

## Information Sheet and Consent Form

<b>Study Title:</b>	A Phase 4, Randomized, Double-blind, Placebo-controlled Study to Evaluate the Efficacy and Safety of Rimegepant in Episodic Migraine Prevention with Multiple Dosing Regimens
<b>Study Sponsor:</b>	Biohaven Pharmaceuticals Holding Company Limited
<b>Protocol Number:</b>	BHV3000-404
<b>EudraCT Number:</b>	2021-005239-22
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<b>Study Site Number:</b>	401
<b>Participant Study Number:</b>	

You are being invited to take part in our clinical research study about migraines. A clinical research study is a way to find out new information about a new medicine, if and how well it works, and if it's safe before it is given to lots of people.

Taking part in clinical research is voluntary. It is up to you to decide whether or not to take part. People who take part in clinical research are called "participants". To help you decide, it is important for you to understand why this research is being done and what it will involve. This information sheet and consent form explains this study to you. After reading the information sheet, you can decide to be in the study, or you can decide not to be in the study. Take whatever time you need to read this information. You may discuss your decision with the study doctor or nurse, your healthcare team, your family, your friends or with anyone else you wish to talk with about it. If you decide to be in the study and then change your mind, that is ok too. You can stop being in the study at any time.

Your study doctor will explain the study to you. Please ask the study doctor or the study nurse to explain anything you do not understand. They will answer any questions you have. You can ask questions about the study at any time. You may also have your family doctor/general practitioner (GP) or other treatment specialist(s) call the study doctor to ask any questions they feel are necessary to evaluate the study and your possible participation in it.

**Table of Contents**

**Information Sheet and Consent Form** ..... 1

1. Who is sponsoring this study? ..... 3

2. Why is this study being done? ..... 3

3. Do you have to take part in this study? ..... 3

4. How many people will take part? ..... 5

5. How long will your participation in this study last? ..... 3

6. What will happen during this study? ..... 5

7. What instructions must you follow while in the study? ..... 13

8. What are the possible benefits of being in this study? ..... 14

9. What are the risks and discomforts of taking part in this study? ..... 14

10. How will we use information about you? ..... 18

11. Where can you find out more information about how your information is used? ..... 19

12. Will your participation in this study be kept confidential? ..... 19

13. What are your choices about how your information is used? ..... **Error! Bookmark not defined.**

14. Where and for how long will my samples be stored? ..... 20

15. Will your GP be informed? ..... 20

16. Who has reviewed this study? ..... 20

17. What will happen to the results of this study? ..... 20

18. How can you find more information about this study? ..... 21

19. What if you do not take part in this study? ..... 21

20. What other treatment options are available? ..... 21

21. What happens if you are hurt or injured due to participation in this study? ..... 21

22. Will you be paid for being in the study? ..... 22

23. What if there are new findings? ..... 22

24. What happens when the study ends? ..... 22

25. Who can you contact if you have questions or concerns about this study? ..... 22

**Consent form for Participants** ..... 24

1. Agreeing to be in the Research Study ..... 24

2. Statement of the Person Obtaining Consent ..... 25

### **1. Who is sponsoring this study?**

The pharmaceutical company, Biohaven Pharmaceuticals Holding Company Limited, based in the United States (US), is funding and organizing this research study. They are referred to as the “Sponsor” throughout this information sheet. Re-Cognition Health is receiving funds from the Sponsor to conduct the study.

### **2. Why is this study being done?**

This clinical research study involves a drug called “rimegepant”. Rimegepant (as (Nurtec® ODT) (orally disintegrating tablet) , has already been approved in the United States (US) for the acute treatment in adults with migraine and for the preventive treatment in adults with episodic migraine. More recently (April 2022), rimegepant (as Vydura®) has also been approved for the same purposes in adults in the European Union (EU) and (June 2022) in the United Kingdom (UK). Rimegepant comes as an orally disintegrating tablet, meaning it is a tablet that is taken by and dissolves in the mouth.

The purpose of this study is to further evaluate how well the drug works in preventing episodic migraine compared to a placebo when taken either every other day or daily. Additionally, this study is evaluating if the study drug is well tolerated and safe. A placebo looks like the study drug but does not contain any active study drug. Researchers use a placebo to see if the study drug works better or is safer than taking nothing. This will allow a careful comparison of the benefits and risks of different dosing regimens of rimegepant as a preventive treatment for episodic migraine. We measure this potential by counting the number of migraine days participants may have each month.

You are being invited to be in this study because you have been diagnosed with migraine (with or without aura).

### **3. Do you have to take part in this study?**

No. If you do not want to be in this study, you do not have to be in it. If you decide to say no, your decision will be respected. If you choose to be in the study, you can ask questions at any time. Participation in this study will not replace your access to standard care.

It is important to note that at any point in time, you have the right to withdraw your consent.

### **4. How long will your participation in this study last?**

Your participation in this study consists of 4 phases:

- 4-week Screening/Observation Phase (2 on-site visits)
- 12-week Double-blind Study Treatment Phase (5 on-site visits)
- 12-week Open-label Extension Phase (1 telephone visit and 4 on-site visits)
- 8-week Follow-up Phase (2 on-site visits)

If all phases are completed, your overall participation could last up to 36 weeks. Over this period, you will be asked to attend the study site for at least 13 ‘onsite’ visits. Study visits will generally last between 1 to 2 hours. (The Screening, Pre-Baseline, Baseline, and 8-Week Follow-up safety visits must be done in person at the study site).

