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Zolgensma flatlines, but Spinraza isn’t the beneficiary

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A fiercely competitive three-horse race in spinal muscular atrophy is Evrysdi’s for the taking.

Just five years ago spinal muscular atrophy was a niche childhood condition with no disease-modifying treatments. Today it is the scene of a fierce battle between three approved drugs, two of which have come under extreme pressure in the US.

And, if last week’s quarterly update for one of them, Biogen’s Spinraza, was disappointing, then today’s numbers from another, Novartis’s Zolgensma, seem little better. A market that has featured clinical missteps, and which has been hit by the Covid-19 pandemic, appears to be Roche’s for the taking.

Roche’s Evrysdi, an oral drug licensed from PTC Therapeutics, posted first-quarter US sales of CHF79m ($86m), a 72% quarter-on-quarter increase in only its second full quarter on the market. Evrysdi is the latest headache to hit Spinraza, an antisense drug that until recently was the standard of care, and the gene therapy Zolgensma, which had briefly challenged Spinraza’s dominance.

Falling from high

Zolgensma was approved in mid-2019, and its launch marked the point at which Spinraza’s US sales started to plummet. Today Novartis boasted of having treated 1,200 SMA patients worldwide with Zolgensma, which posted first-quarter sales of $319m – a 26% increase from the previous quarter, and up 88% year on year.

However, these numbers belie a worrying fact, namely that the gene therapy has stalled in the US, having sold roughly $120m there in each of the last five quarters. As things stand Zolgensma’s US revenue peaked at $150m in the third quarter of 2019 – the therapy’s first full quarter on the market.

On an analyst call today Novartis said Zolgensma sales were being driven by reimbursement wins in Europe. While increased screening of newborns for SMA is expected to help Zolgensma, in the US this will amount to nothing more than treading water for at least the rest of 2021.

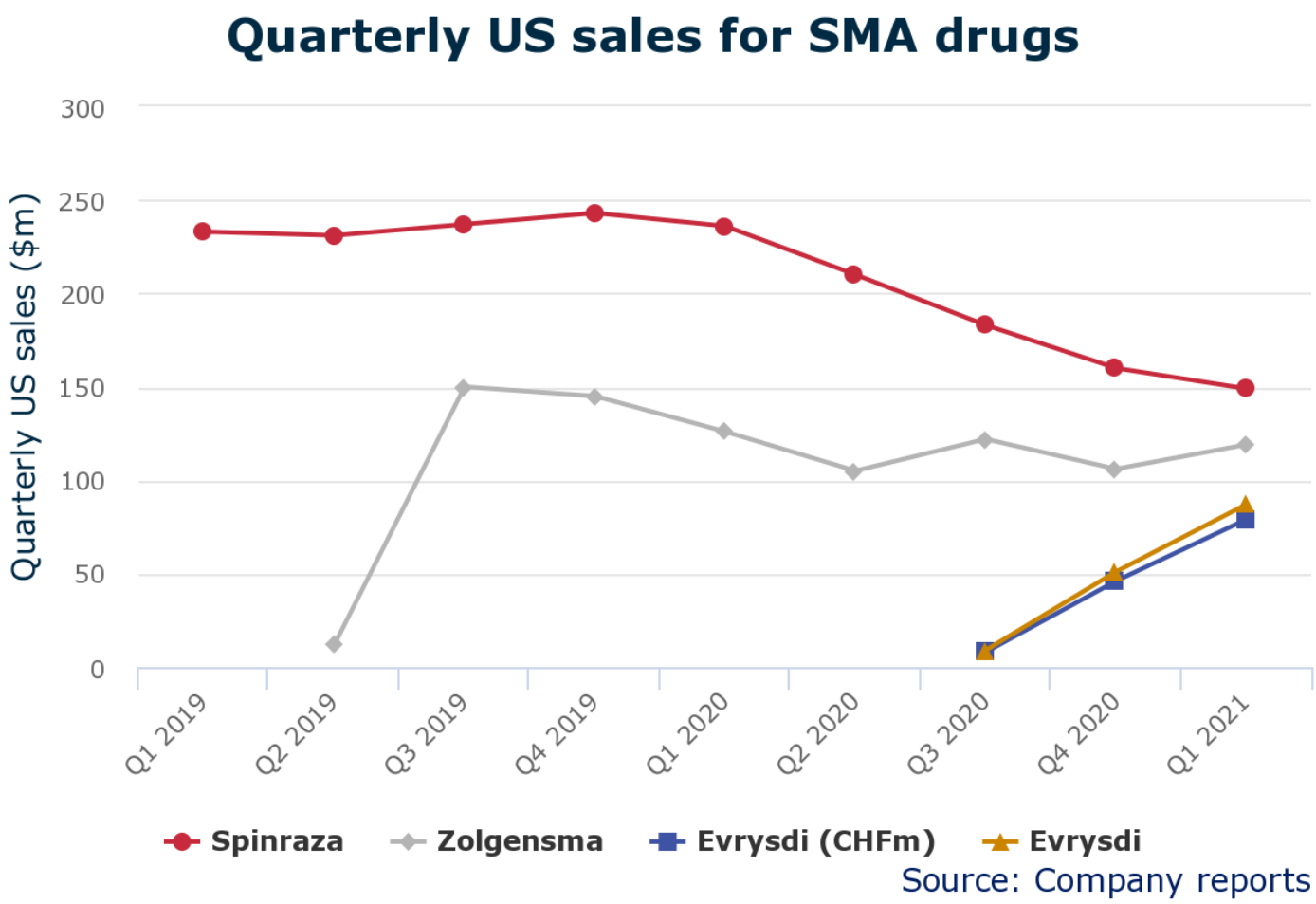
Part of the reason for the ongoing disappointment has been Covid-19, and the onset of the pandemic and concomitant lockdowns over a year ago were said to have slowed new patient starts on Zolgensma and switches from Spinraza.

