UNIVERSITY OF CAMBRIDGE

Cambridge University Hospitals NHS
NHS Foundation Trust

PARTICIPANT INFORMATION SHEET & INFORMED CONSENT FORM

FELL-HD: A trial to assess the tolerability of using felodipine to upregulate autophagy as a treatment of Huntington's disease

You are being invited to take part in a research trial. Before deciding whether to take part, you need to understand why this research is being done and what it involves. Please take time to read the following information carefully and talk to others about the trial if you wish. Please ask us if anything is not clear or if you would like more information. Please take time to decide whether or not you wish to take part.

Section 1 tells you the purpose of this trial and what will happen to you if you take part. Section 2 gives you more detailed information about the conduct of the trial.

Section 1: Purpose of the trial and what will happen

1. What is the purpose of the trial?

Huntington's disease (HD) is a condition that stops parts of the brain working properly over time. It is passed on (inherited) from a person's parents. There is currently no cure for HD or any way to stop it getting worse, but there are treatments available which can help reduce some of the symptoms it causes. There is therefore an urgent need for treatments that slow down the disease (disease-modifying).

The major cause of HD relates to the production of an abnormal protein (called mutant huntingtin or **mHTT**), that builds up over time and causes nerve cells in the brain (neurons) to dysfunction and then die. The production of mHTT is caused by the faulty HD gene which is inherited by people with HD.

Given all this, we believe that one way to try and stop HD progressing is to increase (upregulate) the clearance of mHTT from cells. One normal process that cells use to clear proteins (including mHTT) is called **autophagy**.

A group of scientists based at the University of Cambridge have found that a drug that has been used for many years in the clinic to treat high blood pressure, called **felodipine,** upregulates the autophagy process and so may prove to be a treatment for slowing down HD.

The purpose of this research is therefore to test the safety and tolerability of different doses of felodipine in early-stage HD, before moving on to bigger trials to see whether it may slow down the progression of the disease itself.

2. What is the drug being tested?

Felodipine is licensed in the UK and it is a commonly used drug for the treatment of high blood pressure which is typically administered long-term and is generally well-tolerated. It has been in clinical use for over 20 years.

It is usually prescribed at a standard dose of up to 10 mg/day but can be prescribed at doses of up to 20 mg/day.

There is no 'dummy drug' (placebo) to be used in this trial, therefore everybody taking part in the trial will receive felodipine. The dose you receive will depend on which group you are assigned to.

You will be assigned to one of three dosing groups (see table below) within four weeks of the first visit. Participants will be assigned to one of three dosing groups in an alternating fashion, where participant 1 will be allocated to group 1, participant 2 will be allocated to group 2, participant 3 will be allocated to group 3, participant 4 will be allocated to group 1, and so on.

Time point	Group 1	Group 2	Group 3
Baseline (week 0)	Start on 2.5 mg once a day	Start on 2.5 mg once a day	Start on 2.5 mg once a day
Week 2	Increase to 5 mg once a day and stay on this dose until week 58	Increase to 5 mg once a day	Increase to 5 mg once a day
Week 4	*No change*	Increase to 10 mg once a day and stay on this dose until week 58	Increase to 10 mg once a day
Week 6	*No change*	*No change*	Increase to 20 mg once a day and stay on this dose until week 58
Week 58	Stop felodipine	Stop felodipine	Stop felodipine

Your dose will only be increased if it has been tolerated at the previous lower dose. If you are unable to tolerate a dose, you will be moved back to the last dose that you tolerated. If you are on the lowest dose and are unable to tolerate that, the felodipine will be stopped.

Felodipine should be taken in the morning, without food or following a light meal not rich in fat or carbohydrate. The tablets must not be chewed or crushed and should be swallowed whole with water.

Grapefruit juice can interact with the medication and cause harmful effects. You should not drink grapefruit juice at any time whilst on the trial medication.

If you miss a dose for whatever reason (e.g. as a result of forgetting to take it at the scheduled time), you should take the missed dose up to a maximum of twelve hours after the scheduled dose time. If more than twelve hours have passed, the missed dose should not be taken and you should take your next dose at the scheduled time.

3. Why have I been invited?

You have been invited to participate in this trial because you have been diagnosed with early-stage HD. We believe felodipine may be a suitable treatment to delay disease progression. Before we conduct larger trials to investigate this, we would like to invite

you to participate in this trial to test the safety and tolerability of different doses of felodipine in early-stage HD.

We plan to include 18 participants with early-stage HD to this trial, which will take place at the John van Geest Centre for Brain Repair (VGB), located on the Cambridge Biomedical Campus.

4. Do I have to take part?

No, participating in this trial is completely voluntary. If, after reading this information sheet, you are interested in participating in the trial, you should contact us to discuss the trial in more detail and for us to answer any questions you may have. Alternatively, we will contact you after approximately 2 weeks to ask whether you have any questions about the trial.

