NHSGGC Women & Children's Directorate:
Authorised NCIII List for Paediatrics & Neonates (RHC) – ADMIRAL TRIAL NOW CLOSED, LONGWING ONGOING, NOTIFIED 25.10.2024:

Department	Designated Lead	Nominated Pharmacy Lead(s)	Designated Contacts within On-Site Pharmacy Department	Nominated Nursing Lead(s)	NCIIIs Approved for Use	Indication	Licensed Status LM / ULM / LM but unlicensed indication	Aseptic Manipulation/Preparation Required	Storage in Clinical Area Authorised	Approved * Dose Range	Upper Limit *	Folder/ Information Storage Location	Location of Intralipid for Potential LA Toxicity
Women and children. Clinical trials - RHC Neurology department	Dr Iain Horrocks Administration / PI: Dr Andreas Brunklaus Deputy: Prof Sameer Zuberi Approved by Dr Alan Mathers (CoM) Dr Phil Davies (CD) Jamie Redfern (Director)	Susan Kafka Lead Clinical Pharmacist W&C Samantha Carmichael	Scott Nicol Kirsty Mcleish (on mat leave 2024) Maria Nygren covering Sarah Casey	Patricia Clark Hayley Cranston	Investigational drug product - STK-001 33 mg/mL - a concentrate for solution for injection intended for dilution with artificial cerebrospinal fluid (aCSF) solution followed by IT administration. STK-001 is being investigated as part of the ADMIRAL Trial protocol no: STK-001-DS-102.	Treatment for Dravet's syndrome in children aged between ≥2 and <18 years at Screening	Investigational Medicinal Product (IMP)	Yes – will be prepared in the Aseptic Unit at the RHC.	No	*(a) 3 proposed dose cohorts: 30mg, 45mg, 70mg. Each patient to receive 3 doses in total (Day 1, Week 8, Week 12) with option to include another 2 cohorts based on SMC safety data analysis and recommendations	In each dose cohort the upper limit will be the dose agreed for that cohort i.e. in the 30mg dose cohort – upper dose limit will be 30mg. Maximum dose escalation between any 2 cohorts is 1.8 times the lower dose, with a maximal dose level of 70mg per administration	Folder and documents will be stored in both the Clinical Trials Office main pharmacy QEUH, and Aseptic Pharmacy RHC. Drug will be stored in Aseptic Pharmacy RHC.	N/A
Extension to Admiral Trial, Longwing Study STK-001-DS-502													
Women and children. Clinical trials - RHC Neurology department	Dr Andreas Brunklaus	Susan Kafka Lead Clinical Pharmacist W&C Samantha Carmichael	Scott Nicol Kirsty Mcleish (on mat leave 2024) Maria Nygren covering Sarah Casey	Patricia Clark Hayley Cranston	Investigational drug product - STK-001 33 mg/mL - a concentrate for solution for injection intended for dilution with artificial cerebrospinal fluid (aCSF) solution followed by IT administration. STK-001 is being investigated as part of the LONGWING Trial protocol no: STK-001-DS-502.	Treatment for Dravet's syndrome in children aged between ≥2 and <18 years at Screening	Investigational Medicinal Product (IMP)	Yes – will be prepared in the Aseptic Unit at the RHC.	No	*(b) Patients will receive IT administration of study drug STK-001 at the dose level they received while participating in Study STK-001-DS-102, or at a dose level recommended by the SMC (Protocol Section 6.5.3).	The highest dose administered may not exceed that evaluated previously in Study STK-001-DS-102.	Folder and documents will be stored in both the Clinical Trials Office main pharmacy QEUH, and Aseptic Pharmacy RHC. Drug will be stored in Aseptic Pharmacy RHC.	N/A

* The study is planned to consist of 3 cohorts (Cohorts 1, 2, and 3) with the option to include 2 additional cohorts. The proposed dose levels for each cohort are 30 mg, 45 mg, and 70 mg per drug administration - It is planned that each patient will receive 3 drug administrations in total - one on Day 1, Day 57 (week 8), and Day 85 (week 12). The dose will depend on the cohort the patient is enrolled into to; for example patients enrolled

into the 30mg dose cohort will receive 3 doses in total of 30mg per dose, and those enrolled into the 45mg dose cohort will receive 3 doses in total of 45mg per dose and so on. The proposed cohort dose levels however may be adjusted based on safety review, additional preclinical and/or clinical data, and/or regulatory authorities' recommendation.
The maximal dose escalation between any 2 cohorts will be 1.8 times the lower dose, with a maximal dose level of 70 mg per drug administration. The safety monitoring committee (SMC) may recommend, based on all available safety and PK data, that dose cohorts over 30 mg receive only one dose. An additional one or two optional cohorts may also be enrolled up to a maximum dose of 70 mg per drug administration in order to:
• Escalate or deescalate to a lower and/or to an intermediate dose level of STK-001;
• Repeat a dose level if a safety signal (not meeting a stopping rule) indicates that further dose escalation may affect the safety of study patients; or
• Further characterise PK parameters.

See Clinical Trial Protocol Number STK-001-DS-102 for further information.

* (b) The SMC will meet, at a minimum every 4 months to review all available safety data from this trial, as well as any data from other ongoing trials with STK-001 (as defined in the SMC Charter). The SMC will meet upon the occurrence of dose-limiting toxicities (DLTs) to recommend the acceptability of continued dosing. The occurrence of any of the pause/stopping rules listed in Section 6.6.2 of protocol STK-001-DS-502 at any dose level in patients receiving STK-001 will result in a pause and no further study drug will be administered until a review by the SMC is completed. At the time of the regular review meetings or on an ad-hoc basis, the SMC may advise on the optimal dose level for patients in this Open Label Study based on the emerging benefit/risk profile from the totality of data available from interventional studies of STK-001. The highest dose recommended may not exceed that evaluated previously in Study STK-001-DS-102.

Approval Obtained:

- **Board / NCIII Level Approval:**
- Chief of Medicine W&C - Dr Alan Mathers - approval received, 31.12.21
- Dr Gordon McGinn as joint-lead for implementation of the policy – approval received 02.06.22
- Catherine McLaughlin as joint-lead for implementation of policy – approval of all arrangements being in place received 10.06.2022, and added to the register
- **Paediatric Neurology:**
- Dr Andreas Brunklaus - request received, approval received 31.05.22
- Nominated deputy contact for Dr Brunklaus in case of emergency – Prof Sameer Zuberi – approval received 30.05.22
- Dr Iain Horrocks - Designated Lead for Neurology on NCIII policy – approval received 20.01.2022
- CD for Neurology – Dr Phil Davies – approval received 30.05.22
- Lead Medical Director/General Manager (or deputies), Jamie Redfern - approval received 30.05.22
- **Pharmacy:**
- Steve Bowhay Lead Clinical Pharmacist - approval received, 31.12.21
- **Aseptic Unit Approval:**
- Scott Nicol – approval received 01.06.22
- **Nursing links:**
- Patricia Clark- approval received 31.05.22
- Hayley Cranston – approval received 01.06.22
- **Clinical Trial approval:**
- Dr Sam Carmichael- approval received 31.05.22
- Kirsty McLeish – approval received 02.06.22