National Research Ethics Committee

NREC-CT Meeting

10th April 2024

Attendance

Name	Role
Prof David Brayden	Chairperson, NREC-CT D
Prof David Smith	Deputy Chairperson, NREC-CT D
Dr Christina Skourou	Deputy Chairperson, NREC-CT D
Dr Enda Dooley	Committee Member, NREC-CT D
Prof Andrew Green	Committee Member, NREC-CT D
Prof Cathal Walsh	Committee Member, NREC-CT D
Prof Deirdre Murray	Committee Member, NREC-CT D
Dr Geraldine O'Dea	Committee Member, NREC-CT D
Prof Lina Zgaga	Committee Member, NREC-CT D
Ms Deirdre McLoughlin	Committee Member, NREC-CT D
Prof Tina Hickey	Committee Member, NREC-CT D
Prof Geraldine O'Sullivan Coyne	Committee Member, NREC-CT D
Mary McDonnell Naughton	Committee Member, NREC-CT D
Ms Chanel Watson	Committee Member, NREC-CT D
Ms Aileen Sheehy	Programme Manager, National Office for RECs
Dr Laura Mackey	Programme Officer, National Office for RECs
Dr Susan Quinn	Programme Manager, National Office for RECs
Ms Emma Heffernan	Project Officer, National Office for RECs
Ms Patricia Kenny*	Project Officer, National Office for RECs

Apologies: Gerry Daly

Quorum for decisions: Yes

Agenda

Welcome & Apologies

2023-509256-34-00

2023-504962-52-00

2023-506334-75-00

2023-507684-19-00

2023-506229-12-00

23-NREC-CT-003_Mod-3

2022-502380-37-00 SM-1

2022-501417-31-01 SM-12

2023-506241-30-00 SM-9

AOB

The Chair welcomed the NREC-CT D.

- The minutes from the previous NREC-CT D meeting on 6th March 2024 were approved.
- The NREC Business Report was discussed and noted.

Applications

2023-509256-34-00

Institutions: N/A

Study title: A Phase 1/2 Dose-Exploration and Dose-Expansion Study to Evaluate the Safety and Efficacy of BEAM-302 in Adult Patients with Alpha-1 Antitrypsin Deficiency (AATD)-Associated Lung Disease and/or Liver Disease

Dossiers Submitted: Part I only

- **NREC-CT Decision:**

Favourable

2023-504962-52-00

Principal Investigators & Institutions: University Hospital Galway (Dr Maccon Keane), St Vincent's University Hospital Dublin (Dr Janice Walsh), Bon Secours Hospital Cork (Dr Conleth Murphy)

Study title: A Phase 3, Randomized, Open-label, Study to Compare the Efficacy and Safety of Adjuvant MK-2870 in Combination with Pembrolizumab (MK-3475) Versus Treatment of Physician's Choice (TPC) in Participants With Triple-Negative Breast Cancer (TNBC) Who Received Neoadjuvant Therapy and Did Not Achieve a Pathological Complete Response (pCR) at Surgery

Dossiers Submitted: Part I and II

- **NREC-CT Decision:**

Request for more information

Part I Considerations

Part I Considerations (RFI) for addition to CTIS
1. The Sponsor is requested to update the protocol to clarify how the 60% capping of the TPC arm is determined.

- **Additional Information Required RFI**

Part II Considerations
1. Compliance with national requirements on data protection
• No NREC considerations raised
2. Compliance with use of biological samples
• The NREC-CT noted that pg 13 Section 3.5 of Compliance with use of biological samples document states that some samples will have direct connection as it is stated that they will be labelled as follows *"samples marked with e.g. initials, date*

of birth", however the Main consent ICF pg 17 states that "*Your health information, samples and trial data will be key-coded (pseudonymised) using your month and year of birth to help protect your identity before it is sent to the Sponsor".* The Committee advised that date of birth is identifiable information, and all samples should be pseudonymised (ensuring date of birth is not part of the pseudonymisation). The Committee requested that the documents 'Compliance with use of biological samples', and Main Consent ICF as necessary, be updated to clarify and align.

