National Research Ethics Committee

NREC-CT Meeting

26th November 2025

Attendance

Name	Role
Dr Cliona McGovern	Chairperson, NREC-CT B
Dr John Hayden	Deputy Chairperson, NREC CT-B
Colm O'Donnell	Deputy Chairperson, NREC-CT B
Ms Serena Bennett	Committee Member, NREC-CT B
Dr Åine de Róiste	Committee Member, NREC-CT B
Ms Jasmine Joseph	Committee Member, NREC-CT B
Dr Ciaran Lee	Committee Member, NREC-CT B
Dr Andrew Lindsay	Committee Member, NREC-CT B
Dr Niall McGuinness	Committee Member, NREC-CT B
Prof. Seamus O'Reilly	Committee Member, NREC-CT B
Ms Evelyn O'Shea	Committee Member, NREC-CT B
Mrs Ann Twomey	Committee Member, NREC-CT B
Prof. John Wells	Committee Member, NREC-CT B
Dr Jane Bryant	Programme Officer, National Office for RECs
Dr Laura Mackey	Programme Officer, National Office for RECs
Dr Susan Quinn	Programme Manager, National Office for RECs
Ms Chita Murray	Programme Manager, National Office for RECs
Mr Peadar Rooney*	Project Officer, National Office for RECs
Ms Grainne O'Gorman	CEO, Health Research Board
Ms Rachel McDermott	Project Administrator, National Office for RECs

*Drafted minutes

Apologies: Michaela Higgins, Karina Halley

Quorum for decisions: Yes

Agenda

- Welcome & Apologies
- 2025-522544-40-00
- 2025-521546-23-00
- 2024-519917-72-00
- 2023-506327-29-00 SM-4
- 2024-518589-29-00 SM-1
- 2022-502548-12-00 SM-9
- 2024-516582-36-00 SM-2
- 2024-514435-20-00 SM-2
- 2025-521627-78-00 SM-1
- AOB

- The Chair welcomed the NREC-CT B.
  - The minutes from the previous NREC-CT B meeting on 22nd October 2025 were approved.
  - The NREC Business Report was discussed and noted.

Applications

2025-522544-40-00

Institutions: Tallaght University Hospital

Study title: TRITON-PN: A Phase 3, Global, Randomized, Open-Label Study to Evaluate the Efficacy and Safety of Nucresiran in Patients with Hereditary Transthyretin-Mediated Amyloidosis with Polyneuropathy (hATTR-PN)

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**
- Request for Further Information

- **Additional Information Required**

Part II Considerations

1. **Compliance with national requirements on data protection**
   - No considerations raised by NREC-CT
2. **Compliance with use of biological samples**
   - No considerations raised by NREC-CT
3. **Financial arrangements**

   The NREC-CT noted on page 23 of the Main ICF that there is a limit to compensation for meals of €27 per person per day. The Committee requests that participants are reimbursed for all reasonable out-of-pocket expenses to ensure equity in access to clinical trials across all socioeconomic groups. This information must be provided in the Participant Information Leaflet with clear guidance regarding how these expenses can be claimed, and in the document P1_Compensation for trial participants.
4. **Proof of insurance**

   No considerations raised by NREC-CT
5. **Recruitment arrangements**
   - No considerations raised by NREC-CT
6. **Subject information and informed consent form**
   - Standard Consideration:
     - Where applicable, the Sponsor is requested to submit any Part 2 documentation requiring revision following the outcome of the Part 1 Assessment. Should an additional Request for Information (RFI) be required, please contact the National Office at clinicaltrials@nrec.ie. The request should include a concise summary of the Part 1 consideration(s) that necessitated the update to the Part 2 documentation.
     - All documentation submitted in response to a Request for Information (RFI) must be provided in a format that is both accessible and searchable, such as Microsoft Word or original (non-scanned) PDF files. Please note that scanned documents, including those processed using Optical Character Recognition (OCR), are not acceptable, as they cannot be optimised for compatibility with assistive technologies.

