18 May 2020
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Committee for Orphan Medicinal Products

Orphan Maintenance Assessment Report

Zolgensma (adeno-associated viral vector serotype 9 containing the human *SMN* gene, onasemnogene abeparvovec)
Treatment of spinal muscular atrophy
EU/3/15/1509
Sponsor: AveXis EU Limited

Note

Assessment report as adopted by the COMP with all information of a commercially confidential nature deleted

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1. Product and administrative information

Product	
Active substance	Adeno-associated viral vector serotype 9 containing the human *SMN* gene
International Non-Proprietary Name	Onasemnogene abeparvovec
Orphan condition	Treatment of spinal muscular atrophy
Pharmaceutical form	Solution for infusion
Route of administration	Intravenous use
Pharmaco-therapeutic group (ATC Code)	Other drugs for disorders of the musculo-skeletal system (M09AX09)
Sponsor's details:	AveXis EU Limited Block B, The Crescent Building Northwood, Santry Dublin 9, Co. Dublin D09 C6X8 Ireland
Orphan medicinal product designation procedural history	
Sponsor/applicant	AveXis EU, Ltd
COMP opinion date	13 May 2015
EC decision date	19 June 2015
EC registration number	EU/3/15/1509
Post-designation procedural history	
Transfer of sponsorship	Transfer from AveXis EU Ltd to AveXis Netherlands B.V. – EC decision of 27 September 2018
	2nd transfer from AveXis Netherlands B.V. to AveXis EU Limited – EC decision of 26 September 2019
Marketing authorisation procedural history	
CHMP rapporteurs	J. H. Ovelgonne, E. Flory
Applicant	AveXis EU Limited
Application submission date	15 October 2018
Procedure start date	1 November 2018
Procedure number	EMA/H/C/0004750
Invented name	Zolgensma
Therapeutic indication	Zolgensma is indicated for the treatment of: - patients with 5q spinal muscular atrophy (SMA) with a bi-allelic mutation in the SMN1 gene and a clinical diagnosis of SMA Type 1, or - patients with 5q SMA with a bi-allelic mutation in the SMN1 gene and up to 3 copies of the SMN2 gene. Further information on Zolgensma can be found in the European public assessment report (EPAR) on the Agency's website https://www.ema.europa.eu/en/medicines/human/EPAR/Zolgensma
CHMP opinion date	26 March 2020
COMP review of orphan medicinal product designation procedural history	
COMP rapporteurs	A. Magrelli, F. Naumann-Winter
Sponsor's report submission date	30 November 2018

COMP opinion date (adoption via written procedure)	1 April 2020

2. Grounds for the COMP opinion (orphan medicinal product designation)

The COMP opinion that was the basis for the initial orphan medicinal product in 2015 designation was based on the following grounds:

The sponsor AveXis EU, Ltd submitted on 24 February 2015 an application for designation as an orphan medicinal product to the European Medicines Agency for a medicinal product containing adeno-associated viral vector serotype 9 containing the human SMN gene for treatment of spinal muscular atrophy (hereinafter referred to as "the condition"). The application was submitted on the basis of Article 3(1)(a) first paragraph of Regulation (EC) No 141/2000 on orphan medicinal products.

Having examined the application, the COMP considered that the sponsor has established the following:

- the intention to treat the condition with the medicinal product containing adeno-associated viral vector serotype 9 containing the human SMN gene was considered justified based on preclinical data in a valid in vivo model of the condition, where administration of the product resulted in expression of the missing protein and improved motor function and survival;
- the condition is life-threatening and chronically debilitating due to muscle wasting, weakness, failure to thrive, pulmonary and orthopaedic complications;
- the condition was estimated to be affecting less than 0.4 in 10,000 persons in the European Union, at the time the application was made.

Thus, the requirements under Article 3(1)(a) of Regulation (EC) No 141/2000 on orphan medicinal products are fulfilled.

The sponsor has also established that there exists no satisfactory method of treatment that has been authorised in the European Union for patients affected by the condition.