3. Financial arrangements

- No NREC considerations raised

4. Proof of insurance

- No NREC considerations raised

5. Recruitment arrangements

- No NREC considerations raised

6. Subject information and informed consent form

- The NREC-CT requested that the ICF Optional Screening Consent pg 2 be updated to advise that Pembrolizumab is approved in Ireland.
- The NREC-CT requested that the ICF Optional Screening Consent be updated to inform participants of what will happen to their biological samples and how long they will be kept/stored for.
- The NREC-CT requested that the ICF Optional Greenphire Adults pg 1 bullet point 4 *"If you do not agree to these services, you can still be in the clinical trial"* be updated to included *"and receive reimbursement".*
- The NREC-CT requested that ICF Main consent pg 8 Risk from CT Scan and MUGA Scan be updated to include risk from exposure to radiation.
- The NREC-CT noted that ICF Main consent pg 9 For MK 2870 states *"An investigational drug is one that is not approved by the United States Food and Drug Administration (FDA) and is therefore considered experimental".* The Committee requested that this be updated for Ireland.
- The NREC-CT noted ICF Main consent pg 11 for Pembrolizumab state *"Pembrolizumab, which is approved in the USA and some other countries*". The Committee requested that this be updated to refer to Ireland.
- The NREC-CT requested that the ICF Main consent pg 14 be updated to adequately address the risk profile for capecitabine similar to the other drugs.
- The NREC-CT noted the suggestion of the alternative treatment option of 'olaparib' offered to participants with BRCA mutation (ICF_Main, page 15), and requested that further information is provided to participants regarding the availability of this as a 'standard treatment', or, if alternative treatment options exist for this cohort, that the participants are additionally provided with this information here.
- The NREC-CT requested that the ICF Main consent be updated to inform participants of what will happen to their biological samples and how long they will be kept/stored for.
- The NREC-CT requested that the ICF Main consent pg 2 be updated to advise that Pembrolizumab is approved in Ireland.
- The NREC-CT noted that participants will be required to complete EORTC questionnaire which includes questions regarding mental health. The Committee requested that the ICF Main consent be updated to include acknowledgement that

completion of this assessment may cause distress, and clarification as to the pathway of care and referral offered to participants displaying a mental health issue.

- The NREC-CT requested that the ICF Main consent pg 20 be updated to insert a consent statement that the participant confirms that a copy of the signed Informed consent Form will be provided to them.
- It was not clear to the NREC-CT if participants data, either anonymised or pseudonymised, would be used for future research. The Committee noted the ICF Main consent pg 17 states *"Allow outside researchers to use health data, provided it does not identify you"* and *"Allow other research partners, vendors, or laboratories to use health data to develop new tests related to the trial drug or disease/condition under trial and include the data in reports to health authorities or publications."* The Committee requested that the ICF Main consent and consent form pg 20 be updated to clarify for participants if their data will be used for future research restricted to research in the disease area and/or the study drug and this is clearly stated in the ICF pg 17 and consent page pg 20. The Committee also requested that if anonymised data is to be used that the ICF Main consent page pg 20 be updated to include a specific statement for the participant to explicitly consent to the processing of their personal data from coded to anonymised data it as per Article 4 (2) and (6) General Data Protection Regulation (GDPR).

7. Suitability of the clinical trial sites facilities

- No NREC considerations raised

8. Suitability of the investigator

- No NREC considerations raised

2023-506334-75-00

Principal Investigators & Institutions: Mater Misericordiae University Hospital (Prof. Sean Gaine)

Study title: An Open-label Extension Study Evaluating the Long-term Safety and Efficacy of Seralutinib Orally Inhaled for the Treatment of Pulmonary Arterial Hypertension (PAH)

