National Research Ethics Committee

NREC-CT A Meeting

21st May 2025

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 Maeve Kelleher	Committee Member, NREC-CT A
Dr Dawn Swan	Committee Member, NREC-CT A
Dr Darren Dahly	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 Muireann O'Briain	Committee Member, NREC-CT A
Ms Dympna Devenney	Committee Member, NREC-CT A
Mr Kevin Devlin	Observer
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: Brian Bird, Aisling McMahon, Mandy Daly, Margaret Cooney

Quorum for decisions:

Agenda

- Welcome & Apologies
- 2024-518998-33-00
- 2024-519270-40-00
- 2024-519711-33-00
- 2023-508818-42-00 SM-9
- 2022-502202-33-00 SM-5
- 2022-502851-79-00 SM-9
- 2022-502548-12-00 SM-7
- 2023-509859-13-00 SM-4
- 2023-506987-15-00 SM-4
- AOB

- The Chair welcomed the NREC-CT A.
  - The minutes from the previous NREC-CT A meeting on 16th April 2025 were approved.
  - The NREC Business Report was discussed and noted.

Applications

2024-518998-33-00

Institutions: Beaumont Hospital, Dublin, Portiuncula University Hospital, Galway, Connolly Hospital Dublin, Our Lady of Lourdes Hospital Drogheda, Regional Hospital Mullingar, Longford, St. Vincents University Hospital, Dublin

Study title: A Phase 3b, Multicenter, Randomized, Open-Label Study of Risankizumab Compared to Vedolizumab for the Treatment of Adult Subjects With Moderate to Severe Ulcerative Colitis Who are Naïve to Targeted Therapies

Dossiers Submitted: MSC 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 on page 27 of the protocol. “History of clinically significant (per investigator's judgment) drug or alcohol abuse within the last 6 months.” Clarification is requested on what objective criteria will be used to determine significant alcohol abuse and what mitigation steps are taken to reduce potential investigator bias.
- It was noted the use of technical language and abbreviations throughout the Protocol Lay Summary/Protocol Synopsis, for example on page 1 “the main endpoint is the percentage of patients that achieve endoscopic improvement” and, for example, on page 2, “severely active UC that have not previously had treatment with a TaT.” It is requested that the sponsor revise the Protocol Lay Summary/Protocol Synopsis to reduce the number of abbreviations, acronyms and technical language throughout.
- It was noted on pages 6 and 20 of the protocol the sentence “The primary endpoint is the achievement of endoscopic improvement at Week 48, defined as a centrally read endoscopy subscore of 0 or 1 (score of 1 modified to exclude friability)” It is requested that the sponsor provide clarification on what is a “centrally read” endoscopy, for example the number of clinicians that will be involved and how this may affect between-site variability and bias.
- It is noted that this is an open label trial. The sponsor is requested to clarification on the steps taken to mitigate study team bias.

Part II Considerations

1. **Financial arrangements**

- The NREC-CT noted the options of debit card or payment via Direct Deposit for reimbursements. The NREC-CT requests that these sections on page 19 are

detailed as option 1 and option 2 to ensure it is clear to participants that they have a choice. The NREC-CT requests that the criteria and limits on reimbursement which are detailed in the "Compensation for Trial Participants" is also detailed in this section in the Main PISCF.

2. Recruitment arrangements

- The NREC-CT noted "Eligible subjects include adults aged 18-80". The NREC-CT requests clarification on why the participants over the age of 80 has been 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 that the future use of optional data and samples (including genetic research) is not described in line with regulations / best practice throughout the Main PISCF. The NREC-CT noted that optional and biomarker research is introduced before the study design and study procedures and recommended it is moved further down after the study has been explained to the participant. The NREC-CT requests that future use of samples and optional 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 25 of the Main PISCF "If you withdraw or are withdrawn from the study, the biological samples we have collected from you as part of the study or optional research will continue to be stored and analysed as described in this document unless you specifically withdraw your permission" The

NREC-CT requests that a similar clarifying statement regarding the continued use of personal data, unless withdrawn, is added to this page.