Thus, the requirement under Article 3(1)(b) of Regulation (EC) No 141/2000 on orphan medicinal products is fulfilled.

The COMP concludes that the requirements laid down in Article (3)(1) (a) and (b) of Regulation (EC) No 141/2000 on orphan medicinal products are fulfilled. The COMP therefore recommends the designation of this medicinal product, containing adeno-associated viral vector serotype 9 containing the human *SMN* gene as an orphan medicinal product for the orphan indication: treatment of spinal muscular atrophy.

3. Review of criteria for orphan designation at the time of marketing authorisation

Article 3(1)(a) of Regulation (EC) No 141/2000

Intention to diagnose, prevent or treat a life-threatening or chronically debilitating condition affecting not more than five in 10 thousand people in the Community when the application is made

Condition

Spinal muscular atrophy is a neurodegenerative disease manifesting with progressive alpha motor neuron degeneration and subsequent muscle atrophy. In approximately 95% of cases it is caused by the deletion, -mutation or conversion of the SMN1 gene on chromosome 5q and is inherited as an autosomal recessive disease. SMN1 produces the Survival Motor Neuron protein, which role is multifactorial and still incompletely understood. One of the most studied functions is assembly of small nuclear ribonucleoproteins (snRNPs), which is mediated through a complex of several proteins including Gemin2-8 and unrip (Arnold et al 2015, Muscle Nerve 51:157-167, Howell et al. Future Med Chem. 2014 Jun; 6(9): 1081–1099.).

SMN protein is found in the cytoplasm as well as in the nucleus and has been identified in structures called "Gemini of coiled bodies" or simply "gems". The SMN gene is present in multiple copies in the human genome: one SMN1 (telomeric) and several SMN2 (centromeric). SMN2 transcripts are not able to translate properly, as during mRNA splicing exon7 is not included, resulting in a presumably unstable and not functional protein that is degraded. Consequently, in case SMN1 function is lost, even though several SMN2 copies may exist, they cannot fully compensate for the loss of expression of SMN protein. Correct splicing may vary by the severity of the disease and may be said to occur in as low as only about 10% of SMN2 transcripts (Lunn 2008 Lancet; 371:2120-33).

The disease has been traditionally classified according to the clinical severity and age of onset as: Type I (severe, Werdnig-Hoffmann disease) Type II (intermediate), Type III (mild, Kugelberg-Welander disease) and Type IV (adult).

The proposed therapeutic indication "ZOLGENSMA is indicated for the treatment of:

- patients with 5q spinal muscular atrophy (SMA) with a bi-allelic mutation in the SMN1 gene and a clinical diagnosis of SMA Type 1, or

- patients with 5q SMA with a bi-allelic mutation in the SMN1 gene and up to 3 copies of the SMN2 gene"

falls entirely within the scope of the designated orphan condition "spinal muscular atrophy".

Intention to diagnose, prevent or treat

The intention to treat the condition was accepted based on the positive benefit/risk assessment of the CHMP (see EPAR of Zolgensma).

Chronically debilitating and/or life-threatening nature

The COMP has previously acknowledged that the condition is life-threatening and chronically debilitating due to muscle wasting, weakness, failure to thrive, pulmonary and orthopaedic complications. This view is retained.

Number of people affected or at risk

There are three methods used by the sponsor to give estimates of the number of affected patients: a) review of the current literature mainly focusing on a review paper by Verhaart et al, based on which the sponsor suggests a prevalence range of between less than 0.1 and 0.9 per 10,000; b) an estimation from birth incidence data suggesting a prevalence of approximately 0.2 per 10,000 and c) an estimation of prevalence from carrier frequency studies of 0.2 to 0.44 per 10,000.

In particular, the sponsor cites a review paper by Verhaart and colleagues (Prevalence, incidence and carrier frequency of 5q-linked spinal muscular atrophy - a literature review. Orphanet J Rare Dis.

2017a Jul 4;12(1):124). The applicant used country-specific data from this application and corrected for all subtypes by also taking into consideration the proportions reported in Ogino et al., (Eur J Hum Genet 2004;12:1015–1023). Overall the sponsor provides an estimate between <0.1 and 0.7 per 10,000 (Table 1 below).