Once any questions have been answered, you will be asked whether you wish to take part. If you are still interested, a screening visit will be arranged to see if you are able to take part in the trial.

At the screening visit, you will be asked to sign an informed consent form; however, you are still free to change your mind and leave the trial at any time after this, without giving a reason. If you choose not to participate or to leave the trial, your future medical treatment and normal standard of care will not be affected in any way.

5. What will happen to me if I take part?

If you agree to participate in the trial, you will sign the informed consent form at the end of this document and be given a copy of this to take away and refer to later.

You will attend the VGB 12 times in total over the entire trial. If you consent to the optional MRI scans, two of these visits will also include attending the MRI unit at the Wolfson Brain Imaging Centre, which is also located on the Cambridge Biomedical Campus, within close walking distance of the VGB. In addition, two further visits will occur over the phone, so in all this trial will involve 14 visits.

As felodipine may lower your blood pressure, you will be given a blood pressure monitor following the baseline visit and asked to complete weekly blood pressure readings at home. This will allow the trial team to monitor your blood pressure and adjust your dose of felodipine if necessary.

We strongly recommend you bring a companion to all your trial visits, where possible, as this helps us to gather more information on you and how you are doing. Your companion may be a family member, close friend or carer, and it should be someone who you have regular face-to-face contact with. If your chosen companion is not with you when the trial is first mentioned to you, we will give you an information sheet about the trial to provide to your chosen companion for them to read. If your companion is unable to attend a visit with you, the trial team may follow-up with them over the phone to obtain their input.

The trial duration will be up to 66 weeks, consisting of a 4-week screening period, 58-week treatment period, and a 4-week follow-up period. Once treatment starts you will be seen at the VGB every 2 weeks until week 8, and every 8 weeks thereafter until week 40. Two final in-person visits will be performed at week 57 and week 62. Two telephone visits will also occur at week 48 and week 58.

The situation with COVID-19 is ever changing. If necessary, in-person visits may be rescheduled as remote visits, which could involve using a video platform such as Zoom or Microsoft Teams, or over the phone if you are unable to use these video platforms. Please see section 11 for further information regarding how COVID-19 may impact this trial.

Screening assessments will be carried out once you have signed the informed consent form, so that you can be assessed ('screened') to see if you are eligible to participate in the trial.

Details of the trial visits are described below:

Screening visit (approximately 3.5 hours)

During the first screening visit you will meet with a trial doctor who will review details of your HD (symptoms, tests and medications) with you. He or she will also review the remainder of your medical history, including a check of any other medications you might be taking.

The following assessments will be carried out by the trial team:

- Your vital signs will be recorded, including heart rate, blood pressure and temperature.
- A standard physical examination, to check your overall health, will be performed by the trial doctor. This will involve a check-over of body areas and systems such as your eyes, ears, nose, throat, lungs and heart.
- A blood sample of approximately 10 ml (or 2 teaspoons) will be taken for routine blood tests to ensure that you are suitable for this trial and to monitor the effect of the treatment. There is no need to fast before this, or any other blood test performed during this trial.
- An additional blood sample will be collected from all women of childbearing potential to allow a pregnancy test to be performed.
- The Unified Huntington's Disease Rating Scale (UHDRS) assessment will be performed, which is used to score the features of your HD. The UHDRS is completed by a trained member of the research team and takes approximately 50 minutes. You may be familiar with this as it is typically done at normal HD outpatient clinic appointments.
- A number of other assessments and questionnaires will be performed to assess other features of your HD, including memory, thinking and mood. In total, these will take approximately 65 minutes to complete.

With the results of the screening assessments, a trial doctor will run through a checklist to make sure you are suitable ('eligible') to take part in the trial. Once we know the results, we will contact you, by email or telephone, to confirm whether or not you are eligible to participate in the trial.

If you are eligible for trial entry and are happy to continue in the trial you will be assigned to one of the three dosing groups and will be invited back for a baseline visit within four weeks of screening.

Baseline visit (approximately 2.5 – 3.5 hours)

At this visit you will meet with a member of the trial team who will again check your current health and medications.

During the visit the following activities will occur:

- Your vital signs will be recorded.
- A UHDRS will be repeated. This will take approximately 50 minutes to complete.
- The other assessments and questionnaires completed at screening will be repeated. In total these will take approximately 55 minutes to complete.
- If you agree to this, an MRI (magnetic resonance imaging) scan will be performed. However, the MRI scan is **optional** and it is up to you whether you decide to have this procedure. See further details about this procedure below.
- A blood sample of approximately 10 ml (or 2 teaspoons) will be taken for routine blood tests.
- A urine pregnancy test will be performed for women of childbearing potential (if it has been more than 14 days since the screening pregnancy test).

