

# National Research Ethics Committee

## NREC-CT A Meeting

7<sup>th</sup> January 2026

### Attendance

Name	Role
Prof. Alistair Nichol	Chairperson, 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
Dr Dawn Swan	Committee Member, NREC-CT A
Mrs Erica Bennett	Committee Member, NREC-CT A
Dr David Byrne	Committee Member, NREC-CT A
Dr Sean Lacey	Committee Member, NREC-CT A
Ms Mandy Daly	Committee Member, NREC-CT A
Ms Muireann O'Briain	Committee Member, NREC-CT A
Ms Dympna Devenney	Committee Member, NREC-CT A
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*
Ms Chita Murray	Programme Manager, National Office for RECs
Rachel McDermott	Project Administrator, National Office for RECs

Drafted minutes

**Apologies:** Margaret Cooney, Darren Dahly, Aisling McMahon

**Quorum for decisions:** Yes

### **Agenda**

- Welcome & Apologies
- 2025-523686-15-00
- 2024-513445-37-00
- 2023-509859-13-00 SM-10
- 2023-504816-14-00 SM-22
- 2024-518296-56-00 SM-5
- 2024-519128-26-00 SM-1
- 2023-507536-21-00 SM-7
- AOB

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- The Chair welcomed the NREC-CT A.
    - The minutes from the previous NREC-CT A meeting on 19<sup>th</sup> November 2025 were approved.
    - The NREC Business Report was discussed and noted.
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## Applications

**2025-523686-15-00**

Institutions: Mater Misericordiae University Hospital

Study title: A Phase 1 First-in-Human, Open-Label, Multicenter Study of OP-3136 in Adult Participants with Advanced or Metastatic Solid Tumors

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 was noted that Part 1A of the study includes patients with breast cancer, prostate cancer and NSCLC. However, NSCLC patients have not been included in the Part 2A group. Please provide clarification as to why NSCLC participants have not been included in the Part 2A group.

### Part II Considerations

#### 1. Financial arrangements

- The NREC-CT noted the advanced nature of the potential participants disease progression, and the potential need for supportive care traveling to the site for clinic visits. The NREC-CT requested that reimbursement of travel, accommodation and meal expenses are considered for carers of participants and, if included, that it is elucidated in the P1\_Compensation for trial participants template and relevant PISCFs.

#### 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](mailto: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 PISCF, in particular the study aims, risks, schedule of activities, future research and the consent form are not well written. Article 29 of the Clinical Trials Regulation (CTR) states that informed consent “be kept comprehensive, concise, clear, relevant, and understandable to a layperson”. The PISCF as written does not provide the required conciseness, clarity or understandable to a layperson and should be rewritten with these in mind.
- The NREC-CT noted the statement on page 4 of the Main PISCF “This committee will watch over this study while you are in it.” The NREC CT requested this statement is amended to align with trial oversight under the CTR, and at a National level.
- The NREC-CT noted on page 5 of the Main PISCF the sixteen bullet points that follow “The study aims to find out the following:” contains extensive repetition. The NREC-CT requests that the bullet points are rewritten to reduce the repetition and to be more appropriate for a lay audience.
- The NREC-CT noted the statement on page 5 of the Main PISCF “Monitor and document new bone lesions and PSA response for participants with mCRPC” The NREC-CT requests that when abbreviations are first used, they are accompanied by an explanation.
- The NREC-CT noted the statement on page 8 and page 9 of the Main PISCF in the Blood Tests section “If you stay on the study for 6 months, the approximate maximum amount of blood drawn will be...” The NREC-CT noted the maximum length of the study is stated in the MISCF as 28 to 30 months. The NREC-CT requests that the total maximum blood volume drawn that could be sampled over that period is included in this section. If no more blood samples will be taken after 6 months of sampling, this needs to be explained in lay terms in the blood tests section.
- The NREC-CT noted the statement on page 10 of the Main PISCF “You will also have a fresh tumour biopsy performed approximately 7 to 8 weeks after you start on study treatment, and after your last dose” These two additional tumor biospies need additional explanation in the text as they can be a significant burden for participants. The NREC-CT requests clarification in the text if these biopsies are mandatory or optional and reference the risks of biopsy on page 34 of the Main PISCF.
- The NREC-CT noted the statement on page 10 of the Main PISCF “Patient Reported Outcome Questionnaires: (Breast Cancer Patients Only)” The NREC-CT requests clarification as why only breast cancer participants are completing these questionnaires.
- The NREC-CT noted the statement in the schedule of activities of the Main PISCF “Blood for PBMCs for H3K23Ac assay” and requests that this is explained in lay terminology.
- The NREC-CT noted on page 23 of the Main PISCF “...by looking at your hospital records or publicly available sources such as national registries, newspaper obituaries, and social networking websites.” The NREC-CT requests the removal of the word “obituaries” from this sentence.
- The NREC-CT noted on page 24 of the Main PISCF “Lower back pain irradiating to leg on one side”. The NREC-CT requests that this is rewritten as “Lower back pain travelling to leg on one side”