You will not have study any tests or other procedures done for the study until after you agree to be in the study and sign this consent form.

### **Screening and Observation Phase**

The purpose of the Screening/Observation Phase is for the study doctor and staff to determine if you are eligible for the study, both from a medical and safety standpoint. This phase will be done across 2 study visits, and it will take approximately 28 days.

This study will use 'competitive enrollment', which means that when a target number of participants enter the study, all further enrollment will be closed. Therefore, it is possible that you could be in the Screening/Observation Phase, ready to begin the study, and be discontinued without your consent if the target number of participants has already been reached. If this occurs, you will not be required to complete any other visits.

You will be asked to return your eDiary and paper medication diary at this visit.

### **Double-Blind Treatment Phase**

If you are eligible to participate in the study at the end of the Screening/Observation phase, you will enter the Double-blind treatment phase.

During the 12-week Double-blind Treatment phase, there are 5 on-site study visits. You will be randomly assigned (by chance, like the flip of a coin) to receive treatment. One group will take a 75 mg rimegepant ODT (orally disintegrating tablet) daily, the second group will alternate between a 75 mg rimegepant ODT and the placebo (one day rimegepant, the next day placebo, etc.), and the third group will only take the placebo daily.

This means that you will have a 66% (2 in 3) chance of receiving the active study drug, rimegepant.

During this phase of the study, no one, including you, the study doctor and study staff, will know if you are taking rimegepant or placebo. Scientists refer to this as a "double blind" study, since you and your study doctor are "blinded" to the group you are assigned to. This is done to avoid influencing the study results, even if unintentionally. However, in the event of an emergency, your study doctor will be able to find out which treatment you are receiving if necessary.

The study doctor and/or study staff will give you instructions on how to take the study treatment. You will place each tablet on or under your tongue every day. You will then let this tablet melt and then you will swallow.

### **Open-Label Extension Phase**

After completion of the 12-week Double-Treatment Phase, you will be assessed to determine if you are eligible for the 12-week Open-label Extension Phase which consists of 1 Telephone Visit and 4 on-site visits. During this phase, if you are eligible to continue, you will receive active rimegepant ODT daily. There is no placebo during this part of the study. During this time you, the study doctor, study staff, and the Sponsor will know that you are receiving rimegepant only.

### **Safety Follow-up Phase**

If you are not eligible for extension phase of the study, you will enter into the 8-week Follow-up Phase which consists of 2 additional on-site visits. The purpose of this phase is to check on you, for safety reasons, after you have received study treatment.

If you stop the study early, at any time, you will have an 'Early Termination Visit' to complete end of study treatment assessments. You will also need to return to the study site for the 8-week Follow-up Phase (2 visits).

**Unscheduled Visit(s):** *This can occur at any time during the study.* You may have unscheduled study visits with your study doctor for your safety. The study doctor or nurse will let you know when and why an unscheduled visit is planned.

**Telemedicine Visit(s):** *There could be times when it may be very difficult or impossible to visit the hospital. For example, because of an emergency or due to closures/restrictions caused by the Coronavirus 2019 (COVID-19) pandemic.* If this happens, you will have virtual visits via phone or tele-video conferencing where your study doctor may call to check on you instead or having blood and/or urine tests done at local laboratories or by an in-home vendor, a healthcare provider or a study nurse may come to your home. These types of are called a "telemedicine visits".

## 5. How many people will take part?

The study will take place in approximately 125 study sites (medical facilities) in the US, Canada, European countries, United Kingdom (UK), and Israel. This study will screen approximately 2000 male and female participants who are at least 18 years of age at the time of signing and dating consent. The goal is to evaluate approximately 660 participants who take study drug, with up to 220 participants in each treatment group.

## 6. What will happen during this study?

Before you decide to continue to participate in this research study, you must be given the chance to ask questions. You will need to read, sign and date this consent form, and you will then be given a copy to take home with you. Your study doctor will explain and take you through this 'consent process' at the study site.

### Study Visits, Tests and Procedures

The study doctor or staff need to perform many tests to direct your care. These test results will be collected in addition to the special tests that will be done for research purposes. If you agree to continue to take part in this study, the following tests and procedures will be done (Refer to the Table of Assessments):

#### **Observation Phase:** *Screening Visit and Pre-randomization Evaluation Visit*

- Review of your medical history and past and current medications.
- You will be asked about your typical migraine symptoms, frequency, severity and how your migraines are treated.
- You will have a physical examination performed, including measurement of your vital signs (blood pressure, heart rate, breathing rate, and body temperature), weight and height.