MRI scans

The MRI is completely **optional**. During the course of the trial we plan to perform two MRI scans of your head if you consent to these. The MRI scans will be performed at the Wolfson Brain Imaging Centre, which is located on the Cambridge Biomedical Campus, close to the VGB.

MRI scans are painless and contain no radiation. They use a magnet to produce detailed images of your body and, for this trial, your brain. The scanner consists of a 1.5m long tunnel, through which you pass while lying on a couch. The scan can last from 15-60 minutes and for certain periods it is important you are able to lie still to prevent blurring of the pictures. It can be a little uncomfortable lying still for this length of time. The tunnel in the scanner is quite narrow and can feel quite enclosed. If you are anxious in enclosed spaces, you can be provided with medication to help you relax before you have the scan. Please let us know if you have previously experienced claustrophobia in small spaces. Sedation may also be used to allow completion of the scan, if required. The scanner also makes a banging noise, which is perfectly normal. You will be supplied with earplugs and can listen to music of your choice through headphones if you wish. The technician performing the scan will communicate with you throughout the scan to check that you are comfortable. The scan can be stopped at any point.

During this baseline visit you will be given an initial supply of trial medication and advised to take one tablet daily. You will need to record the number of tablets taken each day, on the medication diary that will be provided to you.

Throughout the trial, do not throw away any empty packaging. Please keep all empty blister strips in their original boxes and return them to the trial team at your next visit. If you have any unused tablets left, please also bring these in their original packaging with you to your next visit.

You should continue to take all of the other drugs you are currently on as normal, including your HD medication/treatment. However, we would ask that you inform the trial team of any new medications (or changes to current medications). This is important as a few drugs do interact with the trial medication.

During this baseline visit you will also be given a blood pressure monitor and instructed on how to use it. You will be asked to perform weekly readings and record the results on the blood pressure diary that will be provided to you. You will not need to complete readings on weeks when you have an in-person trial visit. You should aim to take the readings in the morning, on the same day every week after sitting for about 5 minutes. You should repeat the blood pressure reading twice, and in total collect three readings per session. If you have a drop in blood pressure to below 90/60 mmHg or start to experience symptoms of low blood pressure such as dizziness, fainting and/or light headedness, or blurred vision, you should contact a member of the trial team as soon as possible. You should follow all instructions from the trial team, which may include taking blood pressure readings on a more frequent basis.

During the following thirteen months you will see trial staff in-person nine times: after 2 weeks, 4 weeks, 6 weeks, 8 weeks, 16 weeks, 24 weeks, 32 weeks, 40 weeks, and 57 weeks. You will also have phone visits at 48 weeks and 58 weeks. After 58 weeks of treatment, you will finish the trial medicines and the final visit then follows four weeks later (at 62 weeks).

Week 2, 4 and 6 visit (approximately 30 minutes)

At these visits you will meet with a member of the trial team who will again check your current health and medications and will check if you have had any side effects or problems taking your trial treatment.

During these visits the following activities will occur:

- Your vital signs will be recorded.
- A blood sample of approximately 10 ml (or 2 teaspoons) will be taken for routine blood tests.
- A urine pregnancy test will be performed for women of childbearing potential (week 4 only).

The research team will also check your medication diary with you, to ensure that you are taking the medication correctly. Therefore, **please ensure to bring your completed medication diary, and any unused medication or empty blister strips in the original boxes with you to these visits**.

The trial team will also check your blood pressure diary. Therefore, **please ensure that you bring your completed blood pressure diary with you to these visits.**

At the end of these visits you will receive a further supply of trial medication and be advised to increase your daily dose, if appropriate.

Week 8, 16, 24, 32 and 40 visit (approximately 2.5 hours)

At these visits you will meet with a member of the trial team who will again check your current health and medications and will check if you have had any side effects or problems taking your trial treatment.

During these visits the following activities will occur:

- Your vital signs will be recorded.
- A UHDRS will be repeated. This will take approximately 50 minutes to complete.
- Other assessments and questionnaires will be performed to assess other features of your HD, including memory, thinking and mood, as performed at the screening visit. In total, these will take approximately 55 minutes to complete.
- A blood sample of approximately 10 ml (or 2 teaspoons) will be taken for routine blood tests.
- A urine pregnancy test will be performed for women of childbearing potential.

The research team will also check your medication diary with you, to ensure that you are taking the medication correctly. Therefore, **please ensure to bring your completed medication diary, and any unused medication or empty blister strips in the original boxes with you to these visits**.

The trial team will also check your blood pressure diary. Therefore, **please ensure that you bring your completed blood pressure diary with you to these visits.**

At the end of these visits, you will receive a further supply of trial medication.

Week 48 telephone visit (approximately 15 minutes)

This visit will entail a member of the trial team phoning you to check your current health and medications and to check if you have had any side effects or problems taking your trial treatment. You will also be asked to confirm how many tablets you have left. In addition, you will be asked to confirm that you are completing the weekly blood pressure readings and that your blood pressure has not fallen below 90/60 mmHg. If your blood pressure has fallen to below 90/60 mmHg, you should follow all instructions given to you by the trial team, which may include taking blood pressure readings on a more frequent basis.