Table 1. Adopted from the sponsor's March 2020 maintenance report.

Country/Region	Study time point (point prevalence)	Incidence per live births *	Calculated[C] (Reported[R]) SMA (all types) Prevalence [Subtype]	Reference
Croatia	2016	-	0.93[R]	Draušnik *et al.*, 2019
Estonia	2003	-	0.02 [1][R] 0.03[C]	Verhaart *et al.*, 2017a
France	2018		0.18	Urtizberea *et al.*, 2018
Germany	1987	-	0.02 [1][R] 0.03[C]	Verhaart *et al.*, 2017a
Germany	1980	-	0.16 [2 & 3][R] 0.38[C]	Verhaart *et al.*, 2017a
Germany	2013	-	0.03[C]	Klug *et al.*, 2016
Italy	1989	-	0.66[R]	Verhaart *et al.*, 2017a
Norway	1983	-	0.42[R]	Verhaart *et al.*, 2017a
Poland	1985		0.12 [2 & 3][C] 0.31[C]	Verhaart *et al.*, 2017a
Sweden	1995, 2006	-	0.28 to 0.32[R]	Verhaart *et al.*, 2017a
UK	1971	-	0.12 [2 & 3][R] 0.31[C]	Verhaart *et al.*, 2017a
UK	1994, 2007	-	0.14 to 0.19[R]	Verhaart *et al.*, 2017a

* Where prevalence is reported in the publication, birth incidence is not provided and no calculation of prevalence from incidence was undertaken. All-type SMA Prevalence calculated (C) from reported subtype (R) is based on the proportions reported in Ogino *et al.*, (2004), Klug *et al.*, 2016 states several limitations with their retrospective study including the voluntary nature of the patient registry used for recruitment of study participants.

The sponsor has also derived an estimate from birth incidence, by referring data reported by Verhaart et al (Verhaart et al., J Neurol. 2017 Jul;264(7):1465-1473.) in conjunction with i) Eurostat birth rates for 2016 ii) proportions of subtypes as per Ogino et al., (Eur J Hum Genet 2004;12:1015–1023) and iii) median survival for each subtype reported by Farar et al (J Pediatr 2013;162(1):155-159). This method yields an estimate of 0.24 per 10,000.

A third estimate based on carrier frequencies reported in the recent literature (from mainly non-European studies) and the original orphan drug application (using European data from 2013), is also provided by the sponsor, giving a theoretical prevalence between 0.2 and 0.44 in 10,000.

The COMP has previously considered less than 0.4 per 10,000 and this can be retained for this application, in line with the main review paper cited by the sponsor.

Article 3(1)(b) of Regulation (EC) No 141/2000

Existence of no satisfactory methods of diagnosis prevention or treatment of the condition in question, or, if such methods exist, the medicinal product will be of significant benefit to those affected by the condition.

Existing methods

Spinraza, which is a 2´-O-(2-methoxyethyl) antisense oligonucleotide (ASO) consisting of 18 nucleotides has received a centralised MA in the EU and is indicated for "the treatment of 5q Spinal Muscular Atrophy".

Patients are also managed by supportive care, including provision of nutrition and respiratory assistance as needed and treating or preventing complications of weakness.

Significant benefit

Protocol Assistance was obtained including a question on significant benefit. It was discussed at the time that a) that significant benefit could be based on indirect comparisons between the Spinraza study CS3B (also called ENDEAR) and the CL-101 study of the sponsor and b), any claim of major contribution to patient care should be supported by clinical data supporting improved convenience by reduction of the burden of treatment for patients and caregivers.

At this stage of maintenance (updated report of the sponsor submitted March 13, 2020), an indirect comparison versus nusinersen is presented in line with the above recommendations. With regards to efficacy, comparisons of both symptomatic type 1 patients, as well as pre-symptomatic patients are presented.

