Participant Information Sheet and Consent Form

Study Title:	A 32-week randomized, placebo-controlled double-blinded pilot study to compare the efficacy and safety of low-dose oral minoxidil in male and female patients with patterned hair loss (androgenetic alopecia).
Protocol Number:	MINOXM001
Principal Investigator:	Prof. Rodney Sinclair
Location:	Sinclair Dermatology Level 2, 2 Wellington Parade East Melbourne VIC

Part 1 What does my participation involve?

1 Introduction

You are being asked to participate in this clinical research study. This is because you have androgenetic alopecia (AGA) or more commonly known as patterned hair loss. This study is testing a potential new treatment option for AGA. AGA is the most common cause of hair loss in the community.

This Participant Information Sheet and Consent Form tells you about the study. It explains the purpose of the research, procedures and risks involved. It also describes information about you that will be obtained, how that information will be used and with whom it will be shared. Please read this information carefully. Please feel free to 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, a family member, a friend or your local doctor.
Participation in the research is voluntary (your choice). If you do not wish to take part, you do not have to. You will receive the best possible care whether or not you take part. Please take your time to make your decision.

If you decide you want to take part in the study, 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 study
- 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. For your information, this study is being conducted by Sinclair Dermatology.

2 What is the purpose of this research?

AGA is difficult to treat. Currently the only treatments approved for its treatment is minoxidil lotion and finasteride tablets. These treatments do not work for everybody. This study aims to see whether low-dose (less than 1mg) oral minoxidil may also regrow hair. So far there are no studies that look at whether low-dose minoxidil can be used to treat AGA. Minoxidil lotion is currently approved in Australia for the treatment of AGA. Minoxidil tablets up to 100mg a day are approved in Australia for the treatment of high blood pressure, but they are not approved for the treatment of AGA.

Approximately 40 people will participate in this clinical research study.

3 What happens during the study?

Duration of study

The study will take place over 32 weeks. You will be on medication for 24 weeks following successful screening phase. The screening phase can take up to 28 days before you can commence on your first dose of minoxidil.

There will be a total of seven (7) visits from the first screening and throughout the different study phases of the trial. One of these visits will be a phone call, this will be 2 weeks after your first dose. One of the study staff members will be calling you to check if you have been taking the medication properly and that you are not experiencing any side-effects. Your last visit is a follow-up visit (Visit 7), 28 days after your treatment completes.

Study Procedures

All study procedures will take place in the clinic. There are 2 study groups: 0.45 mg of active medication or placebo. There will be a 50:50 chance that you will be in one of these groups because you will be randomly assigned to a group. Neither the study staff nor you will know what treatment group you have been assigned to. During the trial, you will be given the study medication which you will need to take once a day. You will be required to attend the clinic at specified weeks to allow us to monitor your hair growth.

After you start the medication, both you and your doctor will independently rate how effective the medication is. You will need to fill in some questionnaires during your visits to assess how you feel about your hair loss and whether this has improved. Your study doctor will assess you for any side effects at each visit including monitoring your heart using an ECG machine and asking you how you have been feeling.

Photographs of your head (global photographs) and close-up photographs of your scalp (macrophotographs) will be taken at each study visit and you will be asked to complete some questionnaires. Prior to taken macrophotographs, a small (2cm diameter) area of the hair on the top of your head will be shaven. A small temporary tattoo, about the size of a dot on this page, will then be placed on your scalp. This will be used as a reference point so that the exact same area can be photographed at each visit.

On Study Visit days, you are required to only take your dose in clinic (not at home). You will take your dose once the study doctor has performed the necessary safety assessments.

The blood and urine samples collected for this study will be sent to a local laboratory for safety analysis. The results of these tests will be sent back to the study doctor throughout the study who will discuss any significant results with you. A copy of these results can be made available to you if you wish to keep it for your own records.

Urine pregnancy screening testing will be conducted at every Study Visit except for Week 2 (Visit 3) if you are of childbearing potential.

