Evaluate Vantage

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Upcoming events – Ingrezza's approval and data for Shire's new rare disease asset

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Welcome to your weekly digest of approaching regulatory and clinical readouts. Neurocrine expects a decision on its tardive dyskinesia candidate Ingrezza by April 11, with speculation that it will be approved fuelled by the cancellation of an advisory committee meeting. However, Teva's competitor, which is based on the same compound as Ingrezza, looms.

Also due in the second quarter are phase III data on lanadelumab, Shire's next-generation hereditary angioedema project. Shire has a dominant position in the space but, with patent expiries for its older products and competition heating up, the market is becoming crowded (see table below).

Xenazine derivatives

An advisory committee meeting for Ingrezza had been scheduled for February, but in January the company said this had been cancelled. The FDA has stated that the meeting was "no longer needed", and with no mention of any rescheduling this was interpreted as positive.

Consensus forecasts sit at $706m by 2022, according to *EvaluatePharma; $*656m is assigned to the dyskinesia indication and the remainder to Tourette's, where the project is in phase II. Ingrezza has an NPV of $1.5bn, 42% of the company's market cap.

But it could soon be joined on sale by Teva's SD-809, also a VMAT inhibitor, due its own US decision in tardive dyskinesia by August 30, and forecast to bring in $497m in this indication by 2022. The remaining $170m is set to come in Huntington's chorea.

Forecasts for both assets have been downgraded over the past couple of months – notably, Ingrezza's once sat at $1.3bn by 2022. Both are based on Xenazine, a Huntington's chorea drug that went off patent in 2015. With continued scrutiny over drug pricing, they might struggle to command a premium *(Neurocrine's success sets up showdown of the me-toos, October 9, 2015)*.

Forecast sales for Ingrezza and SD-809

		Annual sales ($m)					
Product	**Company**	**2017**	**2018**	**2019**	**2020**	**2021**	**2022**
Ingrezza	Neurocrine Biosciences	17	100	206	362	543	706
SD-809	Teva Pharmaceutical Industries	38	143	254	396	532	667

Source:EvaluatePharma.

Making HAE

Shire's pivotal phase III Help trial tests lanadelumab, a subcutaneous MAb also known as SHP643, in the rare genetic disorder hereditary angioedema (HAE).

Patients will receive 300mg of lanadelumab every two or four weeks, 150mg every four weeks, or placebo – the primary endpoint is the number of HAE attacks per week versus placebo over 26 weeks. 120 patients are enrolled, and data are expected in the second quarter.

An open-label long-term safety study is also ongoing, testing 300mg every two weeks for 14 months.

A 37-patient phase Ib study reported positive results. From day 8 to day 50 the 300mg and 400mg groups had 100% and 88% fewer attacks respectively than placebo. All patients in the 300mg group and 82% in the 400mg group were attack-free, compared with 27% in the placebo group. The most common adverse events were angioedema, injection-site pain and headache.

2022 forecasts sit at $936m, according to *EvaluatePharma* consensus. Lanadelumab has an NPV of $5.4bn; Shire gained the asset, which has breakthrough and orphan drug designations, through its acquisition of Dyax. While Shire is set to have four of the top five HAE products in 2022, competition is increasing.

Rivals include Berinert SC, also known as Haegarda, a subcutaneous prophylactic treatment from CSL that recently reported positive phase III results. And Biocryst has an oral kallikrein inhibitor, BCX7353, with phase III trials due to start in the second half of the year. Biocryst's first effort, avoralstat, failed *(Biocryst hit with a HAE-maker, February 8, 2016).*

Top five HAE products by 2022

					Annual sales ($m)		
Product	**Company**	**Pharma class**	**Route**	**Use**	**2016**	**2022e**	**Status**
Lanadelumab	Shire	Anti-plasma kallikrein MAb	Subcutaneous	Prophylactic	-	936	Phase III NCT02586805 NCT02741596
Cinryze	Shire	C1 esterase inhibitor	Intravenous	Prophylactic	680	509	Marketed
Firazyr	Shire	Bradykinin B2 antagonist	Subcutaneous	Acute	579	242	Marketed
BCX7353	Biocryst	Kallikrein inhibitor	Oral	Prophylactic	-	198	Phase II NCT02870972
Kalbitor	Shire	Kallikrein inhibitor	Subcutaneous	Acute (black box warning of anaphylaxis)	52	66	Marketed

Source: EvaluatePharma.

Shire's Cinryze, the only approved prophylactic product, is now off patent but a subcutaneous version is in development. Firazyr, its acute treatment, will lose patent protection in 2019.

Pricing these next-generation products could be an issue. In the US the price of Cinryze – estimated at $416,029 per patient last year according to *EvaluatePharma* – is three times greater than in the EU, according to Bernstein analysts. With competitors on the way payers might have a bit more bargaining power.

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