As regards the symptomatic type 1 patients, improved efficacy is argued on the basis of data from study CL-101, juxtaposed to Spinraza studies ENDEAR (CS3B) as well as CS3A. CS3B was the pivotal phase 3 DB study for nusinersen enrolling SMA Type 1 patients, while CS3A was an open label study in type 1 patients.

Study CS3B (ENDEAR) enrolled symptomatic infants (symptom onset before 6 months of age, and ≤7 months of age at screening), diagnosed with SMA-1 (2 copies of the SMN2 gene). In comparison, patient population in study AVXS-101-CL-101 was 6 months of age and younger at the day of vector infusion with Type 1 SMA as defined by: (a) Bi-allelic SMN1 gene mutations with 2 copies of SMN2; (b) Patients 6 months and younger with disease onset up to 6 months of age; (c). Hypotonia by clinical evaluation with delay in motor skills, poor head control, round shoulder posture, and hypermobility of joints (The first 9 patients were enrolled under previous versions of the protocol, which allowed an age range of 9 months or younger).

Survival in ENDEAR was defined as time to either (a) death or (b) permanent ventilation, defined as ≥16 hours ventilation/day continuously for >21 days in the absence of an acute reversible event or tracheostomy. For CS3A, event-free survival was determined by the proportion of patients who were alive and did not require permanent ventilatory support (defined as tracheostomy or the need for ≥16 hours ventilation/Day continuously for at least 2 weeks in the absence of an acute reversible illness).

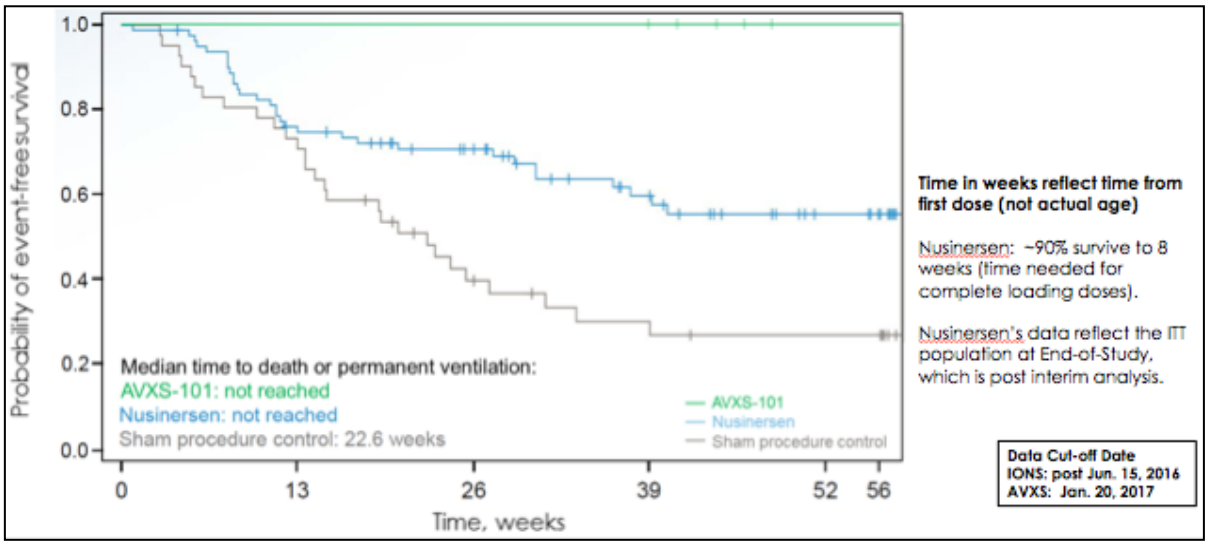
In the AVXS-101-CL-101 study, the primary efficacy endpoint was the time from birth to either (a) requirement of tracheostomy or ≥16-hour respiratory assistance per day (includes bi-level positive airway pressure [BiPAP]) continuously for ≥2 weeks in the absence of an acute reversible illness, excluding perioperative ventilation or (b) death.

