National Research Ethics Committee

NREC-CT A Meeting

17th September 2025

Attendance

Name	Role
Prof. Alistair Nichol	Chairperson, NREC-CT A
Dr Dawn Swan	Committee Member, NREC-CT A
Prof. Aisling McMahon	Committee Member, NREC-CT A
Mrs Erica Bennett	Committee Member, NREC-CT A
Dr David Byrne	Committee Member, NREC-CT A
Ms Margaret Cooney	Committee Member, NREC-CT A
Ms Muireann O'Briain	Committee Member, NREC-CT A
Mr Kevin Devlin	Committee Member, NREC-CT A
Ms Dympna Devenney	Committee Member, NREC-CT A
Ann Twoney	Committee Member, NREC-CT D
Gerry Daly	Committee Member, NREC-CT D
Dr Emily Vereker	Head of Office, National Office for RECs
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
Dr Peadar Rooney*	Project Officer, National Office for RECs

Apologies:

Name	Role
Dr Darren Dahly	Committee Member, NREC-CT A
Ms Caoimhe Gleeson	Deputy Chairperson, NREC-CT A
Prof. Gene Dempsey	Deputy Chairperson, NREC-CT A
Dr Brian Bird	Committee Member, NREC-CT A
Dr Maeve Kelleher	Committee Member, NREC-CT A
Ms Mandy Daly	Committee Member, NREC-CT A

Quorum for decisions: present

Agenda

- Welcome & Apologies
- 2025-521563-13-00
- 2024-520418-22-00
- 2024-519875-24-00
- 2023-509632-26-00 SM-7
- 2023-509133-39-00 SM-2
- 2024-512828-12-00 SM-3
- 2022-501606-35-01 SM-6
- 2024-512998-27-00 SM-8
- 2024-513168-24-00 SM-5
- AOB

- The Chair welcomed the NREC-CT A.
  - The minutes from the previous NREC-CT A meeting on 13th August 2025 were approved.
  - The NREC Business Report was discussed and noted.

Applications

2025-521563-13-00

Institutions: Technological University Dublin

Study title: Safety and efficacy of T10430 eye drops in controlling paediatric myopia progression (MyOPedia)

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required RFI**

Part II Considerations

1. **Proof of insurance**

- The NREC-CT noted on the insurance documents “The insurance is extended to cover travel accident injuries to research subjects, while traveling in relation to Human Clinical Trials covered under the policy” The NREC-CT requests clarification that the insurance is not limited to travel to and from the site. But that insurance has been obtained for the clinical trial and also travel to and from the site.

2. **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 on page 1 of both the Parent/Guardian ICF and the Assent 6-11 ICF, the term myopia used with shortsightedness in brackets. The NREC-CT requests that the lay term shortsightedness be used first, followed by the clinical term myopia in brackets. Additionally, a brief lay explanation of shortsightedness/myopia should be added to page 1, clarifying that myopia will be used throughout the document.
- The NREC-CT noted that the term vehicle is used to refer to placebo throughout both the Parent/Guardian ICF and the Doctor-to-patient letter. The NREC-CT

requests that the word vehicle be replaced with placebo and that a simple lay explanation of placebo to be added to the Parent/Guardian ICF.