- You will have blood samples collected for laboratory tests. If possible, you should arrive for these blood tests after fasting (restricting food and drinks, besides water) for at least 8 hours.
- You will have urine samples collected for:
  - A pregnancy test if you are able to become pregnant. Your test result must show 'not pregnant' for you to qualify and participate in this study.
  - A drug screen to test for drug abuse. The result of the test must meet study entry criteria evaluated by the study doctor for you to participate in this study.
- Your heart function will be assessed with an electrocardiogram ((ECG), a test that measures and records the electrical activity of your heart).
- You will be asked questions about any thoughts or actions about suicide you may have had (Columbia Suicide Severity Rating Scale [C-SSRS]).
- You will be provided an electronic diary (eDiary) and will be trained on how to use the eDiary by the site staff. In the eDiary, you will record if you had a migraine, the intensity of the migraine (mild, moderate, or severe), the characteristics of the migraine (for example, if you have a throbbing headache, location of pain, nausea and/or vomiting, sensitivity to light, and/or sensitivity to sound), if any of your normal activities were affected by the migraine, and if you took medications to treat the migraine. If you took any medications including your standard of care medications to treat the migraine, you will record this information on a paper diary which will be provided to you by the study staff. Please bring the eDiary and paper diary to every study visit. While using this, information about you will be collected and may be shared with the researchers or people outside of the study. This data might include personal health information (daily headache and medication information). A complete description of the data collection and sharing for an eDiary, or device can be found in the Terms of Use, End User License Agreement, or Privacy Policy. If you would like to read these documents, request a copy from the study doctor. This means that some of your personal/medical information will be transferred electronically via the internet. No data or information is completely secure. Once information is released to a third party it may lose its protection and could be disclosed without your permission. The chance of someone misusing your information is very small.
- You will not receive study drug at either of these visits.

***Double-blind Study Treatment Phase: Baseline/Randomization Visit – Week 2, 4, 8, and 12 Visits***

During the Baseline/Randomization visit you will be assessed to determine if you are still eligible to be in the study. The same procedures will occur as during the Observation Phase plus the following assessments:

- You will be asked to complete a questionnaire (Migraine-Specific Quality-of-Life Questionnaire (MSQ) v 2.1) about your migraines and quality of life.
- You will be asked questions about your health (Clinical Global Impression – change (CGI-c scale) and your experiences with the study medication (Satisfaction with Medication (SM) scale).

- You will be assigned to one of the 3 treatment groups noted in Section 4. The study doctor and study staff will give you a supply of study drug and you will take one 75mg ODT of study drug daily even if you do not have a migraine. The date of all doses of study drug taken must be recorded on the study drug wallet. You will be provided with a 'Study Drug Dosing Instructions Card' which provides detailed instructions on how to take the study drug.

**End of Treatment (EOT):** If you stop the Double-blind Treatment Phase early (before Week 12), you will have an 'Early Termination Visit' to complete the End of Treatment assessments. You will have an EOT visit to complete the end of treatment (Week 12) tests which are described in the above (and in the schedule of assessments). You will need to return the eDiary and the Concomitant Medication paper diary. You will also need to return to the study site for the 8-week follow-up phase.

The "schedule of assessments table" for the Double-blind Treatment Phase on the following page describes when each of the tests and procedures will occur for each of the study visits explained in the above.

**After the Week 12 visit, you must wait until the study doctor or nurse contacts you to inform you if you can start the Open-label Treatment Phase.**

**This will be based on your laboratory results which take a few days to come back to your study doctor.**

**Table of Assessments Double-Blind Phase**

Procedure	Screening Phase		Treatment Phase				Follow-up Phase
	Screening Visit	Pre-Randomization Evaluation Visit	Baseline Visit Randomization	Week 2	Week 4 and Week 8	Week 12 (and EOT Visit for Early Discontinuation)	FU Week 2 and FU Week 8 Visits
Day	28 Days Before Day 1	4 Days Before Day 1	Day 1	Day 14	Day 28 Day 56	Day 86	2 Weeks and 8 Weeks After Last Dose
Eligibility	X						
Paper Diary for Medications Taken	X	X	X	X	X	X	X
Physical Examination	X	X				X	
Vital Signs / Physical Measurements	X	X	X	X	X	X	X
Blood draw	2.5 tsp/12.5 mL	2.5 tsp/12.5 mL	2.0 tsp/10 mL	2.0 tsp/10 mL	2.0 tsp/10 mL	2.5 tsp/12.5 mL	2.0 tsp/10 mL
ECG	X	X		X	X	X	
Urine sample		X				X	
Pregnancy Test	X (urine)	X (blood)	X (urine)		X (urine)	X (urine)	X (FU Week 2 urine, FU Week 8 blood)
Adverse Events and Medications taken	X	X	X	X	X	X	X
Columbia Suicide Severity Rating Scale	X		X	X	X	X	X (FU Week 2 only)
Dispense Study Drug			X		X	(X)	
Take study medication				Take study medication daily			
Return unused study drug & empty wallets				X	X	X	
eDiary reviewed		X	X	X	X	X	
Questionnaires			X			X	



	Screening Phase		Treatment Phase				Follow-up Phase
<b>Procedure</b>	<b>Screening Visit</b>	<b>Pre-Randomization Evaluation Visit</b>	<b>Baseline Visit Randomization</b>	<b>Week 2</b>	<b>Week 4 and Week 8</b>	<b>Week 12 (and EOT Visit for Early Discontinuation)</b>	<b>FU Week 2 and FU Week 8 Visits</b>

Abbreviations: ECG=electrocardiogram; FU=Follow-up; tsp=teaspoon;

**Open-label Extension Phase: Weeks 14, 16, 20, 24, and End of Treatment (EOT) Visit**

*(1 Telephone Visit and 4 on-site visits):*

*You must wait to start the study drug until the study staff phone you to confirm your eligibility.*

If you are entering the Open-label Extension Phase, the study doctor and study staff will give you a supply of study drug and you will continue to take one tablet of the study drug, 75 mg rimegepant ODT daily, even if you do not have a migraine that day.