- The NREC-CT noted on page 24 of the Main PISCF “Sudden weakness”. The NREC-CT noted that peripheral neuropathy is not always sudden. The NREC-CT requests that this is rewritten to include information about weakness developing over time.
- The NREC-CT noted on page 25 of the Main PISCF “Thick, whitish vaginal discharge and candidiasis (infection). This implies that there is two different pathologies occurring, thick whitish vaginal discharge and a different issue of candidiasis. The NREC-CT requests that this is rewritten to be clear that this is one pathology in lay terms and also use the common term for candidiasis, thrush.
- The NREC-CT noted on page 25 of the Main PISCF the section “**Risks of Palazestrant**” is written in a different format to the other risks sections. The NREC-CT requests that this section is rewritten to align with how the other risks are presented, using Very common, Common, Uncommon, Rare, Very Rare, or Serious headings as appropriate and presenting risks as 1 in X number of people instead of percentages.
- The NREC-CT noted on page 26 of the Main PISCF “Out of 240 participants treated with palazestrant alone at different doses, 5 participants (2.1%) experienced abnormally low neutropenia (Grade 3), and 20 participants (8.3%) have had dangerously low (also known as Grade 4 neutropenia). This was generally noticed in the participants within the first 6-8 weeks of treatment with palazestrant and most resolved with treatment discontinuation or interruption. The time to resolution of Grade 4 neutropenia ranged from approximately 5 to 42 days. Three (3) out of 240 participants (1.2%) who had neutropenia with serious infections died” The NREC-CT requests that this section is rewritten to explain in lay terms what Grade 3 versus grade 4 neutropenia is. Furthermore, the NREC-CT noted an error in phrasing, given that neutropenia is low count of neutrophils; low neutropenia is considered to be a tautology. The NREC-CT requests that this is corrected and rewritten in clear lay terminology.
- The NREC-CT noted the statement on page 34 of the Main PISCF “Therefore, it is not expected you will be exposed to any additional risk from radiation exposure as compared to if you were not participating in this trial and receiving routine treatment. The NREC-CT notes that as per the Site suitability assessment, these participants are getting increased scans compared to standard of care at the sites in Ireland. This should be clearly stated in the PISCF, to ensure informed consent.
- The NREC-CT noted on page 36 of the Main PISCF the section “**Are there any other treatments?**” details the treatment options for breast cancer and prostate cancer but contains no details for the options of treatment for lung cancer. The NREC-CT requests that this is rewritten to include options for lung cancer such as chemotherapy drugs Docetaxel or Gemcitabine or Vinorelbine as appropriate for Ireland.
- The NREC-CT noted on page 35 of the Main PISCF “Highly effective contraception methods include: Having one of the following procedures at least 6 weeks before starting study treatment: bilateral oophorectomy (removal of both ovaries), hysterectomy (removal of the uterus or womb) bilateral salpingectomy (removal of both fallopian tubes) Bilateral tubal ligation (both fallopian tubes have been cut, tied, or blocked) Non-hormonal intrauterine device (IUD) Total abstinence Vasectomised partner” The NREC-CT requests that this list is ordered with the

non-surgical methods listed first, similar to how the “if you can get others pregnant” section is listed.

