Dear SMA community,

In response to your request for an update on the presentations at the Annual Congress of the ***World Muscle Society, Mendoza, Argentina, October 2-6, 2018***, please find below the information.

NURTURE study data

Interim data from the phase 2 trial, NURTURE, in 25 presymptomatic infants with 5q spinal muscular atrophy was presented at the Annual Congress of the World Muscle Society.[1]

The interim analysis evaluated survival and respiratory intervention rates in infants (n=25) who were genetically diagnosed with presymptomatic SMA and also began treatment in the presymptomatic stage of the disease. As of May 2018, all patients in the study were alive and none required tracheostomy or permanent ventilation. Additionally, 22 of the 25 participants were able to walk with assistance, 17 participants were able to walk independently according to the motor milestone standard of the World Health Organization[2], and all 25 were able to sit without support.[1]

All NURTURE study participants were 14 months or older at the time of the analysis (median (range): 26.0 months (14.0–34.3).[1] Participants included infants with two copies of the SMN2 gene (n=15/25) who are likely to develop an often fatal, early-onset form of SMA known as Type 1, and infants with three copies of the SMN2 gene (n=10/25) who typically develop SMA Type 2 or 3.[3] People living with SMA Types 2 and 3 may never be able to walk or will lose that ability over time.[4] No specific safety concerns were identified.[1]

Access to reimbursed treatment

There are now 22 European countries where patients have access to nusinersen via regular reimbursement. As you can see from the table, there is a range of reimbursed access: in line with the label - 5q spinal muscular atrophy (SMA); for Type I, II, III (excluding IV) and in some cases including age restrictions e.g. <18 yrs. Additionally, in certain countries there are rare disease/ medical committees who apply further inclusion and exclusion clinical criteria. For more details, please see the following table:

Access & Reimbursement Details by Country	
Austria	Reimbursed access - in line with the label - 5q spinal muscular atrophy (SMA)
Belgium	Reimbursed access in line with the label - 5q spinal muscular atrophy (SMA) effective September 1st - inclusion/ exclusion criteria may apply
Bulgaria	Partner in place; preparing for reimbursement dossier submission
Canada	Interim agreement with pCPA. The Provinces will cover limited number of Type 1 SMA patients (according to the current HTA recommendations) and Biogen Canada will cover the most urgent Type 2 and 3 patients – defined as those with the highest risk of losing motor function. Final reimbursement criteria to be defined in January 2019, once the Canadian Agency for Drugs and Technologies

	in Health (CADTH) and the Institut national d'excellence en sante et en services sociaux (INESSS) provide their final assessment, following Biogen's resubmission in September 2018.
Croatia	Reimbursed access -Type I, II, III (<18 yrs.)
Cyprus	Access through Individual Reimbursement
Czech Republic	Reimbursed access -Types I, II and IIIa (subject to clinical criteria)
Denmark	Reimbursed access – presymptomatic, Type I & II (subject to clinical criteria)
England, Wales and Northern Ireland	NICE published its Appraisal Consultation Document (ACD), outlining a 'minded no' for the routine funding of nusinersen. The ACD is an interim decision that does not necessarily reflect the final technology guidance. There has been a consultation period during which anyone could respond with their views on the NICE ACD. NICE committee will meet again on 23 October to review the feedback and reach a final decision. Additionally, ongoing discussions underway
Estonia	Negotiations underway
Finland	Reimbursed access for patients up to, and including, 17 years old, aligned with PALKO positive recommendation.
France	Negotiations underway; current reimbursed access given to Types I, II and III through post ATU
Germany	Reimbursed access in line with the label - 5q spinal muscular atrophy (SMA)
Greece	Reimbursed access for pre-symptomatic, Types I and II; negotiations for Type III underway
Hungary	Biogen & NEAK agreement signed. Final access decisions will be made by NEAK as per the Rare Disease Committee criteria in response to all individual applications
Iceland	Reimbursed access – Types I, II, III under 18 years old
Ireland	Negotiations underway
Israel	Reimbursed access - Types I, II and III
Italy	Reimbursed access - Types I, II and III
Kuwait	Negotiations underway; current access through a named patient programme
Latvia	Submission of P&R dossier - September 2018; negotiations underway
Lithuania	Access through individual reimbursement
Luxembourg	Reimbursed access in line with the label - 5q spinal muscular atrophy (SMA)
Macedonia	Negotiations underway
Montenegro	Negotiations underway
Netherlands	Regular reimbursement for children up to 9·5 years (subject to clinical criteria); involved parties are currently discussing the possibilities of conditional reimbursement for other SMA patients – August 1st 2018
Northern Ireland	Negotiations underway
Norway	Reimbursed access -Types I, II and IIIa (0 to 18 years of age)
Poland	Negotiations underway
Portugal	Negotiations underway
Qatar	Marketing authorisation secured - access through individual reimbursement
Romania	Reimbursed access in line with the label -5q spinal muscular atrophy (SMA) - October 2018

Russia	Partner in place; preparing for reimbursement dossier submission
Saudi Arabia	Negotiations underway; current access through a named patient programme
Scotland	Reimbursed access Type I (later-onset patients funded via the Individual Treatment Fund); negotiations for Type II and III in preparation
Serbia	Access through a named patient programme
Slovakia	Reimbursed access -Types I, II and IIIa - August 1st 2018
Slovenia	Reimbursed access Types I, II and III that are treated in pediatric centers
Spain	Reimbursed access - Types I, II and III
Sweden	Reimbursed access – Pediatric (initiated below 18 years old) Types I, II and IIIa
Switzerland	Reimbursed access (pre-symptomatic and Type I, II, III) up to 20 years old; Individual reimbursement for patients above 20
Turkey	Negotiations ongoing; current access through a named patient programme
Ukraine	Partner in place; preparing for reimbursement dossier submission
UAE	Negotiations underway; current access through a named patient programme

We will continue to be available to provide updates in the future, when requested.

Best regards,
The SMA Biogen Team

References

[1] Swoboda KJ, *et al*. Nusinersen in Infants Who Initiate Treatment in a Presymptomatic Stage of Spinal Muscular Atrophy (SMA): Interim Efficacy and Safety Results From the Phase 2 NURTURE Study. October 6th 2018. 23rd International Annual Congress of the World Muscle Society. 2–6 October 2018. Mendoza, Argentina.

[2] WHO MULTICENTRE GROWTH REFERENCE STUDY GROUP. WHO Motor Development Study: Windows of achievement for six gross motor development milestones. 2006; Suppl 450: 86/95.

[3] Feldkotter M, *et al.* Quantitative Analyses of SMN1 and SMN2 Based on Real-Time LightCycler PCR: Fast and Highly Reliable Carrier Testing and Prediction of Severity of Spinal Muscular Atrophy. Am. J. Hum. Genet. 70:358–368, 2002.

[4] Spinal Muscular Atrophy Support UK and Muscular Dystrophy UK in collaboration with The SMA Trust. Key Facts about Spinal Muscular Atrophy. February 2017.

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