Week 57 visit (approximately 2.5 hours)

At this visit you will meet with a member of the trial team who will again check your current health and medications and will check if you have had any side effects or problems while taking your trial treatment.

During these visits the following activities will occur:

- Your vital signs will be recorded.
- A UHDRS will be repeated. This will take approximately 50 minutes to complete.
- The other assessments and questionnaires completed at screening will be repeated. In total these will take approximately 55 minutes to complete.
- A blood sample of approximately 10 ml (or 2 teaspoons) will be taken for routine blood tests.
- A urine pregnancy test will be performed for women of childbearing potential.

The research team will also check your medication diary with you, to ensure that you are taking the medication correctly. Therefore, **please ensure to bring your completed medication diary, and any unused medication or empty blister strips in the original boxes with you to this visit**.

The trial team will also check your blood pressure diary. Therefore, **please ensure that you bring your completed blood pressure diary with you to these visits.**

Week 58 telephone visit (end of treatment) (approximately 15 minutes)

This visit will entail a member of the trial team phoning you to check your current health and medications and to check if you have had any side effects or problems whilst taking your trial treatment. You will also be asked to confirm that you are completing the weekly blood pressure readings and that your blood pressure has not fallen below 90/60 mmHg. If your blood pressure has fallen to below 90/60 mmHg, you should follow all instructions given to you by the trial team, which may include taking blood pressure readings on a more frequent basis.

At week 58 you will stop taking the trial medication.

Week 62 visit (final trial visit) (approximately 3.5 hours)

At this visit you will meet with a member of the trial team who will again check your current health and medications.

During this visit the following activities will occur:

- Your vital signs will be recorded.
- A UHDRS will be repeated. This will take approximately 50 minutes to complete.
- The other assessments and questionnaires completed at screening will be repeated. In total these will take approximately 55 minutes to complete.
- If you previously consented to the optional MRI scan, and are happy to have this repeated, another will be performed.
- A blood sample of approximately 10 ml (or 2 teaspoons) will be taken for routine blood tests.
- A urine pregnancy test will be performed for women of childbearing potential.

The trial team will also check your medication diary with you, to ensure that you took the medication correctly. Therefore, **please ensure to bring your completed medication diary with you to this visit**. Additionally, **please ensure to return any unused medication and empty blister strips in the original boxes to the trial team at this visit**.

The trial team will also check your blood pressure diary. Therefore, **please ensure that you bring your completed blood pressure diary with you to these visits.**

Schedule of trial procedures according to trial visit

Procedures	Visits								
	Screening	Assigned to dose group	Baseline	Week 2, 4 and 6	Week 8, 16, 24, 32 and 40	Week 48 (telephone visit)	Week 57	Week 58 (telephone visit)	Week 62
You consent to participate	X								
Discuss your health (medical history)	X		X	X	X	X	X	X	X
Check other medications	X		X	X	X	X	X	X	X
Vital signs[1]	X		X	X	X		X		X
Blood pressure diary review				X	X	X[2]	X	X[2]	X
Physical examination	X								
Pregnancy test (women of child-bearing potential)[3]	X		X[4]	X[5]	X		X		X
Blood sample collected	X		X	X	X		X		X
UHDRS	X		X		X		X		X
Assessment of other HD features (including memory, thinking and mood)	X		X		X		X		X
MRI scan (optional)			X						X
Start felodipine			X						
Felodipine dose increase				X[6]					
Stop felodipine								X	
Dispense trial medication			X	X	X				
Trial medication compliance check				X	X		X	X[7]	X
Review of trial medication side effects				X	X	X	X	X	

[1] Following the baseline visit, you will be asked to complete weekly blood pressure readings using a device provided by the trial team. You will not need to complete readings on weeks that you have an in-person trial visit.
[2] Verbal confirmation, no physical check of diary.
[3] At the screening visit, a blood sample will be taken to perform the pregnancy test. A urine pregnancy test will be performed at all other visits.
[4] Only performed if it has been more than 14 days since the screening pregnancy test.
[5] Only performed at week 4 visit.
[6] All groups increase dose at week 2, groups 2 and 3 increase again at week 4, and group 3 increases again at week 6. You will be told which group you are in and therefore when you need to increase your dose.
[7] Verbal confirmation, no physical check of tablets.

6. What will I have to do?

We know that taking part in a trial can be quite daunting, so if you decide to take part we will guide you through what is required from you:

- It is important that you take any trial medication regularly as directed by your trial doctor. You will also need to keep an accurate record of the trial medication you have taken in the medication diary provided to you by the trial team and return any unused medication to your trial doctor at the end of the treatment period.

