Evaluate Vantage

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Snippet roundup: CETP kaput and Biogen buys into amyloid

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

This week, October 23 to 27, 2017, we had thoughts on the following: Amgen puts another CETP out of its misery; Stryker buys Vexim without waiting for US approval; How much is aducanumab worth? At least $8bn, Biogen reckons; Alcon delay puts dampener on Novartis; Soliris sitting pretty with complementary new indication; Smith & Nephew acquires, but divestments could follow; Global Blood drops IPF programme.

These snippets were previously published daily via twitter.

Amgen puts another CETP out of its misery

October 26, 2017

If the once-promising CETP drug class lives on, it might only be in a rather restricted group of heart disease patients with a very specific mutation. Amgen became the last big biopharma group to cancel work on a drug in the HDL-raising class when it announced plans to seek a partner for AMG 899, following the lead of Merck & Co, which recently terminated its work with anacetrapib after disappointing results in the Reveal trial. Although big pharma groups obviously believe that it is unlikely for a CETP inhibitor to succeed commercially, it is not out of the realm of possibility that a partner could emerge for AMG 899 – Roche licensed its project, dalcetrapib, to the Canadian group Dalcor Pharmaceuticals, which has been researching its use in a genetic subtype, patients with an AA polymorphism at the rs1967309 location in the ADCY9 gene. Amgen will write off the $300m it paid for AMG 899's originator, Dezima Pharma, in 2015, which at the time was seen as a cheap bet on the CETP sector. The project had spent recent months in limbo after Amgen put development on hold, saying it was awaiting the outcome of trials of rival agents.

The CETP dream comes to an end

Project	Company	Clinical trials	Fate
Torcetrapib	Pfizer	Illuminate trial terminated when mortality favoured placebo arm, 2006	Company cancelled work
Dalcetrapib	Roche	Dal-Outcomes trial failed, 2012	Outlicensed to Dalcor Pharmaceuticals
Evacetrapib	Eli Lilly	Accelerate trial failed, 2015	Company cancelled work
Anacetrapib	Merck & Co	Reveal trial showed significantly reduced cardiovascular events, 2017	Company cancelled work
AMG 899	Amgen	Completed phase II trial, 2014	Company seeking to outlicense

Stryker buys Vexim without waiting for US approval

October 25, 2017

That Stryker has acquired a company that makes a spinal implant is not likely to raise eyebrows; that it did so before the implant gained US market clearance makes the deal a more unusual move. Vexim's SpineJack, a product sold in Europe since 2010 for the treatment of vertebral fractures, is in a study that could allow for a 510(k) clearance filing next year. Stryker is clearly confident of success: yesterday it bought 50.7% of the French company's share capital and 50.3% of the voting rights, paying €20 ($24) per share, plus €3.91 apiece for 170,745 listed warrants. Today Stryker's French subsidiary will file an all-cash tender offer for all Vexim shares and warrants it does not already own, at the same prices. The deal values Vexim at around €183m – not bad considering sales of SpineJack are only forecast to reach $61m in 2022, according to *EvaluateMedTech*'s sellside consensus.

Spinal devices - total market

		WW annual sales ($m)		
Rank	Company	2016	2022	CAGR
1	Medtronic	2,219	2,519	2%
2	Johnson & Johnson	1,830	1,974	1%
3	Nuvasive	674	1,082	8%
4	Zimmer Biomet	662	1,016	7%
5	Stryker	754	821	1%
...				
13	Vexim	20	61	20%

Source: EvaluateMedTech

Glaxo hints that its future lies in consumer health

October 25, 2017

Glaxosmithkline is not averse to bulking up its consumer offering – but its top priority is improving its pharma business, chief executive Emma Walmsley said today. However, at least part of the decision is out of Glaxo's hands: the UK group would be happy to increase its stake in its consumer joint venture with Novartis, according to Ms Walmsley, but it is up to Novartis whether or not it exercises its option to sell in March 2018. And Novartis's chief exec, Joe Jimenez, hinted yesterday that the Swiss company might hang on to its 36.5% stake. "With the press of a button we can turn that asset into cash," he said during the company's third-quarter earnings call. "But in the meantime, while the margin increases and the top line grows, this is a good investment." Meanwhile, Ms Walmsley would not be drawn on whether Glaxo was interested in acquiring Pfizer or Merck KGaA's consumer units, only saying that she would "look at these assets carefully". She also declined to say whether Glaxo might sacrifice its dividend to make the Pfizer purchase – and a lack of confidence around the group's future dividend likely contributed to a 5% fall in Glaxo's share price today.