Similar procedures will occur as during the Double-Blind Phase (please refer to Table of Assessments for Open-Label Extension Phase).

**End of Treatment (EOT) Visit:** If you stop the Open-label Extension Phase early (before Week 24), you will have an EOT Visit to complete the End of Treatment assessments. You will also need to return for the Follow-up Week 2 and Week 8 Safety Visits.

The “schedule of assessments table” for the Open-label Treatment Phase are on the following page describes when each of the tests and procedures will occur.



**Table of Assessments Open-Label Extension Phase**

	Phone Visit to Confirm Eligibility Based on Laboratory Criteria	Treatment Phase			Follow-up Phase
Procedure		Week 14	Week 16 and 20	Week 24 or End of Treatment Visit	FU Week 2 and FU Week 8 Visits
Day		Day 98	Day 112 and 140	Day 168	2 and 8 Weeks After Last Dose
Paper Diary for Medications Taken		X	X	X	X
Physical Examination			X (Week 16 only)	X	
Vital Signs / Physical Measurements		X	X	X	X
Blood draw		2.5 tsp/12.5 mL	2.0 tsp/10 mL	2.5 tsp/12.5 mL	2.0 tsp/10 mL
ECG		X		X	
Urine sample				X	
Pregnancy Test		X (urine)	X (urine)	X (urine)	X FU Week 2 (urine), FU Week 8 (blood)
Adverse Events and Medications taken		X	X	X	X
Columbia Suicide Severity Rating Scale		X	X	X	X (FU Week 2 only)
Dispense Study Drug			X		
Take study medication		Take study medication daily			
Return unused study drug & empty wallets		X	X	X	
Questionnaires				X	

Abbreviations: ECG=electrocardiogram; FU=Follow-up; tsp=teaspoon.

### **Blood Sampling:**

As part of the study, blood samples will be collected. This will be done by inserting a sterile needle into one of your veins. The quantity and timing of blood draws may vary. A total of 142.5 mL or 28.5 teaspoons in 13 blood samples is expected to be collected throughout the study. The days when blood draws are expected to occur, including the amount (volume) that will be drawn is fully described in the table of assessments for each study phase. These numbers are approximate and may increase or decrease depending on how your clinic chooses to collect the blood samples. The study doctor may need to draw other blood samples for your safety or as part of your medical care at any time during the study. If you do not want to provide these samples, you will not be able to participate in the study.

### **Permitted Medication: Acute Migraine Medication**

Participation in this study will not replace your access to standard (normal) care. This means that you will still need to see your GP and or treatment specialist(s), even if you are in this study. You will also be allowed to take the following medications during the study to treat migraine attacks, if needed:

- Triptans, aspirin, ibuprofen, baclofen, Paracetamol (up to 1000 mg/day for a maximum of 2 consecutive days at a time (this includes Excedrin Migraine), naprosyn (or any other type of non-steroidal anti-inflammatory (NSAID)), antiemetics (e.g. metoclopramide or promethazine), and muscle relaxants.

Your study doctor will have a complete list of these medications and explain this to you.

Please ask the study doctor if you have any questions about the medications that you are allowed to take in this study.

### **Medical Restrictions:**

You should inform the study doctor of all medications (prescription, over-the-counter, and herbal products) that you are currently taking or begin taking during the study. Rimegepant could change how your body handles certain other medicines. This may lead to greater risks from these other medicines. Also, certain medicines may increase the risks of rimegepant. For this reason, certain other medications will not be allowed or limited. Your study doctor will have a complete list of these medications and explain this to you.

Please ask the study doctor if you have any questions about restrictions on medications in this study.

## **7. What instructions must you follow while in the study?**

If you are willing to participate in the clinical study, you must ensure the following:

- Provide true information about your medical history.
- You must not participate in another clinical research project during this study and for a minimum of 30 days after the end of the study.
- Respect all study restrictions and medication restrictions, and do not abuse drugs or alcohol, or smoke/consume marijuana or its components.

- You must agree to complete all study procedures as outlined within this information sheet.
- **For females/those capable of becoming pregnant:** Use adequate contraceptive methods and avoid pregnancy during the study and for 60 days after the last dose of the study drug.
- **For males/those with sexual partners capable of becoming pregnant:** Inform your sexual partner that you are in a research study and you should use adequate contraceptive methods and avoid pregnancy during the study and for 90 days after your last dose of the study drug. Do not donate sperm until after 90 days following the last dose of study drug.
- Inform the study staff of any change in your medical condition, minor or major, during the study and any change to your medications, including over-the-counter medications and supplements.
- If you need to go to the Accident and Emergency department (A&E) at a hospital, you should tell the A&E doctors/nurses that you are in this research study. Contact the study doctor as soon as possible.
- If you no longer want to be in this study, tell the study doctor and come to the clinic for a check-up (early termination visit) and the follow-up safety visits.
- If you have any questions or problems during this study; you should contact the study doctor whose telephone number is on the first page of this information sheet.

## 8. What are the possible benefits of being in this study?

This study is being done for research purposes, and your participation in this study is completely voluntary. If you choose to participate in this study, you may or may not receive any personal benefit. Receiving rimegepant does not guarantee any personal benefit to you. The study drug may or may not help to relieve your symptoms.