- The NREC-CT noted that page 10 of the Main ICF (Study Drug Administration section) states “The study drug is administered with a small needed under the skin”. The NREC-CT requests that this is corrected to “The study drug is administered with a small needle under the skin”.
- The NREC-CT noted that page 14 of the Main ICF uses the terms “Patient Care Sites” and “Central Assessment Sites” when referring to study sites. In Ireland, there is one site i.e. Tallaght University Hospital (TUH). The NREC-CT requests 1) clarification whether TUH will be a Patient Care Site or a Central Assessment Site. 2) clarification whether other Patient Care Sites or Central Assessment Sites are/will be part of the clinical trial in Ireland. If other sites are/will be part of the clinical trial in Ireland, it is requested that appropriate documents for each site is provided to the NREC-CT for review e.g. Site Suitability Assessment per individual site, CV of the Principal Investigator(s) etc.
- The NREC-CT noted that pages 9 (Section 3.2 “List of Study procedures” and 11 (Section 3.3 “Schedule of Assessments”) of the Main ICF provide relevant information about what assessment the participants will undergo and when each will occur, in order to assist the participant when planning their site visits. The Committee requests that the duration which each procedure will take be added to Section 3.2 “List of Study procedures” and the estimated length of time for each visit be added to Section 3.3 “Schedule of Assessments”.
- The NREC-CT noted on page 10 of the Main ICF, “Optional Samples for Future Research: If you agree in a separate consent, additional blood and urine samples will be collected and may be used for possible future research on biomarker testing to learn more about the disease and how the Study Drug works”. It is not clear in the Main ICF or the Biological Sample ICF, when these samples will be collected. The NREC-CT requests that both the Main ICF and the Biological samples ICF is updated with the timing of the sample collection, what site visits or if they are separate site visits, the amount of blood collected, and the frequent of the sample collection.
- The NREC-CT noted that page 2 of the Biological Samples ICF states “Future research aims to advance science and public health using your biosamples and Coded Personal Data from this study. The details of future projects are not determined yet. Future research may occur during or after this study” which is not described in line with regulations / best practice. The Committee requested that future use of samples and personal data is sufficiently explained to participants in the PISCF documents so as to constitute ‘broad’ informed consent, as required under the Health Research Regulations (Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018). Furthermore,
    - It should be confined to a specified disease, related diseases or drug under study in this trial. Consent can only be obtained where future use of samples and data is defined such that participants are fully informed,
    - and/or that an option is provided to enable participants to consent to be contacted in the future about other research studies,
    - The PISCF should also make it clear to participants that subsequent research ethics review will be sought for specific research once clearly defined. For further guidance, please see: NREC guidance on use of biological samples and associated data - https://www.nrecoffice.ie/guidance-on-use-of-biological-samples-and-associated-data/
- The NREC-CT noted references to offsite healthcare visits in the below-listed documents. The NREC-CT requests clarification whether offsite healthcare visits