How much is aducanumab worth? At least $8bn, Biogen reckons

October 25, 2017

If there were doubts about Biogen's commitment to aducanumab, its highly risky beta amyloid-targeting Alzheimer's disease project, this week's dual deal restructuring should dispel them. On Tuesday a tie-up with Eisai was changed, with Biogen gaining an increased share of aducanumab's economics – specifically an extra 5% in the US and 18.5% in the EU, plus a reduction in milestone payments – in return for a reduced Japan profit split (20% instead of 50%) and what Leerink assumes to be an extra $300m of R&D commitment. Biogen yesterday followed this up by renegotiating its deal with aducanumab's originator, Neurimmune, cutting the royalty rate it will owe the Swiss entity by 15%, and potentially a further 5%, for up to $200m up front. Since it is known that the original rate was in the low to mid teens, the price Biogen stands to pay implies a saving of up to $8bn – so aducanumab must be worth more than $8bn for the economics to pay off. Aducanumab's two phase III trials will not read out until late 2019/early 2020, so it will be some time before investors find out whether it was worth it.

Biogen ups its bet on aducanumab

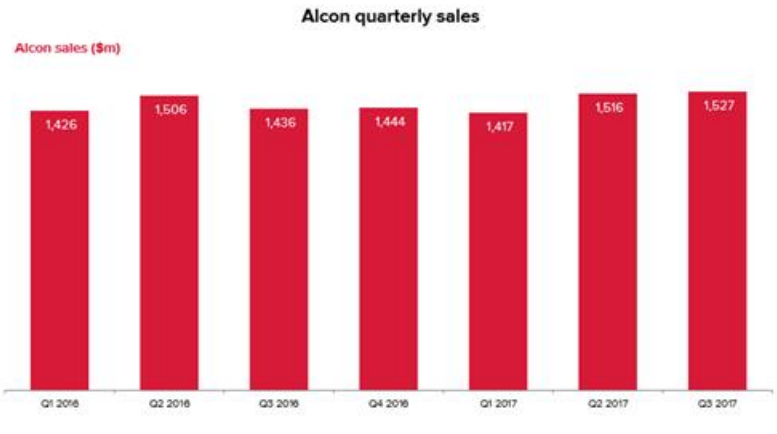
NPV of aducanumab based on *EvaluatePharma* sellside consensus	$10,066m		
Assumed previous royalty ("low to mid teens") due to Neurimmune	13.0%	14.0%	15.0%
Royalty if cut by 15% ($150m cost)	11.1%	11.9%	12.8%
Royalty if cut by further 5% (additional $50m cost)	10.5%	11.3%	12.1%
Total royalty rate eliminated	2.5%	2.7%	2.9%
Implied pretax value of aducanumab to Biogen	**$7,992m**	**$7,421m**	**$6,926m**

Source: EP Vantage valuation based on disclosure in SEC filings.

Alcon delay puts dampener on Novartis

October 24, 2017

Novartis investors awaiting the separation of its Alcon eye care unit will have to wait a little longer: until the first half of 2019 to be precise. The division's turnaround continues, with third-quarter sales up 7% at constant exchange rates year on year, and Novartis appears to have narrowed down the options to either a spin out or IPO. But Alcon needs to show "multiple quarters" of top and bottom-line growth before a separation can take place, the group's outgoing chief executive Joe Jimenez said during Novartis's third-quarter call. "We want the business to come to the market from a position of strength," he added. The Swiss company's stock was down 3% today, which Leerink analysts partly put down to the timing and "lack of absolute clarity" on the Alcon split. Meanwhile, Alcon has regained Novartis's over-the-counter ophthalmic products including the Systane dry eye drop brand – these became part of the main group in early 2016, but continued to be largely managed by Alcon, according to Mr Jimenez. The OTC products sell around $700m per year; the chief exec did not give margin details, but said they should "substantially improve the profit profile of the Alcon business".



Source: Novartis quarterly reports

Soliris sitting pretty with complementary new indication

October 24, 2017

With growth in Soliris's approved indications set to slow, Alexion needed the FDA to give the go-ahead to its cash cow in myasthenia gravis (MG) – and, in spite of mixed phase III data, the agency has obliged. The approval, in refractory generalised MG patients who are anti-acetylcholine receptor (AchR) antibody-positive, will give Alexion access to 5-10% of the total MG population or up to 2,500 US patients, Leerink analysts estimate. *EvaluatePharma* sellside consensus forecasts MG sales of $687m in 2022, 16% of Soliris's total revenues of $4.3bn that year, while Leerink is more bullish, putting 2022 MG sales at $1.2bn and total revenues at $5.3bn. It will be interesting to see how Alexion prices Soliris in the new indication; at up to $600,000 per patient per year in the US, Soliris is one of the most expensive drugs available. The latest approval had been widely expected by analysts after a European green light in August, but investors sent Alexion's shares up 6% in premarket trading today, possibly pleasantly surprised by its broad US label. Soliris is sitting pretty in the complement inhibitor sector with its rivals several years behind, including Alexion's follow-on project, ALXN1210, which is dosed less frequently.

