[Insert local letterhead]

PATIENT INFORMATION SHEET

Title of Study: A RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED, PHASE IIA STUDY EVALUATING THE EFFICACY AND TOLERABILITY OF IRL790 IN PARKINSON'S DISEASE DYSKINESIA

Study Protocol Number: IRL790C003

Sponsor: Integrative Research Laboratories AB

Investigator:

Patient Name:

INTRODUCTION

We would like to invite you to take part in a research study. Before you decide whether you want to take part, 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 others such as family, friends or your GP if you wish.

Ask a member of the research team if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Part 1 tells you the purpose of the study and what will happen if you choose to take part. Part 2 gives you more detailed information about the conduct of the study.

Thank you for reading this.

Part 1

1. WHAT IS THE PURPOSE OF THE STUDY?

In this research study we are testing a new medicine called IRL790 to see if it can reduce the involuntary movements seen in Parkinson's disease, called dyskinesia. These involuntary movements are generally seen when people with Parkinson's have been taking a medicine called Levodopa for several years. Our hope is that IRL790 will help to reduce these movements.

If you agree to take part in this study you will be given either IRL790 or placebo (a placebo is a dummy pill which contains no active ingredient).

The product you will receive will be allocated completely at random, like tossing a coin to decide.

This means there is the same chance of you receiving the dummy treatment as there is of you receiving the new medicine. You will always receive all standard care no matter which treatment you receive.

Once the study has recruited 74 people, those who had IRL790 and those who had placebo will then be compared. To make sure no one can have an effect on the results, this study is also *double-blinded* which means that neither you nor your medical team will know which treatment you are getting (although, if your doctor needs to find out he/she can do so).

2. WHY HAVE I BEEN CHOSEN?

You have been chosen for this study because you have Parkinson's disease and have involuntary movements related to Levodopa.

3. DO I HAVE TO TAKE PART?

No. Taking part in the study is entirely voluntary. It is up to you to decide whether or not to take part. If you decide to take part you are still free to withdraw at any time and without giving a reason. **If you decide not to take part this will not affect your care in any way and your doctor will decide which treatment will be best to offer you.**

4. WHAT WILL HAPPEN TO ME IF I TAKE PART?

You will be given some time with a member of the study team to discuss the study and ask any questions. If you wish to participate in the study you will then be asked to sign an Informed Consent Form. 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 and described

You will be given a copy of this to keep.

If you consent to take part, you will be asked to visit the study team an estimated six times and be contacted by telephone over the next two months.

If your medical team decides that you are eligible for the study then a member of the study team will give you your first dose of the study treatment that you have been allocated to receive (IRL790 or placebo). These are capsules that you will take twice daily for up to 28 days.

The starting dose will be 3 capsules (either IRL790 or placebo) twice daily (morning and afternoon, about 8 hours apart).

Screening visit

Once consented, to check whether you meet the eligibility criteria, you will attend clinic where your Research team will conduct what is called a *Screening visit*.

You will be asked a few questions on your medical history and current medication. You will also undergo a brief physical examination to check your state of health (height, weight, general), vital signs (blood pressure and heart rate), you will have an ECG (test to check your heart), and will be asked to have a blood test and provide a urine sample. Where relevant, one of these samples will be used for a pregnancy test.

The research team will ask you questions from the *Mini-Mental State Examination* (MMSE) which assesses your memory and thought process. You will also be asked questions about your Parkinson's disease and how severe it is will be assessed by completing the Hoehn and Yahr score.

You will also be provided with two diaries to complete. The diary is divided into 30-minute sections over a 24 hour period. We would like to know how much time you spend in the different Parkinson's states and we would also like you to mark when you were asleep. The research team will provide training on how and when to complete the diary. It is important that you complete the diaries on two days in accordance with the instructions given to you by the research team. Only patients who can complete the diary correctly can be included in the study. Should the diary not be completed correctly, the research team will provide more training and you can have another chance to complete the diary.

You will be assigned a *Patient number*, which will protect your identity and any personally identifiable information from anybody involved in the study who is not your immediate Research team, i.e. your treating study doctor and research nurses.

Treatment visit (visit 1)

At Visit 1, you will be *randomised* to the study. This means you are put in one of two groups. One group will receive the study drug, IRL790, the other one a placebo. You will attend clinic and be asked for an update of any medications and any problems you might have had since your last visit. You will also be asked to provide two blood samples the first one before taking your first dose of study medication, and a the second one two hours after.

