National Research Ethics Committee

NREC-CT Meeting

6th August 2025

Attendance

Name	Role
Dr Christina Skourou	Chairperson, NREC-CT
Prof Lina Zgaga	Committee Member, NREC-CT
Mr Gerry Eastwood	Committee Member, NREC-CT
Dr Karina Halley	Committee Member, NREC-CT
Ms Deirdre McLoughlin	Committee Member, NREC-CT
Prof Andrew Green	Committee Member, NREC-CT
Dr Geraldine O'Sullivan Coyne	Committee Member, NREC-CT
Ms Paula Prendeville	Committee Member, NREC-CT
Mr Philip Berman	Committee Member, NREC-CT
Ms Chita Murray	Programme Manager, National Office for RECs
Dr Jane Bryant	Programme Officer, National Office for RECs
Ms Patricia Kenny*	Project Officer, National Office for RECs
Ms Emma Hefferenan	Project Officer, National Office for RECs
Ms Deirdre Ni Fhloinn	Project Officer, National Office for RECs
Mr Peadar Rooney	Project Officer, National Office for RECs

Apologies: Chanel Watson, Margaret Cooney, Deirdre Murray, Ann Twomey, Aine de Roiste, Patrick Forde

Quorum for decisions: Yes

Agenda

- Welcome & Apologies
- 2023-508482-32-00
- 2025-521278-32-00
- 2025-521627-78-00
- 2023-508804-39-00
- 2024-519655-28-00
- 2023-510384-36-00 SM-2
- 2023-508137-14-00 SM-4
- 2024-512412-22-00 SM-2
- 2024-513621-23-00 SM-10
- 2024-514135-17-00 SM-4
- 2023-506288-33-00 SM-4

- The Chair welcomed the NREC-CT D.

Applications

2023-508482-32-00

Institutions: Children's Health Ireland Temple Street

Study title: A Phase 3, randomized, double-blind, placebo-controlled, multicenter study of mavorixafor in participants with congenital and acquired primary autoimmune and idiopathic chronic neutropenic disorders who are experiencing recurrent and/or serious infections.

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required**

Part II Considerations

1. **Compliance with use of biological samples**

- The NREC-CT noted that in Section 2, it is stated that archived diagnostic samples will not be used, however other documentation states that a bone marrow sample taken within 9 months prior to screening can be used. The NREC-CT requested clarification on whether this sample will be accessed, or whether the report from this sample will be accessed for screening purposes.

2. **Financial arrangements**

- The NREC-CT noted the limit of 200 euro per visit, and requested clarification on whether that limit applies to the participant/caregiver/legal representative, or to each one individually. This should also be clarified for participants in the PISCF documents.

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

- The NREC-CT noted that the schedules of activities in the Main PISCF (pg. 8) and Parental PISCF (pg. 30) documents show three bone marrow aspirates, however the main text discusses two aspirates if participants have congenital neutropenia and have not had an aspirate performed in the 9 months prior to screening. The NREC-CT requests that the number of aspirates are consistent across all parts of the PISCF and Assent documents, to ensure this is clear to participants (Main PISCF, page 8; Parental PISCF, page 30).
- The NREC-CT noted that some of the language in the Assent Form may be too advanced and too long for 12-year-olds, and requested that it is simplified and shortened. Some examples of this can be found on page 2 (phrases such as "randomly decide", clarity on whether it is necessary to mention "the outside group of experts", and suggested that the section on dosing by weight could be simplified). The section on pregnancy should also be explained in language that a 12-15 year-old can understand (page 7).

- The NREC-CT noted the following sentence in the Assent Form: ‘you will not know if you are taking mavorixafor or placebo (the study medicine)’, and requested that this is rephrased to indicate that mavorixafor is the study medicine, and not the placebo. (Assent Form, page 2).
- The NREC-CT requested clarification on whether participants will be reconsented once they reach 16 years old, in line with the age of consent as detailed in the Health Research Regulations (Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018).
- The NREC-CT requested further information on how long the daily questionnaires and e-Diary will take to complete, and that this information is communicated to participants in all PISCF/Assent documents.
- The NREC-CT noted that the Principal Investigator will continue to review participants’ medical records after the study is over (Main PISCF, pg. 20; Parental PISCF, pg. 22), and requested that further information is given to participants on which records will be reviewed, and for how long after the end of the study.
- The NREC-CT noted the use of acronyms, such as ‘EOT’ in all three PISCF and Assent documents, and requested that they are removed or explained to participants.
- If applicable, the Sponsor is requested to submit any Part II documentation that require updates as a result of the Part I Assessment. Please include detail of the Part I consideration that triggered the update to the Part II 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.