Dossiers Submitted: Part I and II

- **NREC-CT Decision:**

Request for more information

- **Additional Information Required RFI**

Part II Considerations

1. Compliance with national requirements on data protection

- No NREC considerations raised

2. Compliance with use of biological samples

- No NREC considerations raised

3. Financial arrangements

- No NREC considerations raised

4. Proof of insurance

- No NREC considerations raised

5. Recruitment arrangements

- No NREC considerations raised

6. Subject information and informed consent form

- The NREC-CT requested that the Main ICF be updated to include the EU trial number for participants.
- The NREC-CT requested that the Main ICF be updated to provide information about the availability of the clinical trial results at the end of the trial and location of same.
- The NREC-CT noted the Main ICF pg 4 states that the participant may have access to the study drug "until regulatory agencies approve seralutinib in your country or region". The Committee strongly encourage the sponsor to provide access to the study drug until it available under the drugs payment scheme for those participants who are experiencing benefit from the drug, as there may be a long delay from market authorisation to when it is provided under the drugs payment scheme.
- The NREC-CT noted the Comfort Materials for Subject document refers to comfort items to be provided to participants such as a blanket and water bottle. The NREC-CT requested that these items do not include any identifiers to the study or drug involved.
- The NREC-CT noted that the Pregnant Partner PISCF pg 6 'Who has reviewed this study?' makes reference to the NHS. The Committee requested that as this ICF is specific for Ireland that this be updated to refer to Irish healthcare system.
- The NREC-CT requested that the Main ICF pg 3 references to *"'not being held against you"* you be updated to *"will not affect your care".*
- The NREC-CT noted the listing of COVID-19 as a side effect of the drug in Main ICF pg 10. The Committee were unclear how a drug would cause side effect of COVID-19 and requested that the ICF be updated to clarify. The Committee commented that they would consider this an adverse event while taking the drug rather than a side effect of the drug.
- The NREC-CT noted that Main ICF pg 19 is seeking blanket consent for future use of samples/data for unspecified purposes without further consent *"new commercial drugs or new treatments for diseases".* This type of consent is not in line with best practice, the Declaration of Taipei 2016 and not in compliance with the Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018), where informed participant consent is a mandatory safeguard. The NREC-CT requested that future research is restricted to research in the disease area and/or the study drug and this is clearly stated in the ICF pg 19 and consent page pg 24.
- The NREC-CT requested that the Main ICF pg 21 'What will happen to your data' be updated to remove reference to "Study data, including your coded medical information, may be retained and later used for further research into your medical indication, unless you object". The Committee advised that this is contradictory to the information provided in the ICF pg 19 where participants must provide explicit optional consent to take part in future research rather than "object".

- The NREC-CT requested that the Main ICF pg 24 Consent for Optional Future Research be updated to include a signature and date sections for both the participant and Investigator to sign.

7. Suitability of the clinical trial sites facilities

- No NREC considerations raised

8. Suitability of the investigator

- No NREC considerations raised

2023-507684-19-00

Principal Investigators & Institutions: Mater Misericordiae University Hospital (Dr Waseem Darwish), Mater Private Hospital (Dr Waseem Darwish), Cork University Hospital (Dr Richard Bambury), Tallaght University Hospital (Dr Louise McLoughlin), St Vincent's University Hospital (Prof. Sean McDermott)

Study title: Phase 3, Randomized Study Evaluating the Efficacy and Safety of TAR-210 Erdafitinib Intravesical Delivery System Versus Single Agent Intravesical Chemotherapy in Participants With Intermediate-risk Non-muscle Invasive Bladder Cancer (IR-NMIBC) and Susceptible FGFR Alterations

Dossiers Submitted: Part I and II

- **NREC-CT Decision:**

Request for more information

- **Additional Information Required RFI**

Part II Considerations

1. Compliance with national requirements on data protection

- No NREC considerations raised

2. Compliance with use of biological samples

- The NREC-CT requested that the Compliance with use of Biological Samples document ,pg7, be updated to tick the box to acknowledge the sponsor's plan to store Biological samples where there is "No connection between the sample and the individual participant".

3. Financial arrangements

- No NREC considerations raised

4. Proof of insurance

- No NREC considerations raised

5. Recruitment arrangements

- No NREC considerations raised

6. Subject information and informed consent form

- The NREC-CT requested that the SIS and ICF Molecular Eligibility pg 1 be updated to include the EU trial number for participants.
- The NREC-CT noted reference to HDFN & Nipocalimabon pg 8 and 9 of SIS and ICF Molecular Eligibility. The Committee advised that they found no reference to

HDFN or Nipocalimabon in the IB or protocol supplied. The Committee requested that the SIS and ICF be updated to remove these references or provide further information in relation to their inclusion.