There will also be blood samples taken for pharmacokinetics (PK) testing. This will show us how your body absorbs, breaks down and removes the study drug from your body. These blood samples will be taken after you take your dose in clinic on Weeks 0, 8 and 24. On these Visit days, you will be required to stay in the clinic for longer than usual.

- **For Week 0** (the first day you receive your study medication), blood samples will be collected before, at 5mins, 15mins, 30mins, 1 hour, 2 hours, 4hours, 6hours and 24hours after you take your dose. For the 24-hour timepoint, we ask that you come back to the clinic, this will be a short 15-minute visit.
- **For Weeks 8 and 24** (the last day you receive your study medication) blood samples will be collected before, 5mins, 30mins, 1hour and 4hours after you take your dose.

In order to take multiple blood samples, an intravenous (IV) catheter may be inserted. An IV catheter is a thin plastic tube that is inserted into a vein. A total of about 8- 53 mL or 1½ to 10½ teaspoons of blood will be taken. Some known risks associated with obtaining blood samples include minor bruising, hematoma (accumulation of blood in the surrounding tissue), swelling, tenderness and inflammation at the site of blood collection. These risks typically last several days and will completely heal.

Blood samples may be analysed after the study has completed but will not be kept for longer than 3 years after the final clinical study report has been completed.

A small (2mm) sample of your skin on your scalp will be collected at Week 0 (the first day you receive your study medication) and Week 24 (the last day you receive your study medication). This skin sample, also known as a biopsy, will allow us to see if the study medication is present in the skin. Scalp biopsies will be collected using a standard disposable circular punch blade. The area chosen by the Study doctor will be cleaned with an antiseptic and a local anaesthetic injected to numb the area. The anaesthetic usually used is called lidocaine (or lignocaine). If you have lidocaine or lignocaine allergy, you need to inform the study doctor about it and another anaesthetic will be used. The injection may sting but this sensation will only last a few seconds. After the scalp biopsy, the area will be cleaned again and a dressing applied if necessary. A small 2mm punch biopsy typically heals well with no or minimal scarring. However, make sure to keep the area dry for the first day after the biopsy.

Scalp biopsies will be taken at two (2) timepoints: either 2 hours **or** 4 hours after you take your dose at the clinic. The timepoint you are assigned to will be at random, you or the study staff will not be able to choose this. Scalp biopsies are sent immediately to a local laboratory for analysis, however it may also be analysed after the study has completed. Scalp biopsies will not be kept for longer than 3 years after the final clinical study report has been completed.

Since some of these procedures have to be taken before and after you take the study drug, it is important that you <u>do not take your dose at home on Study Visit days</u>.

You will be given a treatment diary for you to keep a record of when you take your medication and if you experience any side effects. You will need to bring this diary when you come in for all your clinic visits.

The study visit schedule is detailed below.

Visit	1	2	3*	4	5	6	7
Study Period	**± 28 days to Week 0**	**Treatment period (± 5 days)**				**EOT/ET**	**Follow-up visit**
Study Week	**SCR**	**0**	**2**	**8**	**16**	**24**	**28**
Obtain informed consent	x						
Hair loss history. Medical, smoking & alcohol history	x	x					
Eligibility Criteria	x	x					
Demographics	x						
Height and Weight	x					x	x
Clinical assessments (performed by Study Doctor)							
Investigator scalp assessment	x	x		x	x	x	x
Vital signs	x	x		x	x	x	x
ECG	x	x				x	x
Physical examination	x	x		x	x	x	x
Safety blood & urine testing	x	x		x		x	x
Pregnancy testing (urine)	x	x		x	x	x	x
PK Sampling		x		x		x	
Scalp skin Biopsy		x				x	
Review of your health and all medications	x	x	x	x	x	x	x
Participant Questionnaires							
Participant questionnaire, DLQI/WAA-QOL		x		x	x	x	x
Participant questionnaire, KAP		x		x	x	x	x
Participant questionnaire, Sinclair Scale		x		x	x	x	x
Participant questionnaire, Patient Hair Shedding Scale		x		x	x	x	x
Participant questionnaire, MHGQ		x		x	x	x	x
Study procedures							
Scalp temporary tattoo and shave		x		x	x	x	x
Global scalp photography		x		x	x	x	x
Scalp macrophotography		x		x	x	x	x
Randomization		x					
Receive study medication		x		x	x		
Receive adherence diary		x		x	x		

