Appendix 2: Withdrawal of participants from the study, temporary and permanent treatment discontinuation for LIRA 3mg (outside prespecified stopping rules)

Withdrawal of participants from the study

Participants may withdraw consent from the study before study completion if they decide to do so, at any time and for any reason.

Participants will be withdrawn from this study by the research team as agreed by the Principal Investigator (PI) if: i) they are diagnosed with a terminal illness, ii) the PI, Sponsor and/or study clinician deem it unsafe for their continuation in the study for medical, safety, regulatory, or other reasons consistent with applicable laws, regulations or Good Clinical Practice (GCP), iii) they are considered to be lost to follow up as deemed by the clinician, iv) they have lost their capacity during participation in research, v) they receive treatment with medications which the PI determines to require permanent withdrawal from the study (e.g. systemic corticosteroids).

It will be emphasised to participants who withdraw from the study that their standard care will not be affected and that they will return to standard care.

Attempts will be made to assess the primary outcome on all participants whether or not they were compliant and in those who have who have discontinued the treatment (including those participants who have stopped the treatment outside of the pre-specified stopping rules).

Temporary treatment discontinuation for LIRA 3mg (outside of the pre-specified stopping rules)

Temporary discontinuation of LIRA 3mg may be considered by the Principal Investigator (PI) because of suspected Adverse Events (AEs).

Re-initiation of LIRA 3mg at a lower dose, under close and appropriate clinical and/or laboratory monitoring maybe considered at discretion of the PI and if the inclusion and exclusion criteria for the study are still met.

Permanent treatment discontinuation (outside of the pre-specified stopping rules)

Permanent treatment discontinuation is any treatment discontinuation associated with a definitive decision from the PI or the participant not to re-expose the participant to LIRA 3mg treatment. This definition is different to treatment discontinuation due to a participant not meeting the weight-loss targets at the pre-specified stopping rules as per the protocol.

Factors leading to permanent discontinuation of LIRA 3mg include i) pregnancy, ii) episode

of acute pancreatitis and breast malignancy, iii) repeat violation or non-compliance with the protocol, iv) participant being unable to tolerate LIRA 3mg doses and/or v) any other contraindication to the study medication which the PI determines to require permanent treatment discontinuation.