- The NREC-CT noted that SIS and ICF Molecular Eligibility pg 8 is seeking blanket consent for future use of samples/data for unspecified purposes without further consent "HDFN and nipocalimab and similar drugs". This type of consent is not in line with best practice, the Declaration of Taipei 2016 and not in compliance with the Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018), where informed participant consent is a mandatory safeguard. The NREC-CT requested that future research is restricted to research in the disease area and/or the study drug and this is clearly stated in the ICF and consent page. The Committee also requests that any future use of biological samples is reviewed by an ethics committee and requested that this is captured in the ICF.
- The NREC-CT requested that the SIS and ICF Molecular Eligibility pg 5 'Will I be paid' "You *may* be reimbursed" be updated to "You *will* be reimbursed". The Committee also requested that additional information be provided on the reimbursement process for participants and their carers such as how and when it will be paid rather than asking them to discuss with clinical staff.
- The NREC-CT requested that the first reference to REC on pg 2 of the SIS and ICF Molecular Eligibility be updated to provide a definition of the acronym 'REC'.
- The NREC-CT requested that the SIS and ICF Molecular Eligibility-pg3 be updated to clarify the location of Central Laboratory.
- The NREC-CT noted reference to NHS and NHS number on pg 8 and 9 of SIS and ICF Molecular Eligibility. The Committee requested that these references be replaced with Ireland-specific wording.
- The NREC-CT noted that SIS and ICF Molecular Eligibility pg 7 states "The sponsor may generate anonymous data or samples for the purposes of scientific research." The Committee requested that the SIS and ICF Molecular Eligibility pg 11 be updated to include a specific statement for the participant to explicitly consent to the processing of their personal data from coded to anonymised data it as per Article 4 (2) and (6) General Data Protection Regulation (GDPR).
- The NREC-CT requested that the SIS and ICF Main pg 1 be updated to include the EU trial number for participants.
- The NREC-CT noted reference to HDFN & Nipocalimabon pg 22 of SIS and ICF Main. The Committee advised that they found no reference to HDFN or Nipocalimabon in the IB or protocol supplied. The Committee requested that the SIS and ICF be updated to remove these references or provide further information in relation to their inclusion.
- The NREC-CT noted that SIS and ICF Main pg 22 is seeking blanket consent for future use of samples/data for unspecified purposes without further consent "HDFN and nipocalimab and similar drugs". This type of consent is not in line with best practice, the Declaration of Taipei 2016 and not in compliance with the Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018), where informed participant consent is a mandatory safeguard. The NREC-CT requested that future research is restricted to research in the disease area and/or the study drug and this is clearly stated in the ICF and consent page. The Committee also

requests that any future use of biological samples is reviewed by an ethics committee and requested that this is captured in the ICF.

- The NREC-CT requested that the SIS and ICF Main pg 2 be updated to provide detail on the Irish sample size.
- The NREC-CT noted SIS and ICF Main pg 18 says that neither TAR-210 nor the study comparators are available after the study completes, however Protocol pg 33 states that *"after regulatory confirmation and upon further notification by the sponsor, participants in the control arm may have the opportunity to receive TAR-210 for up to one year".* The Committee requested clarification on this, if participants in the control arm may have the opportunity to received TRA-210 for up to one year then this must be made clear to the participant in the ICF.
- The NREC-CT noted the image on SIS and ICF Main pg 8 of the size of TAR-210 system description above it that is "slightly larger than an American quarter or a 2-euro coin". The Committee commented that the item in the image appears to be twice the size of a 2 euro coin not "slightly larger". The Committee requested that the SIS and ICF Main pg 8 be updated ensure clarity for the participant.
- The NREC-CT requested that the SIS and ICF Main pg 14 side effects of the control drugs be updated to include GI symptoms, pain and fatigue symptoms as outlined on page 30 of protocol.
- The NREC-CT noted that the SIS and ICF pg 2 advised that that participants may attend between 17 and 22 times over the course of the study. The Committee requested that the maximum follow up time in months is also detailed for participants here.
- The NREC-CT requested that SIS and ICF Main pg 21 be updated to say that a summary of study results in plain English will be made available and remove reference to "if required by law". The Committee advised they would expect that a summary of study results would be made available to participants regardless if required by law.
- The NREC-CT requested that the SIS and ICF Main be updated to provide a lay language explanation of the following:
    - Pg 2 intravesical delivery system.
    - Pg 4 ECOG
    - Pg 5 TURBT
- The NREC-CT requested that the first reference to REC on pg 2 of the SIS and ICF Main be updated to provide a definition of REC.
- The NREC-CT requested that the SIS and ICF Main pg 8 Wil I be paid "You may be reimbursed" be updated to "You will be reimbursed". The Committee also requested that additional information be provided on the reimbursement process for participants and their carers such as how and when it will be paid rather than asking them to discuss with clinical staff.
- The NREC-CT noted that SIS and ICF Main pg 20 states "The sponsor may generate anonymous data or samples for the purposes of scientific research." The Committee requested that the SIS and ICF Main pg 25 be updated to include a specific statement for the participant to explicitly consent to the processing of their personal data from coded to anonymised data it as per Article 4 (2) and (6) General Data Protection Regulation (GDPR).

