CONTRACT VARIATION AGREEMENT No.3

Contract/Variation Reference: NHS England, Biogen, Spinal Muscular Atrophy UK, TreatSMA, Muscular Dystrophy UK, SMA REACH UK and NICE entered into a managed access agreement dated 3 July 2019 relating to the agreed terms and conditions according to which patients will be entitled to access the drug called nusinersen (Spinraza®) for treatment for 5q Spinal Muscular Atrophy (SMA) NICE TA588 (the "**MAA**").

Contract documentation and documents relied upon	
MAA	Signed: 3 July 2019
Contract Variation 1	Signed: 18 May 2021
Contract Variation 2	Signed: 12 January 2022
Relevant guidance ("Guidance")	
Nusinersen for treating spinal muscular atrophy Technology appraisal guidance (TA588)	24 July 2019

Date of this Variation Agreement: 28, November 2022

This variation agreement relates to the variation of the MAA as set out below (the "Variation Agreement No.3).

Capitalised words and phrases in this Variation Agreement No.3 have the meanings given to them in the MAA.

1. In consideration of their respective obligations under the MAA (as varied by this Variation Agreement No.3) the Parties have agreed to the following variation to the MAA:

   1.1. The following clauses 5.12, 5.13, 5.14 and 5.15 will be deleted in their entirety and replaced with:

   5.12 Biogen is responsible for commissioning separate agreements which will ensure that data is collected during the Term of the MAA period on patient and carer quality of life. Biogen has contracted the UK SMA Patient Registry to collect patient-reported data from individuals with SMA. The SMA Patient Registry is an established database. Data is captured on the Munich Platform, hosted by AIMES Management Services and the patient registry is coordinated from John Walton Muscular Dystrophy Research Centre, Newcastle.

1.2 Clause 3.1 will be deleted and replaced with the following:

3.1. This MAA shall take effect on 3rd July 2019 it will remain in force until the earlier of: (i) publication of a NICE reappraisal of nusinersen; or (ii) the expiry or termination of the MAA. Data collection will be in place for a minimum of three (3) years. For the avoidance of doubt, this MAA shall expire automatically on the 6th anniversary of its term if it has not expired earlier as a result of the publication of the NICE reappraisal of nusinersen. NICE will reissue guidance to the NHS in England based on a review of the data by the end of the sixth year of this MAA. For the purposes of this clause, "Guidance" means the guidance expected to be published by the National Institute for Health and Care Excellence in 2019 in relation to the use of nusinersen ID1069.

1.3 The following abbreviations will be added to **Appendix A – The List of Abbreviations:**

Abbreviation	Definition
Adult SMA Reach	Adult Spinal Muscular Atrophy Reach
SMA Reach UK	Spinal Muscular Atrophy Reach UK

1.4 **Appendix C – Network for data collection** will be deleted in its entirety and replaced with the following:

Data collected as per the MAA will be entered by clinicians into the SMA REACH UK and Adult SMA REACH registries hosted on the Certus platform. SMA REACH UK is a pre-existing disease specific database which collects data from all available paediatric patients with SMA, independent of their treatment regimen. Adult SMA REACH is a new registry aiming to improve understanding of the impact of standards of care and new treatments on the natural history of SMA in the adult population. These registries allow collection of real-world data from routine clinical visits, within a network with transparent governance. They will employ technical solutions to enable cross border scientific and epidemiological partnership.

The data is independently owned by the HCP community. The SMA REACH UK registry is coordinated by UCL Institute for Child Health. The Adult SMA REACH registry is sponsored by The Newcastle upon Tyne Hospitals NHS Foundation Trust.

Current data fields captured cover the majority of fields in this proposed MAA, except for quality of life measures. Data fields currently already available in SMA REACH UK include:

- Patient & assessment details
- Molecular genetic diagnosis
- Motor ability based on the WHO criteria and Vignos
- Mobility
- Nutrition
- Scoliosis
- Respiratory
- Musculoskeletal issues
- Following mobility tests (RHS, HFMSE, RULM, 6MWT, HINE, CHOP-INTEND, EK2)

Relevant data fields will be similar across the two registries. The registries are responsible for ensuring that data linkage is achieved for patients who move from one registry to the other.

1.5 **Appendix D – Endpoints for assessment** the following amendment to bullet point one sub-bullet point five will be amended as follows:

- PROM/ quality of life

2. All other definitions terms and conditions contained in the MAA shall continue to apply in full force and effect.

3. The variations set out in this Variation Agreement No.3 take effect on 28, November 2022

IN WITNESS OF WHICH the Parties have signed this Variation Agreement No.1 on the date(s) shown below

NHS England John Stewart	…….. Signature National Director, Specialised Commissioning, NHS England and NHS Improvement …… Date
Biogen …… Jonathan Randell	…….. Signature …… Title …… Date
Clinical Lead **(SMA REACH UK)** …… Prof Francesco Muntoni	…….. Signature …… Title …… Date
Patient Organisation(s) **Spinal Muscular Atrophy UK** …… Liz Ryburn	…….. Signature …… Title

TreatSMA …… Dr Gennadiy Ilyashenko	…… Date …….. …….. Signature …… Title …… Date
Muscular Dystrophy UK …… Kate Adcock	…….. Signature …… Title …… Date
NICE Thomas Strong	…….. Signature Interim Associate Director, Managed Access …… Date