- The NREC-CT noted on page 2 of the Main PISCF. “AbbVie is paying the study doctor to perform this study.” The NREC-CT requests that this be changed to “AbbVie is paying the study site to perform this study.”
- The NREC-CT requested that page 24 of the PISCF be updated to provide information about the availability of the clinical trial results at euclinicaltrials.eu at the end of the trial and location of same results.
- The NREC-CT noted that “FSH test: if you are assigned female and younger than age 55, to determine if you have completed menopause.” The NREC-CT noted that a standard use of FSH for conformation of menopause is that it is performed on 2 occasions 4-6 weeks apart. The NREC-CT requests clarification regarding how the FSH will be performed.
- The NREC-CT noted on page 19 of the Main PISCF “What happens when the research study stops?” The NREC-CT requests more information be added to this section if there a possibility of a long-term extension for those who have benefitted from this medication.
- The NREC-CT noted references to endoscopy for optional biomarker studies, due to the confusing layout with optional procedures included with mandatory procedures. The NREC-CT requests clarification if all participants will undergo endoscopies, how many times they will undergo them and at what points in the study and for this to be clearly detailed in the Main PICSF.
- The NREC-CT noted on page 7 of the Main PISCF “IUS will be required if the study investigator/site is selected as an IUS site”. The NREC-CT requests that the Main PISCF include details as to what sites are ultrasound sites and if there is an additional risk to participants who will not receive ultrasounds.

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

- The NREC-CT noted on page 7 of the Main PISCF “IUS will be required if the study investigator/site is selected as an IUS site. Please ask your doctor if you will be doing this procedure.” The NREC-CT requests clarification regarding which sites will be IUS sites and the criteria for selecting these sites.

2024-519270-40-00

Institutions: La Nua Day Hospital Mental Health Centre, Galway, Tallaght Adult Mental Health Service, Dublin

Study title: An Efficacy and Safety, Phase III, Multi-center, Double-Blind, Randomized Controlled Study Comparing 2 Active Doses of CYB003 and Placebo in Eligible Participants with Major Depressive Disorder (EMBRACE)

Dossiers Submitted: RMS 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 study is described as “double blinded”. However, due to the nature of the treatment, it would appear that clinicians and participants cannot be blinded to the effect of the IMP, and therefore, the protocol, study documents and structured data should be updated to reflect this.
- The exclusion criteria describe several conditions that must be maintained throughout the study. These are not exclusion criteria, but rather potential protocol violations, and should be dealt with accordingly. Examples of such are exclusion criteria 18. A positive test at screening would be an exclusion. However, the positive test at Day 1 or Day 22 would be a protocol violation. The sponsor should review the eligibility criteria in their entirety, to ensure no similar issues are present.
- It was noted that the sample size accounts for screen fails but not for drop outs. This must be considered when determining sample size and updated accordingly.
- The protocol states that patients with 25% increases in MARDS between screening and time 1 will be discontinued from the study. It is requested that the sponsor provide justification for 1) why a relative increase in MARDS score is used, compared to an absolute or numerical increase and 2) if those participants who are discontinued due to that relative increase will be replaced.
- It is requested that the sponsor provides justification for using random effects per country in the analysis.
- It is requested that the sponsor clarification and details in the protocol regarding how allocation concealment will be ensured.
- The protocol states on page 56, section 6.1.7.1 “Participant Assignment” that patients will be stratified by previous psychedelic use. Depending on the methods used, this could put the allocation concealment at risk due to potential guessing. It is requested that clarification on the method of restricting the randomization list within strata (e.g. random blocks).
- It is noted that the Investigator Brochure focuses solely on study related to MDD. It is requested that the sponsor clarifies if any other human studies of psilocybin based medicines would be relevant for evaluating safety information.
- It is noted that the IDMC won’t be established until four weeks after the first randomized participant. Given the relative scarcity of previous human studies, the IDMC should be established before the first participant is randomized.