- As there is a chance felodipine could cause a drop in your blood pressure you will be required to perform a blood pressure reading at home once a week using a blood pressure monitor supplied by the trial team.

- If applicable, during the trial you should continue taking your normal HD medications in the same way as before. If you or your doctor feels the treatment should be stopped or changed, then you are free to do so. Please inform the trial team of any changes to your HD medications. Additionally, if you are not currently on any HD medications and are started on these during the course of the trial, please inform the trial team of this.

- It is important that you consult with the trial team before starting any new medication. A few drugs interact with the trial medication.

- You should tell the trial team if you feel unwell or different in any way. If you have any major concerns or are feeling very unwell, please contact your trial doctor immediately using the contact numbers at the end of this information sheet.

- Although felodipine is routinely used to treat high blood pressure, its use as a treatment for HD is experimental. Therefore, you should discuss your participation in this trial with any insurance provider you have (e.g. protection insurance, life insurance, income protection, critical illness cover and private medical insurance) and seek advice if necessary, as failure to notify them may affect or invalidate your cover.

Please share this information with your partner if it is appropriate.

- The trial medicine could harm an unborn baby or nursing infant. You will not be able to take part in this trial if you are pregnant or breastfeeding. You should not participate in this trial if you are planning to become pregnant during the trial.

- Women who are able to have a baby must use one of the following, highly effective forms of contraception, for the entire duration of treatment and for 4 weeks after their last treatment with the trial drug:

    - Combined (oestrogen and progestogen containing) hormonal contraception associated with inhibition of ovulation:
        - Oral
        - Intravaginal

        - Transdermal
    - Progestogen-only hormonal contraception associated with inhibition of ovulation:
        - Oral
        - Injectable
        - Implantable
    - Intrauterine device (IUD)
    - Intrauterine hormonal-releasing system
    - Bilateral tube occlusion

- You do not need to use contraception if:
    - you are a woman and you have only one partner, and the man has had an operation to cut the tubes that carry sperm (vasectomy).
    - you are a woman who cannot become pregnant.
    - you practice true abstinence as part of your usual and preferred lifestyle (no sexual activity from 28 days before the first dose until 28 days after the last dose of trial medication). If you become sexually active, you must use contraception as outlined above.

- If you become pregnant during the trial or within 1 month of stopping treatment, you should inform your trial doctor immediately. Your trial doctor will discuss all the options available to you. The outcome and progress of any pregnancy would be followed and you would be asked questions about the pregnancy and baby, if appropriate.

7. What are the side effects of the drug being tested?

Felodipine is a drug which is used commonly in current medical practice. All of the potential complications are documented below, from the most common, to the very rare.

Very common (more than 1 in 10 (10%) of patients)

- Headache
- Flush
- Ankle swelling

Uncommon (less than 1 in 100 (1%) of patients)

- Abnormally rapid heart rate
- Palpitations
- Too low blood pressure (hypotension)
- Nausea
- Abdominal pain
- Burning/prickling/numbness
- Rash or itching
- Fatigue
- Dizziness

Rare (less than 1 in 1000 (0.1%) of patients)

- Fainting
- Vomiting

- Nettle rash
- Pain/stiffness in joints
- Muscular pain
- Impotence/sexual dysfunction
- Lack of oxygen to the heart (myocardial ischaemia)

Very rare (less than 1 in 10,000 (0.01%) of patients)

- Gingivitis (swollen gums)
- Increased liver enzymes as measured on blood tests
- Skin reactions due to increased sensitivity to sunlight
- Inflammation of small blood vessels of the skin
- A need to pass water frequently
- Hypersensitivity reactions such as fever or swelling of the lips and tongue

Felodipine can have a minor or moderate influence on your ability to drive and use machines. If you experience a headache, nausea, dizziness or fatigue your ability to react may be impaired. Caution is recommended with respect to this, especially at the start of treatment.

Felodipine, like other blood-pressure lowering medicinal products, may in rare cases lead to pronounced low blood pressure which in some people may result in an inadequate supply of blood to the heart. Therefore, people with a history of uncompensated heart failure, acute myocardial infarction (heart attack), unstable angina (chest pain) or disease of heart valve/muscle will not be able to participate.

As there is a chance felodipine could cause a drop in your blood pressure, you should let the trial team know as soon as possible if you experience symptoms of this, for example, feeling lightheaded particularly after exercising or eating a heavy meal, or if your weekly blood pressure measurement is below 90/60 mmHg.

Felodipine can interact with other medications, vitamins or herbal remedies you may be taking. An interaction is when a substance changes the way the drug works. This can be harmful or prevent the drug working well.
Be sure to tell your doctor about all medications, vitamins or herbal remedies you are taking.

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

There is a substantial time commitment associated with being part of the trial. It will involve 12 visits to the VGB, plus an additional 2 visits to be performed over the telephone. As well as being time consuming, there are some potential risks associated with the medication, which are documented above.