will be available for participants of the clinical trial in Ireland. If not, the Committee requests that references to offsite healthcare visits be removed from the Main ICF (and other participant-facing documents as applicable) for use in Ireland.
    - page 15 of the Main ICF (Section 3.5 “Off Site Healthcare visits”),
    - page 29 of the Main ICF (Signature section “Offsite Healthcare Services through Illingworth”)
    - page 7 in the Main ICF (Section 3.1: “[remove if site not using Illingworth healthcare home visits] (unless you consent to use optional healthcare nursing support – in this case some visits can be done at your home).”
- The NREC-CT noted on the Main ICF signature page that the signature for agreeing to Offsite Healthcare Services and the signature for consenting to participate in the clinical trial are on the same page. If Offsite Healthcare Services will be available for participants in Ireland, the Committee requests that this be made a separate and explicit consent item in the Informed Consent section of the Main PISCF, with each signature clearly indicating what it is for.
- The NREC-CT noted that Greenphire will be providing a reimbursement service. If a participant does not want to use Greenphire to provide these services, the Committee requests that the Main ICF is revised to include details on how a participant will obtain reimbursement without using Greenphire.
- The NREC-CT noted the below-listed statements in the referenced documents. The Committee requests that the timelines in the Main ICF, the Pregnant ICF and any/all other applicable documents are revised to ensure alignment.
    - page 2 of the Pregnant Partner ICF states “you became pregnant while he was participating in the study or within the 360 days after he stopped treatment with the study drug.”
    - page 6 of the Main ICF states “from the start of Study Drug to 24 months after your last dose”
    - page 18/19 of the Main ICF states “and for 24 months after last dose administration” and “If your partner becomes pregnant during your course of treatment with Nucresiran or up to 24 months after your receiving your last dose” and “If you are female, you must not breastfeed once you receive the study drug through 24 months after receiving the last dose of study drug or until the end of study”.
- The NREC-CT noted on page 8 of the Main ICF that use of the ProofPilot system is optional. The Committee requests clarification on whether a participant who initially declines can later opt in and, if so, how this would be facilitated.
- The NREC-CT noted that page 6 of the Main ICF states “You and anyone in your immediate support network must not share information from or about the study with other participants, on social media, or in the public domain”. As participants are not permitted to discuss their participation as outlined in this statement, the Committee requests the following:
    - Justification for this stipulation
    - Details as to how this will be monitored during the trial
    - That details as to the potential implications for participants (should they fail to adhere to this instruction) be added to the Main ICF.
- The NREC-CT noted that page 8 of the Main ICF states “This web portal may help you keep track of your study visits, receive appointment reminders, access study-related information, and complete questionnaires.” The Committee requests clarification if the ProofPilot system will be used to complete any of the study questionnaires, and details of same.

- The NREC-CT noted that page 9 of the Main ICF states “Questionnaires: You will be asked to fill out questionnaires to assess your quality of life, to describe your hATTR amyloidosis symptoms.” The Committee noted that this includes the use of the Columbia-Suicide Severity Rating Scale (C-SSRS). The Committee requests the following:
  - Clarification whether the questionnaires will be presented through the ProofPilot system or in the presence of a clinical trial team member.
  - Confirmation that the staff administering this questionnaire have completed the specific training required as noted on the C-SSRS “*This scale is intended to be used by individuals who have received training in its administration.”*
  - The Main ICF be updated to contain more context about the nature of the questionnaires, such as how long they will take to complete, how frequently they will be completed, and includes the detail that one of the questionnaires will relate to suicide.
  - The Main ICF be updated to contain details of the support mechanisms which will be in place for participants who have been identified as being at risk by the C-SSRS.
- The NREC-CT noted on page 8 of the Main ICF document “If you are able to become pregnant, you will need to take a home pregnancy test every month and write the results in a paper diary”. The Committee noted that this could be a burden for the participant and should have a larger emphasis in the Main ICF. The Committee also requested clarification whether a reminder could be sent to the participant, for exam by email or via the ProofPilot system, to reduce the overall burden for the participant.
- The NREC-CT noted that page 2 of the Visit Overview Reminder document states “we will check if you are pregnant”. The Committee requests that this is revised to “we will check the recorded results of your pregnancy tests in the Home Pregnancy Test Diary”.
- The NREC-CT noted the inclusion of the Home Pregnancy Test Diary. The Committee requests that additional instructions be added to this document, including how frequently this needs to be done (monthly) and a reminder that the participant will need to bring this with them to the site on their next visit.
- The NREC-CT noted the submission of the Pregnant Partner ICF, and requests a copy of the Pregnant Participant ICF for review, as applicable.
- The NREC-CT noted that page 19 of the Main ICF states “For male participants, no contraception (condom) is required” however, it is also noted on page 18 of the Main ICF “However, certain birth defects, including heart abnormalities, were observed in the offspring of female rabbits that received nucresiran while pregnant. Additionally, some rats that received nucresiran while pregnant experienced loss of embryos or fetuses after uterine implantation. On a test to assess rodent learning and recall, some offspring of rats that received nucresiran while pregnant did not perform as well as offspring of rats that did not receive nucresiran while pregnant.” The Committee requests justification for why male participants are not required to use highly effective birth control methods while female participants are required to.
- The NREC-CT requested clarification whether there will be an option for continuation/extension beyond 38 months for participants who respond positively to this IMP.
- The NREC-CT noted that page 24 of the Main ICF states “Within about 12 months after the study has ended, a summary of the study results will be made available to

