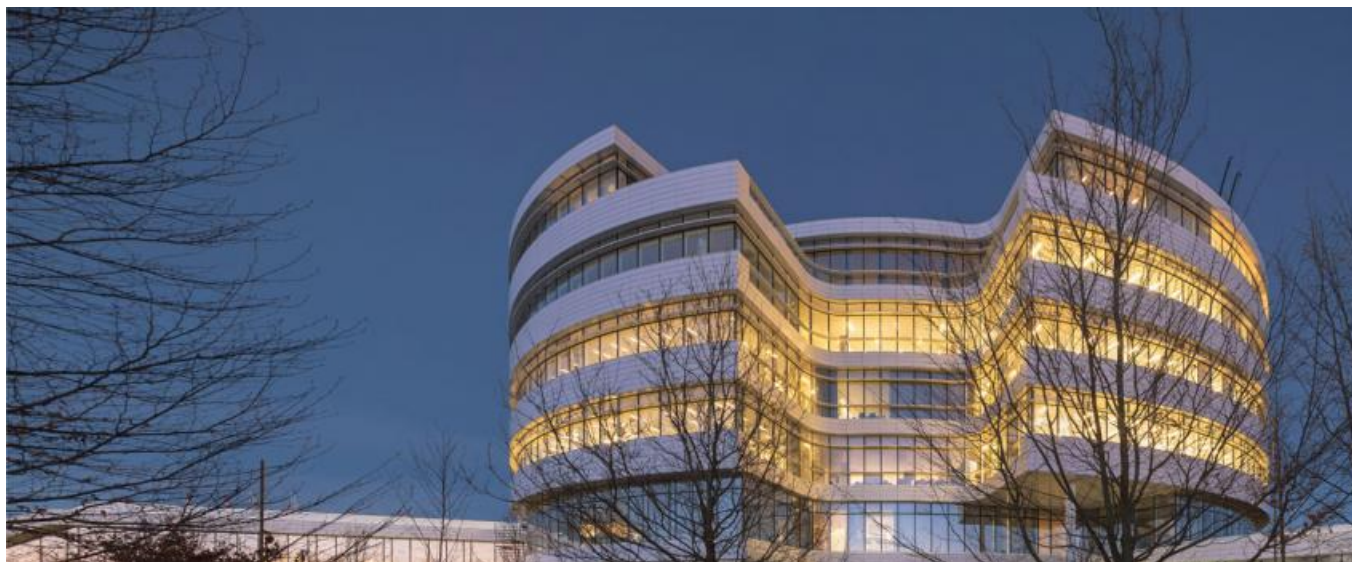


Novo's next big diabetes bet heads to regulators



Amy Brown



Showing a cardiovascular benefit would have been icing on the cake for Novo Nordisk's oral GLP-1 agonist, but the data still look strong enough to support blockbuster sales forecasts.

Success was tinged with slight disappointment for Novo Nordisk late last week as it unveiled results from the final in a series of pivotal studies of oral semaglutide. Pioneer 6 narrowly failed to show a benefit for the project on major adverse cardiovascular events (MACE), though importantly the primary endpoint of the trial, which measured non-inferiority vs placebo, was hit.

Sellside analysts estimate that oral semaglutide and its injected form – branded Ozempic – will be the fastest growing diabetes drugs over the next few years, adding a combined \$6.3bn in sales through 2024, according to *EvaluatePharma*. The impressive 21% reduction in MACE generated by Pioneer 6 should help Novo to meet those numbers.

Gaining weight: diabetes drugs projected to add the most sales

Product	Company	Pharma class	2018e sales (\$bn)	2024e sales (\$bn)	Change in sales 2018-24 (\$bn)
Ozempic	Novo Nordisk	GLP 1 agonist	0.21	4.25	4.04
Semaglutide Oral	Novo Nordisk	GLP 1 agonist	-	2.23	2.23
Trulicity	Eli Lilly	GLP 1 agonist	3.07	4.89	1.82
Jardiance	Boehringer Ingelheim	SGLT 2 inhibitor	1.45	2.90	1.45
Glyxambi	Boehringer Ingelheim	DPP IV & SGLT 2 inhibitor	0.53	1.67	1.14

Source: *EvaluatePharma*.