No direct benefits can therefore be anticipated from participating in this research study except for a health evaluation, and potentially a better understanding of your migraine patterns, associated symptoms, triggers, and risks. The tests provided may help you learn about your general health. This study may help doctors and scientists learn things about the study drug that will help others in the future.

## 9. What are the risks and discomforts of taking part in this study?

Risks are possible side effects from study treatment and from tests done during the study. One of the reasons for doing this study is to learn more about the possible side effects of rimegepant.

There may be rare and unknown side effects of rimegepant, including reactions that may be life-threatening. It is also possible that you may experience a reaction due to the placebo used in this study. The study doctor and staff will closely monitor you for any side effects. The study doctor or study staff may also give you medication or perform certain medical procedures to help lessen side effects.

It is therefore very important that you tell the study doctor and the study staff right away if you feel sick or uncomfortable and about any changes to your health during the study, even if you do not think they are related to the study treatment. If you are not completely truthful about how you feel while you are participating in this study, you may be at greater risk of harm. If you experience one

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IRAS ID: 1004841

BHV3000-404 UK Main PIS ICF\_v1.3\_18 Aug 2022 Final

Page 14 of 26

or more side effects that require urgent medical attention you should call or see your study doctor straightaway or immediately contact the emergency services.

Ask the study doctor or nurse if you have questions about the signs or symptoms of any side effects that you read about in this information sheet.

If a previously unknown medical condition is discovered, during the screening or participation in this research study, the study doctor will discuss:

- Whether you are eligible for study participation
- If you require referral to your usual GP or to a specialist

### **Potential Side-effects of rimegepant**

Rimegepant has been approved in the US, and more recently (April 2022) in the EU, to prevent and treat migraine attacks in adults. As of the end of August 2021, approximately 5,661 people have received rimegepant at any dose while participating in migraine or trigeminal neuralgia (severe facial pain) studies.

To date, rimegepant has been given in multiple doses to 2,471 subjects in 2 completed Phase 2/3 studies. The table below presents the number and percentage of subjects with most frequently reported adverse events (occurring in >2% of subjects):

Adverse event	Subjects receiving rimegepant (%)
<b>Severe adverse event</b>	
Back pain	3 (0.1)
Flu	3 (0.1)
Dizziness	2 (0.1)
Joint pain	2 (0.1)
Urinary tract infection	2 (0.1)
Bronchitis	1 (<0.1)
Nasal sinus swelling	1 (<0.1)
Upper respiratory tract infection	1 (<0.1)
<b>Mild or moderate adverse event</b>	
Upper respiratory tract infection	208 (8.4)
Cold-like symptoms	170 (6.9)
Nasal sinus swelling	113 (4.6)
Urinary tract infection	94 (3.8)
Back pain	83 (3.4)
Flu	81 (3.3)
Nausea	67 (2.7)

CONFIDENTIAL

IRAS ID: 1004841

BHV3000-404 UK Main PIS ICF\_v1.3\_18 Aug 2022 Final

Bronchitis	62 (2.5)
Joint pain	53 (2.1)
Dizziness	51 (2.1)

Temporary elevations (increases) of liver enzymes (an indication of possible liver injury) and muscle enzymes (an indication of possible muscle injury) have been infrequently reported in studies with rimegepant. However, a causal relationship between rimegepant and these laboratory findings has not been found at approved doses of rimegepant.

**Allergic reaction risks:**

With any drug, there is a small but real risk of allergic reactions that can be life-threatening or fatal. Severe reactions have included difficulty breathing and rash and can occur days after administration of the study treatment. Some symptoms of allergic reactions that may be experienced from rimegepant or placebo are:

- Skin itching, redness, rash
- Difficulty breathing
- Dizziness and fainting
- Swelling around the mouth, throat, or eyes
- A fast pulse
- Sweating

**If you have an allergic reaction, you must get emergency medical care immediately!**

**Studies in Animals**

Animal studies have been performed with high doses of rimegepant (approximately 30 to 200 times higher than the doses of rimegepant used in this research study) to try to predict what type of side effects might occur in humans taking rimegepant. In some animals, vomiting and effects on red blood cells, liver, muscle, and lungs were noted. No effects were noted on the embryos of rats exposed to rimegepant who became pregnant. While animal studies do not always predict human response to drugs, the results from these studies in animals and other studies in humans supports the safety of this research study with rimegepant.

**Possible risks of Study Procedures and Assessments:**

You may feel discomfort during some of the tests and there are some risks, such as:

- **Blood samples:** Possible side effects from blood drawing include faintness (feeling faint), swelling of the vein, pain, bruising, or bleeding at the site of puncture. There is also a slight possibility of infection. A numbing cream may be available to reduce the pain. (If a numbing cream/spray is used during blood sample collection there may be skin irritation or the skin may temporarily become itchy and or turn red, pale or develop a rash on the area when the cream/spray was applied to).
- **ECG:** Skin irritation is rare but could occur during an ECG from the electrodes (small sticky patches) or gel that is used.
- **Scales and Questionnaires:** The questionnaires used in this study may be upsetting. You do not need to answer any questions that you are not comfortable with. However, if you decide not to complete certain questionnaires, you may not be eligible to continue to



participate in this study. If you are having suicidal thoughts, you should contact the study doctor at the telephone number listed on the first page of this form.