you." The Committee requests clarification on what this summary will include, whether it will be provided directly to participants or if they will be directed to where it can be accessed, and whether the summary will be written in lay language.
- The NREC-CT noted on page 81 of the Protocol Section 3.1.3. "Tokenization". The NREC-CT requests clarification if this occurring in Ireland. If Tokenization is occurring in Ireland, the NREC-CT requests revision of the Main PISCF to provide more information about Tokenization in a specific section with clear lay language.

7. Suitability of the clinical trial sites facilities

- No considerations raised by NREC-CT

8. Suitability of the investigator

- No considerations raised by NREC-CT

2025-521546-23-00

Institutions: St James's Hospital

Study title: A randomized, double-blind, placebo-controlled Phase III study to evaluate the efficacy and safety of remibrutinib in patients with secondary progressive multiple sclerosis

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**
- Request for Further Information

- **Additional Information Required**

Part I Considerations (RFI) for addition to CTIS

- It is noted that the FDA scientific advice (Feb 2025) provides a recommendation to increase frequency of Liver Function Test (LFTs) laboratory evaluations from every two weeks to weekly in the first 12 weeks of treatment for each period of the study. It is requested that this recommendation is implemented in the protocol, or that a detailed justification for not including the additional liver laboratory evaluations is provided.
- It is noted that the FDA scientific advice (Feb 2025) recommends adding an exclusion criterion that prohibits enrollment of subjects with reported alcohol intake greater than 2 drinks per day for men and greater than 1 drink per day for women. It is requested that this recommendation is implemented in the protocol or that a detailed justification for not revising the exclusion criteria is provided.
  It is requested that the protocol, section 5.3 'Lifestyle Considerations' (p41) is updated to reflect FDA scientific advice (Feb 2025) for alcohol intake guidance, i.e., prohibiting participants from consuming greater than 2 drinks per day for men and greater than 1 drink per day for women during the study, or that a detailed justification for not revising the alcohol intake guidance is provided.

Part II Considerations

1. Compliance with national requirements on data protection

- No considerations raised by NREC-CT

2. Compliance with use of biological samples

- No considerations raised by NREC-CT

3. Financial arrangements

- The NREC-CT noted that participants will not be reimbursed for all expenses, P1_compensation for trial participants details that only two meals will be covered for the entire trial. The NREC-CT requested that participants are reimbursed for all reasonable out of pocket expenses, to ensure equity in access to clinical trials across all socioeconomic groups. This information must be provided in the Participant information leaflet with clear guidance regarding how these expenses can be claimed, and in the document P1_Compensation for trial participants.
- The NREC- CT noted that carers of participants have not been included for travel, accommodation and meal expense reimbursement in the Compensation Form (p1). The Committee requested that reimbursement of travel, accommodation and meal expenses are considered for carers of participants and, if included, that it is elucidated in the Compensation Form and PISCF's.

4. Proof of insurance

- No considerations raised by NREC-CT

5. Recruitment arrangements

- No considerations raised by NREC-CT

6. Subject information and informed consent form

- Standard Consideration:

1. Where applicable, the Sponsor is requested to submit any Part 2 documentation requiring revision following the outcome of the Part 1 Assessment. Should an additional Request for Information (RFI) be required, please contact the National Office at clinicaltrials@nrec.ie. The request should include a concise summary of the Part 1 consideration(s) that necessitated the update to the Part 2 documentation.
2. All documentation submitted in response to a Request for Information (RFI) must be provided in a format that is both accessible and searchable, such as Microsoft Word or original (non-scanned) PDF files. Please note that scanned documents, including those processed using Optical Character Recognition (OCR), are not acceptable, as they cannot be optimised for compatibility with assistive technologies.