- The NREC-CT noted that the Doctor to Patient Letter refers to a low/medium/high dose which may be misleading. To alleviate concerns about the child would receiving a large dose of IMP, the NREC-CT requests that the percentage of active ingredient be included.
- The NREC-CT noted on page 7 of the Assent 6-11 ICF the sentence “I understand that some of my personal data will be collected and used to perform the study” and considered that this is not age appropriate language or terminology that a 6-year-old will understand. The NREC-CT requests that this is rephrased into language suitable for 6–11-year-old participant.
- The NREC-CT noted on page 10 of the Parent/Guardian ICF and on page 4 of the Assent 6-11 ICF, that the participant will receive a daily paper diary. The NREC-CT requests that additional context be provided. including the estimated time required to complete the daily diary entry, and guidance onwhat to do if a diary entry is missed.
- The NREC-CT noted on page 22 of the Parent/Guardian ICF the text states “I agree that if the study doctor is not my child’s family doctor, my child’s family doctor will be told about my child taking part in this study and asked for medical information about my child” and on page 23 of the Parent/Guardian ICF the text states “I agree if my child’s study doctor is not my child’s GP, my child’s GP will be told about their taking part in this study and may be asked for medical information about them” The NREC-CT requests that duplicated text is removed.
- The NREC-CT noted on page 5 of the Parent/Guardian ICF “One drop of the study eye drop solution should be placed into each of your child’s eyes every day at approximately 20:00.” The NREC-CT requests that clarity on the flexibility the timing of administration of the eye drop be included in this section.
- The NREC-CT noted on page 5 of the Parent/Guardian ICF “One drop of the study eye drop solution should be placed into each of your child’s eyes every day at approximately 20:00.” The NREC-CT requests clarification on the rational of administration prior to bedtime, where the early signs of an allergic reaction (as detailed on page 13 of the ICF) might be missed. The NREC-CT requests that signs of allergic reaction to look for and the timeframe for allergic reactions to be briefly detailed on page 5 of the Parent/Guardian ICF.
- The NREC-CT noted on page 9 of the Parent/Guardian “If your child is sexually active and is able to become pregnant, she will have regular urine pregnancy tests to check whether she is pregnant.” The NREC-CT requests that this is rephrased to be more appropriate to the parents/guardian of young children. The NREC-CT requests that this is updated to “Where appropriate, if pregnancy is possible, a regular urine pregnancy tests are recommended”
- The NREC-Ct noted on page 9 of the Parent/Guardian, “she will have regular urine pregnancy tests to check whether she is pregnant.” The NREC-CT requests that more context is added to this section, including how these samples will be destroyed after use.
- The NREC-CT noted on page 13 of Parent/Guardian, section “Reproductive Risks” The NREC-CT request that this is rephrased into more appropriate language for the parents of young children.

- The NREC-CT noted on the Doctor to Patient letter “You can visit the website to learn more about the study:” and “You can also scan the QR code to visit the website and learn more about the study:” The NREC-CT requests alternative arrangements be made available for parents/guardians who might have difficulty accessing online resources.

3. Suitability of the clinical trial sites facilities

- The NREC-CT noted on the Site Suitability Assessment that the site is listed as the Centre for Eye Research Ireland, Technological University Dublin City Campus. - CT request confirmation that this site is covered under the national indemnity scheme or alternative cover. Furthermore, the NREC-CT requested clarification regarding the procedures in place should a participant experience a severe acute medical allergic reaction to the IMP, and confirmation that appropriately qualified staff are available on site to provide emergency care and coordinate transfer to a tertiary hospital facility, if required.
- The NREC-CT noted on page 5 of the Site Suitability Assessment, Section 8 it states that certain equipment is under discussion and may ‘potentially’ be provided by the sponsor. As this equipment is essential for the study, the NREC-CT requests clarification what equipment is required and the timeline for the equipment to be provided, and what alternatives are available if not provided for the sponsor.
- The NREC-CT noted the following in the protocol, section 7.1., page 55 '*referral to another clinic or facility for specific tests or procedures not available onsite*'. Please confirm if additional sites will be included in this study to complete any of the assessments, and if this is the case, what will occur at that site should also be clearly described in the ICF (i.e., participant information leaflet).

4. Suitability of the investigator

- The NREC-CT noted that on the CV, “Current Position” is listed as the Mater Misericordiae University Hospital”, and that the “Current Employment” is listed as Childrens University Hospital, Temple Street” and the Site Suitability Assessment is for the Centre for Eye Research Ireland, Technological University Dublin City Campus”. The NREC-CT requests that this is clarified and that the CV be amended to align if required.

2024-520418-22-00

Institutions: Tallaght University Hospital, Connolly Hospital, Portiuncula University Hospital, Cork University Hospital, Our Lady of Lourdes Hospital, University Hospital Galway

Study title: A randomized, double-blind, placebo-controlled, parallel-group, multicenter study of the efficacy and safety of depemokimab in adult participants with COPD with Type 2 inflammation. (ENDURA-1)

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required RFI**

Part I Considerations (RFI) for addition to CTIS

1.