Part II Considerations

1. **Compliance with national requirements on data protection**

- The NREC-CT noted on page 15 of the Main PICSF and Pregnant Partner PISCF the list of people/organisations that would potentially receive participants personal data. The NREC-CT requests clarification of why each named organisation needs personal data and not coded data. The NREC-CT requests that the list be divided into who will receive participants’ personal information as defined under GDPR and who will receive coded information.

2. Financial arrangements

- The NREC-CT notes there are two eight-hour visits and queried whether the sponsor could consider compensation for accommodation for participants and carers if required. The NREC-CT also requests that the sponsor consider compensation for meal expenses for carers.

3. Proof of insurance

- The NREC-CT noted the insurance certificate was with Lloyd's Insurance Company, the Main PISCF states that the insurance is through Berkley Canada. The NREC-CT requests clarification on the details on insurance for Irish participants and if applicable for the insurance details to be updated. The NREC-CT also requests that insurance details be added to the pregnancy and pregnant partner PISCFs.
- The NREC-CT requests information regarding La Nua Day Hospital Mental Health Centre and if the center is covered under the HSE public liability insurance.

4. 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 on page 3 of the Main PISCF, discussion of the long-term extension study. The NREC-CT request additional information regarding the long-term extension study be added to this section to ensure it is clear to the participant that they are not consenting to the extension with this form and will not be in the long-term extension for an additional 43 weeks.
- The NREC-CT noted on page 7 of the Main PICSF "Clinical administered interviews" The NREC-CT requests clarification on who will be the conducting the interviews, are they part of the study team, external to the study team, a company, what is their training and qualifications. Given the sensitive nature of the interviews, more details are quested for the NREC-CT and in the PICSF.
- The NREC-CT noted in the Main PICSF "Session Monitors" are mentioned in several locations in the PICSF. The NREC-CT requests clarification on who will be the session monitors, are they part of the study team, external to the study team, a company, what is their training and qualifications. Given the sensitive nature of the interviews, more details are quested for the NREC-CT and in the PICSF.
- The NREC-CT noted on page 7 of the Main PICSF "Central Rater" The NREC-CT requests clarification on who will be the central rater, are they part of the study team, external to the study team, a company, what is their training and qualifications. Given the sensitive nature of the interviews, more details are quested for the NREC-CT and in the PICSF.
- The NREC-CT noted on page 7 of the Main PICSF "At least 1 session monitor (lead) will be a licensed therapist." The NREC-CT requests clarification on who will be the licenced therapist. The NREC-CT is specifically requesting details on their

qualifications, licensing, details of the specialised EMBARK training and safety measures that will be taken.