4. Suitability of the investigator

- The NREC-CT noted the limited trial experience of the Principal Investigator at Children’s Health Ireland, and requested confirmation that supports will be available at site, if required.

2025-521278-32-00

Institutions: Connolly Hospital, Letterkenny University Hospital, Tallaght University Hospital, Our Lady of Lourdes Hospital

Study title: A Phase 2 Randomized, Double-blind, Placebo-Controlled Study of the Safety and Efficacy of MTX-463 in Participants with Idiopathic Pulmonary Fibrosis (IPF)

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required**

Part II Considerations

1. Recruitment arrangements

- The NREC-CT noted that the recruitment of individuals lacking capacity is listed as 'not applicable' in the Recruitment Arrangements Form (pg 3). The Committee requested that the intended procedures for the determination of functional assessment of capacity are outlined.
- The NREC-CT noted that translated documents will be provided to participants who do not speak English (Recruitment Arrangements Form, pg 2). The Committee requested that a translator also be considered for these participants to facilitate informed consent.

2. 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 a lack of information in the Main ICF regarding the objectives of the study (pg 2). The Committee requested further information is provided in all relevant PISCF's regarding the study objective using lay terminology.
- The NREC-CT noted an insufficient description of the study drug in the Main ICF (pg 2). The Committee requested further information on the study drug is provided in all relevant PISCF's including a lay description of the mechanism of action.
- The NREC-CT noted insufficient information was provided in relation to the control group in the Main ICF (pg 4). The Committee requested that further information regarding the control group be provided in the Main ICF so that participants can be fully informed.
- The NREC-CT noted a paucity of information regarding risks, side effects and results from both the animal and Phase 1 studies of the IMP (Main ICF pg7, 8). The Committee requested that a lay description of results from the animal and Phase 1 studies of the IMP be elucidated in all relevant PISCF's to facilitate a more comprehensive description of potential risks and side effects. Furthermore, that risks may be unknown because they have not been tested in this population could be further emphasised in all relevant PISCF's.
- The NREC-CT noted that the language used (eg miscarriage, abortion, congenital defects) in the Pregnancy ICF (pg 2) and Pregnant Partner ICF (pg2) may be quite concerning for pregnant individuals who have been exposed to the IMP. The Committee requested that supportive measures (such as an acknowledgement of the worry that may be caused) to be included in appropriate sections of the Pregnancy ICF and Pregnant Partner ICF.
- The NREC-CT noted that the risks section of the Pregnancy ICF (pg 3) and Pregnant Partner ICF (pg3) did not contain sufficient detail on the potential pregnancy risks associated with the IMP. The Committee requested that the potential pregnancy risks associated with the IMP be further elucidated in all relevant PISCF's.

- The NREC-CT noted that the sentence 'your primary care physician and other health care providers that provide health services to you in connection with the study' in the Pregnancy ICF (pg 5), which may lead a participant to incorrectly believe that their primary care physician is involved in the study. The Committee requested that reference to the participants primary care physician is listed separately in all relevant PISCF's to provide clarity for participants regarding the study care team.
- The NREC-CT noted that a courier service will have access to participants personal data (Main ICF pg 14, Pregnancy ICF pg 4, Pregnant Partner ICF pg 4). The Committee requested the role of the courier service be elucidated and an explanation provided for their requirement to access participants personal data.
- The NREC-CT noted that the participant will not have access to the study drug after completion of the trial. The Committee request that this is reconsidered, so that all participants benefiting from the study drug continue to have access.
- The NREC-CT noted reference to questionnaires in the Main ICF (pg6,13) however no questionnaires have been submitted for review. The Committee requested that all relevant questionnaires are submitted for review.
- The NREC-CT noted that personal data including 'data contained in your medical files' may be disclosed in identifiable form to a substantial list of entities (Main ICF pg 14). The Committee request further justification for the disclosure of identifiable personal medical records to entities beyond specific site staff and those required by law or regulation.