Other risks associated with trial procedures include the following:

<u>Risks relating to MRI scanning</u>
If you consent to the optional MRI scans, as part of the baseline and the week 62 assessments you will need to attend the MRI scanning centre at the Wolfson Brain Imaging Centre. This is located on the Cambridge Biomedical Campus, close to the VGB. When possible, we will schedule this on the same day as the other tests, but there may be occasions where this is not possible if the scanner is fully booked or being serviced.

MRI scans involve a large magnet which is used to create high quality pictures of your internal organs, in this case your brain. Some metallic implants in your body may prevent you from taking part in this type of scan. MRIs do not contain any ionising or radioactive radiation and are totally safe. MRI scanners can create a lot of noise but you will be provided with a headset to cover your ears and will be able to stop the scan and communicate with the radiographer at all times.

Like faces, brains come in all shapes and sizes, so that there are many normal variations of what the scan shows. There is a chance of less than 1:100 that your MRI scan may show a significant abnormality of which you are unaware. In such circumstances, you will be appropriately counselled. You will be referred to the appropriate specialist in consultation with your GP, if you are agreeable. Such early detection has the benefit of starting treatment early but, in a small number of cases, may have implications for future employment and insurance.

Risks relating to venepuncture for blood sampling
Blood tests can cause minor discomfort and bruising of skin. Standard protocols will be followed to prevent infections.

Risks of assessments/questionnaires
Some of the assessments and/or questionnaires completed as part of this trial may involve sensitive topics such as depression and suicide, which may be uncomfortable for you to talk about. They will only be carried out by trained individuals from the trial team who will discuss any issues that arise from these with you. Following consultation, you may be referred to your GP or other professional, if appropriate, and if this is in line with your wishes.

9. What are the possible benefits of taking part?

There is no guarantee that you will benefit from taking part in this trial. You may experience relief in your symptoms or a slowing of your disease progression. However, information collected as part of your participation in this trial may benefit people with HD in the future.

10. What are the alternatives for treatment?

Currently, there are no proven treatments which act on the cause of HD and affect its progression.

There are treatments for the symptoms of HD, which you may well already be taking. We will not alter or change these medications if you do decide to participate in the trial.

11. Might coronavirus disease 2019 (COVID-19) affect the trial?

Felodipine does not lead to an increased risk of complications from COVID-19. It is possible that the situation with COVID-19 will change over time. The trial investigators will follow all national and local guidance on testing and research.

Changes may be made to how your trial visits are conducted to allow you to continue participating in the trial during the COVID-19 pandemic. If you are unable to attend a face-to-face visit due to COVID-19, the trial team may contact you over a video platform such as Zoom or Microsoft Teams, or over the phone if you are unable to use these video platforms. You may be able to complete some of the trial assessments that

are important to determine if the trial drug has a positive impact on HD over the video platforms. The trial team will guide you through the process, should this occur. Safety assessments, if required, would continue to be performed following hospital procedures were this to happen. This could involve having blood testing performed off-site.

The trial medication may be couriered to you using the hospital contracted courier service if COVID-19 prevents on-site visits. If this occurs, we will ask for your consent to share your contact details with the courier service.

12. What happens when the trial stops?

You will receive 58 weeks of treatment with felodipine during the trial. However, we will not be able to offer you any further felodipine treatment following the end of the trial.

After this trial, we hope to move on to bigger trials to see whether felodipine may slow down the progression of HD, although this will depend on the results of the current trial.

You will be asked whether you are still happy for us to contact you again to find out whether you may wish to participate in future studies as they arise. Your routine NHS care will continue as usual.

13. Expenses & payment?

You will not receive any payment for participating in this trial; however, we will reimburse any reasonable travel costs incurred by your participation, including mileage to and from the trial site. Parking is available free of charge at the VGB during your visits.

It is important that you keep any travel-related receipts and request a claim form at your hospital visit, if appropriate. Details of how and when payments will be made are available from the trial team.

All payments are made electronically via BACS payment, and so in order to process any travel claims we will need your bank account number and sort code. These will be kept confidential and only used for the purpose of reimbursing you for your travel expenses.

This completes section 1.

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

Section 2: Trial Conduct

14. What if new information becomes available?

Sometimes during the course of a trial, new information becomes available which might affect your decision to continue participating in this trial. Your trial doctor will contact you to discuss the new information and whether you wish to continue participating in the trial. If you still wish to continue in the trial, you will be asked to sign a new informed consent form.

The trial Sponsor organisations, the regulatory authority or the trial doctor may decide to stop the trial at any time. If that happens we will tell you why the trial has been stopped and arrange for appropriate care and treatment for you.

15. What if I decide I no longer wish to participate in the trial?

You are free to come off this trial at any time without giving a reason and without it affecting your future care or medical treatment. If you decide not to participate any further, you will no longer receive the trial treatment.