- The NREC-CT noted that the “Study Tests and Procedures” table in the Main PICSF states that 9 sessions (pre and post) will be provided by the study session monitors. The NREC-CT requests clarification if any another other sessions will be provided by the study session monitors and if there are other sessions, for those sessions to be listed in the “Study Tests and Procedures” table.
- The NREC-CT noted page 10 of the Main PICSF details the risk of allergic reactions. The NREC-CT requests details are included as to the mitigation or response in the event of allergic reaction.
- The NREC-CT noted on Page 11 of the main PICSF “Potential loss of privacy” The NREC-CT requests details of efforts to be undertaken by the research team to mitigate potential loss of privacy.
- The NREC-CT notes on page 17 of the Main PICSF video recordings are processed by AI. The NREC-CT requests the details of the AI tool being used, including the name and vendor supplier details are included in the Main PICSF. The NREC-CT requests assurance that the content won’t be shared with a commercial source and details of how the sponsor will maintain data protection for the participant.
- The NREC-CT noted on page 17 of the Main PICSF that the video recordings will be stored for 7 years. The NREC-CT requested clarification regarding the storage time of 7 years, and the details on the vendor who will be storing the video files to be added to the Main PICSF. Consent for processing and storage of the video recordings should also be added to the Main PISCF, and the PICSF should detail how the sponsor will maintain data protection for the participant.
- The NREC-CT noted that the future use of data is not described in line with regulations / best practice on page 17 of the Main PISCF “The deidentified recordings and/or transcripts may also be used for quality control and research purposes (e.g., for the purposes of identifying biomarkers, and for further research into specific conditions/therapeutic areas).” . 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 it states “Your personal data will only be shared with and disclosed to authorised third parties and recipients” on page 19 of the Main PICSF. The NREC-CT requested clarification for the identity of authorised third parties and if they are the same third parties listed on page 15. If they are the same third parties, the NREC-CT requests that reference to the list on page is included on page 19 in the relevant paragraph. If they are not the same third parties listed on page 15, the NREC-CT requests that they are listed, along with the reason for the sharing of personal data.
- The NREC-CT notes the future research on pg 3 Pregnant Partner is limited to the drug under study. The Committee requests that the Pregnant Partner ICF pg 7 be updated to insert a separate and explicit consent item in the Informed Consent section to make future research optional and to have a separate signatures section, so it is distinct from the main consent to participate in collection of data on the pregnancy.
- The NREC-CT requests that the Main ICF page 16 be updated to include detail that this navigator service is optional.
- The NREC-CT requests that Main ICF page 17 Reimbursement Services be updated to include detail that use of Block Clinical reimbursement company is mandatory for stipend and incidental reimbursement payments.

2024-519711-33-00

Institutions: Children’s Health Ireland - Temple Street and Cooley Road in Dublin

Study title: REVEAL Study: Phase 3 Study of the Efficacy and Safety of ION582 in Children and Adults with Angelman Syndrome

Dossiers Submitted: MSC Part I&II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required RFI**

Part II Considerations

1. Recruitment arrangements

- The NREC-CT noted the following resources listed in the recruitment documentation. The pre-consent brochure, commitment brochure, ION582 overview postcard, REVEAL study video and Informational Patient Website. The NREC-CT requests these participant facing materials are submitted for review when available.
- The NREC-CT requests clarification as to whether there is a limit to how long the participant will be given to review the consent form. Will the participants be given

an opportunity to take the consent forms home to review. The NREC-CT requests that this information is contained in the recruitment arrangements documentation.

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 on page 15 main PISCF “similar drugs have been administered to >14000 people”. The NREC-CT requests additional clarification after this sentence that that ION582 is an orphan drug that has only been used in 55 people in Phase 1 trials and that many of the risks may be unknown and that as more risk become known, participants will be updated. The NREC-CT requests that this is included in lay language.
- The NREC-CT noted on page 15 of the main PISCF “If the study participant is a able to become pregnant, they must refrain from breastfeeding and either be abstinent or, if engaged in sexual relations, use highly effective contraception from the time of signing and dating the informed consent form until at least 40 weeks after their last dose of ION582.” The NREC-CT requests that this is rewritten as “If the study participant is able to become pregnant, they must either be abstinent or, if engaged in sexual relations, use highly effective contraception from the time of signing and dating the informed consent form until at least 40 weeks after their last dose of ION582. They must also refrain from breastfeeding until at least 40 weeks after their last dose of ION582”, so as to separate out the advice for contraception and breastfeeding requirements for participants.
- The NREC-CT noted that participants may require sedation on multiple occasions throughout the study for either the placebo or the IMP. The NREC-CT requests more information be contained in the PICSF about the options for sedation for the participant, the route of sedation administration, the length of time for sedation, if there an opportunity to discuss this with the doctor in advance of any procedure. It should also be emphasised in this section that all participants including those who receive placebo will be receiving sedation.
- The NREC-CT noted technically complex language throughout the main PISCF for example on page 2 “of the maternally derived ubiquitin-protein ligase E3A (UBE3A) allele on a specific chromosome”, on page 4 “Pseudobulbar affect”. The NREC-CT requests that this is explained using lay language.
- The NREC-CT noted of page 2 of the PICSF ‘is not approved for sale by the regulatory agencies’. The NREC-CT requests that this is revised to “Not approved by regulatory agencies”
- The NREC-CT noted in the Main PISCF on page 5. Multiple references to “groups” Pg 4 which may be confusing for participants. The NREC-CT requests that the first line “The study will include 2 groups”, is rewritten to “The study will include 2 age groups”. The NREC-CT requests that the statement “assigned by chance to one of