3. Suitability of the clinical trial sites facilities

- The NREC-CT noted that three of the sites will have unblinded staff prepare the infusions and administer them to participants. The Committee request clarification on the strategies that will be in place to mitigate the risk of unintentional unblinding.

4. Suitability of the investigator

- The NREC-CT noted that the medical council registration for all listed PI's appeared to be expired, missing or listed as not applicable. The Committee requested that medical council registration numbers and expiry dates are included in the CV's for all PI's.
- The NREC-CT note that the CV for the Principal Investigator in Letterkenny Hospital does not list previous experience of a PI role in a clinical trial. The Committee requested additional detail is provided regarding the support which will be provided to the PI by the Sponsor or study staff.

2025-521627-78-00

Institutions: Beaumont Hospital

Study title: 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:**

- Request for Further Information

- **Additional Information Required RFI**

Part II Considerations

1. Subject information and informed consent form

- The NREC-CT noted that the ICF_Main (pg. 1) includes the acronyms IRB & IEC. The Committee requests that the full term is included at the first use of these, and all, acronyms in the document.
- The NREC-CT noted that the ICF-Main (pg. 12) contains a grammatical error which may impede understanding. The Committee requests that the word 'you' is added before 'pass away' in the following sentence: "These calls will occur every 12 weeks after your last dose of the study drug(s) until you withdraw consent, complete three years of follow-up from your first dose, the study staff are not able to contact you or pass away, whichever comes first".
- The NREC-CT noted that the document 'Compensation for Trial Participants' (item #2) indicates that accommodation expenses will be paid for participants, in addition to travel, meals and a monetary payment. The ICF_Main (pg. 28) includes itemised costs, but does not refer to accommodation. In addition, the presentation of this information lacks clarity, and the euro amounts outlined are insufficient if intended to include the above-listed expenses. The Committee requests that the reimbursement amounts be outlined clearly (e.g. in a table), refer to and are sufficient to cover travel, meals, accommodation plus applicable monetary amounts.
- The NREC-CT noted discrepancies in the submitted documents with regard to the duration of data storage (see below examples). The Committee requests that storage periods for data (including samples) presented in the ICF_Main are correct and are aligned with other study documents.
    - ICF_Main (pg. 21) states: "Your samples may be kept for a maximum of 20 years as per GSK standard retention period from the end of the entire study after which time your samples will be destroyed"
    - ICF_Main (pg. 31) section 'How Long Will Your Data Be Used?' states 'GSK must keep your coded data from research studies for at least 30 years'
    - Protocol (pg. 115) states for example 'Records and documents, including signed ICF, pertaining to the conduct of this study must be retained by the investigator for a minimum period of 25 years from the issue of the final CSR/equivalent summary, or in accordance with applicable law, whichever is longer'.
- The NREC-CT noted that the ICF_Main (pg. 24) states that 'GSK may "anonymise" a copy of your coded personal information'. The Committee requests that the processing of anonymising data is included as an explicit consent item in the informed consent section on pg. 32 of the ICF_Main as per the Health Research Regulations (Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018)
- The NREC-CT noted that the future use of data/samples is not described in line with regulations/best practice, as follows below.
    - ICF_Main (pg. 24) section 'Further Use Of Coded Samples And Data' states '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'.
- ICF_Main (pg. 33) includes a consent item which states 'Please indicate if your coded samples and data can be used by GSK and others, such as universities or other companies, for future research NOT related to this study as described in this form

The NREC-CT requests that future use of samples/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,