- The NREC-CT noted on page 6/7,9 and page 19 of the Main PISCF " exploratory biomarkers" are mentioned but not explained, and that the use of these exploratory biomarkers for future research is not described in line with best practice and regulations. The NREC-CT requested that future use of samples related to exploratory biomarkers is sufficiently explained to participants in the PISCF documents so as to constitute 'broad' informed consent, as required under the Health Research Regulations (Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018). Furthermore,
    - it should be made optional
    - it should be confined to a specified disease, related diseases or drug under study in this trial. Consent can only be obtained where future use of samples and data is defined such that participants are fully informed,
    - and/or that an option is provided to enable participants to consent to be contacted in the future about other research studies,

  - optional future research is made into a separate and explicit consent item in the Informed Consent section of the Main PISCF, with separate participant information section and signatures section, so it is distinct from the main consent to participate in the research.
  - The PISCF should also make it clear to participants that subsequent research ethics review will be sought for specific research once clearly defined. For further guidance, please see: NREC guidance on use of biological samples and associated data - https://www.nrecoffice.ie/guidance-on-use-of-biological-samples-and-associated-data/
- The NREC-CT noted that page 1 and 2 of the optional genetic PISCF states “The purpose of this genetic research is mostly to better understand the safety and efficacy (how well it works) of a treatment. It may also be to learn more about human diseases or to help develop ways to detect, monitor and treat diseases” which implies that participants may undergo whole genome / whole exome sequencing. The Committee requested the following:
  - Genomic sequencing is confined to genes involved in the disease being treated or related diseases and /or genes involved in the metabolism of the medicines being used in the trial and this elucidated in the PISCF.
  - Explicit consent, including outlining the risks entailed in such analysis being performed, is added to the PISCF.
  - The possible ownership of such data by private or commercial interests and that this elucidated in the PISCF.
  - The right to withdraw genetic data, and clear information on how to do so, must also be provided in the PISCF.
  - Clarification is provided in the PISCF on the mechanism for anonymisation, storage and security and transfer of genetic material and its associated data.
  - For guidance, please see HSE National Policy for Consent in Health and Social Care Research (V2.0, 2024). Dublin: Health Service Executive https://www2.healthservice.hse.ie/organisation/national-pppgs/hse-national-policy-for-consent-in-health-and-social-care-research
- The NREC-CT noted on page 4, page 21 and page 23 of the Main PISCF, that it mandatory that the participants GP will be informed of the participants involvement in the trial. The NREC-CT requests the GP letter for review.
- The NREC-CT noted that page 13 of the Main PISCF states "Do not drink alcohol excessively throughout the trial" and considers this instruction to be ambiguous and subject to individual interpretation. The Committee requests that context is added to this sentence, including but not limited to:
  - the units of alcohol per time period that is permitted,
  - whether this instruction applies to the core part or the extension part of the study,
  - the potential medical risks or adverse events if a person exceeds the recommended alcohol limit,
  - any repercussions to a participants’ involvement in the study if the alcohol limit is exceeded

7. Suitability of the clinical trial sites facilities

- No considerations raised by NREC-CT

8. Suitability of the investigator

- The Committee notes that the CV for [redacted] does not provide sufficient detail to demonstrate previous clinical trial supervisory experience. Please update the CV to include this evidence. If [redacted] does not have additional prior

supervisory experience in clinical trials, please outline the supports that will be in place from other suitably qualified clinicians to enable [redacted] to undertake the role.