Your Parkinson's disease will be assessed by the research staff completing the Unified Parkinson's disease Rating Scale (MDS-UPDRS) and the Unified Dyskinesia Rating Scale (UDysRS). Part 3 of both Scales must be completed during your "Best ON" state, usually 1 – 2 hours post levodopa.

The MDS-UPDRS is split into four sections as follows:

Part 1 – you will be asked questions about your non-movement Parkinson's symptoms such as your mood and sleep.
Part 2 - you will be asked to complete a questionnaire to assess your motor symptoms and how these affect you in your day to day activities.
Part 3 – is an examination about your movements where you will be asked to move different parts of your body and to speak and walk.
Part 4 – assesses complications arising from your Parkinson's disease for example twitching, jerking, wriggling, spasms or cramps.

The UDysRS is a specific questionnaire to measure the movement complications that arise because of your Parkinson's disease medication (Levodopa). It is split into four parts. Part 3 of the assessment is filmed.

Parts 1 and 2 measure the effect of these symptoms on your daily life.
Part 3 is an objective assessment of your condition and you be asked to perform specific actions and you will be asked to:

- describe a picture;
- pick up and drink some water from a cup;
- put on a laboratory coat and do up three buttons and then take the coat off;
- rise from a chair and walk 15 feet and return and sit back down.

Part 4 is an objective assessment of your disability based on the film of you doing these tasks.

The recorded video footage will then be sent to an expert in Parkinson's disease dyskinesia (selected by the Sponsor, *Integrative Research Laboratories AB* in Göteborg, Sweden). The expert will review the footage to assess the extent of dyskinesia symptoms related to your Parkinson's disease. Steps will be taken to ensure your identity and personal information is kept strictly confidential, and the videos will not breach this. During filming, neither you nor your study doctor will state your names or personally idenitifiable information, and the video files themselves will be coded (to remove your identity, the date of filming, or your location) before being sent out to the expert for review.

You will be provided with a Patient Contact Card with the names and numbers of whom to contact if you need any assistance or questions answered whilst you are on the study.

Treatment visit (visit 2 & 3)

At Visits 2 & 3 you will attend clinic and be asked for an update of any medications and any problems you might have had since your last visit. Your treating doctor may discuss with you about altering the dose of your study treatment.
At Visit 3, you should return your original bottle of capsules, and you will be provided with a new bottle with enough IRL790 capsules until the end of your study treatment period.

The research team will also discuss with you your treatment, and increase or decrease your dose if required.

Phone call (day 21)

On day 21 of your treatment one of our researchers will call you to ask for an update of any medications or any problems you might have experienced since your last visit.

They will ask how you have been doing with your treatment, and ask you to complete two more diaries recording how much time you spend in the different Parkinson's states or asleep. It is important that you complete the diary as you did at the start of the study.

End of treatment (visit 4)

On day 28 you should come into clinic before taking your final dose of treatment. The research team will ask for an update of any medications or any problems you might have experienced since your last visit.

Very much like the Screening visit, there will be another brief physical examination, ECG, assessment of your Parkinson's disease, and you will be asked to have a blood test and provide a urine sample. Where relevant, one of these samples will be used for a pregnancy test.

As with Visit 1, the assessment of your Parkinson's disease will be based on the the Unified Parkinson's disease Rating Scale (MDS-UPDRS) and the Unified Dyskinesia Rating Scale (UDysRS). Part 3 of both Scales must be completed during your "on" state. The filmed parts of the UDysRS will also be repeated at this visit. Your study doctor will assess the overall change in your Parkinson's disease.

You will also be asked to provide a second blood sample two hours after you have been told you can take the last dose of your study treatment.

In the event you choose to withdraw, or are withdrawn from the study, you will be asked to undergo Visit 4 assessments at that time.

Follow Up

A follow up visit will take place a few days after your End of Treatment visit. During this visit you will be asked for an update of any medications you have taken and how you have been feeling. You will have a brief physical examination, ECG, and asked to provide a blood sample and a urine sample.

You will be asked to provide a blood sample at 4 of your visits (Screening, Visit 1, Visit 4, Follow Up). For each blood sample, approximately 1-2 teaspoons (5-10ml) of blood will be drawn. Over the course of the study, the maximum amount taken would fill about 1 cup (250ml).

5. EXPENSES AND PAYMENTS

There are no additional costs associated with taking part in this research project. All medication, tests and medical care required as part of the research project will be provided to you free of charge.

