vitamins or herbal remedies, acupuncture or other alternative treatments. You should also tell your study doctor about any changes to these during your participation in the research project.

1. **What if I withdraw from this research project?**

If you decide to withdraw from the project, 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.

If you do withdraw your consent during the research project, the study doctor and relevant study staff will not collect additional personal information from you, although personal information already collected will be retained to ensure that the results of the research project can be measured properly and to comply with law. You should be aware that data collected by the sponsor up to the time you withdraw will form part of the research project results. If you do not want them to do this, you must tell them before you join the research project.

1. **Could this research project be stopped unexpectedly?**

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 not to be effective
* The drug being shown to work and not need further testing
* Decisions made in the commercial interests of the sponsor or by local regulatory/health authorities
1. **What happens when the research project ends?**

NP202 will not be made available to you after either the research project ends or your participation ends.

The Principal Investigator will share the results of the study with you when requested. The disclosure and/or any published results will be available to all participants when requested. It is usual for a number of months to elapse before definitive results of this type of study are available. These may be published in medical journals that are available to the public. You should feel free to ask the study staff about this.

1. **What will happen to information about me?**

By signing the consent form you consent to the study doctor and relevant research staff collecting and using personal information about you for the research project. Any information obtained in connection with this research project that can identify you will remain confidential. Personal data which may be sensitive will be collected and processed but only for research purposes in connection with this study. All data collected about you will be coded with your study number. The data will be entered into a computer, using secure processes. All records at the study site will be stored in a secure location. All records will be stored for at least 15 years after which they may be destroyed.

Your information will only be used for the purpose of this research project and it will only be disclosed with your permission, except as required by law.

Information about you may be obtained from your health records held at this and other health services for the purpose of this research. By signing the consent form you agree to the study team accessing health records if they are relevant to your participation in this research project.

Your health records and any information obtained during the research project are subject to inspection (for the purpose of verifying the procedures and the data) by the relevant authorities, the institution relevant to this Participant Information Sheet, the John Hunter Hospital, or as required by law. By signing the Consent Form, you authorise release of, or access to, this confidential information to the relevant study personnel and regulatory authorities as noted above.

It is anticipated that the results of this research project may be published and/or presented in a variety of forums. In any publication and/or presentation, information will be provided in such a way that you cannot be identified, except with your permission.

Information about your participation in this research project may be recorded in your health records.

In accordance with relevant Australian and/or New South Wales privacy and other relevant laws, you have the right to request access to your information collected and stored by the research team. You also have the right to request that any information with which you disagree be corrected. Please contact the study team member named at the end of this document if you would like to access your information.

1. **What happens if I am injured as a result of the study?**

Complaints

If you have any complaints you should contact the Research Ethics and Governance Officer listed below.

Treatment Available

If you suffer any injuries or complications as a result of this research project, you should contact the study team as soon as possible and you will be assisted with arranging appropriate medical treatment. If you are eligible for Medicare, you can receive any medical treatment required to treat the injury or complication, free of charge, as a public patient in any Australian public hospital.

1. **Who is organising and funding the research?**

This research project is being conducted by Dr Bradley Wilsmore at John Hunter Hospital, Newcastle. The study medication is supplied and funded by Armaron Bio Pty Ltd. The doctors involved in the research are independent investigators and have no financial relationship with Armaron Bio Pty Ltd.

1. **Who has reviewed the research project?**

All research in Australia involving humans is reviewed by an independent group of people called a Human Research Ethics Committee (HREC). The ethical aspects of this research project have been approved by the Hunter New England Human Research Ethics Committee.

This project will be carried out according to the *National Statement on Ethical Conduct in Human Research (2007)*. This statement has been developed to protect the interests of people who agree to participate in human research studies.

1. **Further information and who to contact**

The person you may need to contact will depend on the nature of your query.

