Evaluate Vantage

September 30, 2016

Snippet roundup: Wins for Amgen, cuts for Novo and confusion over Cabometyx

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

This week, September 26-30, 2016, we had thoughts on the following: Threshold back to the future with tarloxotinib setback; Lupus data release helps Aurinia recover; Novo swings the axe cutting 1,000 jobs as pricing pressure bites; Mixed emotions on Cabo's first line prospects; Amgen looking good for first-to-market in new migraine class; Boston makes a generous offer for EndoChoice; Smoking hot GW could spark takeover interest; Pain to persevere with Remoxy; GE Healthcare spreads its net wider; Humira biosimilar approved, but launch no clearer.

These snippets were previously published daily via twitter.

Threshold back to the future with tarloxotinib setback

September 30, 2016

Threshold Pharmaceuticals will be pursuing a modified plan A after plan B has also suffered a setback. The California based group saw shares fall 44% in morning trading today after it announced that phase II data showed that EGFR inhibitor tarloxotinib failed to show sufficient activity in squamous cell head and neck or skin cancer and EGFR-mutant, T790M-negative non-small cell lung cancer to continue development. In both cases, stable disease was reached in some patients, but a lack of partial responses failed to justify more investment in the project. Just one partial response was achieved in 29 patients in the skin and head and neck trial, and none in the lung cancer trial. Threshold's new strategy involves testing evofosfamide in combination with checkpoint inhibitors. That agent missed in soft-tissue sarcoma last year, which battered the shares badly – following today's share loss, Threshold is now worth one-fifth what was before the evofosfamide failure.

Trial	Setting	ID
TH-CR-602	Squamous cell skin or head and neck cancer	NCT02449681
TH-CR-601	EGFR-mutant, T790M-negative, advanced non-small cell lung cancer	NCT02454842

Source: EvaluatePharma

Lupus data release helps Aurinia recover

September 30, 2016

Shares of Aurinia Pharmaceuticals rose 32% in early trading today with release of more data from the Aura-LV trial of voclosporin in lupus, offsetting previous concerns about a safety signal. Both a low 23.7mg twice daily and a high 39.5mg twice daily dosage of voclosporin achieved five pre-specified secondary endpoints with statistical significance over placebo at 24 weeks. Those measures were time to complete remission, partial remission, time to partial remission, reduction in disease activitiy and urine protein: creatinine ratio. The main flaws in Aurinia's lupus programme were contained in a topline data disclosure made in August: a miss for the high dose in the primary endpoint, complete remission, and the 12 deaths recorded in the active treatment arms compared with the one in the placebo arm. In an analyst presentation today Canada-based Aurinia emphasised that 11 of the deaths occurred in regions with compromised access to standard of care, and that the study's chief investigator and data and safety monitoring board determined that none of the deaths were related to the treatment. In a note after the August release of the topline data that included a discussion of the deaths – after which the shares crashed 56% – HC Wainwright analyst Ed Arce also noted that studies of off-label CellCept and other drugs used in this indication have revealed similar imbalances in death rates.

Lupus sales outlook

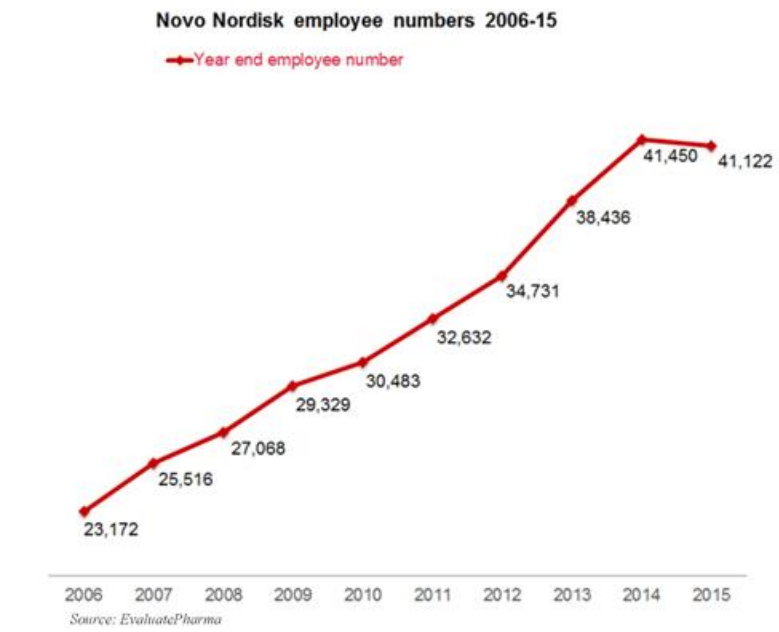
	WW sales ($m)							
Company	2015	2016	2017	2018	2019	2020	2021	2022
Benlysta (GlaxoSmithKline)	351	419	475	526	565	596	619	641
Luveniq (Aurinia Pharmaceuticals)	-	-	-	-	46	99	149	201
Anifrolumab (AstraZeneca)	-	-	-	10	34	77	130	193
Cellcept (Roche)	106	100	93	87	81	75	70	64
Blisibimod (Anthera Pharmaceuticals)	-	-	-	-	7	18	29	42
Other	22	28	29	28	28	30	49	72