- future research 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 if the future research is not defined, 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 that the ICF_Pregnant Participant or Pregnant Partner (pg. 1) includes the following advice: 'Please ask the study doctor or the study staff to explain any words or information that you do not understand'. The Committee requests that this advice be amended to the wording which is used in the ICF_Main (pg. 1) which states 'The study staff will explain the study and the information in this consent form to you. Please ask about anything you do not understand'.
- The NREC-CT noted that the ICF_Pregnant Participant or Pregnant Partner (pg. 2, section ''What is expected from you?') includes wording which is not applicable in this context. The Committee requests that the following amendments are made:
  - Remove the words 'you or' from 'you or your partner will continue with the study assessments/procedures as in the main study informed consent form'
  - Remove the statement 'Your partner may request to continue receiving the study drug'
- The NREC-CT noted that the ICF_Pregnant Participant or Pregnant Partner (pg. 2) states: 'You and your doctor will decide the medical care you and/or your baby will receive'. The Committee requests to view a copy of a General Practitioner (GP) letter which is intended for the GP of the pregnant partner, as the data being sought includes results of tests, details of procedures, medicines taken etc.
- The NREC-CT noted that there are multiple references throughout the submitted documents of the value of collecting participant ethnicity data to observe variations in response to the study drug. The ICF_Pregnant Participant or Pregnant Partner (pg. 3) states that 'The study doctor and other study staff will collect data that can identify you and your baby. This may include…' and lists the data points to be collected. The Committee seeks justification as to why 'ethnicity' has not been included in this list.
- The NREC-CT noted that the ICF_Pregnant Participant or Pregnant Partner (pg. 4) refers to the collection of a number of data points including the Apgar score. The

Committee requests that an explanation of the Apgar test/Agar score be included in the document.

- The NREC-CT noted that the ICF_Pregnant Participant or Pregnant Partner (pg. 6, section 'Annex 1 Additional information about how your coded data may be used') advises the reader to 'Go to the Main Study Informed Consent' to locate the information. Since the pregnant partner will not have received the ICF_Main, the Committee requests that all information which is relevant to the pregnant partner is included in the ICF_Pregnant Participant or Pregnant Partner.
- The NREC-CT noted that the ICF_Pregnant Participant or Pregnant Partner (pg. 6, section 'Why will your and your baby's coded data be collected?') advises the reader to 'Go to the Main Study Informed Consent' to locate the information. The ICF_Main then indicates that samples will be retained for 20 years (pg. 21) and that data may be retained for 30 years (pg. 31). Please note that, under data protection legislation in the Republic of Ireland, individuals gain the right to provide consent for the processing of their personal data, and must be reconsented, once they reach the age of 16. Prior to this age, parental or guardian consent is required. Refer to the Health Research Regulations (Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018) and the HSE National Policy for Consent in Health and Social Care (pg. 64).
- The NREC-CT noted that the ICF_Pregnant Participant or Pregnant Partner (pg. 7) includes the consent line item 'For pregnant participant: I agree that the study doctor may tell my doctor that me and my baby are taking part in a study'. The Committee requests the addition of the same consent line item, for use by the pregnant partner.
- The NREC-CT noted that the ICF_Genetic Research (pg. 2) includes the following statement which is not in line with best practice/regulations: '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'. The NREC-CT requested that future use of samples/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 if the future research is not defined, 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 in the ICF-Genetic (pg. 4, section 'What are the potential risks of genetic research?) that only the risk of giving a blood sample are referred to. The Committee requests that additional detail is included, outlining the potential risks entailed of the genetic analysis being performed.
- 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.

2023-508804-39-00

Institutions: Children's Health Ireland

Study title: A Phase 3b Extension Study to Evaluate the Long-Term Safety of Vedolizumab Subcutaneous in Pediatric Subjects With Ulcerative Colitis or Crohn's Disease

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

- 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 notes that the future use of data / samples is not described in line with regulations / best practice on pg. 1 of SIS and ICF Optional Future Research and pg. 12 of SIS and ICF Parent. The Committee requests that future use of samples / 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/

  Please also update the future research Section 4 of Compliance for use of Biological Samples document to align.

