Vantage
Kickstarting ideas

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Shire dodges pricing questions as lanadelumab's big day nears

Madeleine Armstrong

Shire's big pipeline hope, lanadelumab, should get approved soon – but will sales live up to expectations?

Takeda, whose stock has been battered since it expressed an interest in Shire, might finally get some good news in the next few weeks. The biggest pipeline prospect of its takeover target, the next-generation hereditary angioedema asset lanadelumab, is due an FDA approval decision by August 26.

The project looks likely to get the green light, but whether it can live up to lofty sellside expectations is another matter; *EvaluatePharma* consensus sees sales of $1.6bn by 2024, a tall order in a rare disease that is already served by various products (see tables below). A key issue will be pricing, but Shire is keeping quiet here.

And questions remain over lanadelumab's long-term safety profile. The project is a kallikrein inhibitor, and this class has previously been linked with anaphylaxis.

Project	Lanadelumab
Company	Shire
Market cap	£40.3bn ($52.0bn)
Product NPV	$7.6bn
NPV as a % of market cap	15%
Event	FDA approval decision
Timing	August 26, 2018

No major safety issues have arisen so far with lanadelumab, however, and Shire's chief executive, Flemming Ornskov, said during the company's earnings call last week that he was confident the drug would capture "a very significant share in the US market".

Some of lanadelumab's expected sales will likely eat into Shire's own Cinryze franchise, which is approved in the prophylactic indication that lanadelumab targets.

The chief executive brushed off any concerns about cannibalisation. "This is not a market where one size fits all," he said, adding that in any case lanadelumab should grow the HAE segment by capturing currently untreated patients.

HAE is a genetic condition characterised by episodes where various parts of the body swell. Stifel analysts note that, today, prophylactic HAE drugs are mainly used in more severe patients – those having three or more attacks per month – while lanadelumab has shown promise in milder patients, too.

Top five HAE projects in 2024							
						Indication s	
Product	**Company**	**Pharma class**	**Route of admin**	**Indication**	**Status**	**2018e**	**202**
Lanadelumab	Shire	Anti-plasma kallikrein MAb	Subcutaneous	Prophylactic	Filed	70	645
Ruconest	Pharming	C1 esterase inhibitor	Intravenous	Episodic*	Marketed	162	292
Haegarda	CSL	C1 esterase inhibitor	Subcutaneous	Prophylactic	Marketed	207	311
Cinryze	Shire	C1 esterase inhibitor	Intravenous	Prophylactic	Marketed	658	518
Berinert P	CSL	C1 esterase inhibitor	Intravenous	Episodic	Marketed	350	241
**Filed for prophylaxis. Source: EvaluatePharma.*							

Lanadelumab's efficacy is not in question. The pivotal Help trial met its primary endpoint, showing a statistically significant reduction in HAE attacks versus placebo at all three doses studied; the highest, 300mg every two weeks, reduced mean attack frequency by 87%.

And as a subcutaneous therapy, lanadelumab should help Shire compete with CSL's newcomer, Haegarda, which has been taking market share from Cinryze. As well as capitalising on Haegarda's greater convenience, CSL also benefited last year from supply issues that led to a Cinryze shortage that has now been resolved, at least in the US if not in Europe.

Cinryze and Haegarda are plasma-derived products prone to supply disruptions, something that should not be an issue with lanadelumab, a monoclonal antibody.

Pricing tightrope

All these factors have no doubt contributed to high – some might say overinflated – expectations for lanadelumab. But, with pricing a sensitive topic right now, Shire will have to tread carefully.

Interestingly the US pricing watchdog Icer has already begun evaluating the project, along with other prophylactic HAE therapies, with a report expected in October. Bernstein analysts say the Icer report and resistance from payers are among the biggest potential stumbling blocks for lanadelumab.

When asked about pricing last week Mr Ornskov would only say that lanadelumab would be a "significantly higher-margin product" than Shire's existing HAE drugs, so even at a slight discount to Cinryze lanadelumab could be more profitable. At around $350,000 per year, according to the US pharmacy chain CVS Health, Cinryze is not exactly cheap.

The HAE landscape could change again soon, with a US approval decision due for Pharming's Ruconest for prophylactic use by September 21. Still, this is an intravenous therapy, so lanadelumab should still have the edge on convenience. Ruconest is already approved for acute use in HAE.

Further into the future, Biocryst has an oral kallikrein inhibitor, BCX7353, which could be even more patient friendly. However, phase II results suggested that gastrointestinal side effects might make it hard to find a therapeutic window. A phase III trial, Apex-2, is recruiting.

And Adverum is developing a potentially curative gene therapy, ADVM-053, but this is still in preclinical development. In the meantime, Shire has an opportunity to make its mark with lanadelumab. But, with hopes so high, it cannot afford to put a foot wrong with pricing.

Project	Study	Trial ID
Lanadelumab	Help	NCT02586805
BCX7353	Apex-2	NCT03485911