- The NREC-CT noted on page 35 of the Main PISCF “If you, your unborn child, or your newborn child have a health problem during this time you must tell the study doctor, directly or through your doctor or obstetrician/gynaecologist, and this will be followed until the problem is resolved or becomes stable.” The NREC-CT also noted the submission of the pregnant partner PISCF, the NREC-CT requests a separate pregnant participant PISCF is provided, or alternatively that specific consent items are added to the Main PISCF regarding pregnancy data collection.
- The NREC-CT noted the statement on page 36 of the Main PISCF “You will still need to pay for any medical care not associated with this study. You (and/or your insurance company or government health plan) will be responsible for costs of care that are associated with usual cancer care. This could include any non-study procedures and/or non-study medication that are needed while you are in the study. You should contact your medical insurance company to find out if they will pay for routine medical care while you are in this study.” The NREC-CT requests that this section is rewritten to be appropriate to the Irish healthcare setting.
- The NREC-CT noted the statement on page 40 of the Main PISCF “understand that this study may only be performed by collecting and using my health data. Therefore, by signing this form, I specifically give permission for my data to be checked, transferred, and processed as follows: The authorised representatives of Olema Pharmaceuticals, Inc., the NREC, and inspectors for regulatory authorities may review my health data by directly accessing my health records. Study data, including my coded health data, may be used and shared for legitimate study and scientific purposes.” . The NREC-CT consider this to be overly broad and not specific to the clinical study being undertaken, and requests that this is rewritten to be specific to the clinical study.
- The NREC-CT noted the statement on page 38 of the Main PISCF “Some of your study data will be sent overseas. The data protection laws governing data access and use in other countries may not be the same as those in Ireland. If you have any questions about this, discuss them with your study doctor.” The NREC-CT request that appropriate safeguards (such as the use of standard contractual clauses) be implemented to ensure that data protection standards are equivalent to the standards of GDPR and the Health Research Regulations (Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018) when data/samples are moved outside the EEA, and that the Statement of Compliance for Data Protection is aligned with all relevant ICF’s.
- The NREC-CT noted the statement on page 37 of the Main PISCF “The following people may review your health records to make sure that the study is being run as planned, and that the data collected about you are correct: Government health agencies, regulatory agencies, and their staff. In Ireland this is the Health Products Regulatory Authority (HPRA). Olema staff or designee observing the study (monitors and auditors), including any contract research organisations (CRO). Novotech Clinical Research (Cyprus) Limited is the CRO managing the study in Ireland. Members of the NREC. Contractors and consultants working for Olema and for health authorities. Olema representatives, employees, and Olema’s affiliates, authorised agents, and representatives, who may be with the study

monitors and auditors for quality and training purposes.” The NREC-CT requests that this is revised and divided to provide clarity to the participant regarding access to personal data, and access to pseudo- anonymised or anonymised data.

- The NREC-CT noted the statement on page 34 of the Main PISCF “You should be aware that genetic information may influence insurance companies and/or employers regarding your health or have a negative impact on family or other relationships. Genetic information, like DNA, is unique to you, and may be used to identify you and possibly your family members. There is a risk of potential loss of privacy, as new ways of tracing genetic information are being developed that may make re-identification of genetic information possible.” The NREC-CT requests that this paragraph is rewritten to note any steps that will be taken to safeguard that information under GDPR.
- The NREC-CT noted that page 21 and 34 of the Main PISCF 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 is 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-pppqs/hse-national-policy-for-consent-in-health-and-social-care-research>
- The NREC-CT noted that the future use of data and samples (including genetic research) is not described in line with regulations / best practice on page 21 “We would like to know if you allow the use of any leftover blood and tumour tissue samples for future research. This means that the samples may be tested to: Learn more about cancer and other diseases. Develop new drugs, devices, tests, or processes, including commercial products. Other purposes that are not yet known” and on page 38 “The results may also be analysed again at a later date or may be combined with the data of other studies. Olema and people who work with Olema may use the results of this study to understand the disease better or to review the safety or effectiveness of the study drug, or for other research purposes.” and on page 40 “Olema Pharmaceuticals, Inc. may use samples including tumour and blood samples for additional research” and on page 40 “Olema Pharmaceuticals, Inc., or their representatives, would like you to allow them to use your leftover blood and tumour tissue samples for future research that may help understand more about breast cancer and other diseases” of the Main PISCF. The NREC-CT requested that future use of samples and personal data is sufficiently explained to participants in the PISCF documents so as to constitute broad informed consent,

as required under the Health Research Regulations (Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018). Furthermore,