- The NREC- CT notes that SIS and ICF Optional Future Research (pg. 1) states '*Takeda will also use study data to create anonymised data*". The Committee requests 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 Articles 4(2) and 6 of the General Data Protection Regulation (GDPR).
- The NREC-CT notes that the SIS and ICF Assent 13-15 (pg. 17) Consent form states "I have been informed that my leftover samples collected in this study may be used by the sponsor, TDC Americas, Inc., its agents, and its affiliated companies for future research which may be about the diseases, conditions or drugs that may, or may not, be included in this study" however this is not described in line with best practice/regulations (such as the Health Research Regulations (Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018). The Committee notes there is no reference to future research in the information sheet itself. The Committee requests that the information sheet and consent form sections be updated to provide detail on the future research ensuring that it is described in line with best practice/regulations including that:
    - a) it should be made optional
    - b) 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,
    - c) and/or that an option is provided to enable participants to consent to be contacted in the future about other research studies,
    - d) optional future research is made into a separate and explicit consent item in the Informed Consent section of the SIS and ICF Assent 13-15 with separate participant information section and signatures section, so it is distinct from the main assent 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 requested that the SIS -ICF Main (pg. 1), SIS -ICF Assent 13-15 (pg. 1) and SIS -ICF Parent (pg. 1) be updated to include the EU clinical trial number for participants**.**
- The NREC-CT requests that SIS-ICF Parent and SIS -ICF Optional Future Research be updated to clarify that once the participant turns 16 years old they will be asked to consent for their continued participation in the study and for the processing of their personal data and use of biological samples for secondary research.
- The NREC-CT requests that the SIS- ICF Main (pg. 21) and SIS-ICF Parent (pg. 21) be updated to remove reference to ethics committees inspecting medical records, as the NREC-CT does not have, and is unlikely to have, access to medical records of participants.
- The NREC-CT notes SIS -ICF Assent 13-15 year old (pg. 13) Pregnancy and Sex section states "We realise this is sensitive and we are not assuming you are

sexually active." The Committee requests that the SIS -ICF Main and SIS -ICF Parent pregnancy sections be updated to include this introduction as well.

- The NREC-CT notes that the SIS-ICF Parent (pgs. 1 and 2) in several places states that the child is being asked to take part in the research. The Committee requests that these be rephrased to say that "you and your child" are being asked to take part in the research.
- The NREC-CT requests that the SIS-ICF Parent pg 10 be updated to include a to explain that consents taken as part of the study will not replace consents which are part of standard medical practice, for example, immediately before undergoing a colonoscopy.
- The NREC-CT requests that the SIS-ICF Assent 7-12 yr old be shortened and the language simplified.
- The NREC-CT notes that the SIS-ICF Pregnant Partner (pg. 6) intends to record the "Partner's Signature, on behalf of herself and her baby". The Committee requests that reference to "her baby" be removed, as data processing under GDPR applies to data collected from birth onwards.
- The Committee requests that a SIS -ICF Pregnant Participant be provided for review.

2024-519655-28-00

Institutions: Cork University Hospital, Mater Misericordiae University Hospital, University Hospital Waterford, Midland Regional Hospital, Mater Private Hospital, University Hospital Limerick, St James's Hospital

Study title: OPTIMA YOUNG: Optimal Personalized Treatment of early breast cancer using Multi-parameter Analysis: focus on younger women

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required RFI**

Part II Considerations

1. Financial arrangements

- The NREC-CT noted that compensation will not be offered to participants. The NREC-CT noted that participants will not be reimbursed for expenses and requested that participants are reimbursed for all reasonable out-of-pocket expenses and that this is detailed in the OPTIMA Young ICF, 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.

2. Recruitment arrangements

- The NREC-CT noted that in the website, the following terms/phrases have not been explained: “clinico-pathological”, “speed cancer progression”, “guided by a Prosigna genomic test”, “medico-economic costs”, “toxicities”. The NREC-CT requests that these terms are explained in lay terminology on the website.
- The NREC-CT noted the phrase “Chemotherapy is risky” on the website. The NREC-CT notes that this terminology may cause undue concern. The NREC-CT requests that the risk is explained in lay terminology.
- The NREC-CT noted that a translator will act as an impartial witness for people who don’t speak English. The NREC-CT requests that a translated version of all ICFs and applicable documents be provided for participants who cannot speak English.
- The NREC-CT noted some typos in the website on page 2 such as “the degree activity of some of these genes.” This should be corrected to “the degree **of** activity of some of these genes”. On page 3, the statement “this is known metastatic or secondary” should be corrected to “this is known **as** metastatic or secondary”.
- The NREC-CT noted that incapacitated adults will not be recruited. The NREC-CT requests justification for why they are excluded from the trial.