Out in front: Soliris and its potential rivals

Product	Company	Pharmacology class	Lead indication(s)	2022e sales ($m)
Marketed				
Soliris	Alexion Pharmaceuticals	Anti-complement factor C5 MAb	PNH, HUS, myasthenia gravis	4,291
Phase III				
ALXN1210	Alexion Pharmaceuticals	Anti-complement factor C5 MAb	PNH, HUS	328
OMS721	Omeros	Anti-MBL-associated serine protease 2 MAb	HUS, IgA nephropathy	99
Avacopan	Chemocentryx/Vifor Pharma Group	Complement factor C5a inhibitor	Vasculitis	33
Phase II				
Coversin	Akari Therapeutics	Complement factor C5a & C5b-9 inhibitor	PNH	417
ACH-4471	Achillion Pharmaceuticals	Anti-complement factor D	PNH, chronic kidney disease	166
RA101495	Ra Pharmaceuticals	Complement factor C5 inhibitor	PNH	63
Tesidolumab	Novartis/Morphosys	Anti-complement factor C5 MAb	PNH, AMD, uveitis	42
ALN-CC5/cemdisiran	Alnylam	C-C chemokine receptor type 5 RNAi therapeutic	HUS	-
APL-2	Apellis Pharmaceuticals	Complement factor C3 inhibitor	Haemolytic anaemia	-
RO7112689	Roche/Chugai	Anti-complement factor C5 MAb	PNH	-

HUS: Haemolytic uremic syndrome; PNH: Paroxysmal nocturnal haemoglobinuria. Source: EvaluatePharma

Smith & Nephew acquires, but divestments could follow

October 23, 2017

With an activist investor rumoured to be pushing for divestments to increase its appeal as a takeover target, Smith & Nephew has in fact gone in the opposite direction. S&N has paid $125m cash up front for Rotation Medical, a Minnesota-based company that has developed a shoulder implant that induces growth of new tendon-like tissue to help repair rotator cuff injuries. The implant has 510(k) clearance in the US and an application for European approval is being prepared; it will be sold by S&N's sports medicine reps as well as Rotation Medical's own sales force, and up to $85m in sales-related milestone payments could follow over the next five years. The acquisition is the first S&N has announced for two years, and comes as the activist fund Elliott Management, which is thought to have a 2-3% stake in S&N, is reported to be agitating for divestments. Of course, the timing of the Rotation Medical deal is surely coincidental, rather than S&N seeking deliberately to defy Elliott's alleged agenda, and divestments might yet occur.

10 years, 10 deals: Smith & Nephew's M&A activity

Date announced	Date closed	Target	Value ($m)	M&A Focus
October 23, 2017	Expected Q4 17	Rotation Medical	210	Orthopaedics
October 29, 2015	January 5, 2016	Blue Belt Technologies	275	General & plastic surgery; orthopaedics
July 10, 2015	July 10, 2015	Trauma and orthopaedics business of Deost and DC	-	Orthopaedics
February 3, 2014	May 29, 2014	Arthrocare	1,500	Ear, nose & throat; endoscopy; general & plastic surgery; general hospital & healthcare supply; orthopaedics; wound management
May 2, 2013	May 2, 2013	Sushrut Surgicals	-	General & plastic surgery; orthopaedics
November 28, 2012	December 21, 2012	Healthpoint Biotherapeutics	782	Wound management
May 7, 2012	May 7, 2012	Kalypto Medical	-	Wound management
April 2, 2012	April 2, 2012	Lifemodeler	-	Healthcare IT
June 23, 2011	June 23, 2011	Tenet Medical Engineering	-	Endoscopy; general & plastic surgery; orthopaedics
November 11, 2009	December 22, 2009	Nucryst Pharmaceuticals	21	Wound management

Source: EvaluateMedTech.

Global Blood drops IPF programme

October 23, 2017

Global Blood Therapeutics at least deserves credit for killing a marginal-looking programme fairly early. True, its decision to cancel work in idiopathic pulmonary fibrosis (IPF) after less-than-promising phase I and II data puts more pressure on GBT440 to hit endpoints in its phase III trial in sickle cell disease. But in IPF GBT440, now called voxelotor, would have needed to match or exceed the efficacy of Roche's Esbriet and Boehringer Ingelheim's Ofev in slowing the decline of lung function. GBT's executive team has decided that the improvements in oxygen saturation shown in two of the three early trials were not sufficient to show that GBT440 would be able to do that. If it is successful in sickle cell disease, GBT440 looks like it will be going up against less well-established players, with perhaps Novartis and Pfizer getting to market slightly earlier. Investors had been hoping for some success with IPF, though – GBT shares fell 2% in early trading today.

The race in sickle cell disease

Product	Company	WW Sales ($m) 2018	2019	2020	2021	2022	WW Indication Status
GBT440	Global Blood Therapeutics	-	-	38	157	437	Phase III
SEG101	Novartis	12	40	107	181	265	Phase III
LentiGlobin	Bluebird Bio	-	-	-	52	112	Phase II
Rivipansel	Pfizer	4	17	36	54	70	Phase III

Source: EvaluatePharma

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