the three groups" is rewritten to "assigned by chance to one of the three treatment groups", to ensure clarity for the participant.

- The NREC-CT noted in the main PISCF on page 16 details regarding the EEG. The NREC-CT requests that this section includes the length of time the EEG will be performed.
- The NREC-CT noted on page 14 of the Main PISCF "What will happen at the end of the study?". The NREC-CT requests that this section provide additional context for the participants regarding access to the IMP in the event thatit is found to be effective.
- The NREC-CT noted on page 16 "Some participants in this study will receive…" The NREC-CT requests that this is rewritten as "One third of the participants in this study will receive…", to ensure clarity for participants.
- The NREC-CT noted on page 21 of the Main PISCF "People from the Institutional Review Board (IRB), or Independent Ethics Committee (IEC) and health authorities who have responsibility to protect human participants involved in research" The NREC-CT requests that the independent ethics committee (IEC) be changed to National Research Ethic Committee (NREC) where appropriate in the Main ICF and Caregiver ICF. The NREC-CT also requests that NREC is removed from the list of people or organisation who may review the study participants personal information.
- The NREC-CT noted on page 24 of the Main PISCF "I agree to use the of the Study" The NREC-CT requests that the Main PISCF and Caregiver PISCF be reviewed for typos and double spacing.
- The NREC-CT noted the requirement for sedation and inthrathecal bolus injection in the placebo group, and queried whether this procedure has this been discussed with parent/patient advocacy groups, to ensure parents/caregivers understand the nature of randomization and the requirements of the non-therapeutic placebo arm, and that the PISCF sufficiently explains the requirement for same.
- The NREC-CT noted on page 2 of the GP letter. "Please instruct your patient not to start taking any new medications, including non-prescribed drugs, unless they have received permission from the study doctor". The NREC-CT noted that the onus should not be on the GP alone to provide this advice, and requested that this is rewritten to indicate that the study participant has agreed to not start taking any new medications or non-prescribed drugs without speaking to the Study doctor, and the GP should reiterate this advice.

2023-508818-42-00 SM-9

Institutions: Children's Health Ireland

Study title: An International, Multicenter, Randomized, Double-Blind, Parallel Group, Vehicle-Controlled, Phase 2/3 Study with Open-Label Extension Evaluating the Efficacy and Safety of Diacerein 1% Ointment for the Treatment of Generalized Epidermolysis Bullosa Simplex (EBS)

Dossiers Submitted: MSC 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

- 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 the protocol states (page 7) that participants aged 4 to 12 years will be enrolled, and if participants experience no severe adverse events after 4 weeks of the 8 week protocol, then children 6 months to 4 years will be enrolled. The NREC-CT requests clarification regarding the enrollment of participants aged 6 months to 4 years if severe adverse events do occur.
- The NREC-CT noted in the Parent ICF page 4 tables explains the total blood volume to be drawn. The NREC-CT suggest that it would be valuable knowledge to the participants to know many times they will have their blood drawn as that is important participants and parents/guardians.
- The NREC-CT notes in the parent/guardians ICF page 4 “If genetic testing is performed, your child will be told the results and be requested to provide the report to the investigator…” The NREC-CT requests that this be updated so that parents/guardian of children will be warned about any details in the genetic results that might be concerning, cause emotional distress or indicate any medical risks, before discussion with the child.

