Evaluate Vantage

May 07, 2019

AAN 2019 – Roche confirms its place in spinal muscular atrophy

Amy Brown

A slew of data on spinal muscular atrophy projects over the weekend shows that this tiny market is set for some big competition, with Novartis, Roche and Biogen jostling for position.

The three leading developers of therapies for spinal muscular atrophy were out in force at the Annual Academy of Neurology this weekend, vying for the attention of physicians who treat the rare childhood degenerative disease. All presented compelling new datasets, showing just how competitive this tiny market is set to become.

This will really hot up should Novartis's gene therapy Zolgensma receive US approval in the coming days, and new data at the conference will raise hopes of a broad label, encompassing all subtypes of the disease. Meanwhile, updates from Roche confirm its oral candidate risdiplam as a viable future treatment, albeit one that is a couple of years from the market.

This is all bad news for Biogen, which also presented new analyses of Spinraza, an antisense oligonucleotide that is for the moment the only marketed SMA drug. Comparing across studies is always fraught with difficulties, but with every fresh update from rivals it becomes harder to see how the US biotech can wring much more growth from this product.

The SMA leaders

			Global sales ($m)			
Product	**Company**	**Mechanism**	**2019e**	**2020e**	**2022e**	**2024e**
Spinraza	Biogen	SMN 2 antisense	2,001	2,156	1,816	1,655
Zolgensma	Novartis	SMN gene therapy	125	563	1,446	1,635
Risdiplam	Roche	SMN 2 gene splicing modifier	-	49	464	797

Source: EvaluatePharma.

This is particularly true in the most severe form of the disease, type 1, a subset of patients in most need of treatment and where Novartis's gene therapy is expected to become standard of care. Few type 1 infants survive more than two years, but in an update on the Str1ve study in these patients, 13 of 15 Zolgensma-treated infants survived to 13.6 months without requiring permanent ventilation.

Infants continued to achieve motor milestones not typically seen, and it seems that the effectiveness of this gene therapy – at least in the first few months after treatment – is largely confirmed.

Updates from Roche's risdiplam in type 1 infants were also very encouraging; the company presented some longer-term data from the Firefish study, notably from a group of subjects who received the dose that was selected for the confirmatory second stage of the study. Highlights include survival of 88% and the ability of one infant to stand unassisted – a huge milestone for those with this condition.

The table below shows that risdiplam appears to be beating Spinraza. Final data from Firefish are not due until the end of the year, but it seems that in the not too distant future Biogen will have to fight hard for patients who do not qualify for gene therapy.

Selected data points from SMA type 1 trials			
	Spinraza	**Risdiplam**	**Zolgensma**
	Phase III Endear study, 12mth post treatment	**Infants on dose selected for confirmatory part 2, after 12mth**	**Str1ve study, March 8, 2019 data cut**
Survival	61% (n=80)	88% (n=17)	95% (n=20, to 10.5 months)
Rolling	10% (n=73)	59% (n=17)	41% (n=22)
Sitting unassisted*	8% (n=73)	41% (n=17)*	50% (n=22)
Standing assisted	1% (n=73)	6% (n=17)	5% (n=22)
**Spinraza and Zolgensma trials use sitting for 30 seconds, risdiplam for at least five seconds. Source: AAN presentations, company press releases.*			

Beyond the type 1 patients Biogen's future position does not appear any stronger. A first look at data from Novartis's Strong trial, in subjects with type 2, seem to support the view that the regulator will be comfortable granting Zolgensma a broad label; the price that Novartis choses might cause payers to be less generous.

Clinically meaningful improvements in motor function make for impressive reading, and look similar to data generated by Spinraza in these patients. 60% of those in the older cohort, who were 24-60 months old at dosing, improved by more than three points on the HFMSE motor function scale after seven months; in Biogen's Cherish study, which recruited similar patients, 57% had at least a three-point improvement.

Important differences in trial design and enrolment make comparisons difficult, but Zolgensma certainly looks competitive enough here, and importantly its once-and-done offering is much more attractive than Biogen's monthly spinal injections. Analysts at Evercore ISI point out that Novartis has started a higher-dose cohort in this trial, so it seems that there is room for further improvement.

Again, Roche cannot be forgotten in this setting: an update from the Sunfish study, enrolling type 2 and type 3 patients, also generated very encouraging survival data, and improvements on motor scores. A different motor scale was used, called MFM32; among 43 patients for whom 12-month follow-up was available, 58% saw an improvement of at least three points. The broad population in Sunfish makes comparisons particularly difficult, though the overall conclusion is that risdiplam looks good.

With threats coming from two angles, it is no wonder that numbers for Biogen's Spinraza have come down: over the past 12 months 2024 consensus has fallen by 22%, to sales of $1.7bn, according to *EvaluatePharma*.

Defenders of Spinraza point out that the therapy is well entrenched, and that it is the only SMA agent to have been put through rigorous, placebo-controlled studies. But these arguments have lost water as Roche and Novartis have continued to generate competitive data over ever longer periods, and updates over the weekend will do nothing to plug the leak.

The table has been corrected to clarify that the Str1ve data were out to 10.5 months.

More from Evaluate Vantage

Evaluate HQ
44-(0)20-7377-0800

Evaluate Americas
+1-617-573-9450

Evaluate APAC
+81-(0)80-1164-4754