4 What do I have to do?

At your screening visit, your doctor will ask you what other medicines you are taking. Certain medications will exclude you from participating in the trial. These include blood pressure medications, products that promote scalp hair growth (eg. finasteride or minoxidil), spironolactone, flutamide, cyproterone acetate and cimetidine.

During the study, you will be asked to keep your current hairstyle, hair colour and not to use medicated hair products or shampoos.

Except for the screening visit, you will be required to fast for a minimum of 8 hours before your scheduled Study Visits for Weeks 0, 8, 24 and 28. If you are participating in the trial you will not be able to donate blood during the period of the study.

At Study Visits 4,5 and 6 (Weeks 8, 16 and 24) you will be required to bring back all unused study medication and any empty medication vessels to the study site.

If you need to commence any new medications while the trial is being conducted please let the study doctor know.

The dose used in this study (0.45mg) is very low in comparison to the approved FDA and TGA doses of up to 10mg daily for the treatment of hypertension. To date, there is no known effects of Minoxidil on fertility, including future fertility in humans.

The effects of Minoxidil 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. You must not participate in the research if you are pregnant or trying to become pregnant, or breastfeeding. If you are female and child-bearing is a possibility, you must be willing to have a urine pregnancy test prior to commencing the research project and at every Study Visit. If you are male, you should not father a child or donate sperm for at least 3 months after the last dose of study drug. Both male and female participants must avoid pregnancy during the course of the research and for a period of 3 months after completion of the research project, as there is potential risk for an abnormal child being born. The study doctor will discuss effective methods of avoiding pregnancy with you.

[For female participants] You must use a highly effective method of contraception/birth control (methods which result in low failure rate, i.e. less than 1% per year, when used consistently and

correctly) and if currently lactating, you should not breast feed your baby while on this study and for 3 months after the last dose of study drug has been taken. Accepted methods of contraception include:

1. Established use of oral, injected or implanted hormonal methods of contraception.
2. Placement of an intrauterine device (IUD) or intrauterine system (IUS).
3. Sterilised male partner (with the appropriate post-vasectomy documentation of the absence of sperm in the ejaculate).

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. Even if you are no longer in the study, your study doctor will contact you after your baby is born to find out about the baby's health.

[For male participants] It is highly recommended that you inform your partner of your participation in the study and the need to avoid pregnancy. The use of contraception is strongly recommended. It is recommended that a condom be worn for all sexual intercourse as the study medication may affect your sperm risking the potential for an abnormal child being born. Further, you must agree that if your partner becomes pregnant while you are on the study, you will advise the study doctor who will then provide you with an authorisation form to present to your partner. If she is in agreement, that authorisation will function as consent to approve the study doctor's access to medical information to allow monitoring of the pregnancy, and the birth and the health of the baby.

5 Do I have to take part in this study?

Participation in any clinical study 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 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, 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 Samson Clinical or Sinclair Dermatology.

6 What are the alternatives to participation?

You do not have to take part in this study to receive treatment at this clinic. Other options are available; these include finasteride tablets and minoxidil lotion. Your study doctor will discuss these options with you before you decide whether or not to take part in this study. You can also discuss the options with your local doctor.