3. 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 reference on page 2 of the OPTIMA Young ICF to “the trusted support person you have designated”. The NREC-CT requests more clarification on this, specifically but not limited to the below. The NREC-CT requests that this information is clarified in the ICF in the appropriate section.
  - does the “trust support person” have to be specifically designated?
  - can “the trusted support person” can change for each appointment?
  - does the “trusted support person” have any decision-making capability for the participant?
- The NREC-CT noted on page 5 of the OPTIMA Young ICF that “The standard treatment for this type of cancer is surgery, followed by chemotherapy, then what is known as optimal hormone therapy, i.e. a combination of tablets and injections to stop the ovaries producing hormone (i.e. stopping menstruation).” The NREC-CT requests clarification if radiotherapy is a potential treatment option for participants in this trial as part of standard treatment.
- The NREC-CT noted on page 11 of the OPTIMA Young ICF “Your study doctor will ask for your permission to monitor your pregnancy and will transmit certain information to the sponsor." The NREC-CT requests clarification if a specific pregnancy consent ICF is available for review by the NREC-CT and if it is not currently available, the NREC-CT requests that it be made available for review at the next substantial modification. The NREC-CT requests clarification on how long the pregnancy follow-up time period will be, and what information will be collected.

- The NREC-CT requests that the following words in the OPTIMA Young ICF be added to the glossary and explained in lay terminology.
    - Efficacy (pg. 5)
    - Osteoporosis (pg. 5)
    - Cardiovascular disease (pg. 5)
    - Perception (pg. 5)
    - Toxicities (pg. 5)
    - Genomic (pg. 3)
    - Constitute (pg. 5)
    - Methodological (pg. 6)
    - Incompatibility of logistics (pg. 6)
    - Trial methodology (pg. 8)
    - Non-exhaustive (pg. 8)
- The NREC-CT requests that the following words in the OPTIMIZE ICF be added to the glossary and explained in lay terminology.
    - Autonomy
    - Contraindication
- The NREC-CT requests that the explanation for "randomisation" in the OPTIMA Young ICF and OPTIMIZE ICF be explained in layman's terms. In specific the NREC-CT requests
    - Please use the term 'participant' instead of 'subject'
    - Remove "(like flipping a coin or drawing of lots)" and instead give direct odds like 1 in 2 chance or 50/50 chance of being in one group or the other.
    - Explain the justification for randomisation using clear lay terminology for why this decision is done randomly instead of participant picked by the study doctor.
- The NREC-CT noted that in both the OPTIMA Young ICF (pg. 26) and the OPTIMIZE ICF (pg. 17), there is space for a third additional signature for an impartial witness. The NREC-CT requests information be added to all relevant PISCF's explaining the context where an impartial witness signature would be needed (as per CTR: Annex I,L 62(b)).
- The NREC-CT noted some of the language of the OPTIMA Young ICF has unclear meaning, and requests that they be rewritten using simpler language which is accessible to the layperson.
    - Page 10: "Today, it remains impossible to affirm that a woman receiving the trial treatments can start a pregnancy without running risks"
    - Page 11: "To date, there is no information to suggest that the small amounts of treatment that may be excreted in breast milk are harmful to a child."
- The NREC-CT noted the following statement on page 13 of the OPTIMA Young ICF: "your sample will…be used for further research into breast cancer, and in particular into biomarkers*, i.e. molecular factors that can predict the course of the disease"**.** The NREC-CT requests that this is rewritten as "…be used for further research into breast cancer, and in particular into biomarkers*, i.e. molecular factors that can predict the course of breast cancer".
- The NREC-CT noted the following statement on page 10 of the OPTIMIZE ICF: "Data relating to your identity (first name, surname, medical record number, etc.) is

never collected by Unicancer." The NREC-CT also noted that page 10 of the OPTIMIZE ICF states "Unicancer is responsible for processing your data in the context of this sub-study" and the section "Who has access to your personal data?" states "2. the Unicancer teams in charge of this trial". These statements do not align. The NREC-CT requests that the section "Part 2: Information about your personal data" be reviewed for clarity and rewritten to remove contradictory statements.

