Evaluate Vantage

December 21, 2017

Snippet roundup: Approvals for Merck/Pfizer and Biom Up, but Shire disappoints

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Welcome to your weekly roundup of *EP Vantage*'s snippets – short takes on smaller news items.

This week, December 18-22, 2017, we had thoughts on the following: one down in Biogen's Alzheimer's chase; approval only the beginning for Merck and Pfizer's ertugliflozin; Shire fails to make progress in Hunter syndrome; Biom Up has a blast with approval; Ultragenyx sells its voucher for $130m a month after getting it.

These snippets were previously published daily via twitter.

One down in Biogen's Alzheimer's chase

December 21, 2017

Biogen's Alzheimer's focus will shift to the 2019 pivotal readout of aducanumab now that BAN2401 has missed its primary endpoint in a phase II trial. Compared with placebo BAN2401 did not show an 80% probability of achieving a clinically significant difference in Alzheimer's disease composite score at 12 months. The Bayesian design of the 856-patient trial means that this can now proceed to an 18-month data cut-off, expected towards the end of 2018 – but this is only a secondary endpoint, according to its clinicaltrials.gov record. Failure of BAN2401 in a mid-stage trial could be seen as yet another strike against the beta amyloid hypothesis, as the antibody was more selective for protofibrils of the substance, believed to be more toxic to nerve cells than monomers targeted by such agents as Lilly's failed solanezumab. Mizuho analyst Salim Syed said there was not much read-through from the BAN2401 trial to aducanumab because the two agents bind at different locations and target different types of beta amyloid, and the trials enrolled different populations and will use different endpoints. Nevertheless, Biogen shares were down 3% in early trading today.

Biogen's Alzheimer's disease pipeline

Status	Product	Pharma Class
Phase III	Aducanumab*	Anti-beta-amyloid MAb
	Elenbecestat*	Beta secretase cleaving enzyme inhibitor
	BIIB080	Tau antisense oligonucleotide RNAi therapeutic
Phase II	BAN2401*	Anti-beta-amyloid protofibrils MAb
	BIIB092 (gosuranemab)	Anti-tau MAb
Phase I	BIIB076*	Anti-tau MAb

**Collaboration with Eisai. Source: EvaluatePharma*

Approval only the beginning for Merck and Pfizer's ertugliflozin

December 21, 2017

It says something about the competition in the diabetes space when the approval of your drug is not the main event. Yesterday Merck & Pfizer, two latecomers to the SGLT-2 party, announced that their product ertugliflozin had gained a US green light, becoming the fourth SGLT-2 to be launched. The drug, which will carry the brand name Steglatro, has been approved as monotherapy and in combination with Januvia or metformin. Combining the product with a DPP-4 inhibitor theoretically should have given it a better chance of competing in a highly crowded market, but Lilly has a rival product in the form of Glyxambi, a mix of Jardiance and the DPP-4 Tradjenta. And recently consensus forecasts for the Steglatro combination have halved. This could be due to Steglatro not currently boasting a cardiovascular benefit, something that Jardiance does. With other SGLT-2 drugs in the market also demonstrating, or about to report, CV benefits, Steglatro is unlikely to make a real splash unless its own CV outcomes data blow all others out of the water. And investors will have to wait until

2019 for that to happen – the real main event.

Biggest diabetes products featuring SGLT2

			Annual sales $(m)	
Product	Generic Name	Company	2016	2022
Farxiga/Forxiga	dapagliflozin propanediol	AstraZeneca/Ono Pharmaceutical	907	1,789
Jardiance	empagliflozin	Boehringer Ingelheim	256	1,720
Glyxambi	empagliflozin; linagliptin	Boehringer Ingelheim	139	1,730
Invokana	canagliflozin	Johnson & Johnson/Mitsubishi Tanabe Pharma	1,438	1,103
Ertugliflozin & Sitagliptin	ertugliflozin; sitagliptin phosphate	Merck & Co/Pfizer	-	558
Ertugliflozin	ertugliflozin	Merck & Co/Pfizer	-	398

Source: EvaluatePharma

Shire fails to make progress in Hunter syndrome

December 19, 2017

Today's announcement that Shire's experimental drug SHP609 had failed to slow cognitive decline in children with Hunter syndrome will be devastating for parents looking for advances in this rare disease. SHP609 is a reformulation of Elaprase, which has shown improvements in walking distance. Shire had been hoping that there could also be benefits from Elaprase in cognition. However, Elaprase cannot cross the blood-brain barrier; reformulating Elaprase into SHP609 enables delivery via the spinal cord, circumventing this issue. Unfortunately, the study missed both its primary and secondary endpoints. With the failure of SHP609 the next potential innovation in Hunter syndrome could come in the form of Sangamo Therapeutics' phase I/II gene-editing projects SB-913 and SB-318, which effectively hack cells, making them produce therapeutic levels of corrective proteins. For those dealing with Hunter syndrome SB-913 and SB-318's progress through the clinic will be watched with the keenest of interest.