But Zolgensma has been troubled from the beginning, when Novartis acquired its originator, Avexis. A data

manipulation scandal followed, and months after IV Zolgensma got approved its intrathecal version was put on clinical hold because of a preclinical toxicity signal.

Then, last September, the US FDA put another roadblock in the way of intrathecal Zolgensma, requesting an additional confirmatory study. This is thought to have delayed launch by two years from early 2022, before considering the effect of the clinical hold, which 18 months after being imposed remains in place with no signs of being lifted.

The intrathecal formulation is vital for Novartis to regain lost ground, as it would allow babies over the age of two, the limit for IV Zolgensma, to be treated.



Still, if Novartis has a mountain to climb with Zolgensma, for Spinraza the situation seems even worse. With no sign of stabilisation in US sales, which are continuing to fall even as Covid-19 recedes, Biogen continues to cite a competitive market, and analysts say revenue growth is the optimistic scenario.

Adding to this gloom were figures Biogen released last week, showing that the number of patients on Spinraza has remained stuck at about 11,200 for the past three quarters. Spinraza is priced broadly in line with Zolgensma if the annual cost of the necessary maintenance treatment is taken into account.

Against this backdrop Roche launched Evrysdi at a discount of 25-60% versus Spinraza and Zolgensma, if five years of therapy is considered.

Little wonder that the sellside has boosted forecasts for Evrysdi, which had been expected to bring in $866m in 2024, according to *Evaluate Pharma's* archived 2019 consensus; today the 2024 forecasts stands at $1.7bn.

True, it is still early days for Evrysdi, but the prospect of a relatively cheap, oral drug seems to be a winning formula. Novartis does have its own mRNA splicing modifier, branaplam, in phase 2, but this will not be filed for SMA until 2025 or later.

Approved SMA products			
Product	**Patient population**	**List cost**	**2026e sales ($m)**
Spinraza (Biogen/Ionis)	All SMA types, all ages	$750,000 in first year, then $375,000/yr	1,307
Zolgensma (Novartis)	Type 1/2 children aged two or under	$2.1m one-off cost (spread over 5 yrs)	1,904
Evrysdi (Roche/PTC)	All SMA types, all ages	Up to $340,000/yr	2,071
Source: Evaluate Pharma & company documents.			