- The NREC-CT noted that page 17 of OPTIMA Young ICF, states "The personal data* about you collected by Unicancer includes administrative and demographic data (e.g. gender, age, etc.) and health data, including genomic data, strictly necessary for the conduct of the trial in which you are participating" and underneath it states "Unicancer never collects data relating to your identity (first name, surname, medical record number, etc.)" These statements do not align. The NREC-CT requests that the section "Part 2: Information about your personal data" be reviewed for clarity and rewritten to remove contradictory statements.
- The NREC-CT noted that page 27 of the OPTIMA Young ICF states "We invite you to read the corresponding information leaflet, to discuss your participation in this optional research with your study doctor and, if you wish to participate, to sign the corresponding consent form. The use of your data for this research is optional and does not affect your participation in the OPTIMA-YOUNG trial. In other words, if you do not consent to this optional research, you will still be able to answer the OPTIMA-YOUNG questionnaires on WeShare." The NREC-CT requests clarification if the WeShare programme is optional, if this is optional, the NREC-CT requests that an optional consent box is added. If participation in the WeShare programme is not optional, the NREC-CT requests that appendix 2 is rewritten to ensure that mandatory participation in the WeShare programme is clearly indicated in the OPTIMA Young ICF.

2023-510384-36-00 SM-2

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

Study title: A Phase 3 Study of Teclistamab in Combination With Lenalidomide and Teclistamab Alone versus Lenalidomide Alone in Participants With Newly Diagnosed Multiple Myeloma as Maintenance Therapy Following Autologous Stem Cell Transplantation – MajesTEC-4

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Favourable

2023-508137-14-00 SM-4

Institutions: Beaumont Hospital

Study title: A Phase 2, Single-Arm, Open-Label Extension Study, Evaluating the Long-Term Safety and Clinical Efficacy of SAR447537 (INBRX-101) in Adults with Alpha-1 Antitrypsin Deficiency (AATD) Emphysema

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Favourable

2024-512412-22-00 SM-2

Institutions: Children's Health Ireland Temple Street, Children's Health Ireland Crumlin

Study title: A Phase 3 study to evaluate the efficacy of INM004 (Shiga antitoxin) in pediatric patients with Hemolytic Uremic Syndrome associated to infection by Shiga toxin-producing Escherichia coli

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**

- 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 an interpreter will be utilised for families who do not speak English (Clarification Letter- Informed Consent Process, pg 2). The Committee requested that translated documents (in addition to an interpreter) be provided for families who do not speak English to ensure informed consent.
- The NREC-CT noted that there is no EU-CT number listed on the Clarification Letter- Informed Consent Process. The Committee requested that the EU-CT number is included on all documents pertaining to the trial.

2024-513621-23-00 SM-10

Institutions: Beaumont Hospital, Tallaght University Hospital, Cork University Hospital, Mater Misericordiae University Hospital

Study title: TACTI-004, a double-blinded, randomized phase 3 trial in patients with advanced/metastatic non-small cell lung cancer (NSCLC) receiving eftilagimod alfa (MHC class II agonist) in combination with pembrolizumab (PD-1 antagonist) and chemotherapy

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Favourable

2024-514135-17-00 SM-4

Institutions: Cork University Hospital, Beaumont Hospital, University Hospital Waterford, University Hospital Galway

Study title: A Phase 3, Randomized, Double-Blind, Placebo-Controlled Study of Povetacicept in Adults with Immunoglobulin A Nephropathy (RAINIER)

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
• 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 page 21 of the Main ICF states “You have the right to request that your data is deleted, unless this request would make it impossible or make it very difficult to conduct the research. Each request will be considered on a case by case basis”. Please amend this text to align to include clarification under which circumstances this right to request deletion of data would be denied. • The NREC-CT noted that page 21 of the Main ICF states “If you consent, we (the sponsor) will use your samples and data collected for this study for research purposes, in accordance with applicable Irish data protection laws and ethical approval”. The NREC-CT requested that future use of samples / 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). Specifically,

- 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 if the future research is not defined, that an option is provided to enable participants to consent to be contacted in the future about other research studies,
- 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/

2023-506288-33-00 SM-4

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

Study title: MK-5684-01A Substudy: A Phase 1/2 Umbrella Substudy of MK-5684-U01 Master Protocol to Evaluate the Safety and Efficacy of MK-5684-based Treatment Combinations or MK-5684 Alone in Participants With Metastatic Castration-resistant Prostate Cancer (mCRPC) (OMAHA-01A)

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Favourable

AOB

- None