- The NREC-CT noted reference to NHS and NHS number on pg 22 of SIS and ICF Main. The Committee requested that these references be replaced with Ireland specific wording.
- The NREC-CT requested that the SIS and ICF Pregnancy pg 1 be updated to include the EU trial number for participants.
- The NREC-CT noted that SIS and ICF Pregnancy pg 4 is seeking blanket consent for future use of samples/data for unspecified purposes without further consent "HDFN and nipocalimab and similar drugs". This type of consent is not in line with best practice, the Declaration of Taipei 2016 and not in compliance with the Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018), where informed participant consent is a mandatory safeguard. The NREC-CT requested that future research is restricted to research in the disease area and/or the study drug and this is clearly stated in the ICF and consent page. The Committee also requests that any future use of biological samples is reviewed by an ethics committee and requested that this is captured in the ICF.
- The NREC-CT requested that the SIS and ICF Pregnancy be updated to provide a lay language explanation of intravesical delivery system.
- The NREC-CT noted reference to NHS and NHS number on pg 4 of SIS and ICF Pregnancy. The Committee requested that these references be replaced with Ireland specific wording.
- The NREC-CT noted reference to HDFN & Nipocalimabon pg 4 of SIS and ICF Pregnancy. The Committee advised that they found no reference to HDFN or Nipocalimabon in the IB or protocol supplied. The Committee requested that the SIS and ICF be updated to remove these references or provide further information in relation to their inclusion.
- The NREC-CT noted that SIS and ICF Pregnancy pg 4 states that *"sensitive data such as racial or ethnic origin … …. necessary for evaluating study results"* will be collected. The Committee commented that the pregnant woman is not a research participant and as such this sensitive data should not be collected. The NREC-CT requested that the SIS and ICF Pregnancy be updated to remove reference to the collection of this data.

7. Suitability of the clinical trial sites facilities

- The NREC-CT noted the SSA for Tallaght University Hospital specifically states that device insertion will be carried out by the Urology Surgical Dept. The Committee requested that the SSAs for Mater Misericordiae University Hospital, Mater Private Hospital, Cork University Hospital and St Vincent's University Hospital be updated to clarify the device insertion.

8. Suitability of the investigator

- No NREC considerations raised

2023-506229-12-00

Principal Investigators & Institutions: N/A

Study title: A phase II, randomized, open-label study to assess the efficacy, safety, and pharmacokinetics (PK) of maintenance cabozantinib (XL184) plus best supportive care (BSC) versus BSC in children, adolescents and young adults (AYA) with unresectable residual osteosarcoma either at diagnosis or at first relapse after standard treatment.

Dossiers Submitted: Part I only

- **NREC-CT Decision:**

Request for more information

- **Additional Information Required RFI**

Part 1

- The Sponsor is requested to update the Main protocol section 10.5 Genetic testing to make it clear under whose governance both the DNA samples and the associated data are held.