2024-519917-72-00

Institutions: St James's Hospital, Mater Misericordiae University Hospital

Study title: TRITON-CM: A Phase 3 Global, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of Nucresiran in Patients with Transthyretin-Mediated Amyloidosis with Cardiomyopathy (ATTR amyloidosis with cardiomyopathy)

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**
- Request for Further Information

- **Additional Information Required**

Part II Considerations
1. Compliance with national requirements on data protection
• No considerations raised by NREC-CT
2. Compliance with use of biological samples
• No considerations raised by NREC-CT
3. Financial arrangements
• The NREC-CT noted on page 15 of the Main PISCF, that participants will not be reimbursed for all expenses, and that monetary limits are proposed for expenses such as travel, accommodation and meals. The NREC-CT requested that participants are reimbursed for all reasonable out-of-pocket expenses, to ensure equity in access to clinical trials across all socioeconomic groups. This information must be provided in the participant information leaflet with clear guidance regarding how these expenses can be claimed, and in the document P1_Compensation for trial participants.
4. Proof of insurance
• No considerations raised by NREC-CT
5. Recruitment arrangements
• No considerations raised by NREC-CT
6. Subject information and informed consent form
– Standard Consideration: – Where applicable, the Sponsor is requested to submit any Part 2 documentation requiring revision following the outcome of the Part 1 Assessment. Should an additional Request for Information (RFI) be required, please contact the National Office at clinicaltrials@nrec.ie. The request should include a concise summary of the Part 1 consideration(s) that necessitated the update to the Part 2 documentation. – All documentation submitted in response to a Request for Information (RFI) must be provided in a format that is both accessible and searchable, such

as Microsoft Word or original (non-scanned) PDF files. Please note that scanned documents, including those processed using Optical Character Recognition (OCR), are not acceptable, as they cannot be optimised for compatibility with assistive technologies.

- The NREC-CT noted the following terms have been included in the Main PISCF without explanation and requested that the terms be explained on first use using appropriate language suitable for a lay audience.
    - Page 10: SiRNA
    - Page 7: biomarker
    - Page 14: pharmacokinetic
    - Page 14: neurofilament light chain
    - Page 14: anti-drug antibodies
- The NREC-CT noted the below-listed statements in the referenced documents. The Committee requests that the timelines in the Main PISCF, the Pregnant PISCF and any/all other applicable documents are revised as applicable to ensure alignment.
    - page 2 of the Pregnant Partner PISCF states “you became pregnant while he was participating in the study or within the 360 days after he stopped treatment with the study drug.”
    - page 4 of the Main PISCF states “from the start of Study Medication to 24 months after your last dose”
    - page 11 of the Main PISCF states “and for 24 months after last dose administration or until the end of the study, whichever is longer”
    - page 12 of the Main PISCF “and for up to 24 months after the last dose of study drug”
    - Page 12 of the Main PISCF “If your partner becomes pregnant during your course of treatment with nucresiran or up to 24 months after your receiving your last dose of Study Medication (or until study completion, whichever is longer)”

- The NREC-CT noted on page 14/15 of the Main PISCF that Greenphire will be providing a reimbursement service. The Committee requests that the Main PISCF be revised to include details of how a participant will obtain reimbursement without using Greenphire, in the event that a participant does not wish to use Greenphire to provide these services.
- The NREC-CT noted that page 4 of the Main PISCF states “You and anyone in your immediate support network must not share information from or about the study with other participants, on social media, or in the public domain”. As participants are not permitted to discuss their participation as outlined in this statement, the Committee requests the following:
    - Details as to how this will be monitored during the trial
    - That details as to the potential implications for participants (should they fail to adhere to this instruction) be added to the Main PISCF
- The NREC-CT noted that page 14 of the Main PISCF states "Medical Costs: The Sponsor will pay for the Study Medication, tests, and procedures needed in this study." The Committee requests that the following wording be added for clarification "and that the participant will incur no costs for taking part in this study"