You will not receive payment for your participation in this study but you may be reimbursed for travel expenses (including parking) for any additional medical visits associated with the study.

6. WHAT DO I HAVE TO DO?

To take part in this study you will have to provide informed consent using a written form known as an Informed Consent Form.

If you are eligible and wish to take part in the study, you will be expected to take the medication twice

daily (morning and afternoon, 8 hours apart) orally, with 200mL of water.

You will be expected to attend clinic and meet your treating physician and/or Research Nurse at the scheduled visits (Screening Visit, Visit 1, Visit 2, Visit 3, Visit 4, Follow Up).

If you or your partner becomes pregnant during the study or within three months of receiving their final dose, you will be asked to inform the investigator as soon as possible and consent to follow-up of the pregnancy outcome by the Sponsor.

It is important for your own safety that you tell us of your complete medical history and all medications/supplements/herbal preparations that you are taking. If you notice any health problems please notify your study doctor immediately. You must always follow the instructions of the study doctor and staff.

7. WHAT IS THE PRODUCT THAT IS BEING TESTED?

The study drug being tested is called IRL790, and will be tested against a placebo. Both will come as capsules, identical in appearance, to be taken orally with 200mL of water.

IRL790 has been selected for development aimed as a treatment to reduce Levodopa induced dyskinesia.

The starting dose will be three x 2.5mg capsules (7.5mg), twice daily (morning and afternoon, about 8 hours apart). At Visit 2 and Visit 3, following a review by your study doctor, the dose may increase (to 10mg twice daily) or decrease (to 5mg twice daily) by one capsule per dose administration.

8. WHAT ARE THE ALTERNATIVES FOR DIAGNOSIS OR TREATMENT?

You will continue to use your usual treatment with Levodopa at the same dosage. Similarly, you will receive all standard care for Parkinson's Disease at this hospital irrespective of whether you take part in this study or not.

9. WHAT ARE THE POSSIBLE DISADVANTAGES AND RISKS OF TAKING PART?

Avoid Direct Sunlight: Due to a small risk of sunburn when taking IRL790, patients must avoid direct exposure to sunlight whilst taking the study drug. During this time patients should wear protecting clothing, sun glasses and sun protection cream on exposed parts of the body if they are going outdoors in direct sunlight.

It is possible that if you take this treatment whilst pregnant, it may harm the unborn child. Pregnant women may therefore not take part in this study neither should women who plan to become pregnant during the study. Women who are at risk of pregnancy will be asked to have a test before taking part to exclude the possibility of pregnancy. Women who could become pregnant must use two effective contraceptive methods during the course of this study. Any woman who finds that she has become

pregnant while taking part in the study should immediately tell her study doctor.

Male patients are expected to use both barrier and contraceptive methods to prevent pregnancy and drug exposure to a partner and refrain from donating sperm from the date of dosing until three months after last dosing of IMP. Male patients whose female partner(s) is (are) pregnant must use a condom from the time of the first administration of treatment or study medication until three months (90 days) following administration of the last treatment or dose of study medication.

Having a blood sample taken may cause some discomfort, bruising, minor infection or bleeding. If this happens, it can be easily treated.

10. WHAT ARE THE SIDE EFFECTS OF ANY TREATMENT RECEIVED WHILST TAKING PART?

Previous studies testing IRL790 in both healthy volunteers and those with Parkinson's disease dyskinesia showed good tolerability of the drug, and mild, short-lived side effects. Potential side effects which you may experience, currently associated with IRL790 treatment, are:

Parkinsonism, tremor, muscular rigidity, insomnia, drowsiness, headache, slurred thinking, dissociation, balance disorder, dizziness, concentration difficulties. You might also experience dizziness when switching from lying down or sitting to standing, laboured breathing, general lack of energy, fatigue, and swelling.

As this is a new drug that has limited information, new and unknown side effects may occur.

If you do experience any symptoms, you should report them to your medical team or GP or at any of your study visits. If you are in any way concerned please contact your study nurse or doctor.

You can contact a member of the study team by telephoning:

<<Emergency Contact Number>>

11. WHAT ARE THE POSSIBLE BENEFITS OF TAKING PART?

We hope that the treatment will help you in reducing your Levodopa induced dyskinesias, as past research into the study drug IRL790 has shown, however, this cannot be guaranteed. The information we receive from this study may help us to treat future patients with advanced Parkinson's disease and levodopa induced dyskinesia.

