INFORMED CONSENT

Sponsor / Study Title:	**Renew Research, LLC, Renew Health Ltd., Renew Group Private Ltd. / A Randomized Pivotal Study of Renew™ NCP-5 System for the Treatment of Mild Cognitive Impairment due to Alzheimer's Disease or Mild Dementia of the Alzheimer's Type**
Protocol Number:	**Renew™ NCP-5 -1001**
Principal Investigator: (Study Doctor)	**«PiFullName»**
Telephone:	**«SitePhoneNumber»**
Address:	**«PiLocations»**

INTRODUCTION

Before agreeing to participate in this research study, it is important that you read and understand the specific research study explanation shown below. This consent document describes the purpose, duration, procedures, and alternative procedures available to you, risks (including discomforts and precautions of the study) and benefits. It also describes your right to withdraw from the study at any time. Because this study is experimental, the clinical research study team cannot guarantee that the study treatment to be applied will work for your health condition.

It is very important that you are completely truthful with your Investigator about your health history, so that your harm is minimized by taking part in this study.

PURPOSE OF THE STUDY

You are being asked to participate in this research study because you have been clinically diagnosed with Mild Cognitive Impairment (MCI) due to Alzheimer's disease, or mild dementia of the Alzheimer's type.

The purpose of this research study is to test how safe and effective the Renew™ NCP-5, an External Counterpulsation (ECP) device is for the treatment of mild cognitive impairment due to Alzheimer's disease, and mild dementia of the Alzheimer's type. Specifically, this study will evaluate how the Renew™ NCP-5 device works in relation to your ability to think, remember, understand and learn (cognition).

The Renew™ NCP-5 device is a United States Food and Drug Administration (FDA) cleared device for treatment of severe chest, arm, shoulder pain caused by inadequate blood flow to the heart that does not respond to standard medical or surgical therapy.

For treatment of MCI due to Alzheimer's disease and mild dementia of the Alzheimer's type, the Renew™ NCP-5 device is a new investigational medical device because the device is not yet approved by the FDA to be used in standard clinical treatment for this indication.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. 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.

NUMBER OF SUBJECTS / LENGTH OF PARTICIPATION

About 100 to 250 subjects will participate in this study. If you qualify and decide to participate in the study, you will be randomly assigned by chance (similar to the flip of a coin) to either the Renew™ NCP-5 device study treatment or the sham procedure using the same device. You will have a 50% (1:1 ratio) chance of receiving Renew™ NCP-5 device study treatment and a 50% (1:1 ratio) chance of receiving the sham procedure.

Your participation in this study will last approximately 1 year. During the initial treatment period, you will be treated five days per week with a maximum of 35 treatments administered during the initial 12-week treatment period. At a minimum you will receive treatments three days per week. Each treatment session will last for 60-minutes. Once you have completed the first 35 treatments, you will start the maintenance period where you will receive two treatments per week up to Week 24. At nine (9) months and twelve (12) months after your first study treatment, you will return for follow up assessments.

You will also perform study related assessments and receive standard medical tests as described below under "procedures" to measure your ability to move, think, remember, understand and learn (cognition). These assessments and medical tests will occur based on a clinical schedule during the study period.

VOLUNTARY PARTICIPATION

Your participation in this study is entirely voluntary. Your decision not to participate will not have any negative effect on your medical benefits, or your medical care. You can decide to participate now, but withdraw your consent later and stop being in the study without any loss of benefits or medical care to which you are entitled.

PROCEDURES

If you choose to participate, the Principal Investigator and his/her research study staff will describe all procedures to be followed.

- **Medical History** – A review of the health conditions you presently have or have had in the past will be collected.

- **Physical Examination** – A physical examination, including a neurological assessment, will be done to ensure you are healthy enough to participate in the study.

- **Medication, treatment and procedure history** – A review of your medications and supplements will be collected. You will be asked to keep taking your medications for your chronic conditions throughout the study. We will also collect information on any past treatments and procedures you may have had.

- **Vital Signs** – Blood pressure, heart rate, respirations, and temperature will be taken. These are standard medical procedures. Vitals signs will be checked (blood pressure, temperature, heart rate and respiration rate) at baseline and at non-study treatment visits while you are sitting. Before and after each study treatment blood pressure and heart rate will be taken to ensure your safety and that none of the procedures done are causing any problems with your vital signs. Vital signs will be taken while you are lying down during the treatment visits.