- It is noted that the Protocol title is recorded in the Protocol as “A randomized, double-blind, placebo-controlled, parallel-group, multicenter study of the efficacy and safety of depemokimab in adult participants with COPD with Type 2 inflammation” and that the Charter for the IDMC has the study title as “A randomized, double-blind, placebo-controlled, parallel-group, multicenter study of the efficacy and safety of depemokimab in adult participants with COPD with type 2 inflammation characterized by an eosinophilic phenotype”. It is requested that these titles are aligned.
- It is noted that PPD is mentioned throughout the Charter for the IDMC and the unblinded PPD SDTM team responsible for laboratory and immunogenicity data. Clarification is requested regarding the role of PPD in managing the study, and in particular, if there is a clear firewall between the DSMB and the study management, i.e., who the IDMC project coordinator is and their relationship to the CRO running the clinical study.
- It is noted in the protocol in section 5.1.1 participants must be between 40 and 80 years of age. It is requested that the sponsor clarifies why potential symptomatic participants less than 40 years of age are excluded from this study.
- It is noted in the protocol in section 5.1.8 (i.e., the substudy) that participants must be between 40 years of age and 70 years of age. It is requested that the sponsor clarifies the difference in age parameters between the study and the substudy.
- It is noted in the protocol in section 8.1.2 that the sponsor will “obtain the participant’s medical history by interviewing the participant and/or review of the participant’s medical records.” As it is best practice to make considerable efforts to obtain and review the participants’ medical records prior to enrolment, it is requested that the sponsor updates the protocol section 8.1.2 to reflect that all efforts will be made to obtain records for pre-existing conditions, signs and/or symptoms present prior to the first dose.

- It is noted in the protocol in section 8.1.4 that Tokenisation is planned for some participants. It is requested that the sponsor clarifies what countries this will occur in.
- It is noted in section 8.10 (i.e., medical resource utilisation and health economics) that the 'resource utilisation worksheet' will collect data about utilisation of unscheduled healthcare resources associated with COPD exacerbations, and that these data may be used to conduct exploratory economic analysis. This appears to be out of scope of the aim of the study, and justification is requested.
- It is noted on page 123 that Pregnant participants have a follow-up of pregnancies no longer than 6 to 8 weeks. It is requested that this section is revised to also include pregnant partners.
- It is noted in section 10.3.5.5 that the sponsor will be is “obligated to perform or arrange for the conduct of supplemental measurements and/or evaluations as medically indicated or as requested by GSK to elucidate the nature and/or causality of the AE or SAE as fully as possible”. It is requested that the sponsor clarifies if this includes postmortem including histopathology, in the event a participant dies.

Part II Considerations

1. Subject information and informed consent form

- If applicable, the Sponsor is requested to submit any Part 2 documentation that require updates as a result of the Part 1 Assessment.Please include detail of the Part 1 consideration that triggered the update to the Part 2 documentation.
- The National Office requests that all documentation provided in response to RFI is presented in an accessible and searchable format (Word or original PDF). We are unable to accept scanned documents (including documents modified using Optical Character Recognition) as these documents cannot be optimised for use with assistive software.
- The NREC-CT noted that technical language in the Main ICF needs review. The NREC-CT requests that the Main ICF language is reviewed and simplified. Examples are provided below.
    - Page 12 of the Main ICF - Reproductive studies
    - Page 14 of the Main ICF - Inflammatory proteins
    - Page 15 of the Main ICF - RNA sequencing
    - Page 10 of the Main ICF - Non-allergic generalised systemic rash
    - Page 14 of the Main ICF - Sputum
    - Page 6 of the Main ICF - health assessments
    - Page 7 of the Main ICF – “Fractional exhaled nitric oxide” and in this paragraph, explain “inflammation”
    - Page 3 of the Main ICF – “run-in period”
    - Page 4 of the Main ICF – “count of some blood cells called Eosinophils”
    - Page 4 of the Main ICF - “Suitable to participate”
    - Please consider using more simple language such as “expected duration” to be changed to how “long it will last”.
- The NREC-CT noted on page 12 of the Main ICF options for birth control methods are listed. The NREC-CT requests that it be clarified in on page 12 of the Main ICF

that women who are not of childbearing potential do not need to use birth control methods or take urine pregnancy tests.