- it should be confined to a specified disease, related diseases or drug under study in this trial. Consent can only be obtained where future use of samples and data is defined such that participants are fully informed,
  - and/or that an option is provided to enable participants to consent to be contacted in the future about other research studies,
  - optional future research is made into a separate and explicit consent item in the Informed Consent section of the Main PISCF, with separate participant information section and signatures section, so it is distinct from the main consent to participate in the research.
  - The PISCF should also make it clear to participants that subsequent research ethics review will be sought for specific research once clearly defined. For further guidance, please see: NREC guidance on use of biological samples and associated data - <https://www.nrecoffice.ie/guidance-on-use-of-biological-samples-and-associated-data/>
- The NREC-CT noted that the Main PISCF has used a bundled approach to consent in the Informed Consent Section of the PISCF and requested that a layered approach to consent is used (in that each consent item is listed and a box for participants to provide their initials is included alongside each consent item) in line with HSE policy Please see HSE National Policy for Consent in Health and Social Care Research (V2.1, 2025). Dublin: Health Service Executive [www2.healthservice.hse.ie/files/157/](http://www2.healthservice.hse.ie/files/157/)
  - The NREC-CT noted that page 41 of the Main PISCF and page 7 of the Pregnant Partner PISCF includes a witness signature line. The NREC-CT requests information be added to all relevant PISCF's explaining the context where a witness signature would be needed (as per CTR: Annex I,L 62(b)).
  - The NREC- CT noted that pages 21,37,38 and 40 of the Main PISCF and page 4 of the pregnant partner PISCF refers to 'coded data' and requested that it is clarified in all relevant PISCFs whether this refers to use of 'pseudonymised' or 'anonymised' data. If 'coded data' refers to anonymised data, the NREC-CT 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 on page 3 of the Main PISCF "You will not be paid, but you may get travel costs back" and on page 36 of the Main PISCF "You will not be paid for expenses like lost wages, disability, discomfort due to injury, or meals obtained while waiting at the study clinic. You may be reimbursed for the reasonable cost of travel required to participate in this study, such as bus, train, and taxi fares." The NREC-CT noted in the Compensation for Trial Participants document submitted, that Travel expenses, accommodation expenses and meal expenses will be

offered to participants with not conditions on the payment of compensation. The NREC-CT requests that this is rewritten to align with the Compensation for Trial Participants documentation and encourages that participants are compensated for all out-of-pocket expenses as a result of taking part in the trial.

- The NREC-CT noted on page 3 of the Pregnant Partner PISCF “This means that you, your insurance company, or your government’s health plan may have to pay for these.” The NREC-CT requests that this is rewritten to be applicable to the Irish healthcare context and remove reference to a “government’s health plan”.
- The NREC-CT noted on page 4 of the Pregnant Partner PISCF “Olema and people who work with Olema may use the results of this safety monitoring to understand the disease better, to review the safety or effectiveness of the study drug, or for other research purposes”. The NREC-CT noted that the purpose of the safety monitoring consentis specifically regarding the pregnant partner and the foetus/child. The NREC-CT requests that is rewritten to ensure clarity for the pregnant participant that this is safety data monitoring for the pregnancy and child only.

## 2024-513445-37-00

Institutions: Beaumont Hospital, University Hospital Galway

Study title: A prospective, open-label, randomized, multicenter phase-III trial to evaluate the efficacy of pirtobrutinib and epcoritamab compared with R-(mini)-CHOP for treatment of patients with Richter Transformation - CLLRT2

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 participants will not be reimbursed for expenses. The NREC-CT noted that the participants of this clinical trial will be advised not to drive as per the SPMC for pirtobrutinib “Jaypirca has a minor influence on the ability to drive and use machines. Fatigue, dizziness, and asthenia have been reported in some patients during treatment with Jaypirca and should be considered when assessing a patient’s ability to drive or operate machines”. Taking this into consideration, the committee requested that participants are reimbursed for all reasonable out-of-pocket expenses including travel (Main PISCF page 16), to ensure travel is not an undue burden and 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. 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](mailto: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 overly complicated language is used in the Main PISCF. Article 29 of the Clinical Trials Regulation (CTR) states that informed consent “be kept comprehensive, concise, clear, relevant, and understandable to a layperson”. The PISCF as written does not provide the required conciseness nor is it easily understandable to a layperson and should be rewritten with this in mind. This includes but is not limited to the following:
  - Page 3 “about the efficacy and tolerability of drugs”
  - Page 4 “optimise the response rates and tolerability of RT treatment,”
  - Page 4 “proliferation of CLL cells”
  - Page 5 “Cytogenetics &”
  - Page 5 “serum parameters thymidine kinase”
  - Page 4 “Efficacy and safety of the combination of pirtobrutinub and epcoritamab...”
  - Page 5 “No contraindications”
  - Page 5 “Gene sequencing to identify new prognostic factors”
  - Page 6 “In the standard arm, the treatment regimen consists of 6 cycles of R-(mini)-CHOP (21-day cycles) with radiation of the remaining PET-positive lesions”
  - Page 6 “Consolidation with allogeneic stem cell transplantation is permitted in both arms”
  - Page 7 “Epcoritamab is administered subcutaneously”
  - The NREC-CT requests that the PISCF is reviewed in its entirety for technical language and be rewritten for the participants in lay language.
  - The NREC-CT also request that the term participant is used throughout all PISCF and participant facing material to refer to the clinical trial participant, instead of “patient”.
- The NREC-CT noted that this study is a phase 3, the NREC-CT requested that a brief lay summary of the results of the phase 1 and phase 2 studies should be added to the Main PISCF.
- The NREC-CT noted the schema on page 3 of the Main PISCF, and that this is the same schema as Figure 2 in the Protocol. This schema is considered by the