2022-502202-33-00 SM-5

Institutions: Children’s Health Ireland, Dublin

Study title: AttaCH: A Phase 2, Multicenter, Long-Term, Open Label Extension Trial Evaluating Safety, Tolerability, and Efficacy of Subcutaneous Doses of TransCon CNP Administered Once Weekly in Children and Adolescents with Achondroplasia

Dossiers Submitted: MSC 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

- 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 on all Parent ICF's and Legal Age ICF's that on page 3, it explains the total blood volume to be drawn. The NREC-CT suggest that it would be valuable knowledge to the participants to know many times they will have their blood drawn performed as that is important participants and parents/guardians.
- The NREC-CT noted that on page 1 of the Long Term Follow UP PISCF. "We would like to give you and your child the opportunity to continue participation without treatment and with no regular or planned visits to the research site." The NREC-CT requests that this wording in this paragraph be rephrased to ensure that a participants right to withdraw without any follow-up is not infringed, that if the participant does not want to continue they will be assured of their rights and as part of their options for further medical care, one of the options offered along with standard of care would be other clinical trials, the long term extension of this study, and any other options their medical doctor deems appropriate.
- The NREC-CT noted the optional consent in the Long-term follow up PIL "I agree to have my child's primary care physician (paediatrician, GP) be informed about my child's participation in this clinical study". The NREC-CT requests clarification regarding why this consent is optional, and that the reason for informing the participant's GP is included in the document.
- The NREC-CT requests that on page 2 of the Long term follow up PIL in the section "Your Responsibilities" it is made clear to the participant and participant's parents/caregivers that they can withdraw from the trial at any time without penalty.
- The NREC-CT notes page 2 of the Long Term Follow up PIL states under "Policy Regarding Pregnancy: There are no policies for handling of pregnancies in this additional data collection." The NREC-CT requests context is added to this section to make it clear to participants why this section is not applicable for them.
- The NREC-CT noted it was unclear in the long term follow up PIL how long the participant is expected to provide data for and requested that the duration of the data collection is made clear to participants and their parents/caregivers.

2022-502851-79-00 SM-9

Institutions: St. Vincents University Hospital, Dublin, Our Lady's Hospital Manorhamilton, Sligo, Connolly Hospital Dublin

Study title: A Phase 3, Single-Arm, Multicenter, Open-label Extension of Study ARGX-113-2007 to Investigate the Long-term Safety, Tolerability, and Efficacy of Efgartigimod PH20 SC in Participants Aged 18 Years and Older With Active Idiopathic Inflammatory Myopathy

Dossiers Submitted: MSC 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

- 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 inconsistencies throughout the documentation regarding the length of the study. In the Study visit guide in the first column in the table at the bottom of page 1 it states “The study treatment period will last up to 51 months…” and “The study treatment period will last 41 weeks…” on page 2 of the Study visit guide it states“The study treatment period will last up to 51 months…” and “The study treatment period will last 51 weeks…”” on page 3 of the ICF the text says “the study will last up to 53 months” The NREC-CT requests that the study guide and ICF figures and text align.

2022-502548-12-00 SM-7

Institutions: University Hospital Waterford, Waterford, St. James's Hospital, Dublin

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

Dossiers Submitted: MSC Part I&II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required RFI**

Part II Considerations raised

1. **Proof of insurance**

- The NREC-CT noted the dates on the Insurance certificate is from October 2023-September 2024. The NREC-CT requests an updated insurance certificate.