7 What are the possible benefits of taking part?

We cannot guarantee or promise that you will receive any benefits from this study; however possible benefits may include prevention of hair loss and hair regrowth. On Weeks 0, 8 and 24 where additional blood samples will be taken for PK testing, you will be provided with refreshments. There will be no additional costs to you for your participation in the study. However, you will be reimbursed (up to $50) for your time and travel to the clinic on each completed scheduled Study Visit days.

8 What are the possible risks and disadvantages of taking part?

Medical treatments often cause side effects. Minoxidil is currently used to treat high blood pressure. The doses used to treat high blood pressure are much higher than the doses you will potentially be taking. There are also potential heart-related side effects of minoxidil on people with any kidney or heart conditions. Some of the common side effects of minoxidil are:

- dizziness
- heart palpitations
- swelling of the feet
- nausea/vomiting

In addition, the recommended doses (10mg) of Minoxidil for high blood pressure have been shown to result in growth of unwanted body hair. However, we do not anticipate that you will have any of these side effects at the doses you will be taking. But if you have any of these side effects, or are worried about them, talk with your study doctor. You will also be asked to record these side effects in a diary. Your study doctor will also be looking out for side effects.

A skin scalp biopsy is generally a safe procedure but sometimes complications can occur. Some of these complications include: bleeding from the biopsy site, bruising, infection, scarring and a local reaction to the anaesthetic. If this occurs, you are required to contact the Clinic to seek advice for medical attention.

9 What if new information arises during this study?

Sometimes during the course of a study, 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 study. 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 study you will be asked to sign an updated consent form.

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

10 Can I have other treatments during this study?

Whilst you are participating in this study, you may not be able to take some or all of the medications or treatments you have been taking for your condition or for other reasons. 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, herbal remedies, acupuncture or other alternative treatments. You also need to tell your study doctor about any changes to these medications during your participation in the study. Your study doctor will explain to you, which treatments or medications need to be stopped while you are involved in the study.

11 What if I withdraw from this study?

If you decide to withdraw from the study, please discuss with the study doctor or study staff before you withdraw. This will allow discussion of any health risks or special requirements related to withdrawing. If you withdraw from the study during the treatment period (in between Weeks 0 and Week 24), then you will be asked to come to the study site as soon as possible so that the assessments for the Early Termination visit (Week 24) can be done. You will then be asked to continue into the Follow-Up period of the study which includes the final visit (Week 28).

If you withdraw, the study doctor and relevant study staff will not collect additional personal information from you. Personal information already collected will be retained to ensure that the results of the study can be measured properly and to comply with the law. Also, data collected by the sponsor up to the time you withdraw will form part of the study results. If you do not wish for them to do this, you must tell them before you join the study.

12 Could this study be stopped unexpectedly?

This clinical study 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 do not need further testing.
- Decisions made in the commercial interests of the sponsor or by local regulatory/health authorities.

13 What happens when the study ends?

When the study ends, you can still continue to have your regular medical follow up visits with your usual dermatologist. Other treatment options available to treat AGA will be made available to you.

Part 2 How is the study being conducted?

14 What will happen to information about me?

By signing the consent form, you allow the study doctor and relevant research staff to collect and use your personal information needed for the study. Any information obtained in connection with this study that can identify you will remain confidential. The information will be kept on a password-secured computer. Your name will be de-identified and coded. Any data stored on hard copies will be kept under lock and key. All information will be kept for seven (7) years after which they will be erased from the computer. All hard copies will be shredded and disposed accordingly.

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 study.

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

Information about your participation may be recorded in your health records. In accordance with relevant Australian and Victorian 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 which you disagree with to be corrected. Please contact the study staff named at the end of this document if you would like access to your information.

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

A description of this clinical trial is also required on the website mentioned above by the Australian National Statement on Ethical Conduct in Human Research 3.3.12.

It is anticipated that the results of this study will be published and/or presented in 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.