If you choose to stop the trial treatment, or the trial doctor decides it is no longer appropriate for you to take the trial treatment, you will have three options regarding further trial involvement. This decision is completely yours to make. Your options are as follows:

1. Should you be willing, you will continue with your trial assessments and will follow the same schedule as if you were still on treatment.
2. If you no longer wish to follow the full trial schedule but are willing to undergo a limited follow-up, we will invite you for a final visit prior to your full trial withdrawal.
3. If you wish to fully withdraw from the trial, no further tests will be performed on you and no further research samples will be collected.

Any data already collected or results from tests already performed on you or your samples will continue to be used in the trial analysis.

The trial doctor may also choose to withdraw you from the trial if they feel it is in your best interests or if you have been unable to comply with the requirements of the trial. Reasons for trial withdrawal could include:

- You have experienced a serious side effect
- You are unable to complete the visits, medication or trial documentation as required
- You become pregnant or plan to become pregnant

If you have experienced any serious side effects during the course of the trial which require you to withdraw from the trial, your trial doctor will follow-up with you regarding your progress until the side effect has stabilised or resolved.

16. What if there is a problem?

Any complaint about the way you have been dealt with during the trial or any possible harm you might suffer will be addressed. If you have any concerns about any aspect of this trial you should speak to your trial doctor who will do their best to answer your questions.

In the event that something does go wrong and you are harmed by taking part in the research and this is due to someone's negligence then you may have grounds for a legal action for compensation against Cambridge University Hospitals NHS Foundation Trust. If your claim is

successful your legal costs will be met. The normal National Health Service complaints mechanisms will still be available to you (if appropriate). The University has obtained insurance which provides no-fault compensation i.e. for non-negligent harm, you may be entitled to make a claim for this.

The NHS does not provide no-fault compensation i.e. for non-negligent harm, and NHS bodies are unable to agree in advance to pay compensation for non-negligent harm. They are able to consider an ex-gratia payment in the case of a claim.

If you wish to complain or have any concerns about any aspect of the way you have been approached or treated during this trial, you can do this through the NHS complaints procedure. In the first instance it may be helpful to contact the Patient Advice and Liaison Service (PALS) at your hospital. Contact details can be found at the end of this information sheet.

17. How will we use information about you?

Cambridge University Hospitals NHS Foundation Trust (CUH) and the University of Cambridge are the Sponsors for this clinical trial, based in the United Kingdom.

We will need to use information from you and your medical records for this research project.

This information will include your name, NHS number and contact details which will be held by the site. People (Sponsor organisations, regulatory authorities and research personnel) will use this information to do the research or to check your records to make sure that the research is being done properly.

People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead.

We will keep all information about you safe and secure.

Once we have finished the trial, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the trial.

De-identified information about your health and care may be made available for other research studies run by CUH and/or the University of Cambridge, or other organisations. These organisations may be NHS or other public sector organisations, academic institutions, charities and commercial companies in the UK or abroad. Before your data is shared with other organisations all personal identifiers, such as names, addresses and dates of birth, will be removed. Making information from trials available for further research helps maximise the benefit of conducting trials and allows other researchers to verify results and avoid duplicating research. To facilitate this, some trial datasets are made available to researchers via a public online database and become “open data”. Data are thoroughly de-identified before they are submitted to an open data platform and once the data are uploaded we do not have control over how they are used.

18. What are your choices about how your information is used?

- You can stop being part of the trial 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.

19. 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-participants/
- our leaflet available from www.hra.nhs.uk/participantdataandresearch
  or please visit:
  for Cambridge University Hospitals NHS Foundation Trust:
  https://www.cuh.nhs.uk/participant-privacy/
  for University of Cambridge:
  https://www.medschl.cam.ac.uk/research/information-governance
  or email the Information Governance team at:
  researchgovernance@medschl.cam.ac.uk
- by asking one of the research team (see contact details at the end of this information sheet)
- by sending an email to gdpr.enquiries@addenbrookes.nhs.uk

20. What will happen to my samples?

During the trial the blood samples collected from you will be sent to the local laboratory within Cambridge University Hospitals NHS Foundation Trust, where they will undergo routine blood tests. No blood samples will be stored as part of the FELL-HD trial.

Your trial doctor will inform you of any abnormalities discovered as part of this testing and will counsel you on the appropriate action to take. If required, you will be referred to the appropriate specialist in consultation with your GP, if you are agreeable.

21. What will happen to the results of the trial?

The results of the trial will be thoroughly anonymised and you will not be able to be identified from any of the data produced. When the results of this trial are available they may be published in peer reviewed medical journals and used for medical presentations and conferences. They will also be published in a clinical trial registry. Some data from the trial may be used by investigators in the trial team undertaking related research into treatments for Huntington's disease.

De-identified datasets from the trial may also be made available to other researchers in line with national and international data transparency initiatives.