- The NREC-CT noted on page 5 of the Main ICF "The total volume of blood during the entire period of your participation is estimated to be". The NREC-CT requests that his is simplified to "the amount of blood you will have to give over the entire time you are in the study".
- The NREC-CT noted on page 17 of the Main ICF "Copies of your medical records may be sent to trusted third parties working with GSK for the purpose of independent review and adjudication by expert committee or for evaluation." The NREC-CT request that this language is revised to suitable lay terminology. The NREC-CT requests that more context is added to this section to ensure it is clear to participants why their medical records are sent to third parties.
- The NREC-CT noted on page 19 of the Main ICF "Your samples may be tested for indications of other diseases, including infectious diseases such as HIV (the virus that causes AIDS) and Hepatitis B and C (viruses that can damage the liver as a part of further research). This may occur many years after your participation in the study. This medical test may give information that is very important to the participant and should be delivered in a reasonable time". The NREC-CT requests that HIV, Hepatitis B and C tests are limited to a reasonable time period and that this time period is detailed in the ICF.
- The NREC-CT noted on page 23 of the Main ICF that Scout Clinical may be used for reimbursement of expenses and stipend. The NREC-CT requests clarification as to whether the participant will be required to sign a Scout Clinical ICF in order to use Scout Clinical services as part of this clinical study. If so, the NREC-CT requests the Scout Clinical ICF be submitted for review. The NREC-CT also requests that the details of how the participant will receive reimbursement and/or stipends if they choose not to use Scout Clinical Services.
- The NREC-CT noted on page 18 of the Main ICF refers to 'coded data' and requested that it is clarified in the PISCF whether this refers to use of pseudonymised' or 'anonymised' data.
    - If 'coded data' refers to anonymised data, the Committee requested that:
    - The ICF be updated to include a consent statement for the participant to explicitly consent to the processing of their personal data from pseudonymised /coded data to anonymised data as per Article 4 (2) and 6 General Data Protection Regulation (GDPR).
    - An explanation of the process is provided to participants in the PISCF using plain English suitable for a lay audience. This should include an explanation of the term 'anonymised'.
- The NREC-CT noted that the future use of data / samples is not described in line with regulations or best practice on page 29 of the Main ICF "for further research NOT related to this study", page 15 of the Main ICF "do additional research on your samples/data other than just what is done for this study.", page 19 of the Main ICF "If you agree to the use of your coded samples and data for further research that is NOT related to this study, this will be used by GSK and others, for example universities or other companies, to: Study other diseases and treatments: Develop new research methods and tests." The NREC-CT requests that future use of samples / personal data is sufficiently explained to participants in the ICF

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,
- optional future research is made into a separate and explicit consent item in the Informed Consent section of the Main ICF, with separate participant information section and signatures section, so it is distinct from the main consent to participate in the research.
- The ICF 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 on page 3 of the Genetic Research ICF "Further use of your coded samples and data for research NOT related to this study will be used by GSK or others to: Study other diseases and treatments. Develop new genetic research methods and tests", on page 6 of the Genetic Research ICF, "Test and improve GSK computer systems that support clinical study processes" and on page 7 of the Genetic Research ICF "for further research NOT related to this study including study of other diseases and treatments and to develop new genetic research methods and tests," The NREC-CT requested that future use of samples / personal data is sufficiently explained to participants in the ICF 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,
    - optional future research is made into a separate and explicit consent item in the Informed Consent section of the Main ICF, with separate participant information section and signatures section, so it is distinct from the main consent to participate in the research.
    - The ICF 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 on page 4 of the Pharmacokinetic Substudy ICF and on page 6 of the Pregnancy Participant ICF "for further research NOT related to this study including study of other diseases and treatments and to develop new genetic research methods and tests," The NREC-CT requested that future use of samples / personal data is sufficiently explained to participants in the ICF 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,
  - optional future research is made into a separate and explicit consent item in the Informed Consent section of the Main ICF, with separate participant information section and signatures section, so it is distinct from the main consent to participate in the research.
  - The ICF 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 of the Genetic Research ICF states that participants may undergo whole genome sequencing and 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.
  - The possible ownership of such data by private or commercial interests and that this elucidated in the ICF.
  - Clarification is provided in the ICF on the mechanism for anonymisation, storage and security and transfer of genetic material and its associated data.
  - Please note it is requested that any consent form is a stand-alone document and does not refer to other consent forms for more information, as on page 3 of the Genetic Research ICF.
  - 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

2. Suitability of the clinical trial sites facilities

- The NREC-CT noted on page 28 of the Protocolthat parasitic screening is needed for participants who have visited high risk countries in the last six months. The NREC-CT requests that additional details are added to the site suitable assessment form as to whether sites have the ability to perform parasitic testing if required.
- The NREC-CT requested further information is provided in the site suitability assessment form as to how recruitment will be managed by the sites.
- The NREC-CT noted that if Scout Clinical is not used by the participant, the site will have to manage the process. The NREC-CT requests clarification that the sites have sufficient resources to manage this process.