The Danish diabetes giant has long been cautioning not to expect Pioneer 6, a relatively short and small outcome study, to show a cardiovascular benefit. Such a result would have made it much easier for Novo to achieve a label claim, however, something it still hopes to do by pooling these results with Sustain 6, the CV outcome study run with Ozempic.

This did manage to show a benefit on the MACE endpoint, with 26% risk reduction. As the two projects use the same active ingredient, Novo now plans to speak to regulators to see if the pooled results will be enough to support a claim across both oral and injected versions.

There are reasons why the regulators might turn this down, however. Only a few datasets are available on Pioneer 6 so far, but it seems that several measures go in the opposite direction from Sustain 6.

So for example while Pioneer 6 was driven by a statistically significant 51% reduction in cardiovascular death, Sustain 6 saw very little difference on this measure. Again, on all-cause mortality, Pioneer 6 generated 49% reduction in risk, but Sustain 6 was more balanced. On stroke, as with the overall MACE endpoint, Sustain generated statistically significant differences, whereas the opposite was seen with Pioneer 6.

Given that the US remains the most lucrative diabetes market, the FDA is the regulator to convince here, and Novo said that discussions are ongoing. The company has already outlined plans for a much larger CV outcome study with oral semaglutide, which would be expected to show superiority. But this would recruit 12-15,000 patients and take several years.

Win or loss?

Another unknown in this situation is the result that once-weekly rival Trulicity has generated in the Rewind study. Eli Lilly's announcement built expectations of a strong read out, so perhaps Novo really has no choice but to generate further evidence ([Rewind helps Lilly move forward in diabetes, November 5, 2018](#))

Still, there is another camp that questions how much difference such a claim would really make. Neither Jardiance nor Victoza saw big upticks in sales after they were able to boast a cardioprotective benefit, analyst Wimal Kapadia at Bernstein pointed out.

Umer Raffat at Evercore ISI agreed: "It's not clear if having CV benefit language on label has had a direct correlation with launch curves in this setting."

Semaglutide, in both forms, has at the very least proven to be heart safe. Arguably more importantly, the drug's ability to lower blood sugar and facilitate weight loss has been shown to be very competitive.

At this stage, Trulicity is forecast to be the biggest selling diabetes drug in 2024, with Ozempic not far behind. But Novo is the competitor with it all still to do here. A cardiovascular claim on the label would make these numbers look a lot more secure.

Biggest selling diabetes products in 2024					
Product	Company	Description	Annual Sales WW (\$bn)		
			2018e	2021e	2024e
Trulicity	Eli Lilly	GLP 1 agonist (once-weekly injection)	3.07	4.48	4.89
Ozempic	Novo Nordisk	GLP 1 agonist (once-weekly injection)	0.21	2.71	4.25
Jardiance	Boehringer Ingelheim	SGLT 2 inhibitor (once-daily pill)	1.45	2.28	2.90
Tresiba	Novo Nordisk	Insulin analogue	1.36	2.24	2.90
Farxiga	AstraZeneca	SGLT 2 inhibitor (once-daily pill)	1.39	2.10	2.49
NovoRapid	Novo Nordisk	Insulin analogue	3.01	2.65	2.41
Semaglutide Oral	Novo Nordisk	GLP 1 agonist (once-daily pill)	-	0.66	2.23
Lantus	Sanofi	Insulin analogue	4.24	2.82	2.14
Humalog	Eli Lilly	Insulin analogue	3.04	2.35	1.79
Glyxambi	Boehringer Ingelheim	DPP IV & SGLT 2 inhibitor (once-daily pill)	0.53	1.38	1.67
		Total diabetes market	49.12	56.20	56.30

Source: EvaluatePharma.

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