- **Electrocardiogram (ECG)** – This is a standard medical procedure to check the functioning of your heart and make sure you are healthy enough to participate in the study. It records the electric activity of the heart.

- **Cardiovascular Risk Assessment** – A brief assessment of your cardiovascular (heart) health will be completed using your age, gender, race, blood pressure, some results from your medical history and lab work using a computer program.

- **Cognitive Assessments** – You will be given some tests to confirm that you have Mild Cognitive Impairment due to Alzheimer's disease, or mild dementia of the Alzheimer's type and to test your ability to think, remember, understand and learn (cognition). It is anticipated that it will take two hours to complete these tests. Cognitive testing will occur at the Screening, Baseline, Weeks 6, 12, 18, 24, 9 month, and 12 month visits. Cognitive testing may be done on treatment days but must be completed after the treatment.

- **Exercise** – You will be asked about your level of exercise, including cognitive exercises such as language exercises, Sudoku puzzles or online brain training programs (e.g. Lumosity), number of times you exercise per week (if any), and length of each exercise session. The aim is to have you maintain the same level of exercise over the course of the study. You will also be asked to complete two exercises to assess your ability to move.

- **Patient Questionnaires –** You will be asked to complete a self-evaluation questionnaire regarding your use of health-related services during the course of the study.

- **Blood Sample**: This is a standard medical procedure. A sample of your blood will be collected at various times (6 times in total) during the study. It is anticipated needing approximately 8 to 16 teaspoons of blood over the course of the one-year study. Collected blood samples will be transferred to a clinical laboratory for testing. Blood will only be collected for the objectives of this study and no additional blood tests will be done. If the laboratory has problems processing your blood sample, you may be asked to give a repeated sample.

- **MRI** (Magnetic Resonance Imaging): This is a standard medical procedure. The goal of this procedure is to make sure there are no abnormalities in your brain. At several sites, the MRI will also be used to measure the blood flow in your brain and the rate at which blood moves through your blood vessels. You will be informed if the MRI will be used for this purpose. The MRI is a medical device that uses a large magnet to deliver strong magnetic waves to scan your brain. You will need to wear comfortable clothing, remove any metal objects from your body and lie still on a bed adopting a comfortable position. You will lie still for 90 minutes while the scanner takes photos of your brain and you will hear loud tapping noises during the procedure. The MRI operator will give you earplugs or headphones to wear. The MRI is painless. You will have an MRI at your initial visit and at Week 24 and 12 months from your first treatment.

Magnetic fields do not cause harmful effects at the levels used in the MRI. However, the magnets used are very strong and will attract some metals. Tell your study doctor if you have a cardiac pacemaker or implants or other metal in your body. Having these devices or implants may mean you should not have an MRI scan performed. You should also tell your study doctor if you have any tattoos or other permanent makeup which may become warm or irritated during the MRI. In the event the machine does not capture the image properly, you may be asked to have the scan repeated.

Renew™ NCP-5 treatment: This is the experimental device used in this study to treat mild cognitive impairment due to Alzheimer's disease, and mild dementia of the Alzheimer's type. The goal of this study treatment is to increase the blood flow to your brain and determine if this action improves your ability to think, remember, understand and learn (cognition). The study treatment is done as follows: While you are lying flat, pneumatic, blood pressure like cuffs, will be placed on three places on your legs: your calfs, your lower thighs and buttocks. The operator will also place three sticky patches (electrodes) on your chest that will be connected to a monitor that records your heart rate and rhythm. The cuffs will be inflated and deflated based on the actions of your heart (between heartbeats). Each study treatment session will take approximately one hour and there will be up to 5 study treatment sessions per week for up to 12 weeks (initial study treatment period) and 2 study treatment sessions per week (maintenance period) until Week 24 week. Compression pressure will be given at different levels depending on which group you are randomized to and your overall ability to tolerate the study treatment. You will then be asked some questions by your provider/research team.

For selected sites, you may be asked to complete the following assessments, which will add additional time to your visit:

- **Ultrasound** of your brain uses high frequency sound waves to measure the amount of blood flow through arteries and veins. It is non-invasive and takes about 30 minutes to complete. It will be performed 6 times during the study.

- **Ultrasound measurement** of how well your blood vessels function will be performed by placing a blood pressure cuff on your forearm and inflating and deflating it while you are lying flat on a table. This test will take approximately 30-60 minutes. This test will be performed 6 times during the study.

SCREENING (will help to determine if you are eligible to participate in the study).