- The NREC-CT noted on page 34 of the protocol the section entitled ‘Tokenization’ (Section 3.1.3). The Committee requests clarification whether tokenisation will be occurring in Ireland. If yes, the Committee requests revision of the Main PISCF to provide more information about tokenization in a specific section with clear lay language.
- The NREC-CT noted that page 15 of the Main PISCF states “Within about 12 months after the study has ended, a summary of the study results will be made available to you.” The Committee requests clarification on what this summary will include, whether it will be provided directly to participants or if participants will be directed to where it can be accessed, and whether the summary will be written in lay language.
- The NREC-CT noted the following statements in the Main PISCF: “For male patients, no contraception (condom) is required” (page 19) and “However, certain birth defects, including heart abnormalities, were observed in the offspring of female rabbits that received nucresiran while pregnant. Additionally, some rats that received nucresiran while pregnant experienced loss of embryos or foetuses after uterine implantation. In a test to assess rodent learning and recall, some offspring of rats that received nucresiran while pregnant did not perform as well as offspring of rats that did not receive nucresiran while pregnant” (page 11). The Committee requests justification as to why male participants are not required to use highly effective birth control methods while female participants are required to. As presented, the Committee felt the Main PISCF implies no risk related in children born of a male participating in the trial – which is out of alignment of the pregnant partner PISCF which states that risks are unknown. The Committee suggests these wordings are aligned so participants are aware if risks are known or unknown at the point of study entry,
- The NREC-CT noted the submission of the Pregnant Partner PISCF and requests a Pregnant Participant PISCF is submitted for review.
- The NREC-CT noted on page 8 of the Main PISCF that use of the ProofPilot system is optional. The Committee requests clarification as to whether a participant who initially declines can later opt in and, if so, how this would be facilitated.
- The NREC-CT noted that page 5 of the Main PISCF states “This web portal may help you keep track of your study visits, receive appointment reminders, access study-related information, and complete questionnaires.” The Committee requests clarification whether the ProofPilot system will be used to complete any of the study questionnaires, and details of same.
- The NREC-CT noted references to offsite healthcare visits in the below-listed documents. The NREC-CT requests clarification whether offsite healthcare visits will be available for participants of the clinical trial in Ireland. If not, the Committee requests that references to offsite healthcare visits be removed from the Main PISCF (and other participant-facing documents as applicable) for use in Ireland.
    - page 9 of the Main PISCF (Section 3.4 “Home Healthcare services”),
    - page 20 of the Main PISCF (Signature section “Home Healthcare Services through Illingworth:”)
    - page 5 in the Main PISCF (Section 3.1: Optional Home Healthcare Support section)

- The NREC-CT noted that pages 6 (Section 3.2 “List of Study procedures”) and page 8 (Section 3.3 “Schedule of Assessments”) of the Main PISCF provide relevant information about what assessment the participants will undergo and when each will occur, in order to assist the participant when planning their site visits. The Committee requests that the duration which each procedure will take be added to Section 3.2 “List of Study procedures” and the estimated length of time for each visit be added to Section 3.3 “Schedule of Assessments”.
- The NREC-CT noted that page 7 of the Main PISCF states “Optional Samples for Future Research: If you agree in a separate consent, additional blood and urine samples will be collected and may be used for possible future research on biomarker testing to learn more about the disease and how the Study Drug works”. It is not clear in the Main PISCF or the Biological Sample PISCF, when these samples will be collected. The Committee requests that both the Main PISCF and the Biological samples ICF is updated with the timing of the sample collection, what site visits or if they are separate site visits, the amount of blood collected, and the frequency of the sample collection.
- The NREC-CT noted that page 2 of the Biological Samples PISCF states “Future research aims to advance science and public health using your biosamples and Coded Personal Data from this study. The details of future projects are not determined yet. Future research may occur during or after this study” which is not described in line with regulations / best practice. The Committee requested that future use of samples and personal data is sufficiently explained to participants in the PISCF documents so as to constitute ‘broad’ informed consent, as required under the Health Research Regulations (Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018). Furthermore,
    - It should be confined to a specified disease, related diseases or drug under study in this trial. Consent can only be obtained where future use of samples and data is defined such that participants are fully informed,
    - and/or that an option is provided to enable participants to consent to be contacted in the future about other research studies,
    - The PISCF should also make it clear to participants that subsequent research ethics review will be sought for specific research once clearly defined. For further guidance, please see: NREC guidance on use of biological samples and associated data - https://www.nrecoffice.ie/guidance-on-use-of-biological-samples-and-associated-data/

- The NREC-CT requested clarification whether there will be an option for continuation/extension beyond 38 months for participants who respond positively to this IMP and, if so, that this information is included in the Main PISCF.

