Evaluate Vantage

August 02, 2013

BioCryst eyes HAE market as Viropharma struggles to innovate

Joanne Fagg

The hereditary angioedema (HAE) space sees a surprising amount of activity, considering the market for drugs to treat the swelling disorder effectively did not exist five years ago and is still worth less than $1bn. In the US, four companies are already battling over an estimated 6,500 patients, but others are still keen to enter the fray – BioCryst said last week it planned to take a novel oral therapy into proof of concept studies later this year.

Elsewhere this week Viropharma announced that a subcutaneously delivered version of its market-leading infusion therapy, Cinryze, will be scrapped after patients in a phase II study developed antibodies. The HAE market might be young but it is moving fast, and incumbents like Viropharma need to keep innovating to stay on top (see tables).

Back-up plan

Viropharma executives said on a conference call yesterday that antibody signals had been seen before so this outcome was always possible with the Halozyme-partnered product. As a result, back up versions were already in development, and an alternative low-volume, subcutaneous product should still be able to move into phase III in the same time frame, in the middle of next year.

The possibility of using a low volume version of Cinryze to allow subcutaneous delivery has always existed, but Viropharma had previously said the challenges this presented meant the Halozyme technology offered a better chance of success. Vincent Milano, chief executive, said work on low volume products over the last year had "proved fruitful" and yielded a formulation with a "high probability" of being a single injection, hence the ability to push on.

Time will tell whether this really is a viable alternative and whether the FDA will allow the company to move straight into phase III off the back of a bioequivalence study. So far, investors seemed only mildly concerned by the setback – shares in the company dipped 7% on the news yesterday. But as the table below shows, analysts are expecting great things from a subcutaneous version of Cinryze, and any further setbacks would not be taken as lightly.

Keeping growing

Cinryze became the first FDA-approved to treat the inherited swelling disorder in 2008, and since then Viropharma and the other companies that followed have established a market in the US where none existed previously (*Lev wins approval for first HAE treatment in US, October 13, 2008*). Cinryze is the only product approved to treat the condition prophylactically – the others are used after a swelling attack has started – and has managed to comfortably establish itself as the market leader.

However the product – derived from human blood plasma, it replaces the missing dysfunctional C1 esterase enzymes – loses orphan drug exclusivity in the US in late 2015, after which sales are expected to plateau. A subcutaneous version would allow Viropharma to keep its franchise growing – the failure of the project is a disappointing outcome.

The remainder of the products available compete within the acute space, so at this stage do not specifically come up against with Cinryze. However the most recent entrant to the US market, Shire's Firazyr, is growing strongly – second-quarter sales surged 54% to $50m – and its subcutaneous formulation and self-administration approval means it is shaping up to be a strong player.

While Viropharma will no doubt be keeping an eye on Firazyr, it will also have taken a close look at the news from BioCryst last week, which announced encouraging phase I results on an oral product – a development that would certainly add a new dimension to the HAE space.

In a placebo-controlled study that recruited 87 healthy volunteers, the company said BCX4161 appeared safe and well tolerated, and that drug exposure and kallikrein inhibition was observed throughout the dosing interval, over seven days. BioCryst will now run a phase II proof of concept study to test the drug's ability to

reduce the frequency of oedema attacks – the same setting in which Cinryze is used. It plans to enrol 25 HAE patients who have a high frequency of attacks, and test a 400mg dose of BCX4161 administered three times daily for 28 days. The company says it also has other, second generation oral kallikrein inhibitors ready to enter pre-clinical development.

Watching progress

The positive data sent BioCryst shares up a staggering 88%, an impressive display of investor optimism considering the stage of the drug and the battered reputation of the company, which has been struggling to recover from a botched takeover attempt, a string of development setbacks and uninspiring strategic review (*BioCryst labours and brings forth a mouse, December 10, 2012*).

BioCryst predictably leapt on the opportunity to raise well-needed cash and swiftly announced a placement to raise up to $20m, which did nothing to supress investor enthusiasm – shares closed at a 17-month high of $5.33 yesterday.

BCX4161 has a long way to travel and success is far from guaranteed. But the HAE space is active enough to keep the current participants' eyes on its progress. If Viropharma's attempts to improve Cinryze's delivery fail to bear fruit, an oral alternative will be exactly the sort of thing it needs.

Selected HAE products

Product	Pharmacological Class	Company	2012	2014	2016	2018	Status
Cinryze	C1 esterase inhibitor	ViroPharma	327	489	487	465	Marketed
Firazyr	Bradykinin B2 antagonist	Shire	116	237	328	386	Marketed
Berinert P	C1 esterase inhibitor	CSL	124	157	186	215	Marketed
Cinryze + rHuPH20	C1 esterase inhibitor	ViroPharma	-	-	119	210	Phase II
Kalbitor	Kallikrein inhibitor	Dyax	40	60	70	80	Marketed
Ruconest	C1 esterase inhibitor	Santarus	-	10	29	50	Filed (US*)
Cetor	C1 esterase inhibitor	Sanquin Blood Supply Foundation	-	-	-	-	Marketed**
Berinert SC	C1 esterase inhibitor	CSL	-	-	-	-	Unclear
BCX4161	Kallikrein inhibitor	BioCryst Pharmaceuticals	-	-	-	-	Phase I
		Total	*607*	*953*	*1,219*	*1,406*	

* Marketed in the EU by Swedish Orphan Biovitrum
** Sales not available

All data sourced to EvaluatePharma.

To contact the writer of this story email Amy Brown in London at AmyB@epvantage.com or follow @AmyEPVantage on Twitter