23-NREC-CT-003_Mod-3

Principal Investigators & Institutions: Prof Trevor Duffy

Study title: A Phase 2/3, Randomized, Double-Blinded, Placebo-Controlled, Parallel-Group, 2-Arm, Multicenter, Operationally Seamless Study to Evaluate the Efficacy, Safety, Tolerability, Pharmacodynamics, Pharmacokinetics, and Immunogenicity of Efgartigimod PH20 SC in Participants Aged 18 Years and Older With Active Idiopathic Inflammatory Myopathy

- **NREC-CT Decision:**

Request for more information

- **Additional Information Required RFI**
- The NREC-CT noted that the Protocol pg 34 refers to screening period of 4-6 weeks however there is no reference to the screening in the Main Phase III ICF. The Committee requested that detail about the screening period be included in the ICF and that participants are informed that no screening procedures will take place before the ICF is signed.
- The NREC-CT noted that the Protocol refers to blood being tested for hepatitis and HIV infections during screening however this information is not detailed in the ICF. The Committee requested that Main Phase III ICF be updated to add a statement informing participants that their blood will be tested for hepatis and HIV and that the study team are required to report any positive HIV, Hep A or Hep C test result and certain personal details about the participant to the relevant authority. This is because they are mandatory notifiable diseases (Infectious Diseases (Amendment) Regulations 2022 (S.I. No. 258 of 2022) May 2022).
- The NREC-CT noted that the Main Phase III ICF pg 2 refers to a sample size of 240. The Committee requests that the ICF be updated to provide detail on the estimated global sample as well as the projected Irish sample.

- The NREC-CT requested that the Main Phase III ICF pg 2 be updated to include an explanation of the randomisation process similar to what is included in the flyer *"Participants enrolled in the study will be randomly assigned by a computer to receive either the investigational study drug or placebo. Half of the participants will be assigned to receive the investigational study drug and half will receive placebo."*
- The NREC-CT noted that the Main Phase III ICF pg 3 refers to questionnaires to be completed. The Committee requested that the ICF be updated to include a brief explanation on what topics the questionnaires cover and an estimate of time taken to complete.
- The NREC-CT requested that the Main Phase III ICF pg 4 be updated to provide more detail around actigraphy including what data will be collected via this, security of data transfer and access to the actigraphy data by the actigraphy provider.
- The NREC-CT noted that the Main Phase III ICF pg 4 provides detail about end of treatment visits for those that stop the study drug early or withdraw. The Committee requested that this section be updated to include information around end of treatment visits/requirements for those participants who received all the planned doses of study drug.
- The NREC-CT requested that Main Phase III ICF pg 4 be updated to provide justification for those participants who stop taking the study drug early to visit the site every 8 weeks and to provide detail about what tests will happen at these additional follow up visits. Please consider inserting a table in an Appendix listing tests and measures applied at each study visit for clarity.
- The NREC-CT requested that the Main Phase III ICF pg 4 be updated to clarify the possibility of receiving efgartigimod during the follow up study, for both those who were on placebo or IP during the current study.
- The NREC-CT requested that the Main Phase III ICF pg 4 be updated to clarify if patients should have up to date COVID and other vaccinations before participating in the study due to the increased chance of infections.
- The NREC-CT noted a typo on pg 5 of Main Phase III ICF "paint, rash & bruising"
- The NREC-CT noted on Main Phase III ICF pg 5 the key under the table includes Very Common/Common/Uncommon however the introduction to the table refers only to the "most commonly reported side effects". The Committee requested that the ICF be updated to clarify which side effects are presented in the table.
- The NREC-CT noted the wording on pg 6 of the Main Phase III ICF "you may not become pregnant" which may be misleading. The Committee requested that the ICF be updated to reword as "You must not become pregnant".
- The NREC-CT requested that the Main Phase III ICF pg 7 "Will I be paid to be in study" and page 9 be updated to provide detail on the reimbursement process for participants for expenses related to their participation in the study such as what will be covered, how and when it will be paid etc.
- The NREC-CT requested that the Main Phase III ICF pg 7, What happens if I am injured while in the study, be updated to provide more detail on the compensation for participants, when it may and may not be paid including detail that the sponsor will

provide compensation in accordance with the Irish Pharmaceutical Healthcare Association guidelines.