NREC-CT to be overly complicated and not suitable for a lay audience and requests that it is redesigned to be appropriate for a lay participant.

- The NREC-CT noted the submission of quality-of-life questionnaires as part of the application. The NREC-CT note there is no detail provided regarding the requirement to complete these questionnaires as part of the study. The NREC-CT requests that the frequency, timing, burden, and presentation of the quality-of-life questionnaires are detailed clearly and in lay language in the Main PISCF.
- The NREC-CT noted that in the SPMC for pirtobrutinib “Jaypirca has a minor influence on the ability to drive and use machines. Fatigue, dizziness, and asthenia have been reported in some patients during treatment with Jaypirca and should be considered when assessing a patient’s ability to drive or operate machines”. The NREC-CT requested that if participants cannot drive during the study, this could be a significant burden for participants depending on their travel distance to the site and the public transport options available to the participant. The NREC-CT requests that this is clearly and explicitly detailed in the PISCF.
- The NREC-CT noted the statement on page 5 of the Main PISCF that a blood sample will be taken for “scientific research programs and experimental studies”. The NREC-CT requests that further details are provided in lay terminology in the PISCF, and that consent is sought if provision of this blood sample is optional.
- The NREC-CT noted the statement on page 6 of the Main PISCF “Another tissue sample is necessary for participation in the study” The NREC-CT requests more context be provided for this biopsy including the type of sample required, the timing of collection, and clarification on whether this refers to the lymph node biopsy mentioned on page 6, the bone marrow biopsy on page 15, or the biopsy samples discussed on page 21.
- The NREC-CT noted the statement on page 8 of the Main PISCF “Your doctor will monitor your blood count during treatment and intervene if necessary”. The NREC-CT considers this wording to be vague and requests that further context be provided, including which blood cell parameters will be monitored and the intended purpose of any interventions.
- The NREC-CT noted the contraception and pregnancy information on page 8 and 9 of the Main PISCF. The NREC-CT requests that this information is restructured for male participants and female participants in distinct sections.
- The NREC-CT noted the statement on page 10 of the Main PISCF “The following section first describes the side effects that commonly occur during therapy”. The committee requests that the “General explanation of the risks” should be rewritten to include a relative approximation of the risks using the same language in other sections, namely using the Very Common, Common, Less Common headings and the “X out of 100 people treated (percentage)” format.
- The NREC-CT noted on page 15 of the Main PISCF the stated risk of “skin cancer or skin tumours”. Furthermore, the NREC-CT noted that on page 5 of the SPMC for Pirtobrutinib that it was advised that “Patients should be monitored for the appearance of skin cancers and advise protection from sun exposure” and on page 31 “Use sun protection and make regular skin examinations.” The NREC-CT requests that this information is added to the appropriate section of the Main PISCF to ensure participants are adequately informed.

