PARTICIPANT INFORMATION SHEET

Cannabidiol for Parkinson's Disease Psychosis

(CAN-PDP): PHASE II

You are being invited to take part in the above research study. Before you decide whether to participate it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with friends and relatives if you wish. Please ask a member of the study team if there is anything that is not clear or if you would like more information. Take your time to decide whether or not you wish to take part. If you decide to take part, you may keep this information sheet.

What is the purpose of the study?

Parkinson's disease psychosis is a symptom of Parkinson's disease that causes patients to experience hallucinations and/or delusions. More than half of all patients with Parkinson's disease eventually develop these symptoms over the course of their disease. These problems can be difficult to manage and can impact quality of life. Currently, existing medications to treat these symptoms are either not very effective or have significant side effects.

This is a research study to test an investigational medicine called cannabidiol (CBD). Previous studies not only suggest that CBD may be useful in treating psychosis, they also suggest that it is safe to use in older adults.

The purpose of this trial is to look at how safe and well CBD works in patients with Parkinson's disease psychosis, and how well it is tolerated. The investigational medicine is not expected to modify the progression of Parkinson's disease.

What is the investigational medicine?

Cannabidiol (CBD) is extracted from the cannabis plant but is not responsible for the effects produced by cannabis, such as 'feeling high'. The study will also include a placebo. A placebo is an investigational medicine look-a-like but contains no active ingredients. In this information sheet, the term "study medicine" refers to either CBD or placebo. Because this is a research study, study medicine will only be given to you during this study and not after the study is over.

Why have I been invited?

You are being invited to participate in this research study because you have Parkinson's disease and experience symptoms of psychosis (such as delusions or hallucinations).

Do I have to take part?

It is up to you to decide whether or not to take part. If you decide to take part, you will be given this information sheet to keep and will be asked to sign a consent form. If you decide to take part, you are still free to withdraw at any time, without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the future medical care that you receive.

What will happen to me if I take part?

The aim of this study is to investigate the effect of CBD on symptoms of Parkinson's disease psychosis. To investigate this, participants will be randomly allocated to one of two treatment groups. The first group will receive cannabidiol (CBD) capsules and the second group will receive placebo capsules. Participants will have a 50/50 chance of receiving either CBD or placebo capsules. You will be asked to take the study medicine for 12 weeks (84 days).

This is a double-blind study which means that you and the study team will not know which treatment group you are in. In case of an emergency however, the study team can get this information.

If you agree to participate, you will be invited to attend six study visits, which can take place either at home or in a clinical setting. To minimise the length of time taken for face-to-face visits, we will aim to conduct the majority of assessments and questionnaires remotely (i.e. over the telephone, videocall or email) where this is feasible.

We also have a sub-study that aims to investigate the effect of CBD on brain function. To investigate this, participants will also undergo two brain scans using magnetic resonance imaging (MRI) at King's College London. If interested in participating in the sub-study, we will provide you with a separate information leaflet and consent form.

- **Screening visit (up to two weeks before the start of treatment)**

If you agree to participate in this study, we will perform a screening visit which will take approximately 2 to 3 hours. You will be asked some questions to review your eligibility to take part in this research project and, if eligible, asked to read and sign a consent form.

We will ask questions to get basic background information about you, your general health and medications that you are currently taking. We will need to carry out a short physical examination (including heart rate, blood pressure, temperature, neurological assessment), and take a small blood sample.

You and your caregiver will also be asked to complete some questionnaires to measure your memory and any behavioural or psychological problems that you may currently be experiencing.

- **Baseline visit (day 1)**

The baseline visit will take place on day 1 of the study and will take approximately between 3 and 4 hours.

During this visit we will ask you and your caregiver to participate in an interview where we will discuss any behavioural or psychological problems that you may currently be experiencing. We will also ask you and your caregiver to fill in some questionnaires and rating scales relating to your memory, quality of your life and daily functional skills. As before, we will do a short physical examination, and take a small blood sample.

At the end of the baseline visit you will be given a two-week supply of either CBD (400 mg/day) or placebo capsules. We ask that you take the study medicine once a day around mealtime.

- **Follow-up visit 1 (day 15)**

Follow-up visit 1 will take place on day 15 of the study and should only take approximately 1 to 2 hours.

As before, we will do a short physical examination. Any negative effects of the study medicine will be discussed during this visit and any unused study medication should be returned. At the end of this visit you will be given a four-week supply of CBD (400 mg/day) or placebo capsules.

- **Follow-up visit 2 (day 43)**

Follow-up visit 2 will take place on day 43 of the study and should only take approximately 1 to 2 hours.

As before, we will need to carry out a short physical examination (including heart rate, blood pressure, temperature) and take a small blood sample. Any negative effects of the study medicine will be discussed during this visit and any unused study medication should be returned. At the end of this visit you will be given a six-week supply of either CBD (800mg per day) or placebo capsules.

- **Follow-up visit 3 (day 85)**

Follow-up visit 3 will take place on day 85 of the study and should take approximately between 3 to 4 hours.