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 in section 5.8.2 of the MZL and FL ICF's the revised text states that birth control must be used "for up to 1 month". The NREC-CT request this is revised to "for a least 1 month" to ensure it is clear to the participant for how long contraception use is required.
- The NREC-CT noted in section 5.8.3 of the MZL and FL ICF's the revised text advising the participant to refrain from breast feeding for "up to 1 month after the last dose". The NREC-CT request that this is revised to advise the participant refrain from breast feeding "for a minimum period, e.g. at least 1 month after the last dose"
- The NREC-CT noted in section 5.8.3 of the MZL and FL ICFs the revised text "and according to the approved rituximab product/PI," The NREC-CT requests that this is clarified and that any guidelines are clearly stated in the ICFs.
- The NREC-CT noted in section 5.8.2 of the MZL and FL ICFS "the above-indicated period for each drug after completing study treatment". The NREC-CT requests that this is clarified and that the timelines are clearly stated in the paragraph.
- The NREC-CT noted in section 5.8.2 of the MZL and FL ICFs that the advice for male contraception has been revised from 90 days down to "up to 1 week". The NREC-CT requests clarification on the reduction of time. Furthermore, the NREC-CT requests that this is revised to read "study treatment, and for at least 1 week after the last dose…" to ensure a minimum timeframe is provided.
- The NREC-CT noted in section 5.8.2 of the MZL and FL ICFs "and for >28 days after the last dose of lenalidomide, and according to the approved rituximab product/PI, whichever is longer." The NREC-CT requests that this be revised into lay language and that any timelines are clearly stated in easy-to-understand language for the participant.
- The NREC-CT noted on page 16 of the TL ICF "Cytokine release syndrome (acute infusion reaction)" is not lay language. The NREC-CT requests that this be revised into lay language.

2023-509859-13-00 SM-4

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

Study title: A Phase 3, Two-Stage, Randomized, Multicenter, Open-Label Study Comparing Mezigdomide (CC-92480), Bortezomib And Dexamethasone (MeziVd) Versus Pomalidomide, Bortezomib And Dexamethasone (PVd) In Subjects With Relapsed Or Refractory Multiple Myeloma (RRMM): Successor-1

Dossiers Submitted: MSC 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

- 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 requests that the phrase “demographic data” on page 1 of the revised PICSF be rephrased into lay language phase such as “personal information”.
- The NREC-CT noted on page 15 of the main ICF “Very important to participate so researchers can continue to see how your disease was affected by the treatment. You will not participate in the PFS if you stopped treatment due to worsening of your disease” The NREC-CT requests replacing “will not participate” with “need not participate” to avoid the possible interpretation of the language implying blame.
- The NREC-CT noted the addition of IDMC recommendations regarding Pneumocystis jirovecii pneumonia (PJP) prophylaxis and granulocyte colony-stimulating factor (GCSF), (Protocol, page 7) and queried whether the participant’s GP will be advised of same in a revised GP letter.
- The NREC-CT noted in the Study Overview recruitment material, there is no mention of consent and this being voluntary. The NREC-CT requests that the voluntary nature of the clinical trial and that consent must be obtained prior to the start of the study is contained in the recruitment material.

2023-506987-15-00 SM-4

Institutions: Tallaght University Hospital, Dublin

Study title: Phase Ib/II Trial of Pembrolizumab (MK-3475) Combination Therapies in Metastatic Castration-Resistant Prostate Cancer (mCRPC) (KEYNOTE-365)

Dossiers Submitted: MSC 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

- 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 in item 12, page 29 of the Main Adult ICF the text does not appear to be finalized. The NREC-CT requests that this section be reviewed and finalised for review.
- The NREC-CT noted on page 2 of Main Adult ICF “if you agree to participate” This text is misleading and the NREC-CT requests that this section be rewritten into the past tense as Cohort J has been discontinued.
- The NREC-CT request clarification if participants already on arm J will be given an opportunity to join another arm of study.
- The NREC-CT noted an updated IB for Olaparib, the NREC-CT requests clarification why the PIL does not contain updated information about Olaparib.

- AOB:
  - XXX
  - XXX