- If you feel in crisis, you can **call 999** and/or **Samaritans on 116 123**
- **Placebo:** If you receive placebo (the inactive substance) as part of this study, your symptoms may not improve.

### **Pregnancy and Contraception (birth control) Information**

#### ***Females: People who can become pregnant should know***

Taking the study drug may involve unknown risks to a pregnancy, an embryo, a foetus (unborn baby), or a breastfeeding infant. Therefore, if you are pregnant, planning to become pregnant, or breastfeeding a child, you cannot take part in this study. Pregnancy tests will be done for all participants who are able to become pregnant (that is, those who have had their first menstrual period). This test might not detect an early pregnancy. Pregnancy tests will be repeated during the study.

You must agree to practice abstinence (avoid any heterosexual activity that may lead to pregnancy) or to use an acceptable method of birth control while taking part in this study and for 60 days after the last dose of study drug. It is strongly recommended that your male partner also uses an acceptable contraceptive method.

#### ***Males / People who can get other people pregnant should know:***

If you choose to have sex during the study and have sex with a person who can become pregnant, you must agree to practice abstinence (avoid any heterosexual activity that may lead to pregnancy) or you and your partner should agree to use an acceptable method of contraception throughout the study and for 90 days after your last dose of the study drug.

You must not donate sperm until 90 days following the last study drug administration. If you agree to participate in this study, you are expected to inform your sexual partner(s) who can become pregnant that you are participating in a clinical research study of a drug, and that the effects of the drug on pregnancy and an unborn baby are unknown. It is strongly recommended that your female partner also uses an acceptable method of contraception. You are also expected to provide your sexual partner, who can become pregnant, with the information in the Pregnancy/Birth Control section of this Information Sheet and to provide them with contact information for the study doctor for any additional questions you may have.

#### ***Contraception***

If you are already using a method of birth control, the study doctor or study staff will discuss with you if your current method of birth control is acceptable for use during this study. The study doctor will explain what you need to do.

Methods of acceptable birth control include:

- Abstinence.
- The combination of a male condom and hormonal birth controls to prevent ovulation (estrogen and progestogen or progestogen-only) or a male condom and an intra-uterine

contraceptive device (IUD, with or a without hormone release system) inserted at least 4 weeks prior to study drug administration.

- The simultaneous use of a male condom and, for the partner capable of becoming pregnant, a diaphragm or cervical cap with intravaginal applied spermicide.

If you are abstinent (not sexually active), the study doctor will require you to use acceptable methods of birth control if you become sexually active during the study.

### ***Pregnancy follow-up***

If you become pregnant or if you get someone pregnant during the study, you should tell the study doctor or staff as soon as possible.

If you become pregnant, the study drug will be stopped, and your involvement in this study will end. You will be asked to complete the final study procedures and assessments (EOT visit) and the two follow-up Safety Visits. The study doctor will also notify the Sponsor of the pregnancy, discuss any follow-up with you, and ask you for information until the end of the pregnancy including the health of your baby.

If your partner becomes pregnant, the study staff will ask permission to collect information from your pregnant partner about the pregnancy, its outcome, and the health of the baby after birth. Your partner will also be asked to sign and date a separate consent form to allow the collection of this information.

### ***Other Safety Considerations:***

It is important that you respect all restrictions since it could affect the study results or have consequences on your safety. If you do not follow these restrictions, you should tell the study staff as soon as possible.

Before taking any medicine or before any medical procedure (for example, surgery), it is recommended that you tell their doctor, pharmacist, and/or dentist that you are taking part in a clinical research study.

You will be given a study card, which you should always carry with you in case of an emergency. This card can help healthcare professionals who are not involved in your study treatment to identify that you are taking part in a clinical research study.

**If you feel dizzy or drowsy, you should not perform activities requiring mental alertness, judgment, and physical coordination such as driving or operating machinery until you feel secure and safe to do so.**

## **10. How will we use information about you?**

We will need to use Information from your medical records for this research project.

This information will include your:

- Name
- Initials
- Contact Details
- Date of Birth
- Sex
- Race
- NHS Number

- Physiological characteristics, which means your height, weight, and other results from ongoing study tests such as health tests (blood and heart tests).

People 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.

Some of your information, will be sent to the US. They must follow our rules about keeping your information safe.

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

### **11. 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.
- If you choose to stop taking part in the study, we would like to continue collecting information about your health at Re-Cognition Health. If you do not want this to happen, tell us and data collection will stop.
- The Sponsor and associated vendors need to manage your records in specific ways for the research to be reliable. This means that you won't be able to see or change the data we hold about you.
- The right to file a complaint with a data protection office within the government.

### **12. Where can you find out more information about how your information is used?**

- You can find out more about how your information is used at [www.hra.nhs.uk/information-about-patients/](http://www.hra.nhs.uk/information-about-patients/)
- The leaflet available from the HRA here [www.hra.nhs.uk/patientdataandresearch](http://www.hra.nhs.uk/patientdataandresearch)
- by asking one of the research team
- by sending an email to (the Sponsor's Data Protection Officer (DPO)) [ricardo.garvao@biohavenpharma.com](mailto:ricardo.garvao@biohavenpharma.com) or
- by ringing us on +44 (0)20 3355 3536

If you have questions about the use of your information, please first contact the data protection officer at your study site. This is due to the requirement to use a unique code which protects your personal data confidentially. The Sponsor does not have access to the unique code. Therefore, only the study team know your identity and they can fully access and provide information respectively. For additional questions you may also contact the Sponsor's DPO.

