Evaluate Vantage

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Snippet roundup: Sighs of relief for Astra and Glaxo

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

This week, May 8 to 12, 2017, we had thoughts on the following: galcanezumab win won't stop Lilly's headache; Astra breathes easier on Imfinzi; FDA's halt on Advair generics leaves Teva as the biggest threat; Array sets sail for the US with Columbus; Depomed reshuffle reveals tough times in opioids; Soon-Shiong adds patent loss to his woes; Rex goes down under; the expected leaves Active shareholders nursing surprising losses.

These snippets were previously published daily via twitter.

Galcanezumab win won't stop Lilly's headache

12 May

Phase III success for Lilly's anti-CGRP migraine candidate galcanezumab puts it on track for a filing in the second half of the year. But the project showed a seemingly similar effect to Amgen and Novartis's rival erenumab, which is slightly ahead in development, doing little to change the view that this will be a highly competitive class with a marginal benefit for patients at best. And the companies involved might end up fighting over a smaller pie than expected – Amgen recently distanced itself from its deal with Novartis, suggesting that sellside expectations are overdone. Lilly's stock was up as much as 2% in premarket trading this morning on results from the Evolve-1 and Evolve-2 trials in episodic migraine, and the Regain chronic migraine study, but opened flat. The next data in the anti-CGRP space should come from Alder, which expects to report results from its phase III Promise 1 trial of eptinezumab in episodic migraine in the second quarter. Eptinezumab is given intravenously, while the other three candidates are subcutaneous, putting Alder at a disadvantage. It will need to show something special if it is to make headway against its larger rivals.

The anti-CGRP sector

Project	Company	Status	2022e sales ($m)	Notes
Erenumab	Amgen/Novartis	Phase III	1,250	Filing due Q2 2017
TEV-48125	Teva Pharmaceutical Industries	Phase III	820	
Eptinezumab	Alder BioPharmaceuticals	Phase III	771	Phase III Promise 1 data due Q2 2017
Galcanezumab	Eli Lilly	Phase III	690	Filing due H2 2017

Source: EvaluatePharma

Astra breathes easier on Imfinzi

12 May

An early win in the Pacific lung cancer trial has increased confidence in Astrazeneca's PD-L1 inhibitor Imfinzi, and could provide Astra with its first approval in this disease. But the setting of the study, stage III unresectable NSCLC after chemo but before progression, might not provide the company with a huge market. Investors are still waiting for the big one, readout of the first-line Mystic tremelimumab combination study in mid-year – but this didn't stop them pushing Astra's share price up 5% this morning. *EvaluatePharma* sellside consensus estimates that NSCLC will account for 56% of Imfinzi's sales by 2022, at $1.30bn. Stage III unresectable disease is responsible for around 30% of NSCLC cases – but many of these patients initially receive targeted therapies, so it is unclear how many could be left for Imfinzi. And the rival PD-1 agents Keytruda and Opdivo already have NSCLC on their labels. While the result – along with the recent accelerated approval in bladder cancer – is good news for Astra, everything still hinges on Mystic.

Imfinzi lung cancer readouts

Study	Setting	Trial ID	Data due
Pacific	Monotherapy; stage III unresectable NSCLC after platinum-based chemo and radiotherapy	NCT02125461	Reported
Mystic	+/- tremelimumab; first-line NSCLC	NCT02453282	Mid-17
Arctic	+/- tremelimumab; third-line, PD-L1-low/negative	NCT02352948	H2 2017
Neptune	+/- tremelimumab; first-line NSCLC	NCT02542293	2018
Poseidon	+/- tremelimumab; first-line, I-O/I-O/chemo triplet	-	2018+
Pearl	Monotherapy; first-line, Asia	NCT03003962	2018+
Adjuvant	Monotherapy; adjuvant setting	-	2018+