- The NREC-CT requested that the Main Phase III ICF pg 8 be updated to provide more detail of where the laboratories that the samples are being sent to and stored are located.
- The NREC-CT noted the collection of data on ethnicity in Main Phase III ICF pg 9. In line with GDPR special category data requirements, the NREC-CT requested justification regarding collection of race and ethnicity data. The Committee also requested that the Main Phase III ICF be updated to include this justification in line with GDPR requirements.
- The NREC-CT noted a typo on pg 9 of Main Phase III ICF “subic origin”.
- The NREC-CT requested that the Main Phase III ICF pg 10 be updated to provide detail about what countries patients coded data may be sent to and what precautions/measures are taken to protect their data regardless of the country the data will be transferred to.
- The NREC-CT requested that the Main Phase III ICF pg 11 be updated to move the consent for optional future research to the following page with a separate signature box to enable participants to explicitly consent to this optional component.
- The NREC-CT noted that the Main Phase III ICF pg 11 states “My personal data may be transferred to a country where laws protecting these data may differ from those in my own country.” The Committee advised that participants personal data should not be transferred outside of the site, only coded or pseudonymised data can be transferred outside of the site. Please update the ICF to reflect this.
- The NREC-CT noted the future research section (page 8) has been amended to the area of ‘immunology’ rather than the disease area of ‘myositis’, This type of consent is not in line with best practice, the Declaration of Taipei 2016 and not in compliance with the Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018), where informed participant consent is a mandatory safeguard. The NREC-CT requested that future research is restricted to research in the disease area and/or the study drug and this is clearly stated in the ICF. The Committee advised that alternatively an option could be provided to enable participants to consent to be contacted in the future about new research studies once the future research is clearly defined. The Committee also requests that any future use of samples or data is reviewed by an ethics committee and requested that this is captured in the PISCFs.
- The NREC-CT requested that the Main Phase III ICF pg 11 be updated to include a consent statement that the participant has been told in words and writing about the study, its goals, its length and any risks and benefits.
- The NREC-CT requested that the Main Phase III ICF pg 11 be updated to include a consent statement that the participant understands that their participation is voluntary and they can withdraw from the study at any time.
- The NREC-CT recommended that the Main Phase III ICF pg 11 consent page would benefit from each statement having an initial or tick box to confirm understanding and explicit consent for each statement rather than just listed in a paragraph

- It was unclear to the NREC-CT if the Non PII website document submitted is for use in Ireland. Please clarify.
- The NREC-CT requested that the Non PII website be updated to replace “you may be reimbursed” with you “will be reimbursed”.
- The NREC-CT requested that the Genetic Testing Addendum pg 1 “The information in that document still applies, and so does your consent” be updated to include “unless you choose to withdraw from the study”.
- The NREC-CT noted that the Non PII website document shows caregivers. It was unclear to the Committee if caregivers expenses for lengthy study visits will be reimbursed. Please clarify. The Committee requested that the Main Phase III ICF be updated to clarify for participants if their caregiver expenses will be reimbursed.
- The NREC-CT noted that the Genetic Testing Addendum pg 1 states that “If you do not agree to allow genetic testing, you will not be able to continue in the study”. The Committee were unclear whether participants whose disease is found to be of genetic origin would be requested to leave the study also. Please update the Genetic Testing Addendum to clarify.
- The NREC-CT requested that the Genetic Testing Addendum pg 1 be updated to provide lay language explanations for DNA sample and genetic testing.
- It was unclear to the NREC-CT if the participant will be given the result of the genetic test. The Committee requested that the Genetic Testing Addendum be updated to clarify if the results will be provided to them.
- The NREC-CT requested that the sponsor details in the Addendum what plans are in place to refer participants to appropriate treatment/support if their genetic test shows their myopathy is of genetic origin.