- The NREC-CT noted the statement on page 16 of the Main PISCF “During clinical trials of a drug, all study participants are insured in accordance with the German Drug Law” The NREC-CT requests that this is rewritten in accordance with appropriate Irish legislation and/or European legislation.
- The NREC-CT noted the statement on page 18 of the Main PISCF “you may only undergo other medical treatment—except in emergencies—after prior consultation with the study doctor”. The NREC-CT requests that this is rewritten to ensure clarity to participants regarding their rights to access other medical treatments, that this should be discussed with their study team, and any consequences this may have on study participation.
- The NREC-CT noted the statements on page 25 of the Main PISCF “For this purpose, I release the study doctor from his/her medical confidentiality obligations” and on page 7 of the pregnancy ICF: “For this purpose, I release the doctors treating me and my child from their medical confidentiality obligations”. The NREC-CT request that this is rewritten to be specific to this clinical trial and for the purpose of reporting the study results.
- The NREC-CT requested that the Long term data storage and use of samples PISCF 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 Long term data storage and use of sample PISCF it 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 is elucidated in the Long term data storage and use of sample PISCF.
  - Explicit consent, including outlining the risks entailed in such analysis being performed, is added to the Long term data storage and use of sample PISCF.
  - The possible ownership of such data by private or commercial interests and that this elucidated in the Long term data storage and use of sample PISCF.
  - The right to withdraw genetic data, and clear information on how to do so, must also be provided in the Long term data storage and use of sample PISCF.
- The NREC-CT noted on page 6 of the Long term data storage and use of sample PISCF it states, “For further follow-up, we also ask you to participate in the German CLL Study Group registry”. The NREC-CT requests that this is rewritten to include the voluntary nature of the future follow-up and inclusion in the registry.

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

- The NREC-CT noted on page 68 of the protocol “The screening assessments (especially local blood tests, clinical examination and imaging data) should not be older than 35 days prior to the day of signing the informed consent”. The NREC-CT noted that this timeline could be challenging in some hospital sites, depending on hospital imaging arrangements. The NREC-CT requests clarification that both sites have agreed to this specific timeline for consent and imaging PET-CT or MRI within 35 days.

### **2023-509859-13-00 SM-10**

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

Study title: A Phase 3, Two-Stage, Randomized, Multicenter, Open-Label Study Comparing CC-92480, Bortezomib and Dexamethasone (480Vd) Versus Pomalidomide, Bortezomib And Dexamethasone (PVd) In Subjects With Relapsed Or Refractory Multiple Myeloma (RRMM)

Dossiers Submitted: Part I & II

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

### **2023-504816-14-00 SM-22**

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

Study title: A Phase 3, Randomized, Active-controlled, Open-label, Multicenter Study to Compare the Efficacy and Safety of MK-2870 Monotherapy Versus Treatment of Physician's Choice in Participants With Endometrial Cancer Who Have Received Prior Platinum-based Chemotherapy and Immunotherapy (MK-2870-005/ENGOT-en23/GOG-3095)

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:

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- 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 pages 10-13 of the Main ICF, that the revised side effects are presented with inconsistent formats. On page 11 of the Main ICF “Increased level of a substance (enzyme) in the blood” and on page 11 “An increased lab finding that may be related to kidney function problems”. The NREC-CT requests that the same for wording for an increase or decrease is used consistently throughout the ICF.
- The NREC-CT noted on pages 10-13 of the Main ICF, that the revised side effects are presenting with medical language used without explanation. Including but not limited to
  - Page 10 “Arrythmia”
  - Page 10 “Atrial Fibrillation”
  - Page 10 “Extrasystoles”
  - Page 10 “Tachycardia”
  - Page 11 “Enzyme”
  - Page 11 “alanine aminotransferase”
  - Page 11 “aspartate aminotransferase”
  - Page 11 “bilirubin”,
  - Page 11 “gamma-glutamyl transferase”
  - Page 11 “abnormal hepatic function”
  - Page 11 “Albumin”
  - Page 11 “Alkaline phosphatase”
- The NREC-CT requests that all terminology is explained in lay terminology when first used in the document.

#### **2024-518296-56-00 SM-5**

Institutions: Beaumont Hospital

Study title: A Phase 3, Randomized, Double-Blind, Placebo-Controlled Program to Evaluate the Efficacy and Safety of Tulisokibart in Participants with Moderately to Severely Active Crohn’s Disease

Dossiers Submitted: Part I & II

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

#### **2024-519128-26-00 SM-1**

Institutions: Institute of Eye Surgery Waterford

Study title: A phase 2, double-masked, randomized, multicenter, parallel group, placebo controlled study to investigate the efficacy and safety of GAL-101, 2%, ophthalmic solution in patients with non-foveal geographic atrophy secondary to non neovascular age-related macular degeneration: eDREAM study

- **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](mailto: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.