### **13. Duration of data storage**

Your information /data will be stored by the trial site and Sponsor for a minimum of 25 years after completion or termination of this trial. The health authority or the hospital can require that this period is longer if necessary, after that, your personal data will then be deleted

You may revoke this consent for use in writing through your study doctor at any time.

#### **14. Where and for how long will my samples be stored?**

Your blood and urine samples will be collected by your study doctor or nurse and labelled in with a unique study code in a way that will not identify you. These samples will be processed at the study site and then shipped securely by courier to a central laboratory in the UK (ACM Global Laboratory Limited (23 Hospital Fields Road York, YO10 4DZ, UK) and US (ACM Medical Laboratory (160 Elmgrove Park Rochester, NY 14624, USA) for analysis (testing) and storage.

Any remaining materials will be destroyed after completion or termination of this trial.

You may revoke your consent for the use of your sample(s) at any time by contacting the study doctor. If you revoke your consent to use the samples before they have been analysed, the study doctor will ensure that they are destroyed and that you are notified of the process. If, however, analyses on the samples have already been carried out, the Sponsor is not obliged to destroy the results of this research.

#### **15. Will your GP be informed?**

If you agree, your GP or migraine treatment specialists (if applicable) will be informed of your participation in this research study. A letter will be sent which will notify your GP and or treatment specialist(s) of your participation in this study. Your GP does not have to agree to your taking part in study.

#### **16. Who has reviewed this study?**

Before any research is allowed to take place it must be reviewed by an independent Research Ethics Committee (REC). This is done to help protect the rights and interests of research participants. This study has been approved by Westminster Research Ethics Committee.

The study has also been approved by the Medicines and Health Regulatory Agency (MHRA).

#### **17. What will happen to the results of this study?**

The data collected in this study will be used for future medical and scientific research. Information from this trial may be presented at meetings or published in medical journals. This information will not include your name or information that can easily be traced back to you.

The study results may be shared with other government health agencies as part of applications to gain approval of new medicines or to meet other reporting requirements such as reporting side effects. You can also request details of the study results from your study doctor at the end of the study.

Based on regulatory requirements and the Sponsor's policy, your coded information will be kept for a period of 25 years or longer. This allows the Sponsor to fully answer questions from health authorities about the way the drug works in this study.

## 18. How can you find more information about this study?

Take the time you need to make your choice. Ask the study doctor or nurse about any questions you have. A description of this research study will be available on the US clinical trials register at <http://www.clinicaltrials.gov/> on the EU clinical trials register <https://www.clinicaltrialsregister.eu/> and the International Standard Randomised Controlled Trial Number (ISRTN) register at <https://www.isrctn.com/>. These websites will not include information about you. At most, the website will include a summary of the results. You can search these websites at any time.

## 19. What if you do not take part in this study?

Your participation in this study is voluntary. You may decide not to participate, or you may leave the study at any time. Your decision will not result in any penalty or loss of benefits to which you are otherwise entitled. Your decision will not prevent you from receiving standard of care for your migraine from your GP and or treatment specialist(s). However, the study treatment will not be available to you.

The Sponsor or study doctor can withdraw you from this study at any time without your consent for any reason including, but not limited to:

- The sponsor or the study doctor decides to stop your participation in the study for your safety
- Your failure to follow the instructions of the study doctors.
- If the study is stopped by the Sponsor or study doctors before you complete the study.
- If it is found that you do not meet the study requirements.
- If you have any side effects of concern to the study doctor.
- You do not consent to changes made in the study plan that may affect you.

If you leave or are withdrawn from the study early:

- The study doctor or a member of the study team will ask for your permission to contact you to see how you are doing and to determine if additional procedures need to be done.
- The study doctor will discuss your further treatment options with you.

## 20. What other treatment options are available?

You are being asked to take part in this study to help further education and understanding of the drug rimegepant. You do not have to be in this study to receive treatment for your migraine. There are alternative treatments available, including prescription, non-prescription medications, and other research studies for the treatment or prevention of migraine.

Talk to the study doctor or your GP or other treatment specialist(s) if applicable, about the options that may be available to you. Your study doctor or GP or other treatment specialist(s) will discuss the risks and benefits of these other options with you.

## 21. What happens if you are hurt or injured due to participation in this study?

If you suffer an injury as a direct result of taking part in the study, the Sponsor will pay for the reasonable costs of medical treatment in accordance with the Guidelines of the Association of the British Pharmaceutical Industry (ABPI). The Sponsor has insurance to cover these costs, and will make these payments where the research-related injury resulted from:

- A drug being tested or administered as part of the trial protocol;
- Any test or procedure you received as part of the trial

The Sponsor would not be bound by these guidelines to pay compensation where the injury resulted from a drug or procedure outside the trial protocol or where the protocol wasn't followed.

The Sponsor will not provide compensation for personal discomfort, or for injuries or problems related to your underlying medical condition.