7. Suitability of the clinical trial sites facilities

- No considerations raised by NREC-CT

8. Suitability of the investigator

- No considerations raised by NREC-CT

2023-506327-29-00 SM-4

Institutions: St James's Hospital, Tallaght University Hospital, Cork University Hospital

Study title: A Phase 3 Randomized Double-blind Study of Adjuvant Pembrolizumab With or Without V940 in Participants With Resectable Stage II to IIIB (N2) NSCLC not Achieving pCR After Receiving Neoadjuvant Pembrolizumab With Platinum-based Doublet Chemotherapy (INTerpath-009)

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**
- Favourable

2024-518589-29-00 SM-1

Institutions: Connolly Hospital, St Vincent's University Hospital, Cork University Hospital

Study title: A Phase III, randomized, double-blind, placebo-controlled study to assess the Efficacy, Safety, and Tolerability of BI 1291583 2.5 mg administered once daily for up to 76 weeks in patients with Bronchiectasis (The AIRTIVITY® Study)

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**
- Request for Further Information

- **Additional Information Required**

Part II Considerations raised

1. **Subject information and informed consent form**

- Standard Consideration:
  - Where applicable, the Sponsor is requested to submit any Part 2 documentation requiring revision following the outcome of the Part 1 Assessment. Should an additional Request for Information (RFI) be required, please contact the National Office at clinicaltrials@nrec.ie. The request should include a concise summary of the Part 1 consideration(s) that necessitated the update to the Part 2 documentation.
  - All documentation submitted in response to a Request for Information (RFI) must be provided in a format that is both accessible and searchable, such as Microsoft Word or original (non-scanned) PDF files. Please note that scanned documents, including those processed using Optical Character Recognition (OCR), are not acceptable, as they cannot be optimised for compatibility with assistive technologies.
- The NREC-CT noted submission of the Paediatric Investigation Plan and the Pediatric Quality of Life Inventory Questionnaire. However, the NREC-CT also noted that K1_Recruitment arrangements document for Ireland (at Section 3.0: for

clinical trials which will involve minors) was not revised, and that Assent ICF and/or Parent/Guardians consent for minors documents have not been submitted. The Committee seeks clarification whether minors will be recruited to the trial in Ireland. If minors are to be recruited in Ireland, the Committee requests that K1_Recruitment arrangements document be revised and that Assent ICFs and Parent/Guardians consent ICF for minors documents are submitted for review.

2022-502548-12-00 SM-9

Institutions: University Hospital Waterford, St James's Hospital

Study title: A Phase 3 Randomized, Open-Label, Multicenter Study of Zanubrutinib (BGB 3111) Plus Anti-CD20 Antibodies Versus Lenalidomide Plus Rituximab in Patients With Relapsed/Refractory Follicular or Marginal Zone Lymphoma

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**
- Favourable

2024-516582-36-00 SM-2

Institutions: St Vincent's University Hospital, Beaumont Hospital, Cork University Hospital, University Hospital Limerick, St James's Hospital

Study title: A Single arm phase 2 trial of neoadjuvant trastuzumab deruxtecan (T-DXd) with response-directed definitive therapy in early stage HER2-positive breast cancer: a standard chemotherapy-sparing approach to curative-intent treatment – SHAMROCK study

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**
- Favourable

2024-514435-20-00 SM-2

Institutions: Children's Health Ireland

Study title: A Phase 3b Open-Label Study of Long-Term Neurocognitive Outcomes in Children With Phenylketonuria Treated With Sepiapterin

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**
- Favourable

2025-521627-78-00 SM-1

Institutions: Beaumont Hospital

Study title: A Phase 3, Multicenter, Randomized, Open-label Clinical Study of GSK5764227, a B7-H3 Antibody Drug Conjugate (ADC), compared with Topotecan in Participants with Relapsed Small Cell Lung Cancer (SCLC)

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**
- Favourable