It should be noted that the main efficacy survival endpoint for the nusinersen ENDEAR study was slightly less restrictive than the criteria used in the AveXis AVXS-101-CL-101 study (permanent ventilation, defined as ≥16 hours ventilation/day continuously for >21 days compared with the conventional 14 day criteria used in the AveXis study).

The sponsor discusses that all 12 patients (100%) in AVXS-101-CL-101 Cohort 2 (the therapeutic dose) were event-free over a 24-month follow-up period, compared with 61% of nusinersen-treated patients and 32% of control patients in ENDEAR over a ~13-month observation period. In the nusinersen CS3A study, 3 patients died during the study period. Event-free survival at Day 910 was 69% in CS3A Cohort 2 (64% when the 2 children with 3 copies of SMN2 are excluded), with all events occurring by study Day 546. In the 12 mg nusinersen cohort, 2 participants had a tracheostomy at 6.3 months and 17.4 months

In the AVXS-101-CL-101 study all patients (15/15) were alive and without the need for permanent ventilatory support at the final study visit 24 months post-dose (one patient in Cohort 1 required permanent ventilation at approximately 28 months [22 months post-dose] for hypersalivation; however, the child's ventilatory requirement lessened to below the 16 hours/day threshold after surgical ligation of the salivary glands, thus meeting the survival endpoint). All 12 patients in the therapeutic dose arm remained alive and without the need for permanent ventilation throughout the 24-month follow-up period of the study. No patients failed therapy and no other additional SMA targeted therapies (such as nusinersen) were given.

Figure 1. Kaplan-Meier Curves for Time to Death or Permanent Ventilation: Nusinersen vs. AVXS-101



Further to the comparison of the main endpoint, the sponsor also notes:

- Improvements in motor function, as assessed by CHOP-INTEND total score. The score increased shortly after AVXS-101 administration and was sustained over time for all 12 patients in AVXS-101-CL-101 Cohort 2 and that the level of motor function improvement achieved by AVXS-101-treated patients substantially exceeded that achieved by nusinersen-treated patients in either ENDEAR or Study CS3A.
- Ventilation improvements: It is reported that 7 of 12 AVXS-101-treated patients (58%) did not require any chronic ventilatory support (and thus required <10% of time on ventilator support) assessed when all patients had reached at least 13.6 months of age. Among the 5 patients that did, all were single instances of intubation while the patient was hospitalised, with the duration of use ranging from 1 to 9 days. By comparison, only 33% of nusinersen-treated patients in ENDEAR required <10% of time on ventilator support, and 31% required ventilatory support for >50% of the time.
- It is also argued that all of the comparable developmental milestones showed an advantage for AVXS-101 over nusinersen. For example, 92% of AVXS-101-treated patients achieved

independent sitting versus 10% of nusinersen-treated patients in the final analysis of the ENDEAR study and 36% at the interim analysis in Study CS3A. Two of 12 (17%) AVXS-101-treated patients were able to walk independently at the time of the primary efficacy endpoint of 13.6 months, whereas no nusinersen-treated patients achieved this milestone after similar treatment periods.

- An improvement in the number of hospitalisations is also discussed. Patients treated with the therapeutic dose of AVXS-101 required an average of 2.1 hospitalisations per patient year (up to 24 months follow-up), whereas nusinersen-treated patients in ENDEAR required an average of 4.5 hospitalisations per patient year (up to 13 months follow-up). The mean proportion of time hospitalized for nusinersen-treated patients was 11.4% (range, 0-50.0%); 59% were hospitalized <10% of the time, and 18% were hospitalized ≥20% of the time. For AVXS-101-treated patients, the mean proportion of time hospitalized was 4.4% (range, 0-18.3%); 83% were hospitalized <10% of the time; none were hospitalized ≥20% of the time (Arjunji et al., 2019). Sixteen percent of AVXS-101-treated patients required no hospitalisations, whereas only 2% of nusinersen-treated patients required no hospitalisations