Source: EvaluatePharma

Novo swings the axe cutting 1,000 jobs as pricing pressure bites

September 29, 2016

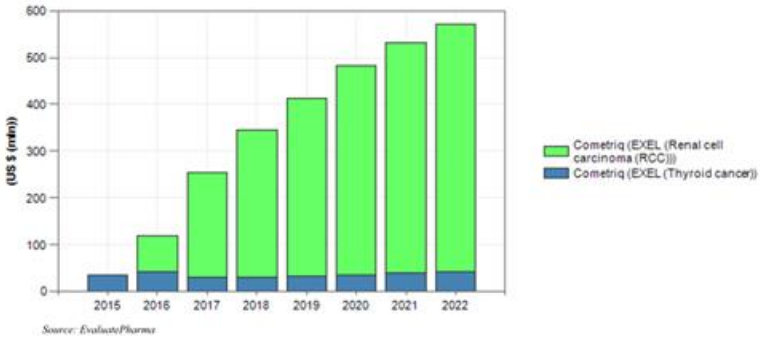
Until recently Novo Nordisk's diabetes franchise looked unassailable. Today the Danish group announced it would be cutting 1,000 of its 42,000 workforce. Like others in the diabetes space Novo has been hammered by payers, particularly in its core insulin business. Novo is also facing the looming threat of biosimilars – further destabilising the insulin division. Luckily, it has its GLP-1 franchise to fall back on. The company's primary focus will now be getting cardiovascular benefits on the label of Victoza and its other GLP-1 products, an event that could enable it charge premium prices and hopefully offset the falls in the insulin business. However, today's job cuts will be across the board and there is a danger that by reducing its R&D function the group will not be able to create innovative products like once-weekly semaglutide that will be central to defending itself from price cuts.



Mixed emotions on Cabo's first line prospects

September 29, 2016

Investors are clearly both optimistic and anxious about the potential of Exelixis/Ipsen's Cabometyx in renal cell carcinoma. The 13% fall in Exelexis' stock price yesterday, which wiped over $400m from its market capitalisation, was prompted by the disclosure in the ESMO abstracts of early clinical data on a possible competitive threat in first line use. But wait, surely data on Cabometyx in the first line setting has not even been revealed yet? Indeed, those data are among the late breakers at the very-same cancer conference. But Exelixis' stock has trebled since the US biotech reported a PFS win over Sutent – the shift to first line use has already been being priced in. The competitive threat: it came from an initial study with Keytruda and Inlyta, a combination that being tested by Merck in the Phase III Keynote-426 trial. Exelixis' investors could be in for more turbulence in the coming weeks.



Amgen looking good for first-to-market in new migraine class

September 29, 2016

The first look at phase III data from the anti-CGRP class changes little for the outlook of this hotly contested new migraine approach. Top-line data on AMG 334, or erenumab, showed the Amgen drug reduced monthly

episodic migraine days by a statistically significant, placebo-adjusted 1.1 days, repeating the result seen in phase II. A second phase III study called Strive testing a higher dose and measuring the response over a longer time period will report before year end. Amgen and partner Novartis will be hoping to see some differentiating qualities emerge – the data generated to date by the four competitors in this space looks very similar although the others have yet to report pivotal results. So unless rivals produce something substantially different, erenumab's edge will remain largely an issue of timing. In a crowded, undifferentiated market, this is not to be sniffed at.

CGRP-targeting antimigraine MAbs

Company	Project	Migraine type	Efficacy***	Phase of data	Next steps	2022e sales*
Amgen/Novartis	Erenumab	Episodic	1.1 days	III	PIII data YE; file for approval H1'17	$483m
		Chronic	2.4 days	II		
Lilly	LY2951742	Episodic	1.2-1.3 days	II	PIII data H1'17	$420m
		Chronic	n/a		PIII data H1'17	
Alder	ALD403	Episodic	1.0 days	II	PIII data Q1'17	$993m**
		Chronic	~2-2.8 days^	II	PIII to start Q4'16	
Teva	TEV-48125	Episodic	2.6-2.8 days	II	PIII data Q4'17	$1,054m
		Chronic	1.7-2.0 days	II	PIII data Q4'17	

**EvaluatePharma sellside consensus; **Forecast includes the assumption of an EU licensing deal ***reduction in monthly migraine days vs placebo ^Estimates from data presentation*

Source: Evercore ISI, Bernstein, Morgan Stanley

Boston makes a generous offer for EndoChoice

September 27, 2016

Following $112m of venture funding and a $95m IPO, EndoChoice has finally hooked itself a buyer. The endoscopy group is being taken out by Boston Scientific for $210m, with the $8 per share offer representing a 90% premium over the price at close yesterday. Sales of endoscopy technologies are growing fast – EvaluateMedTech's consensus forecasts put this segment's annual growth rate at 6.8% – so Boston's move to augment its endoscopy business with EndoChoice's portfolio might be smart. EndoChoice had sales of around $75m last year, whereas Boston's endoscopy unit sold $1.2bn-worth of devices, but this is the type of small tuck-in deal that ought to give hope to medtech start-ups.