If you want any further information concerning this project or if you have any medical problems which may be related to your involvement in the project (for example, any side effects), you can contact the principal study doctor on 02 4921 4720 or any of the following people:

 **Clinical contact person**

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| --- | --- |
| Name | Dr Bradley Wilsmore |
| Position | Cardiologist  |
| Telephone | 02 4921 4720 |
| Email | Bradley.Wilsmore@hnehealth.nsw.gov.au |

**24-hour contact person**

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| --- | --- |
| Name | Dr Austin May |
| Position | Cardiology Fellow  |
| Telephone | 02 4921 3000 |
| Email | Austin.May@health.nsw.gov.au |

**Complaints contact person**

If you have any complaints about any aspect of the project, the way it is being conducted or any questions about being a research participant in general, then you may contact:

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| --- | --- |
| Name | Dr Nicole Gerrand |
| Position | Manager, Research Ethics and Governance Unit |
| Telephone | 02 4921 4950 |
| Email | hnelhd-hrec@hnehealth.nsw.gov.au |
| Please quote | Reference No: 17/11/15/3.01 |

**Consent Form**

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| **Title** | A Phase II Randomised, Double-Blind, Placebo-Controlled Study of the Efficacy, Safety and Tolerability of Oral NP202 in Adults who have paroxysmal atrial fibrillation and a cardiac device |
| **Short Title** | NP202 for Atrial Fibrillation |
| **Principal Investigators** | Dr Bradley WilsmoreDr Austin May |
| **Location** | John Hunter Hospital, Newcastle |

**Declaration by Participant**

I have read the Participant Information Sheet or someone has read it to me in a language that I understand.

I understand the purposes, procedures and risks of the research described in the project.

I give permission for my doctors, other health professionals, hospitals or laboratories outside this hospital to release information to John Hunter Hospitalconcerning my disease and treatment for the purposes of this project. I understand that such information will remain confidential.

I have had an opportunity to ask questions and I am satisfied with the answers I have received.

I freely agree to participate in this research project as described and understand that I am free to withdraw at any time during the study without affecting my future health care.

I understand that I will be given a signed copy of this document to keep.

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|  |
|  | Name of Participant (please print) |  |  |  |  |
|  |
|  | Signature |  |  Date |  |  |
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**Declaration by Study Doctor/Senior Researcher †**

I have given a verbal explanation of the research project, its procedures and risks and I believe that the participant has understood that explanation.

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|  | Name of Study Doctor/Senior Researcher† (please print) |  |  |
|  |  |
|  | Signature |  |  Date |  |  |
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† A senior member of the research team must provide the explanation of and information concerning the research project.

Note: All parties signing the consent section must date their own signature.

**Form for Withdrawal of Participation**

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| **Title** | A Phase II Randomised, Double-Blind, Placebo-Controlled Study of the Efficacy, Safety and Tolerability of Oral NP202 in Adults who have paroxysmal atrial fibrillation and a cardiac device |
| **Short Title** | NP202 for Atrial Fibrillation |
| **Protocol Number** | NP202-002 |
| **Location** | John Hunter Hospital, Newcastle |

**Declaration by Participant**

I wish to withdraw from participation in the above research project and understand that such withdrawal will not affect my routine treatment, my relationship with those treating me or my relationship with John Hunter Hospital.

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|  | Name of Participant (please print) |  |  |  |  |
|  |
|  | Signature |  |  Date |  |  |
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In the event that the participant’s decision to withdraw is communicated verbally, the Study Doctor/Senior Researcher will need to provide a description of the circumstances below.

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**Declaration by Study Doctor/Senior Researcher†**

I have given a verbal explanation of the implications of withdrawal from the research project and I believe that the participant has understood that explanation.

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|  |
|  | Name of Study Doctor/Senior Researcher† (please print) |  |  |
|  |  |
|  | Signature |  |  Date |  |  |
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† A senior member of the research team must provide the explanation of and information concerning withdrawal from the research project.

Note: All parties signing the consent section must date their own signature.