• Sign Informed Consent	• Vitals
• Demographics	• EKG
• Medical, Treatment and Procedure History	• Labs
• Medication History	• MRI
• Cognitive Assessments	• Physical Exam

BASELINE, Weeks 6, 12, 18, 24, Month 9 and Month 12:

• Cognitive Assessments/tests	• Randomization (Baseline only)
• Vital signs	• Adverse Event
• Physical Exam (Month 12 only)	• Concomitant Medications and treatment
• Labs (Weeks 12, 24 and 12 Month only)	• Ultrasound (selected sites only at Day 1)
• Exercise Regimen with mobility assessments	• Study Termination (Month 12/Early termination only)
• Health Resource Utilization Survey (Baseline, Weeks 12, 24, Months 9 and 12)	Patient Satisfaction Survey (Month 12 only)

STUDY TREATMENT and MAINTENANCE: You will participate and receive the following research and standard medical procedures, which will occur during the Study Treatment & Maintenance periods of this study.

We anticipate that each study treatment visit will last for 1-2 hours. Visits at Screening, Baseline, Weeks 6, 12, 18 and 24, 9 month and 12 months or early termination will last approximately to 2 – 3 hours.

YOUR RESPONSIBILITIES AS A STUDY PARTICIPANT

As a participant in this study, your responsibilities include:

- Disclose all health information to the best of your ability to the Principal Investigator or study staff
- Comply with all study procedures
- Follow the instructions of the Principal Investigator and study staff
- Keep your study appointments. If you have to miss an appointment, call the research study staff to reschedule
- Tell the Principal Investigator or research study staff about any side-effects, changes in treatments, medications or exercise, doctor visits or hospitalizations you may have
- Ask questions as you think of them

WITHDRAWAL FROM STUDY

If you agree to participate in the study and then change your mind, you are free to withdraw your consent and discontinue your participation at any time. Your decision will not affect your ability to receive medical care for your disease and you will not lose any benefits to which you are otherwise entitled. If you want to withdraw from treatments, you will be encouraged to come in for the assessment visits only which would enable us to track your progress.

The Investigator or the sponsor can stop your participation at any time without your consent for the following reasons:

- If it appears to be medically harmful to you;
- If you fail to follow directions for participating in the study;
- If it is discovered that you do not meet the study requirements;
- If the study is canceled

If you withdraw from the study or the Principal Investigator determines you should be withdrawn from the study, you will be asked to:

- Complete the exams to test your ability to think, remember, understand and learn (cognitive tests)
- Have a final MRI and, if applicable ultrasound assessments.

POSSIBLE RISKS, SIDE EFFECTS AND/OR DISCOMFORTS

There are different levels of risks, discomforts and inconveniences associated with any research study. You should talk to the Principal Investigator if you have any questions. Some possible risks are:

- Some people experience side effects from the use of ECP which are mild and resolve quickly including:
    - Fatigue
    - Headache and dizziness
    - Muscle aches
    - Skin irritation, swelling, bruising where cuffs are applied
- When blood samples are taken, some people experience pain, bruising, or bleeding at the site of puncture. There is also a minimal possibility of infection. Some people may feel faint.
- Skin irritation is rare but could occur during an electrocardiogram (ECG) from the electrodes or gel that is used.

- While no significant risks have been found from the use of MRI scans, you may be bothered by the MRI machine noise and by feelings of being closed in (claustrophobia).
- The FDA has determined that this study presents no significant risk to participants. However, since the study device, Renew™ NCP-5, is investigational when taken alone or in combination with medications, there may be other risks that are unknown.

POTENTIAL BENEFITS

The clinical research study team cannot and does not guarantee or promise that you will receive any benefits from this study. However, you will have access to this device, Renew™ NCP-5, which you might not otherwise have had and which may provide a benefit to you.

ALTERNATIVE TREATMENT

You do not have to be in this study to receive treatment for mild cognitive impairment or Alzheimer Disease**.** Please consult with your physician for other treatment options. The Investigator will discuss with you the risks and benefits of alternative treatments.

NEW FINDINGS

Any new important information that is discovered during the study and which may influence your willingness to continue participation in the study will be made available to you.

COMPENSATION FOR PARTICIPATION

You and your caregiver/family member will be reimbursed for costs you incur that are related to your participation in the study. Transportation, meals, parking fees and other relevant costs will be paid for by the study. If you do not finish the study, you will only be paid for the visits you completed.