A second indirect comparison with the effects on presymptomatic patients is also performed between the ongoing studies CL-304 of the sponsor and nusinersen's study CS5 (NURTURE). AVXS-101-CL-304 is a global Phase 3, open-label, single-arm study of a single IV infusion of AVXS-101 in pre-symptomatic SMA patients with genetically diagnosed Types 1 and 2 who are aged ≤6 weeks. The study is ongoing and was fully enrolled as of 08 November 2019 with a total of 30 patients enrolled. This is juxtaposed to nusinersen study CS5 (NURTURE) which is an ongoing, Phase 2, open-label, single-arm, multinational study of intrathecal nusinersen in infants who initiate treatment early. NURTURE consists of a 5-year treatment period and a post-treatment follow-up evaluation. Participants received nusinersen 12 mg administered as intrathecal injections by lumbar puncture, with four loading doses (administered on Days 1, 15, 29, and 64), followed by a maintenance dose every 119 days over five years.

The NURTURE study has been ongoing for over 24 months and at the time of the recently published interim results from March 2019, all infants were ≥25 months old (De Vivo et al., J Neuromuscul Disord. 2019; 29(11):842-856). The AVXS-101-CL-304 study has been ongoing for about 18 months and the patients are younger than those reported in the NURTURE study. The sponsor notes a "comparable" efficacy across the efficacy parameters presented, that are common to both trials in pre-symptomatic SMA infants (survival, attainment of developmental milestones, motor function).

Such a "comparable" efficacy is not helpful to establish significant benefit. For example with regards to survival, at an interim analysis of the CS5 (NURTURE) study when patients had been on study for a median of 27.1 months and were of a median age at last visit of 26.0 months, all 25 patients (2 SMN2 gene copies, n=15; 3 SMN2 gene copies, n=10) were alive without permanent ventilation. The primary endpoint of time to death or respiratory intervention could not be estimated at the interim analysis as there were too few events.

Another group of arguments is based on a major contribution to patient care. It is postulated that only a single dose of AVXS-101 is highly likely to reduce the burden of treatment for patients and caregivers when compared with nusinersen and is not limited by the potential for interruption of therapy. AVXS-101 shows improvement in outcomes expected to impact patient care (including swallowing function, nutritional support, frequency and duration of hospitalisations, pulmonary events and ventilatory support and bulbar function). However, there is little or no data available in the literature for nusinersen for these other outcomes, that would allow for a comparison.

- In CL-101, parent(s)/legal guardian(s) reported the number of hours per day the patient required ventilation support over the two weeks prior to the visit if support was being used (Al-Zaidy et al., Pediatr Pulmonol 2019;54(2):179-185). At baseline (mean age 3.4 months, range [0.9-7.9]), 10 of 12 (83%) patients in Cohort 2 did not require noninvasive ventilation (NIV), and no patient required a tracheostomy at any time throughout the 2-year study period. As of their final study visit, 7 of the 10 patients who did not require ventilator support before dosing completed the study without any ventilator support. All three patients who did not require NIV at baseline but required it postdosing had an early onset of symptoms in the first month of life and a rapid disease progression characterized by diffuse muscle weakness, respiratory insufficiency, and inability to swallow. The NIV was required in the context of viral illnesses and was maintained thereafter. All five infants who required NIV at the final study visit remained stable post-dosing (Al-Zaidy et al. Pediatr Pulmonol 2019;54(2):179-185).
- CL-101 included videofluoroscopic swallow test assessment to determine swallowing integrity and the need for supplemental enteral feeding. This test was performed at baseline and at the end of study (Al-Zaidy et al., Pediatr Pulmonol 2019;54(2):179-185). At baseline, 7 of 12 (58%) patients were able to feed orally and did not require supplemental nutritional support, defined as enteral feeding. Of these 7 patients who entered the study requiring no nutritional support, 6 (86%) continued to receive no nutritional support and exclusively fed by mouth (the seventh patient continues to feed orally). Video-fluoroscopic swallow studies showed that the number of patients who achieved safe swallow function using thin liquids increased from 4 (33%) patients pre-treatment to 10 (83%) patients at the end of the follow-up period. The number of patients able to safely swallow to allow for at least partial oral feeding increased from 7 (58%) patients at baseline to 11 (92%) patients at the end of the follow-up period. Of the 5 patients who entered study AVXS-101-CL-101 receiving non-oral feeding support, 4 developed or maintained the ability to feed by mouth.
- Speech following AVXS-101 treatment was also analysed and 11 of 12 (92%) patients were able to speak by the end of the study (Al-Zaidy et al. Pediatr Pulmonol 2019;54(2):179-185).

