Evaluate Vantage

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Snippet roundup: The FDA says no to Acelrx whereas Merck decides not to ask

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

This week, October 9 to 13, 2017, we had thoughts on the following: Acelrx trips up, again; Merck ignores call of history and shelves anacetrapib; Cryolife falls despite Jotec deal; Smith & Nephew could see increased growth, if not a takeover; Pfizer split back on again; no icing for Xarelto cake.

These snippets were previously published daily via twitter.

Acelrx trips up, again

October 12, 2017

Shareholders have been savagely disabused of the notion that Acelrx learned anything from the US rejection of its first pain project, Zalviso. Another FDA complete response letter has been received, this time for Dsuvia, asking for more safety data and a human factors study, causing shares to crater 55%. The drop leaves the company with a market value of $108m, not much above the $68m in cash it has in the bank. This all sounds horribly familiar – Zalviso got a CRL in 2015 that ultimately required a whole new clinical trial, hence investors' unwillingness to swallow the company's promise of a swift resubmission before it has had the chance to understand the FDA's concerns fully. Zalviso is at least heading back to the regulator after its latest phase III success in August – the hand-held device allows post-surgical patients to self-administer the opioid sufentanil in a 15mg sublingual form. Dsuvia administers a higher dose of the same drug, also sublingually, via disposable applicators, and is being aimed at emergency settings or ambulatory surgical centres. Given widespread concerns about opioid misuse intense regulatory scrutiny here is not surprising. Acelrx should have ensured that its second application was watertight.

Zalviso

Dsuvia

Merck ignores call of history and shelves anacetrapib

October 12, 2017

In what must be a big relief for investors Merck & Co yesterday said it would not be filing anacetrapib for regulatory approval. The decision is clearly commercial and eminently sensible. The kudos of having the only CETP inhibitor to churn out a positive phase III result – a feat that has stumped three other contenders – appears not have been enough to balance out anacetrapib's feeble clinical benefit and concerns over the project's continued accumulation in tissue. At best anacetrapib looks like a weak LDL-lowerer, boasting a modest 9% risk reduction in time to first major coronary event. And with other generics on the market, including statins and Merck's own Zetia, it is hard to see why doctors would prescribe a product that could have future issues with tissue accumulation or, with other more cost-effective alternatives available, why payers would reimburse the product. So despite its clinical triumph in a space the industry had largely written off anacetrapib will not make history as the industry's first approved CETP inhibitor. All eyes will now turn to Amgen's AMG 899/TA-8995 – in July Amgen was still saying this project was "delayed pending competitor clinical trials" – and Dalcor Pharmaceuticals' dalcetrapib.

CETP inhibitor late-stage pipeline

Product	Company	Phase
Dalcetrapib	Dalcor Pharmaceuticals	Phase III
AMG 899/ TA-8995	Amgen/Mitsubishi Tanabe Pharma	Phase II
CKD-519	Chong Kun Dang	Phase II
Abandoned		
Anacetrapib	Merck & Co	Abandoned phase III
Evacetrapib	Eli Lilly	Abandoned phase III
Dalcetrapib	Roche/Japan Tobacco	Abandoned phase III
Torcetrapib	Pfizer	Abandoned phase II

Source: EvaluatePharma

Cryolife falls despite Jotec deal

October 12, 2017

News of Cryolife's $225m cash-and-stock acquisition of the private German stent graft company Jotec has failed to placate shareholders alarmed by its missed revenue guidance. Cryolife's shares crashed 14% yesterday after the company said third-quarter revenues came in at $45.1m against guidance of $46.5-47.5m, partially owing to hurricane damage to its sites in Florida and Texas. Cryolife will also buy back inventory that was previously sold to distributors with whom it has cancelled agreements in connection with the Jotec transaction, lowering preliminary third-quarter revenue to $44m. Cryolife, which makes cardiovascular technologies including valves and allografts, will likely update its 2017 guidance and issue guidance for the combined company in the coming weeks. Jotec had sales of €43m ($51m) for the 12 months ended June 30, but several products are approaching the US market. Cryolife says it will help shepherd these through the US approval process and reap the rewards of increased sales.