12. WHAT HAPPENS WHEN THE RESEARCH STUDY STOPS?

Your participation in the study will end, and you will not receive any further treatment in relation to this study. The study visits will end either when you have completed all scheduled study treatment and visits, or your doctor feels it is in your best interests to do so. Alternatively, the sponsoring company, Integrative Research Laboratories AB (IRLAB) may wish to end the study as a whole. If this occurs, the reasons will be explained to you. At this point, your normal care will resume. You will not be able to

find out if you were on the active drug, IRL790, or the placebo.

13. WHAT IF THERE IS A PROBLEM?

Any complaint about the way you have been dealt with during the study or any possible harm you might have experienced will be addressed. The detailed information on this is given in Part 2.

14. WILL MY TAKING PART IN THE STUDY BE KEPT CONFIDENTIAL?

Yes. We will follow ethical and legal practice and all information about you will be handled in confidence. The details are included in Part 2.

This completes Part 1. If the information in Part 1 has interested you and you are considering participation, please read the additional information in Part 2 before making any decision.

Part 2

15. WHAT IF NEW INFORMATION BECOMES AVAILABLE?

Sometimes during the course of a research project, new significant information becomes available about the treatment that is being studied. If this happens, your study doctor will discuss this with you and whether you want to continue in the study. If you decide not to carry on, your study doctor will make arrangements for your 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 might consider it to be in your best interests to withdraw you from the study. He/she will explain the reasons if this is the case.

16. WHAT WILL HAPPEN IF I DON'T WANT TO CARRY ON WITH THE STUDY?

Taking part in the study is entirely voluntary. It is up to you to decide whether or not to take part. If you decide to take part you are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time or a decision not to take part will not affect the standard of care you receive.

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 but may ask you to complete a final Follow up Visit. Personal information already collected will be retained to ensure that the results of the research project can be measured properly. You may ask that any retained samples be destroyed and that previous data collected are not used, but otherwise any samples collected will be retained for analysis and data collected by the sponsor up to the time you withdraw will form part of the research project results.

17. WHAT IF THERE IS A PROBLEM?

It is not expected that you will suffer any health damage as a result of participation in this study. If you become ill or injured whilst you are on this study, you will receive the medical care that you need straight away.

At your first Treatment Visit (Visit 1), the study team looking after you will provide you with a Patient Contact Card with the names and numbers of whom to contact if you need any assistance or questions answered whilst you are on the study.

If you think that you may have been harmed by the study medication, or otherwise by taking part in the study, the study sponsor Integrative Research Laboratories AB has insurance (Newline Underwriting Management Ltd.) and will compensate you in accordance with guidelines of the Association of the British Pharmaceutical Industry (ABPI)/ Association of British HealthCare Industries (ABHI), as follows:

- If your injury is attributable to administration of the study medication

- If you were harmed by any procedure that is part of the study, which you would not have had but for your inclusion in the study
- If you followed instructions
- If your injury is not the result of the natural course of any underlying disease and/or pre-existing disease process present prior administration of the study medication

You can get a copy of the guidelines from your clinic, or write to ABHI, 250 Waterloo Road, London SE1 8RD; Tel 020 7960 4360 or email enquiries@abhi.org.uk

If you think you have become injured or sick as a direct result of your participation in the study, please contact the study clinic immediately using the contact details at the end of this information sheet. In the event that your participation in this study results in a medical problem, treatment will be made available. Your study doctor will explain the treatment options available, and where you can go to get information and be treated.

If you remain unhappy and wish to complain formally this should be addressed in writing to PALS (Patient Advice and Liaison Service): [Details for nearest PALS]

18. WILL MY TAKING PART IN THIS STUDY BE KEPT CONFIDENTIAL?

If you consent to take part in the research, any of your medical records may be inspected by relevant personnel of Integrative Research Laboratories AB, (the company sponsoring the research) or their representative for purposes of analysing the study results. They may also be looked at by relevant regulatory authorities and your clinic's ethics committee to check that the study is being carried out correctly.

You will be given an individual subject number that will be used on all your study documentation and your name will not be disclosed outside the clinic. Any information about you, which leaves the clinic, will have your name and address removed so that you cannot be recognised from it. All information that is collected about you during the course of the study will be kept strictly confidential.

Data collected during the study will be anonymised, and no personal information is attached to the study data, but may be sent to associated researchers to countries where the laws don't protect your privacy to the same extent as the law in the UK. The company will take all reasonable steps to protect your privacy. This data will not be shared with anyone else.