During this visit we will ask you and your caregiver to participate in an interview where we will discuss any behavioural or psychological problems that you may currently be experiencing. We will also ask you and your caregiver to fill in some questionnaires and rating scales relating to your memory, quality of your life and daily functional skills. As before, we will do a short physical examination, and take a small blood sample. Any negative effects of the study medicine will be discussed, and any unused study medication should be returned.

- **Follow-up visit 4 (day 113)**

Follow-up visit 4 will take place on day 113 of the study and should only take approximately 1 hour.

During this visit we may take a small blood sample in case the blood test results from the previous follow-up visit 3 are abnormal, and any negative effects of the study medicine will be discussed.

What do I have to do?

If you participate in this study, you will be expected to:

• Keep all scheduled appointments.

• Take the study medicine every day around mealtime and call the study team if you have any questions about how to take the study medicine. You should not stop taking the study medicine without talking to the study team first.

• Do not give the study medicine to anyone else. Only the participant can take the study medicine. Keep the study medicine out of the reach of children and persons who may not be able to read or understand the label.

• Bring all unused study medicine to Follow-up visit 1, 2 and 3.

• Tell your study team about any changes in your health, even if you think they are not important.

• Tell the study team about any other medicines that you take, even if it is medicine that you buy without a prescription, including any vitamins and supplements.

• Inform the study team if you move or change your phone number during the study.

• If you think you are or might be pregnant during the study, you must tell the study team immediately. If you become pregnant, you will have to stop participating in the study. The study team may ask for information about the pregnancy and the birth of the baby. The study team may share this information with the study sponsor.

•Some people receiving CBD may experience side-effects such as feeling sleepy or tired, which may affect your judgement and performance of skilled tasks. You should not drive, operate heavy machinery or engage in hazardous activities if you are experiencing significant side-effects such as sleepiness.

What are the possible benefits of taking part in the study?

You may or may not receive any benefits from taking CBD as part of the study. CBD might improve some of the symptoms of Parkinson's disease psychosis. The information we obtain in this study may help us to treat Parkinson's disease patients with psychosis more effectively in the future, reducing both patient and caregiver distress.

What are the possible disadvantages and risks of taking part in this study?

1) CBD: Previous research has shown that the effects of CBD are very subtle. Nevertheless, like all medicines, the active medication may cause side effects in some people, including mild sleepiness or tiredness, gastrointestinal problems, headache or nausea.

If you find CBD unpleasant or develop any side effects, let us know. The Study Doctor will be available by telephone and you can call at any time. In addition, we will properly assess any potential side effects during the study visits. The purpose of this is to make sure that you find the CBD acceptable. We don't want people to feel pressured into taking CBD if they find it unpleasant. It is not uncommon for people to

drop out of studies because of the side-effects of a drug. In the most unlikely scenario admission to a local ward can be arranged if necessary.

2) Blood samples: The physical risks and discomforts of giving the blood samples are the same as those for any other blood sample taken from a vein. There may be minor bruising or irritation.

3) Some of the questionnaires and rating scales may involve you answering questions that are sensitive and of a personal nature. You should only answer those questions that you are comfortable with. You do not need to answer any questions you do not wish to.

What happens when the study stops?

Because this is a research study, the study medicine will not be available at the end of the study. When the study ends, you will continue with your usual care from your GP or hospital.

What will happen to blood samples I give?

Samples will be analysed either internally or externally, depending on what is needed. When processing and storing your samples, the study will comply with the relevant laws to protect the confidentiality of research participants. We will carry out biomarker analyses including genetic/DNA analyses. Genetic research results are for research purposes only and not for clinical diagnosis or treatment. All samples that we collect from you will be anonymised and coded. Personal information will not be available to laboratory research workers or anybody outside of the research project.

Future use of samples

We anticipate that the samples we collect for future use will contribute to research for many years to come. Future research involving the information supplied may involve other research groups seeking to understand diseases like Parkinson's. These could be our collaborators or independent researchers from other academic and/or commercial groups. Your anonymised information would be made available only to bona fide research groups with full ethical approval for the research undertaken.

If you withdraw from the study, information collected may still be used. However, any stored blood or tissue samples that can still be identified as yours will be destroyed if you wish.

What are the risks if I become pregnant?

Taking the study medicine may involve unknown risks to a pregnant woman, an embryo, foetus (unborn baby) or nursing infant. Therefore, if you are pregnant, planning to become pregnant or are breastfeeding a child, you cannot participate in this study. We also ask that if you are of childbearing potential (i.e. premenopausal/menopausal), you are taking appropriate contraceptive measures. If you become pregnant during this study, you should notify the study team as soon as possible. The study medicine will be stopped and your participation in this study will be ended. Information about your pregnancy and its outcome will be collected and used to learn more about the effects of the study medicine on pregnancy.

What if something goes wrong?

In the event you experience any side effects, please contact the study team. You may also contact the NHS Patient Advice and Liaison Service (PALS) for independent advice. South London and Maudsley (SLaM) NHS Foundation Trust PALS can be contacted on free-phone 0800 731 2864 or by email at pals@slam.nhs.uk. Alternatively, you can dial NHS 111 to find the nearest PALS.