Cryolife

		WW sales ($m)				
Segment (Company) Tiers - Level 3	EvaluateMedTech Device Classification - L3	2016	2018	2020	2022	CAGR
Cardiac tissue	Cardiac Prosthetic Devices (unspecified)	30	35	39	43	6%
Vascular tissue	Cardiac Prosthetic Devices (unspecified)	37	40	43	47	4%
BioGlue and BioFoam	Surgical Sealants	63	69	76	83	5%
PerClot	Hemostats	4	4	5	6	7%
CardioGenesis cardiac laser therapy/ Revascularization technology	Cardiovascular Lasers	8	7	7	7	-2%
PhotoFix	Intercardiac Patches	2	2	3	4	12%
On-X Direct	Mechanical Heart Valves	33	44	58	71	14%
On-X OEM	Mechanical Heart Valves	2	1	1	1	-5%
Total Company Revenues	Total Company Revenues	178	202	232	262	6%

Source: EvaluateMedTech

Smith & Nephew could see increased growth, if not a takeover

October 11, 2017

Shareholders in Smith & Nephew appear to view the activist hedge fund Elliott Management building a stake in the orthopaedics group as a sign that it could soon be reinvigorated. The company's shares are up 4% in London so far today, and its ADRs closed up 5% yesterday. This is perhaps surprising as the size of Elliott's stake and what agenda the fund might push are unknown. But, added to the fact that S&N's chief executive, Olivier Bohuon, is to step down in 2018 after seven years in the role, the news has also reignited speculation – never long dormant – around a potential takeover. Mr Bohuon was president of Smithkline Beecham at the time of its merger with Glaxo Wellcome in 2000, but strongly discouraged any takeover attempts at S&N – most recently a rumoured $18bn bid by Stryker in late 2015. Even if Elliott does not push for a trade sale, S&N ought to benefit from increased emphasis on growth, with its organic growth averaging only 2-3% in recent years, according to Bernstein, and 2017 guidance at just 3-4%.

Smith & Nephew: past and forecast growth

	WW sales ($bn)			WW sales ($bn)		
Sector	2012	2016	CAGR 2012-16	2017e	2022e	CAGR 2017-21
Endoscopy	0.9	1.2	7%	1.3	1.6	5%
Orthopaedics	2.0	2.0	0%	2.1	2.4	3%
Wound management	1.0	1.2	5%	1.3	1.6	4%
Other medtech	0.2	0.2	7%	0.2	0.3	8%
Total	4.1	4.7	3%	4.8	5.9	4%

Source: EvaluateMedTech

Pfizer split back on again

October 10, 2017

Pfizer's decision not to split up lasted just over a year, with the company now saying it is reviewing options for its consumer healthcare business. It is probably no wonder that the pharma giant wants to exit the sector – 2016 sales of $3.4bn made it only the number-seven player – but it is unclear who would want to acquire the unit, which encompasses brands like Chapstick and Advil. Companies lying below Pfizer in the rankings are unlikely to be interested: Boehringer left the sector earlier this year, while Merck KGaA recently said it was thinking of doing the same. One of the larger consumer players might want to build scale – perhaps Reckitt

Benckiser or Glaxosmithkline under its new chief exec, Emma Walmsley, who previously headed up its consumer division; Nestlé is also rumoured to be interested. Pfizer said it might also choose to spin off the unit, or ultimately keep it. If it does offload it, the money could come in handy for pharma-focused acquisitions; there has recently been talk about Pfizer being interested in Bristol-Myers Squibb.

Top consumer healthcare players

Company	Total consumer healthcare sales ($bn)		Market share	
	2016	2022e	2016	2022e
Johnson & Johnson	13.31	15.90	12%	14%
Glaxosmithkline	9.74	11.46	9%	10%
Bayer	6.68	7.48	6%	6%
Reckitt Benckiser	4.51	4.68	4%	4%
Perrigo	4.16	3.54	4%	3%
Sanofi	3.68	6.51	3%	6%
Pfizer	3.41	4.09	3%	4%

Source: EvaluatePharma

No icing for Xarelto cake

October 9, 2017

Having scored the big win in coronary and peripheral artery disease last month, it looked as if Bayer and J&J were mounting a successful revival of Xarelto sales against its main rival, Eliquis. So news that the drug failed to prove itself against aspirin in reducing the risk of stroke and systemic embolism in the phase III Navigate Esus trial has put a dent in plans to secure another label expansion. Navigate Esus was stopped early after an interim analysis showed that, not only was there no difference between Xarelto and aspirin in reducing the risk of stroke and systemic embolism, but that bleeding rates were higher in the Xarelto arm. Despite the setback Bayer and J&J are maintaining their ambitious sales targets for Xarelto, thanks chiefly to the results of the Compass trial in CAD and PAD, which analysts have forecast could add over $1bn to sales. But with Eliquis still clutching a superiority claim over warfarin in two big indications, compared with Xarelto's non-inferiority label, Xarelto needs to ace the next four other studies it has lined up to expand its use –both to justify the huge investment J&J and Bayer are making in the trials and to avoid being the sector's also-ran.

Eliquis v Xarelto

		Sales forecast ($bn)					
Product	Company	2017	2018	2019	2020	2021	2022
Eliquis	Bristol-Myers Squibb	4.8	5.9	6.8	7.6	8.3	8.8
Xarelto	Johnson & Johnson/Bayer	5.5	6.1	6.7	7.4	7.9	8.5

Source: EvaluatePharma

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