Visit Name	Participant Stipend
Visit 1 / Screening	$xx.xx
Visit 2 / Baseline	$xx.xx
NCP-5 Treatment *(Paid per every treatment visit completed; up to 5 visits per week from Week 1 – Week 11 and up to 2 visits per week from Week 13 – Week 23)* *$xx.xx See below*	
Week 6 Assessment	$xx.xx
Week 12 Assessment	$xx.xx
Week 18 Assessment	$xx.xx
Week 24 Assessment	$xx.xx
9 Month Follow Up	$xx.xx
12 Month Follow Up / Early Term	$xx.xx

You will be paid [Time of Payment (i.e. following each completed visit, annually, monthly, etc.)].

CONFIDENTIALITY

Records of your participation in this study will be held confidential except when sharing the information as required by law, or as described in this informed consent. The Investigator, the sponsor, or persons working on behalf of the sponsor, and under certain circumstances, the FDA, the Institutional Review Board (IRB) and other regulatory authorities will be able to inspect and copy confidential study-related records which identify you by name. If the results of this study are published or presented at meetings, you will not be identified.

If you would like to know how the sponsor will protect the privacy of your records, ask the study doctor how to get this information.

All attempts will be made to anonymize the data immediately upon acquisition in order to maintain participant confidentiality.

You have the right to see and copy your records. However, if you sign this form, you might not be able to see or copy some of your records until after all participants finish the study.

COMPENSATION FOR INJURY

If you suffer an adverse reaction, illness, or injury which, in the reasonable judgment of Institution, was directly caused by the Study Device or any properly performed procedures required by the Protocol, Sponsor shall reimburse for the reasonable and necessary costs of diagnosis and treatment of any Study subject injury, including hospitalization, but only to the extent such expenses are not attributable to (i) Institution's negligence or willful misconduct or (ii) the natural progression of an underlying or pre-existing condition or events, unless exacerbated by participating in the Study. However, Sponsor shall not reimburse for other injury or illness related costs (such as lost wages).

You will not lose any of your legal rights or release the sponsor, the Investigator, the study staff, or study site from liability for mistakes by signing this consent document.

To pay medical expenses, the sponsor will need to know some information about you like your name, date of birth, and Medicare Beneficiary Identifier (MBI). This is because the sponsor has to check to see if you receive Medicare and if you do, report the payment it makes to Medicare.

COSTS

There will be no charge to you for your participation in this study. The study device, study-related procedures, and study visits will be provided at no charge to you.

EMERGENCY CONTACT / IRB CONTACT

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns or complaints about the study, please contact the Investigator at the telephone number listed on page one of this consent document. If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in a research study being conducted by the Investigator listed on page one of this document.

An institutional review board (IRB) is an independent committee established to help protect the rights of research subjects. If you have any questions about your rights as a research subject, and/or concerns or complaints regarding this research study, you should contact:

- By mail:
  Study Subject Adviser
  Advarra IRB
  6940 Columbia Gateway Drive, Suite 110
  Columbia, MD 21046
- or call **toll free**: 877-992-4724
- or by **email**: adviser@advarra.com

Please reference the following number when contacting the Study Subject Adviser: Pro00027434.

PRIMARY CARE PHYSICIAN / SPECIALIST NOTIFICATION OPTION

Please indicate below whether you want the clinical research study team to notify your primary care physician, or your specialist of your participation in this study.

_____ Yes, I want the Investigator to inform my primary care physician/specialist of my participation in this study.

_____ No, I do not want the Investigator to inform my primary care physician/specialist of my participation in this study.

_____ I do not have a primary care physician/specialist.

_____ The Investigator is my primary care physician/specialist.

PHOTOGRAPHS

During your participation in the study, you may be periodically asked if the study team can take pictures of you to send to the study Sponsor. The photographs will be on the treatment area and used for quality assurance purposes. No identifying information will be captured on the photographs.

RISKS

There are no known physical risks from participating in the photography part of the study.

There are non-physical risks associated with participating in this part of the study, such as the risk of accidental disclosure of your personally identifiable medical information.

There may be risks that are currently unforeseeable.
Please indicate below whether you consent to allowing the clinical research team to take photographs of your lower body throughout the study if needed, to monitor treatment and safety. No identifiable information will be captured.

_____ Yes, I consent to having a photograph taken of my lower body for study related purposes.

_____ No, I do not consent to having a photograph taken of my lower body for study related purposes.

CONSENT

I have read and understand the information in this informed consent document. I have had an opportunity to ask questions and all of my questions have been answered to my satisfaction. I voluntarily agree to participate in this study until I decide otherwise. I do not give up any of my legal rights by signing this consent document. I will receive a copy of this signed consent document.