If you would like to obtain a copy of the published results please contact your trial doctor directly who will be able to arrange this for you. We will also provide updates via our group's website (http://www.thebarkerwilliamsgraylab.co.uk/) and will share results of the trial in our HD annual newsletter.

22. Who is organising and funding the trial?

This trial is sponsored by Cambridge University Hospitals NHS Foundation Trust and the University of Cambridge.

The trial is funded by the UK Dementia Research Institute (UK DRI) and by the National Institute for Health Research (NIHR) Cambridge Biomedical Research Centre – Dementia and Neurodegeneration Theme. The funders will not be responsible for any part of the trial or involved in any data management or interpretation of the results of the trial.

23. Who has reviewed this trial?

This trial has been peer reviewed by independent representatives of the UK DRI as part of the funding application process. All research within the NHS is reviewed by an independent group of people called a Research Ethics Committee, to protect your interests. This trial has been reviewed and given favourable opinion by London – Brent REC. The Medicines and Healthcare Products Regulatory Agency (MHRA) who are responsible for regulating medicines in the UK have also reviewed this trial.

24. Further information and contact details

Please feel free to ask questions about this consent form or the trial at any time. You may ask questions before you decide to start the trial or at any time after the trial has started.

In case of any question about the investigation (e.g. risks, side effects, injury, patient rights, etc.) you can contact:

Professor Roger Barker (Chief Investigator)

Telephone: 01223 331160
Email: rab46@cam.ac.uk

Katie Andresen (Trial Coordinator)

Telephone: 01223 331141
Email: kera2@cam.ac.uk

If you are unhappy and wish to complain formally, you can do this via the Patient Advice and Liaison Service (PALS):

Tel. 01223 216756
Email: pals@addenbrookes.nhs.uk

In the event of an emergency:

In the event of an emergency please follow your normal emergency procedure. If you need urgent medical attention, go to the nearest accident & emergency (A&E) department.

If you need to contact the trial team outside of normal working hours, please contact the Addenbrooke's switchboard on **01223 245151** and ask for a member of the FELL-HD trial team.

Thank you for taking the time to read this document, and for considering taking part in the trial.

INFORMED CONSENT FORM

Trial Title: FELL-HD: A trial to assess the tolerability of using felodipine to upregulate autophagy as a treatment of Huntington's disease

Principal Investigator: Professor Roger Barker **Participant Number:** _____

If you agree with each sentence below, please initial the box		**INITIALS**
1	I have read and understood the Participant Information Sheet version 2.0, dated 09 June 2022 for the above trial and I confirm that the trial procedures and information have been explained to me. I have had the opportunity to ask questions and I am satisfied with the answers and explanations provided.	
2	I understand that my participation in this trial is voluntary and that I am free to withdraw at any time, without giving a reason and without my medical care or legal rights being affected and that any data and samples already collected or tests already performed will continue to be used in the trial as described in this information sheet.	
3	I understand that personal information about me will be collected and used in accordance with this information sheet. This information will be kept in the strictest confidence and I will not be identifiable in any results published.	
4	I understand that sections of my medical notes or information related directly to my participation in this trial may be looked at by responsible individuals from the Sponsor organisations, regulatory authorities and research personnel where it is relevant to my taking part in research and that they will keep my personal information confidential. I give permission for these individuals to have access to my records.	
5	I understand that my GP will be informed of my participation in this trial and sent details of the FELL-HD trial, including any clinically significant abnormalities found during trial procedures.	
6	I have read and understood the compensation arrangements for this trial as specified in the Participant Information Sheet.	
7	I understand that the doctors in charge of this trial may close the trial or stop my participation in it at any time without my consent.	
8	I have read and understood my responsibilities for the trial including using appropriate contraception as listed in section 6.	
9	I understand that I will have access to the trial drug felodipine for the time I am on the trial only.	
10	I understand that some identifiable data will be stored on internal secure servers, only accessible by authorised members of the trial team.	
11	I understand that, if necessary, some visits may be conducted remotely and that this may involve the completion of assessments over video platforms (such as Zoom or Microsoft Teams)	
12	I understand that de-identified information collected about me may be shared with collaborators to support other research in the future, including research conducted by both commercial and non-commercial organisations in the UK and abroad.	

OPTIONAL		INITIALS
13	I agree to undergo the **optional** MRI scans as part of this trial.	
14	I wish to receive the newsletter at the end of the trial, which will include the results of the trial after it has been completed.	
15	I agree to allow the trial investigators to contact me in the future with respect to further follow-up studies for this trial or related ethically-approved studies.	

I agree to participate in this trial:

_____	_____	_____
Name of participant	Signature	Date
_____	_____	_____
Name of person taking consent	Signature	Date

Time of Consent (24hr clock) _____:_____

1 copy for the participant, 1 copy for the trial team, 1 copy to be retained in the hospital notes.