As discussed above, while there are no comparisons to be made on the patient care presented data, the sponsor has included an indirect comparison of the pivotal trial of nusinersen versus CL-101 data, that supports an improvement in the time to death or permanent ventilation. This may be considered as a clinically relevant advantage. However, it also has to be noted that during the evaluation the CL-101 study was considered to be a supportive study due to the manufacturing process of the used product.

It is of note that some of the above data stem from a different process of manufacturing than the commercial (process B) product. This is the reason why CL-101 was considered during the assessment procedure to be a supportive study, and study CL-303 a pivotal study. The latter is a recently completed (last patient last visit 12 Nov 2019) Phase 3, open-label, single-arm, single-dose study in patients with SMA Type 1 with 1 or 2 copies of the survival motor neuron 2 (SMN2) gene conducted in the United States.

With regards to the CL-303-study results:

- Co-primary efficacy endpoints were the proportion of patients who achieved functional independent sitting for ≥ 30 seconds at the 18 months of age study visit and survival at 14 months of age. Of the 22 enrolled patients, it was reported that 20 (90.9%) were alive without permanent ventilation at 14 months of age. The applicant also reported that 14 patients (63.6%) achieved the co-primary endpoint, sitting without support for at least 30 seconds.

- Co-secondary efficacy endpoints include the proportion of patients maintaining the ability to thrive, and the proportion of patients who are independent of ventilatory support. Nine patients (40.9%) met all criteria for ability to thrive at 18 months of age. Seventeen of 22 patients (77.3%) were independent of ventilatory support (as assessed by Trilogy BiPAP data) at 18 months of age. It is also reported by the sponsor that 21 patients (95.5%) achieved a CHOP-INTEND score $\geq$ 40, 14 patients (63.6%) had achieved a CHOP-INTEND score $\geq$ 50, and 5 patients (22.7%) had achieved a CHOP-INTEND score $\geq$ 60.

Despite the fact that the sponsor does not use the CL-303 study to perform comparisons versus nusinersen, the improvement in survival with regards to the CL-101 comparisons, as presented above, can be considered as a clinically relevant advantage of improved efficacy.

4. COMP list of issues

Not applicable.

5. COMP position adopted on 1 April 2020

The COMP concluded that:

- the proposed therapeutic indication falls entirely within the scope of the orphan condition of the designated Orphan Medicinal Product;
- the prevalence of spinal muscular atrophy (hereinafter referred to as "the condition") was estimated to remain below 5 in 10,000 and was concluded to be less than 0.4 in 10,000 persons in the European Union, at the time of the review of the designation criteria;
- the condition is life-threatening and chronically debilitating due to muscle wasting, weakness, failure to thrive, pulmonary and orthopaedic complications;
- although satisfactory methods of treatment of the condition have been authorised in the European Union, the assumption that Zolgensma may be of potential significant benefit to those affected by the orphan condition still holds. The sponsor has presented an indirect comparison versus nusinersen, supporting an improvement in survival or time to permanent ventilation in treated patients with type I disease. The Committee considers that this constitutes a clinically relevant advantage.

The COMP, having considered the information submitted by the sponsor and on the basis of Article 5(12)(b) of Regulation (EC) No 141/2000, is of the opinion that:

- the criteria for designation as set out in the first paragraph of Article 3(1)(a) are satisfied;
- the criteria for designation as set out in Article 3(1)(b) are satisfied.

The Committee for Orphan Medicinal Products has recommended that Zolgensma, adeno-associated viral vector serotype 9 containing the human *SMN* gene, onasemnogene abeparvovec, EU/3/15/1509 for treatment of spinal muscular atrophy is not removed from the Community Register of Orphan Medicinal Products.