### 2. Suitability of the clinical trial sites facilities

- The NREC-CT noted the addition of the UPMC Kildare Site, which is referred to as a satellite site in the application. The NREC-CT stated that given that clinical trial activities will take place at this site, the site must be listed as a site on CTIS, with a designated Principal Investigator. Article 73 of the Clinical Trials Regulation, states that “A principal investigator shall ensure compliance of a clinical trial at a clinical trial site with the requirements of this Regulation”. Therefore, the NREC-CT requests that the Kildare site is added as a site to CTIS, so that both the Institute of eye surgery site at UPMC Whitfield/Waterford Hospital, and the Institute of eye surgery at UPMC Kildare Hospital are listed as sites with designated principal investigators. The SSA for Kildare should be updated accordingly to reflect these changes. Please see sections 1.2 “Sponsor and other organisation(s) registration in OMS” and section 2.4.6 “Populating Part II section of a CT application” of the Sponsor Handbook.
- The NREC-CT request confirmation that UPMC Kildare is covered under the national indemnity scheme or has sought alternative indemnity coverage. Furthermore, the NREC-CT requests clarification if storage for the clinical trial samples will be facilitated by UPMC hospitals or if the samples are being transferred to the Waterford site.

### 3. Suitability of the investigator

- The NREC-CT requests clarification on who is designated as the principal investigator at the Kildare Site. If [REDACTED] is acting as the Principal Investigator for both the Kildare Site and the Waterford Site, please provide clarification on how

the clinical trial is managed under his supervision at both sites simultaneously. If an additional PI is designated for the Kildare Site, please provide the relevant CV and DOI.

## **2023-507536-21-00 SM-7**

Institutions: Mater Misericordiae University Hospital

Study title: A Phase 1/2 Open Label, Dose Escalation and Expansion Study of MDNA11, IL-2 Superkine, Administered Alone or in Combination with an Immune Checkpoint Inhibitor in Patients with Advanced Solid Tumors

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](mailto: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 13,14 of the Main ICF the revised risks are presented as technical terminology first and then lay terminology or have no explanation in lay terms. Including but not limited to the following.
  - Page 13 “Increase in blood alanine aminotransferase and aspartate aminotransferase level (changes in liver function test/blood test marker)”
  - Page 13” Cytokine release syndrome (changes that may happen when your immune system responds aggressively to MDNA11, which may include fever, low blood pressure, low oxygen level, or changes in liver and kidney functions)”
  - Page 13 “Fatigue (Tiredness)”
  - Page 13 “Hypotension”

- Page 14 “Increase in blood bilirubin level (changes in liver function test/blood test marker)”
- Page 14 “Sinus tachycardia (when the heart beats faster than normal)”
- Page 14 “Increase in blood creatinine levels (changes in kidney function test/blood test marker)”
- Page 14 “Hypophosphatemia (when you have a lower than normal level of phosphate in your blood)”
- Page 14 “Dyspnea (when you experience shortness of breath or difficulty breathing)”
- Page 14 “Pruritus (the feeling of itchiness and wanting to scratch)”
- Page 18 of the Main ICF. “Myocarditis-myositis-myasthenia gravis overlap syndrome is when the body’s immune system attacks its own heart muscle (myocarditis), skeletal muscles (myositis), and the nerves that control muscles (myasthenia gravis) all at once. This may cause you to experience chest pain, swelling of the legs, fast or irregular heartbeat, dizziness, fainting, weakness, pain in your muscles, tiredness, drooping of the eyelids, blurred or double vision, difficulty swallowing, slurred speech, weakness in your arms and legs, or difficulty breathing.
- The NREC-CT requests that the lay language is presented first and then the technical terminology is presented second in brackets.
- the NREC-CT requests that the lay language and lay explanation is presented first and then the technical terminology is presented second in brackets.
- The NREC-CT noted on page 12 and page 18 of the Main ICF “Side effects (reported in >30 % of patients)” and “Side effects (reported in >15% of patients)” and on page 14 of the Main ICF “Less common side effects (reported in > 10% of patients):” The NREC-CT requests that this revised text is reverted to the more easily understood format of “out of 100 people who received MDNA11, at least X but less than Y have experienced the following”, previously used in the last version of the Main ICF and to align with the risks not revised on page 16 and 17 of the Main ICF

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- **AOB:**
  - None