2024-519875-24-00

Institutions: St Vincent's University Hospital

Study title: A Randomized, Parallel Group, Placebo-Controlled Study to Evaluate the Efficacy and Safety of Paltusotine in Adults with Carcinoid Syndrome due to Well-Differentiated Neuroendocrine Tumors (CAREFNDR)

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required RFI**

Part II Considerations

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 that in section 2.2.1 of the Main ICF it explains that the participant will be in the blinded part of the study for 16 weeks. The NREC-CT requests that the study schedule on page 2 of the recruitment materials brochure, or a similar graphic be included in the initial sections of the Main ICF.
- The NREC-CT noted in section 2.2.1 of the Main ICF, the term "blinded" is used. The NREC-CT requests that blinded study is given a lay terminology explanation on first use in the Main ICF.
- The NREC-CT noted in section 2.2.1 of the Main ICF, the term "placebo" is used. The NREC-CT requests that "placebo" is given a lay terminology explanation on first use in the Main ICF.
- The NREC-CT noted in section 3.7 of the Main ICF "You will be informed of any new information about any of the rescue medications that might adversely affect your well-being." The NREC-CT requests that rescue medication is given a lay terminology explanation in the Main ICF.
- The NREC-CT noted in section 2.7 of the Main ICF "If you have any questions about your rights as a study participant before, during, or after this study or lodge a complaint with the Office of the Data Protection Commission, 21 Fitzwilliam Square South, Dublin 2, Ireland, please contact the website of the Data Protection Commission (DPC) (https;//www.dataprotection.ie) for data protection rights." The

NREC-CT requests that this information is moved to a more appropriate section, such as section 7.2; What information is being collected and what are my rights.