_____
Subject's Printed Name

_____ _____
Subject's Signature Date (MM/DD/YYYY)

_____
Printed Name of Legally Authorized Representative

_____ _____
Signature of Legally Authorized Representative Date (MM/DD/YYYY)

_____
(Authority of Legally Authorized Representative to act on behalf of Subject)

*Authority to act on behalf of another includes, but is not limited to parent, guardian, or durable power of attorney for health care.

_____
Printed Name of the Person Conducting the
Consent Discussion

_____ _____
Signature of the Person Conducting the Date (MM/DD/YYYY)
Consent Discussion

AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION

During your participation in this research study, the Investigator and study staff will collect or create personal health information about you (for example, medical histories and results of any tests, examinations or procedures you undergo while in the study) and record it on study documents. The Investigator will keep this personal health information in your study-related records (that we will refer to as "your study records"). In addition, the Investigator may obtain, and include in your records, information regarding your past, present and/or future physical or mental health and/or condition. Your Investigator may ask you to sign a separate authorization to obtain some or all of your medical records from your doctor. Your study records may include other personal information (such as social security number, medical record numbers, date of birth, etc.), which could be used to identify you. Health information that could identify you is called "Protected Health Information" (or "PHI").

Under federal law (the "Privacy Rule"), your PHI that is created or obtained during this research study cannot be "used" to conduct the research or "disclosed" (given to anyone) for research purposes without your permission. This permission is called an "Authorization". Therefore, you may not participate in this study unless you give your permission to use and disclose your PHI by signing this Authorization. By signing, you are agreeing to allow the Investigator and staff to use your PHI to conduct this study.

By signing this Authorization, you also are agreeing to allow the Investigator to disclose PHI as described below:

- The sponsor of this study and anyone working on behalf of the sponsor to conduct this study (referred to as "the sponsor"). The sponsor will analyze and evaluate the PHI and may use it to develop new tests, procedures and commercial products. The study staff will assign a code number and/or letters to your records, which means that you will not ordinarily be identified in the records sent to the sponsor. The sponsor may, however, look at your complete study records that identify you. In addition, the sponsor may visit the study site to oversee the way the study is being conducted and may review your PHI during these visits to make sure the information is correct.
- The Institutional Review Board ("IRB") may have access to your PHI in relation to its responsibilities as an Institutional Review Board.

Your health data will be used to conduct and oversee the research, including for instance:

- To see if the device works and is safe.
- To compare the device to other devices.
- For other research activities related to the device.

The Investigator or sponsor may disclose your PHI to the United States Food and Drug Administration ("FDA") or similar regulatory agencies in the United States and/or foreign countries.

These disclosures also help ensure that the information related to the research is available to all parties who may need it for research purposes.

Except for the disclosures described above, your PHI will not be shared with others unless required by law. If your PHI is given to the parties listed above and/or to others who are not required to comply with the federal law, your PHI will no longer be protected by this law and could possibly be used or disclosed in ways other than those listed here.

You have a right to see and make copies of your PHI. You are agreeing, however, by signing this document, not to see or copy some or all of your PHI until the sponsor has completed all work related to this study. At that time, you may ask to see your records.

You have a right to revoke your Authorization at any time. If you revoke it, your PHI will no longer be used for this study, except to the extent the parties to the research have already taken action based upon your Authorization or need the information to complete analysis and reports for this research. To revoke your Authorization, you must write to the Investigator, stating that you are revoking your Authorization to Use and Disclose Protected Health Information. If you revoke this Authorization, you will not be allowed to continue to be in this study.

You will receive a copy of this Authorization after you have signed it.

I have read this form and its contents were explained. My questions have been answered. I voluntarily agree to allow study staff to collect, use and share my health data as specified in this form. I will receive a signed and dated copy of this form for my records. I am not giving up any of my legal rights by signing this form.

_____

Subject's Printed Name

_____ _____

Subject's Signature Date (MM/DD/YYYY)

Printed Name of Legally Authorized Representative

_____ _____
Signature of Legally Authorized Representative Date (MM/DD/YYYY)

_____
(Authority of Legally Authorized Representative to act on behalf of Subject)

*Authority to act on behalf of another includes, but is not limited to parent, guardian, or durable power of attorney for health care.

_____
Printed Name of the Person Conducting the Consent Discussion

_____ _____
Signature of the Person Conducting the Consent Discussion Date (MM/DD/YYYY)