Source: endochoice.com

Smoking hot GW could spark takeover interest

September 26, 2016

GW Pharma's third trial win with anti-epilepsy drug Epidiolex is likely to have two consequences. The first, and most important for the company, will be further de-risking its most valuable asset. The second will be further fanning the flames of the rumours that the company is gearing up to be taken out. Certainly another clinical win in a rare disorder that has no current treatments is bound to make some specialty pharma companies salivate. But GW is no longer the bargain it used to be. Today's results from a second study in Lennox-Gastaut syndrome pushed the shares up to record highs, valuing the UK biotech poster boy at about £2.4bn ($3.1bn). GW is also in a unique position to continue walking its path alone, given the small sales force needed to sell Epidiolex. Additionally, the onerous requirements of managing the regulatory process for products that are made from cannabis might be a deterrent for a larger company. That said, if GW continues to look this good none of that will be unsurmountable and the investment bank the group is rumoured to have called in earlier this month might get a lot busier.

Source: Google finance

Pain to persevere with Remoxy

September 26, 2016

After a third complete response letter for its opioid Remoxy, Pain Therapeutics is determined to continue development of its supposedly abuse-proof oxycodone. On the positive side, problems with manufacturing and stability, raised in the previous CRLs in 2008 and 2011, are behind it, chief executive Remi Barbier believes. But the FDA is now focused on Remoxy's abuse-deterrent label claims and has requested new studies exploring three possible routes of abuse: injection, inhalation and snorting. The former two could be completed in a matter of months, Mr Barbier said during a conference call, but the snorting study in humans would take longer – it is possible that Pain might focus on the first two label claims if it wants to refile Remoxy quickly. All three studies would take a year and around $5m to carry out, the company estimates – and with almost $25m in the bank at the end of June, it has the resources needed. If Pain does succeed, an attractive market beckons, fuelled by the growing opioid crisis in the US. But another setback might finish the group off. Its stock was down as much as 67% in premarket trading this morning.

GE Healthcare spreads its net wider

September 26, 2016

GE Healthcare has one of the more active corporate VC operations in the medtech industry, but generally restricts its venture investments to US and Israeli companies (see table). It is thus reassuring to see the imaging group branch out into emerging markets with a new incubator programme, including a potential $50m investment fund. Cost pressures in the West are making it harder to sell expensive imaging machinery, so GE is perhaps wise to look at cheaper technologies that appeal to a new customer base. Called five.eight, the programme is intended to aid development of – among other things – low-cost healthcare technologies and digital applications, and will begin by choosing 10 start-ups which will be eligible for investment of up to $5m apiece. The first target is Bangalore-based Tricog, which uses cloud-connected electrocardiographs to help speed diagnosis of myocardial infarction.

GE Ventures' investments, 2014-2016

Date	Company	Country	Round	Investment ($m)
August 3, 2016	Ornim	Israel	Series C	20.0
March 22, 2016	Acutus Medical	USA	Series C	75.0
April 27, 2015	Neuronetics	USA	Series F	34.3
October 19, 2014	Check-Cap	Israel	Undisclosed	-
June 12, 2014	Chrono Therapeutics	USA	Series A	32.0
March 3, 2014	RainDance Technologies	USA	Series E	16.5

Source: EvaluateMedtech

Humira biosimilar approved, but launch no clearer

September 26, 2016

The approval of Amgen's Humira biosimilar, Amjevita, was widely predicted following a positive panel vote in July. But what is harder to forecast is when the product, previously known as ABP 501, might be launched. The earliest possibility looks like March 2017, 180 days after Amgen gives Abbvie notice that it intends to commercialise a competitor, which can only be done upon approval. But Abbvie hopes to hold off biosimilar competition for longer and has said it has patent protection up to 2022. This seems optimistic, as the key composition-of-matter patent falls in December 2016 in the US. The truth is likely to lie somewhere in between – EvaluatePharma consensus has Humira sales peaking at $18.2bn in 2018 before declining thereafter, and Amjevita sales beginning at $45m in 2017.

FDA-approved biosimilars

Product	Company	Biosimilar of	Approval date	2022e sales ($m)
Amjevita	Amgen	Humira	Sept 23, 2016	829
Erelzi	Novartis	Enbrel	Aug 20, 2016	-
Inflectra	Pfizer	Remicade	Apr 5, 2016	427
Basaglar	Eli Lilly	Insulin	Dec 16, 2015	1,107
Zarxio	Novartis	Neupogen	Mar 6, 2015	-

Source: EvaluatePharma.

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