- The NREC-CT noted in section 4.2 of the Main ICF "This study medication, like many medications, can occasionally cause severe side effects, which may be life-threatening. Side effects may occur almost immediately after the study medication is administered, or days later.". The NREC-CT stated that this does not provide sufficient information regarding the risk of side effects in order for the potential participant to make an informed decision. The NREC-CT requests that the sponsor list the most common severe side effects, and their frequency, in the Main ICF.
- The NREC-CT noted in section 4.6 of the Main ICF "You will not be charged for this treatment. You will not receive any compensation for this injury." The NREC-CT requests that section is amended to ensure the information provided is relevant in the Irish healthcare context.
- The NREC-CT noted in section 3.3 of the Main ICF "Your samples will be stored in a secure laboratory until 1 year after the completion of the study and after that, they will be destroyed" The NREC-CT requests that the location of the samples and the laboratory is detailed in this section of the Main ICF.
- The NREC-CT noted that in section 7.3 of the Main ICF "By signing this form, you understand that medical information about you obtained during this study may be made available to…" The NREC-CT request clarification on what is meant by medical information, and if this information be anonymised or pseudo-anonymised.
- The NREC-CT noted in section 7.1 and 7.3 the term "coded information" is used, and requested that it is clarified in the PISCF whether this refers to use of 'pseudonymised' or 'anonymised' data. If 'coded data' refers to anonymised data, the Committee requested that:
    - The ICF be updated to include a consent statement for the participant to explicitly consent to the processing of their personal data from pseudonymised /coded data to anonymised data as per Article 4 (2) and 6 General Data Protection Regulation (GDPR).
    - An explanation of the process is provided to participants in the PISCF using plain English suitable for a lay audience. This should include an explanation of the term 'anonymised'.
- The NREC-CT noted that on page 28 of the Main ICF it states "I confirm that I have received the informed consent form in my preferred (or native) language". NREC-CT requests that the consent section contains a witness signature line. The NREC-CT requests information be added to all relevant ICF's explaining the context where a witness signature would be needed (as per CTR: Annex I,L 62(b)).
- The NRE-CT noted on page 27 in the consent section of the Main ICF "I agree that my General Practitioner will be informed of my participation in this study. I authorise the release of my medical records to Crinetics, agents of Crinetics, inspectors of health authorities, the Food and Drug Administration, other governmental agencies, and the /IEC." The NREC-CT requests clarification on why consent is being sought to release the personal medical records of a participant to these groups.
- The NREC-CT noted in section 3.4 of the Main ICF states that participants may undergo whole genome / whole exome sequencing and 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 in section 3.5 of the Main ICF “You will not be charged for your participation in the study.” The NREC-CT request that his is rephrased to be “no cost to the participant”.
- The NREC-CT noted in section 7.3.1 of the Main ICF “you may be provided with participant concierge (travel arrangement) services from Scout Clinical, a vendor engaged by Crinetics. This vendor will collect information about you (and your caregiver, if necessary), such as your name, address, and contact details (e.g., phone number).” The NREC-CT requests clarification as to whether the participant will sign a Scout Clinical consent form. If the participant will sign a relevant consent form which includesthe collection of their personal data, NREC-CT requests a copy of the Scout Clinical Consent form for review.
- The NREC-CT noted on page 27 in the consent section of the Main ICF, “I agree to participate in the travel reimbursement program and allow Scout Clinical to process my personal data for this purpose as described in this ICF” and “I agree to participate in the optional participant concierge (travel arrangement) service and allow Scout Clinical to process my personal data for this purpose as described in this ICF.” The NREC-CT requests that as this is an optional part of the study and is a separate part of the consent process, that the participant is given an opportunity to refuse with a yes or no option. The NREC-CT requests that if a participant does not want to use Scout Clinical or have their financial data transferred outside of the EU, that an alternative option be detailed in the Main ICF.
- The NREC-CT noted in section 7.3 “This medical information may be made available to Crinetics or persons acting on behalf of Crinetics (including contractors) for lawful purposes including conducting the study and analysing study results, future research,” and on page 28 in the consent section of the Main ICF “I agree to the sharing of my personal data obtained from this research with researchers” and “I consent to the re-use of my personal data obtained from this research”. The NREC-CT noted that the future use of data / samples (including genetic research) is not described in line with regulations / best practice. The NREC-CT requested that future use of samples / personal data is sufficiently explained to participants in the ICF 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 ICF, with separate participant information section and signatures section, so it is distinct from the main consent to participate in the research.
    - The ICF 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 that the Main ICF page 28 be updated to include specific statement that the participant/legally designated representative confirms that a copy of the signed and dated Informed Consent Form will be provided to them and that a copy will be retained by the study doctor.
- The NREC-CT noted in section 4.6.1 in the Main ICF “The insurance covers damage resulting from the study. Not all damage is covered.” The NREC-CT requests that examples of what is not covered by insurance taken out by the sponsor for this clinical study is provided for the participant.
- The NREC-CT notedthat a pregnant partner ICF was submitted for review. The NREC-CT request clarification if a pregnant participant ICF is to be submitted for review.
- The NREC-CT noted Pregnant partner ICF states "I agree with the use of my or my baby’s personal data obtained in this study for other future research activities and associated scientific publications" The NREC-CT that the use of the child’s personal data for future research is not described in line with regulations / best practice. The NREC-CT requested that future use of personal data is sufficiently explained to participants in the ICF 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 ICF, with separate participant information section and signatures section, so it is distinct from the main consent to participate in the research.

- When seeking consent for the use of a child's personal data for future research, when the child reaches the age of consent, please detail how consent will be obtained from the child who has reached the age of consent for the continued use of the data in future research
- The ICF 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/

2023-509632-26-00 SM-7

Institutions: Galway University Hospital, Tallaght University Hospital, Mater Misericordiae University Hospital, Cork University Hospital, St Vincent's Hospital

Study title: A Phase 1b/2 pan-tumor, open-label study to evaluate the efficacy and safety of ifinatamab deruxtecan (I DXd) in subjects with recurrent or metastatic solid tumors

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Favourable

2023-509133-39-00 SM-2

Institutions: Beaumont Hospital, St James's Hospital, St Vincent's Hospital

Study title: EPIK-B5: A Phase III, randomized, double-blind, placebo-controlled study of alpelisib (BYL719) in combination with fulvestrant for men and postmenopausal women with HR-positive, HER2-negative advanced breast cancer with a PIK3CA mutation, who progressed on or after aromatase inhibitor and a CDK4/6 inhibitor

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required RFI**

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 that the participants who are currently on placebo will be receiving alpelisib or remaining on fulvestrant alone, and as stated in the protocol (page 51) cross-over is based on investigators judegement and discusion with patient. The NREC-CT requests that the details of the crossover is added as a tick box in the consent form, to ensure participant consent for the crossover is recorded.
- The NREC-CT noted on page 5 of the PIL "You have an "equal" or 50% chance (like flipping a coin) of being treated with either alpelisib, or alpelisib-matching placebo" and "You will take 1 to 3 pills of alpelisib-matching placebo by mouth once a day" the NREC-CT requests instructions that are no longer relevant be removed from the PIL.
- The NREC-CT noted on page 5 of the PIL "Recruitment in this study was stopped in February-2025. This decision was not related to any new or unexpected safety findings. No new participants will be recruited." The NREC-CT requests that more context be added to this section, explaining the reason for the stopping of recruitment in lay non-technical terms.