Hunter syndrome pipeline

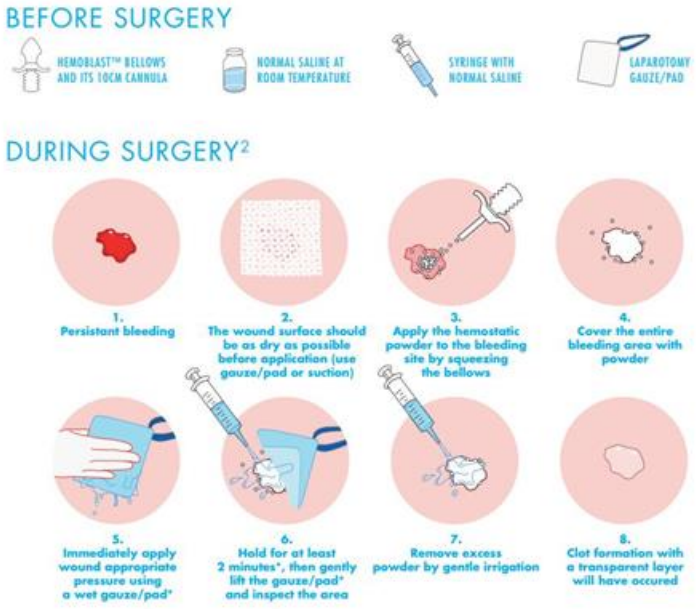
			WW sales ($m)	
Product	Company	Phase	2016	2022
Elaprase	Shire/Sanofi	Marketed	704	789
SHP609	Shire	Phase II/III	-	107
SB-913	Sangamo Therapeutics	Phase I/II	-	2

Source: EvaluatePharma

Biom Up has a blast with approval

December 19, 2017

Biom Up appears to be on a bit of a roll, having followed its €42.5m ($50.2m) Euronext IPO in October with achievement of FDA premarket approval for its flagship product six months ahead of schedule. Hemoblast Bellows, a device loaded with three haemostatic compounds used to control bleeding during surgery, was expected to hit the US mid-2018, but the FDA approved it just nine months after submission. The device is used to apply a powder formulation of a combination of thrombin, collagen and chondroitin sulphate to the source of the bleeding in patients undergoing cardiac, general and orthopaedic procedures, among others. Its pivotal trial was a speedy affair too, having been stopped early for efficacy after interim results showed that 93% of patients achieved haemostasis within six minutes of application of Hemoblast versus 74% for control subjects, who were treated with an absorbable gelatine sponge with thrombin. Biom Up, whose shares rose 6% on the approval, intends to begin selling the device in the summer.



Ultragenyx sells its voucher for $130m a month after getting it

December 18, 2017

Ultragenyx did not hold on to its priority review voucher for long, perhaps deciding to get what it could for the asset in case the fall in value of these vouchers over the past couple of years accelerated. Awarded just last month when the company's enzyme replacement therapy Mepsevii was approved by the FDA for Sly syndrome, the voucher was today sold to Novartis for $130m. Ultragenyx has managed to drive a better deal – very slightly – than Sarepta and Biomarin, both of whom also sold rare paediatric vouchers this year, for $125m apiece. It is not yet clear what Novartis's plans for the voucher are. One option might be advancing the approval of BAF312, its phase III-stage secondary progressive multiple sclerosis candidate. BAF312 is a sphingosine-1-phosphate modulator and a follow-up to Novartis's Gilenya, and is forecast to generate blockbuster sales by 2022, according to *EvaluatePharma*'s consensus of sellside data. Another possibility could be speeding canakinumab to market for cardiovascular disease. Still, none of that is Ultragenyx's concern. The California group can now concentrate on its X-linked hypophosphataemia candidate burosumab, for which an FDA approval decision is due by April. If this gets approved too the company will find itself with a second priority review voucher – and perhaps second deal to sell it on.

The fate of disclosed priority review vouchers

Date sold	Price ($m)	Date issued	Voucher type	Issued company	Action
–	–	Apr 2009	Tropical disease	Novartis	Redeemed by Novartis in BLA for Ilaris (gout)
Jul 2014	67.5	Feb 2014	Rare paediatric	Biomarin	Sold to Sanofi & Regeneron
Sep 2014	Not disclosed	Sep 2015	Rare paediatric	Wellstat	Transferred to AstraZeneca in licensing deal
Nov 2014	125.0	Mar 2014	Tropical disease	Knight	Sold to Gilead
May 2015	245.0	Mar 2015	Rare paediatric	Asklepion	Sold to Sanofi
Aug 2015	350.0	Mar 2015	Rare paediatric	United Therapeutics	Sold to Abbvie
Q2 2016*	~200**	Jun 2016	Tropical disease	Paxvax	Likely sold to Gilead*
Feb 2017	125.0	Sep 2016	Rare paediatric	Sarepta	Sold to Gilead
Nov 2017	125.0	Apr 2017	Rare paediatric	Biomarin	Sold to undisclosed buyer
Dec 2017	130.0	Nov 2017	Rare paediatric	Ultragenyx	Sold to Novartis

*Notes: *Gilead revealed purchase of undisclosed PRV in Q2 statement; **based on Gilead disclosure of $624m increase in R&D spend, less $400m Nimbus purchase and undisclosed clinical trial progression.*

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