## **22. Will you be paid for being in the study?**

There are no costs to you. Any expenses and costs associated with the study are covered by the study Sponsor. This includes the cost of the study drug and any procedures and tests that are performed during the study. You will be reimbursed for your travel expenses (up to a maximum of £75 per visit), for meals and or other reasonable expenses related to your participation in this study. If you withdraw from the study early, you will be reimbursed for the expenses for the portion of the study that you completed.

You will also receive an inconvenience payment of £50 depending on the type of visit related to your participation in this study. This is to help cover the cost of time and any associated expenses (which may include time off school or work or childcare if applicable, for study visits).

## **23. What if there are new findings?**

The study doctor will inform you of any new significant information, when it becomes available, which may affect your willingness to continue to participate in this study. You will be told as soon as possible so you can decide whether to leave the study or continue. If you continue, you will may be required to sign and date a new consent form. This new information may also mean that you can no longer participate in this research. It could also mean that the Sponsor may suspend or prematurely end the study. If this occurs, the person(s) supervising the research will stop your participation.

## **24. What happens when the study ends?**

When your participation in the study ends, the study sponsor will no longer provide the study drug, and you will no longer have access to rimegepant through the study. You will however continue to receive normal, standard care, from your primary doctor/GP and or migraine treatment specialist(s).

## **25. Who can you contact if you have questions or concerns about this study?**

If you have any questions or problems during this study; you should contact the study doctor whose telephone number is on the first page of this information sheet.

If remain unhappy and wish to make a formal complaint you can do this by contact:

- Information Commissioners Office (ICO) or,
- Patient Advice and Liaison Service (PALS) office for England Support Service on 0800 019 3282 or,
- Patient Advice and Liaison Support Service (PASS) office for Scotland on 0800 917 2127 or,

- If applicable, follow the NHS complaints procedure. These details can be obtained from the NHS website.

**Thank you for taking the time to read this information sheet**

**If you have understood what is involved in this study and would like to take part, please review and sign the consent form.**

**If you choose to sign the consent form, you will receive a signed and dated copy of the form for your records.**

## Consent form for Participants

**Study Title:** A Phase 4, Randomized, Double-blind, Placebo-controlled Study to Evaluate the Efficacy and Safety of Rimegepant in Episodic Migraine Prevention with Multiple Dosing Regimens

**Study Sponsor:** Biohaven Pharmaceuticals Holding Company Limited

**Protocol Number:** BHV3000-404

**EudraCT Number:** 2021-005239-22

**Principal Investigator:  
(Study Doctor)** Dr Manpreet Kaur

**Study Site Number:** 401

**Participant Study Number:**

### 1. Agreeing to be in the Research Study

Please initial  
each box

1. I confirm that I have read and understood this Participant Information Sheet and Consent Form dated 18-AUG-2022 (version 1.3) for the above study or someone has read it to me in a language that I understand. I have had sufficient time and the opportunity to consider the information, ask questions. I have had these questions answered to my satisfaction.	
2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected.	
3. I understand the purposes, procedures as well as the nature, significance, risks, and implications of the research described in the research study.	
4. I understand that relevant sections of my medical notes and data collected as part of this research study; may be looked at by the Sponsor of the study and its authorized representatives, by regulatory authorities or from the NHS Trust or Hospital, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.	
5. I understand that coded data/samples will be transferred outside of the UK as described in the information sheet. I understand that data protection laws outside the UK may not be as comprehensive.	



6. I understand and consent to collection, analysis, distribution and storage of my blood and urine samples as described for this study.	
7. I understand my information/data will be stored by the trial site and Sponsor for a minimum of 25 years after completion or termination of this trial.	
8. I agree for my GP and or treatment specialist(s) (if applicable) to being informed of my participation in this study.	
9. I give permission for my GP and or other treatment specialist(s), other health professionals, hospitals or laboratories outside this hospital to release information to this study site concerning my condition and treatment for the purpose of this study. I understand that such information will remain confidential.	
10. I understand that, upon request, I will be able to receive a copy of the summary of the study results from the study doctor once the results become available.	
11. I understand that I will be given a signed copy of this document to keep.	
12. I agree to voluntarily take part in this research study.	

\_\_\_\_\_  
Participant's name (printed in block letters)

\_\_\_\_\_  
Participant's signature for consent

\_\_\_\_\_  
Date (DD/MMM/YYYY)

## 2. Statement of the Person Obtaining Consent

I confirm that I have explained the purpose and plan of the study for the participant named above.

I certify that the participant has agreed to participate in the study by signing and dating the consent form to acknowledge the verbal explanation and their consent to take part in the study.

The participant signing this 'Information Sheet and Consent Form' has been given the opportunity to ask questions and appears to understand the nature, purpose, and demands of participating in this study.

\_\_\_\_\_  
Name of the person obtaining consent  
(printed in block letters)

\_\_\_\_\_  
Signature of the person obtaining consent

\_\_\_\_\_  
Date (DD/MMM/YYYY)

**Complete the section below, only if applicable. If not applicable, leave blank.**

\_\_\_\_\_  
Name of witness (if applicable)  
(printed in block letters)

\_\_\_\_\_  
Signature of the witness

\_\_\_\_\_  
Date (DD/MMM/YYYY)

*By signing the consent form, the witness confirms that all the information contained in the Participant Information Sheet/Consent Form has been read in its entirety to, and apparently understood by the participant and that informed consent was freely given.*

**1 copy for participant; 1 (original) for Investigator file; 1 to be kept in medical notes**