19. INVOLVMENT OF THE FAMILY DOCTOR

You should also note that your consent will be taken to notify your General Practitioner about your participation in the study and for information to be shared as needed.

20. WHAT WILL HAPPEN TO ANY SAMPLES I GIVE?

Blood and urine samples will be taken at the Screening Visit, Visit 4, and Follow Up visit. Pregnancy tests will also be performed at these visits, if applicable.

Blood samples will also be taken at Visit 1 and Visit 4. The samples will be stored at -20°C until used for the purpose of measuring the levels of IRL790 in your blood. The samples will be safely disposed of after the clinical study report has been finalised.

If you withdraw consent to the use of biological samples donated, the samples will be disposed of/destroyed, if not already analysed and documented.

21. WHAT WILL HAPPEN TO THE RESULTS OF THE RESEARCH STUDY?

A description of this clinical study will be available on http://www.ClinicalTrials.gov which is a registry of clinical trials and studies. You can search this Web site at any time. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results.

The results of the study may be sent outside the European Union for use by Integrative Research Laboratories AB or other responsible third party. Your confidentiality will be maintained as the information will not contain anything that can be used to identify you.

At the end of the study, the results will be analysed and may be used by Integrative Research Laboratories AB as the basis for another study or for approval of the product for sale. The results may also be published in reputable scientific journals.

22. WHO IS ORGANISING AND FUNDING THE RESEARCH?

The study is being sponsored by a company called Integrative Research Laboratories AB (Arvid Wallgrens Backe 20, 413 46 Göteborg, Sweden). It will be performed by their associates and the study doctor and clinical team treating you.

The sponsors of this study will pay (name of hospital department or research fund) for including you in this study.

23. WHO HAS REVIEWED THE STUDY?

The study has been approved by the Wales Research Ethics Committee and the Medicines and Healthcare products Regulatory Agency – MHRA (a UK central government office responsible for overseeing the development of new medicines). It has been agreed that it may go ahead. The Study also has the support of the NHS National Institute for Health Research.

24. CONTACT FOR FURTHER INFORMATION

If you have any questions about the research, or in the event of a research related injury please

contact:

During normal working hours:

Name:

Telephone:

Outside normal working hours:

Name:

Telephone:

If you would like independent advice on the research, please contact [contact details]. You may also contact your GP for independent advice before entering the study.

If you have a concern about any aspect of the research, you should speak to [contact] in charge of the research.

[Insert local letterhead]

Centre Number: xx

Patient Identification Number for this study: xxxxx

Study Number: IRL790C003

Name of Investigator: [Principal investigator]

Sponsor: Integrative Research Laboratories AB

PATIENT INFORMED CONSENT FORM

Study title: A RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED, PHASE IIA STUDY EVALUATING THE EFFICACY AND TOLERABILITY OF IRL790 IN PARKINSON'S DISEASE DYSKINESIA

Please initial the box next to each statement if you agree to it.

1.	I confirm that I have read and received a copy of the patient information sheet dated, 20/NOV/2017 (version 1.3) for the above study. I fully understand what is involved and have had the opportunity to ask questions, which have been answered satisfactorily.	
2.	I understand that my participation is voluntary and that I am free to withdraw at any time without giving reason and without my medical care or legal rights being affected.	
3.	I understand that sections of my medical notes and data collected may be looked at by individuals from regulatory authorities, the ethics committee and the sponsor or designates where it is relevant to my taking part in research. I give permission for these individuals to have access to my records	
4.	I understand that my data will be held confidentially on a computer at the hospital and by the sponsor or designate. I give my permission for this data to be held on computer by these parties.	

5.	I give my permission for the staff treating me to contact my General Practitioner (GP) and agree that relevant information can be shared.	
6.	A description of this clinical study will be available on http://www.ClinicalTrials.gov. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.	
7.	By signing this consent form I agree that my study data, including videos and data relating to my physical or mental health or condition, and race or ethnic origin, may be transferred and used as described in the information sheet for the study.	
8.	I agree to my data being sent outside the European Union for use by the sponsor, as long as confidentiality is maintained.	
9.	I agree that the video with the assessment will be sent to a qualified Rater based in Sweden.	
10.	I agree to take part in the above study.	

Name of Patient	Date	Signature

Name of the Investigator	Date	Signature

Distribution of copies: one for patient; one for researcher; one to be kept with hospital notes