15 Complaints and compensation

If you suffer an injury as a result of participating in this study, hospital care and treatment will be provided. If you are injured or become seriously unwell as a result of your participation in this trial, you may have a right to seek compensation. It is the recommendation of the independent ethics committee responsible for the review of this trial that you seek independent legal advice before taking any steps towards compensation for injury.

You can contact your study doctor at any time throughout the study if you have any concerns or you feel you may have a study-related injury.

16 Who is organising and funding the research?

This research is being conducted and funded by Samson Clinical. Professor Sinclair is the sole Director and Shareholder of Samson Clinical and owner and director of Dr. Rodney Sinclair Pty Ltd, trading as Sinclair Dermatology. Professor Sinclair was also the inventor of oral minoxidil tablets for the treatment of AGA (Patent 2011100917, 26, July 2011).

No other member of the research team will receive a personal financial benefit from your involvement in this study (other than their ordinary wages).

17 Who has reviewed the study?

All research in Australia involving humans is reviewed by an independent group of people called the Human Research Ethics Committee (HREC). The ethical aspects of this clinical study have been approved by Bellberry 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.

18 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 that may be related to your involvement in the project (for example, any side effects), you can contact the principal study doctor on (03) 96542426 or any of the following people:

Clinical contact person

Name	Jennifer Kierran
Position	Practice Manager
Telephone	(03) 96542426
Email	manager@sinclairdermatology.com.au

For matters relating to research at the site at which you are participating, the details of the local site complaints person are:

Name	Joanne Kenny
Position	Study Coordinator
Telephone	(03) 96542426
Email	joanne.kenny@sinclairdermatology.com.au

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:

HREC Office contact (Single Site - Research Governance Officer)

Position	Committee Chair, Bellberry Human Research Ethics Committee
Telephone	(08) 8361 3222.

Consent Form - *Adult providing own consent*

Title	A 32-week randomized, placebo-controlled double-blinded pilot study to compare the efficacy and safety of low-dose oral minoxidil in male and female patients with patterned hair loss (androgenetic alopecia).
Short Title	Treatment of pattern hair loss (androgenetic alopecia) with oral minoxidil.
Protocol Number	MINOXM001
Project Sponsor	Samson Clinical
Coordinating Principal Investigator/ Principal Investigator	Prof. Rodney Sinclair
Location	Sinclair Dermatology

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 Sinclair Dermatology concerning 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 study 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.

Name of Participant (please print) _____

Signature _____ Date _____

If required:

Name of Witness* to Participant's Signature (please print) _____

Signature _____ Date _____

* Witness is not to be the investigator, a member of the study team or their delegate. In the event that an interpreter is used, the interpreter may not act as a witness to the consent process. Witness must be 18 years or older.

Declaration by Study Doctor/Senior Researcher†

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

Name of Study Doctor/Senior Researcher (please print) _____

Signature _____ Date _____

† A senior member of the research team must provide the explanation of and information concerning withdrawal from the study.

Form for Withdrawal of Participation - *Adult providing own consent*

Title	A 32-week randomized, placebo-controlled double-blinded pilot study to compare the efficacy and safety of low-dose oral minoxidil in male and female patients with patterned hair loss (androgenetic alopecia).
Short Title	Treatment of pattern hair loss (androgenetic alopecia) with oral minoxidil.
Protocol Number	MINOXM001
Project Sponsor	Samson Clinical
Coordinating Principal Investigator/ Principal Investigator	Prof. Rodney Sinclair
Location	A/Prof. Leslie Jones Sinclair Dermatology

Declaration by Participant

I wish to withdraw from participation in the above study and understand that such withdrawal will not affect my routine treatment, my relationship with those treating me or my relationship with Samson Clinical or Sinclair Dermatology.

Name of Participant (please print) _____

Signature _____ Date _____

Declaration by Study Doctor/Senior Researcher†

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

Name of Study Doctor/
Senior Researcher† (please print) _____

Signature _____ Date _____

† A senior member of the research team must provide the explanation of and information concerning withdrawal from study.

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