2022-502380-37-00 SM-1

Principal Investigators & Institutions: Jasna Pavicic-Astalos - Institute of Eye Surgery

Study title: A Phase 3b Study to Evaluate the Duration of Effect of Bimatoprost SR in Participants with Open-Angle Glaucoma or Ocular Hypertension

- **NREC-CT Decision:**

Request for more information

- **Additional Information Required RFI**

Part II Considerations
1. Compliance with use of biological samples
• This document represents information already approved under CTD
2. Subject information and informed consent form

- The NREC-CT requested that the Main PIS-ICF be updated to include detail around the urgent safety measure and provide an explanation to the participant regarding the reason the 3rd cycle of treatment has been discontinued.
- The NREC-CT noted the addition on Main PIS-ICF pg 4-6 'What will my participation in the study involve'. The Committee requested that this section be updated and rewritten to be clearer for participants including lay language, proper punctuation, providing explanations for all acronyms such as PRN and lay language explanations for technical terms such as gonioscopic photography and anterior segment imaging.
- The NREC-CT noted duplication of first three paragraphs in Main PIS-ICF pg 14 'Are there other side effects I should know about'. The Committee requested that this be updated to remove the duplication.
- The NREC-CT requested that Main PIS-ICF pg 15, 'Side effects of antibiotic drops' be updated to include the reason for using these drops.
- The NREC-CT requested that the Main PIS-ICF pg 17 be updated to reinsert the delete wording regarding 'Washout risks'.
- The NREC-CT noted that the Main PIS-ICF pg 23 refers to optional research. The Committee requested the Main PIS-ICF be updated to clarify what this optional research is for, how participants will consent to it and whether the data of any EU participants will be used in optional research.
- The NREC-CT requested that Main PIS-ICF be updated to reinsert the information that participant data may be transferred outside the EU to jurisdictions where the level of data protection may be lower, which has been deleted from pg 29.
- The NREC-CT noted the addition of wording on pg 26 Main PIS-ICF around continued follow up and collection of information about a participant if they become pregnant and are withdrawn from the study. The Committee advised that participants should consent separately to the continued follow up and collection of data in event of pregnancy. The Committee requested that a Pregnant Participant ICF be provided for review.
- The NREC-CT requested that the Main PIS-ICF pg 32 consent statement 2 be updated to remove reference to optional research as optional research consent must be obtained and documented separately to the consent for main study.
- The NREC-CT requested that the Main ICF pg 33 be updated to include consent statements for any optional research with signature and date sections for both the participant and Investigator to sign.
- The NREC-CT requested that the Main PIS-ICF pg 32 be updated to reinsert the following statement *"I have been informed about the nature and purpose of this clinical trial. I have also been informed about the product and the procedures involved in this clinical trial. The benefits and risks have been explained to me."*
- The NREC-CT requested that the Main PIS-ICF pg 32 be updated to replace point 3 *"I acknowledge that my Personal Data and biological samples will be accessed, collected, processed and transferred as described in the Patient Information Sheet"* with *"I understand and agree that my medical and sensitive data and biological material that are relevant for this research study may be transferred outside of Europe to AbbVie Ltd and partners, to countries that do not have the same level of protection as the EU, although the Sponsor has implemented*

technical and organisational safeguards to protect my Personal Information and is ultimately responsible for protecting my Personal Information".

3. **Suitability of the clinical trial sites facilities**

- No NREC-CT considerations raised

4. **Suitability of the investigator**

- This document represents information already approved under CTD

2022-501417-31-01 SM-12

Principal Investigators & Institutions: St James' Hospital (Prof. Fergal Kelleher), Beaumont Hospital (Dr Jarushka Naidoo)

Study title: A Phase 3, Randomised, Double-blind, Active-Comparator-Controlled Clinical Study of Adjuvant MK 7684A (Vibostolimab with Pembrolizumab) Versus Adjuvant Pembrolizumab in Participants with High-risk Stage II-IV Melanoma (KEYVIBE-010

- **NREC-CT Decision:**

Favourable

- **Additional Information Required**
- None

2023-506241-30-00 SM-9

Principal Investigators & Institutions: Prof. Ray McDermott

Study title: MRTX849 in Combination with Cetuximab Versus Chemotherapy in Patients with Advanced Colorectal Cancer with KRAS G12C Mutation with Disease Progression On or After Standard First-Line Therapy

- **NREC-CT Decision:**

Favourable

- **Additional Information Required**
- None

AOB:

- None