Regarding any side effects as a result of taking part in this study, King's College London will provide compensation for claims in respect of non-negligent harm and there is insurance for negligent action. Regardless of this, if you wish to complain, or have any concerns about any aspect of the study we would encourage you to discuss this with us as soon as possible and we will do our best to rectify matters or change procedures as appropriate.

Regarding insurance cover, King's College London (KCL)/ SLaM will maintain adequate insurance in relation to the trial, KCL through its own professional indemnity (Clinical Trials) and no-fault compensation, and the Trust having a duty of care to patients via NHS indemnity cover.

How will we use information about you?

We will need to use information from you and your medical records for this research project. We will keep all information about you safe and secure.

KCL/ SLaM is the sponsor for this study based in the United Kingdom. We will be using information from you and your NHS Trust medical records in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it

properly. KCL/ SLaM will keep identifiable information about you for a minimum of 25 years after the study has finished.

The NHS participating Trust will use your name, NHS number and/ or date of birth and contact details to contact you about the research study, and make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study. Individuals from KCL/ SLaM and regulatory organisations may look at your medical and research records to check the accuracy of the research study. The NHS Trust will pass these details to KCL/ SLaM along with the information collected from you and your medical records. The only people in KCL/ SLaM who will have access to information that identifies you will be people who need to contact you for trial monitoring purposes or audit the data collection process.

People who do not need to know who you are (for example, the people who analyse the information) will not be able to see your name or contact details. Your data will have a code number instead.

What are your choices about how your information is used?

- You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have.
- We need to manage your records in specific ways for the research to be reliable. This means that we won't be able to let you see or change the data we hold about you.
- If you agree to take part in this study, you will have the option to take part in future research using your data that is saved from this study on the KCL database.

Where can you find out more about how your information is used?

You can find out more about how we use your information

- at www.hra.nhs.uk/information-about-patients/
- by asking one of the research team
- by ringing us on 07936545178

- by contacting King's College London's Data Protection Officer, Mr Albert Chan at info-compliance@kcl.ac.uk

What will happen if I do not want to carry on with this study?

Your decision to participate in this study is voluntary. You may choose not to participate, or you may withdraw from the study for any reason, without penalty or loss of benefits to which you are otherwise entitled and without any effect on your future medical care.

If you stop taking the study medicine before completing the last study visit for any reason (for example if the study team feels it is in your best interest, you decide not to continue or the study is stopped) you will be required to return all unused study medicine.

You and your caregiver will also be asked to return for a follow-up visit. The following information will be collected:

• Current medication usage

• Assessments relating to your memory, behavioural or psychological symptoms, quality of your life and daily functional skills

• Information on any sickness or health problems you may have experienced since the last visit

If you decide to withdraw from the study, your medical data and any samples collected prior to withdrawal may still be processed and/or analysed along with other data collected as part of the study. No additional medical data or samples will be collected after you have withdrawn from the study. Upon your withdrawal, you have the right to request that your collected, untested samples are destroyed. If you would like your samples to be destroyed, please let your study team know. Information that has already been sent to the study Sponsor cannot be withdrawn. You may also revoke the authorisation to use or disclose personal information about your health. If you choose to withdraw your authorisation, you must notify the study team in writing.

The study team or the sponsor can stop your study 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 cancelled

What will happen to the results of the research study?

We will publish the results of the study in international scientific journals and present the findings at scientific conferences. You will not be identified in any publications or presentations.

Who is organising and funding the research?

Parkinson's UK is funding this research.

Who has reviewed the study?

The London Hampstead Research Ethics Committee (REC) and Medicines and Healthcare products Regulatory Agency (MHRA) have authorised this Clinical Trial.

Will I be paid for my participation in this study?

You will be given a £25 gift voucher at baseline and follow-up visit 4. This should help to cover any reasonable costs of participating in the trial.
If preferred, we are happy to refund any travel or other reasonable expenses you incur in order to attend the research visits. We ask that you keep your receipts.

Will my GP be informed about my participation?

With your consent, your GP will be informed that you have decided to take part in this study. We would do so to ensure that we and your GP can best manage your overall healthcare. Your GP will not routinely receive any information or results from your assessments or investigations, but we will advise them of any information relevant to your health. We also ask the GP to inform us of any information that is relevant to your participation in the study. This may involve the exchange of identifiable data/information between your GP and the study doctor. If there are significant concerns about your or someone else's safety or welfare, the research team may deem it necessary to share information with your care team or the relevant authorities.

Contact for Further Information

If you wish to participate, you will be asked to sign a consent form. You can keep the information sheet for your records.

Thank you for reading this and for your interest in the study.

For further information, please contact:

CAN-PDP Trial Manager

Department of Psychosis Studies

Institute of Psychiatry, Psychology & Neuroscience (6th Floor)

16 De Crespigny Park, London, SE5 8AF

Tel: 07936545178

Email: canpdp.trialoffice@kcl.ac.uk