2024-512828-12-00 SM-3

Institutions: Children's Health Ireland

Study title: An open-label study to collect safety and effectiveness information on long-term treatment with vamorolone in boys with Duchenne Muscular Dystrophy who have completed prior studies with vamorolone (The GUARDIAN Study)

Dossiers Submitted: Part II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required RFI**

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 on page 18 of the Parent/Guardian ICF, the statement "to support future scientific or medical research, related or unrelated to this study" is not in line with regulations / best practice. The NREC-CT requested that future use of 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 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 on page 1 of the modification form “Where allowed by the study site, we are introducing the possibility of remote consenting”. However, the Parent/Guardian ICF does not include any details on how this will be implemented. The NREC-CT requests clarification on whether remote consenting is taking place at Irish sites. If remote consenting is being implemented in Ireland, the NREC-CT requests additional information be provided in the recruitment arrangements form. Please include details on how remote consent will be conducted, how signatures will be recorded, how parents/guardians will sign the form and what safeguards are in place to ensure confidentiality and verify identity.

2022-501606-35-01 SM-6

Institutions: Bon Secours Hospital Cork, Beaumont Hospital, St James's Hospital, University Hospital Waterford, University Hospital Galway, Sligo University Hospital, Cork University Hospital

Study title: Randomized, multicenter, open-label, Phase 3 study of mirvetuximab soravtansine in combination with bevacizumab versus bevacizumab alone as maintenance therapy for patients with FRα-high recurrent platinum-sensitive epithelial ovarian, fallopian tube, or primary peritoneal cancers who have not progressed after second-line platinum-based chemotherapy plus bevacizumab (GLORIOSA)

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Favourable

2024-512998-27-00 SM-8

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

Study title: A Prospective, Open-Label, Randomized, Phase 3 Trial of Acasunlimab (GEN1046) in Combination With Pembrolizumab Versus Docetaxel in Subjects With PD-L1 Positive Metastatic Non-Small Cell Lung Cancer After Treatment With a PD-1/PD-L1 Inhibitor and Platinum-Containing Chemotherapy (ABBIL1TY NSCLC-06)

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required RFI**

Part II Considerations raised

1. **Recruitment arrangements**

The NREC-CT noted the submission of new recruitment material. The NREC-CT requests clarification regarding the intended use of the social media content including:

- Who will be requested to post the material online?
- Will potential participants provide their consent to participate by electronic means?
- Whether the site will supervise or participate in the advertising of the content?
- Whether approval from the clinical institutions will be required before study team members use their own social media platforms to advertise for participants?

2. **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 deletion of the section entitled 'Findings' in pages 11 and 12 of the Main ICF. Given that the text appears not to be participant-facing, and appears to be addressed to the P.I., the NREC-CT requests clarification as

to whether this section is in fact a tracked change from a previous version of the Main ICF. Is there consent for the P.I. to correspond with the patient's G.P. other than only on the fact that the patient is a participant in the trial?

- The NREC-CT noted that, on page 134 in the IB, the revised text states "The hepatic safety profile of acasunlimab underscores the importance of scheduled liver function testing". To reflect the significance of the risk, the NREC-CT requests that the hepatic safety risk be given greater prominence in the risks section, and details about liver function testing be added to both the Risks section and the "Tests and checks during the follow-up period" section (page 11) of the ICF.

2024-513168-24-00 SM-5

Institutions: St Vincent's University Hospital, Mater Misericordiae University Hospital, University Hospital Galway

Study title: A randomised, controlled, parallel group, open-label trial evaluating the impact of treatment with the GLP-1 analogue semaglutide on weight loss in people living with HIV and obesity (SWIFT Study)

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required RFI**

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 the PIL does not contain sufficient detail regarding additional contact details available to the participant, if required, including those related to recovery of expenses, and complaints relating to data protection.

- AOB:
  - XXX
  - XXX