Source: Astrazeneca Q1 presentation, 27 April 2017

FDA's halt on Advair generics leaves Teva as the biggest threat

11 May

Glaxosmithkline could not have hoped for better news – with the second substitutable Advair generic knocked back by the FDA, it seems highly unlikely that the company's respiratory cash cow will see direct competition in the US this year. Hikma said today that the regulator categorised its CRL as a "major" response, which means any resubmission will have a 10-month review. The company, partnered with Vectura on the device, stressed that substitutability was not in question, so what is still to be ironed out remains unclear. Mylan seems to be in a similar position, although it is fighting to have its "major" classification downgraded on a technicality; it is awaiting a meeting with the regulator, which could happen "any day". Either way, the immediate threat to Advair is now Teva's Airduo Respiclick, which was launched at the end of April. This delivers the same active ingredients as Advair; the Israeli firm is marketing it as both a brand and a deeply discounted generic at two different prices. Glaxo has largely brushed off the threat of this product, pointing to its lack of substitutability and different dosages, but Teva's two-pronged strategy has the potential to make a dent. The UK pharma giant is widely expected to have an authorised generic waiting in the wings, but it will be understandably reluctant to pull the trigger on this until it really has to; can strong demand for Airduo force its hand?

The US respiratory battlefield

	GSK	Teva		Astra	Merck	GSK	Mylan	Hikma
	Advair	Airduo brand	Airduo generic	Symbicort	Dulera	Breo	Wixela Inhub	Gx Advair
Low dose price	$291	$285	$90	$270	$291	$322	?	?
Med dose price	$361	$285	$90	$309	$291	$322	?	?
High dose price	$475	$285	$90	-	-	-	?	?
2020 US sales forecast	$426m*	$156m		$592m	$165m	$988m	$234m*	$148m*

*Source: Pricing - Evercore ISI. Sales - EvaluatePharma. *Consensus pre-dates CRLs, so these numbers will now shift up/down*

Array sets sail for the US with Columbus

10 May

A second hit in the Columbus trial means Array Biopharma's Braf-Mek combo of encorafenib and binimetinib is odds-on for approval in melanoma. Topline results from the 344 patients in the second part of the phase III study showed that the combination gave median progression-free survival of 12.9 months compared with 9.2 months for encorafenib monotherapy, a significant difference. This endpoint was missed in part one of Columbus, in which encorafenib was administered at a higher dose. In part one, however, Array's combo did show a significant PFS benefit over Roche's Zelboraf. The company is to file an NDA for the combination in June or July, but approval, if it comes, will not be the end of Array's work: the Braf-Mek segment is dominated by Novartis, whose combo is forecast to hit blockbuster sales in 2022, and Roche is not far behind. Nevertheless, Array's investors sent its shares up 11% in the pre-market, perhaps also factoring in the possibility of a takeout. This is not an entirely blind hope: Merck has shown some interest in the company, signing a deal on Monday under which combinations of binimetinib and Keytruda will be studied in colorectal cancer.

The Braf pack

		Annual WW sales for melanoma ($m)			
Company	Product	2016	2018	2020	2022
Novartis	Tafinlar + Mekinist	672	877	996	1057
Roche	Zelboraf + Cotellic	262	381	623	701
Array BioPharma	Encorafenib + binimetinib	-	118	280	348

Source: EvaluatePharma

Depomed reshuffle reveals tough times in opioids

10 May

Depomed's first quarterly earnings report since a board control fight and C-suite reshuffle has not been taken well. Shares fell 12% post-market on a guidance cut of 17%, news of declining sales for its two top products, Nucynta and Gralise, and announcement of a strategic reorganisation. Depomed will cut its headquarters staff by 30 positions, or 20%, while adding 20 to its neurology sales force, which will now handle Gralise as well as Cambia. The recently upsized pain sales force, at 258 representatives, will handle only the opioids Nucynta ER and IR. Depomed will stop promoting the inhaled fentanyl product Lazanda because of "significant deterioration" in that market. Finally, the group is looking at modifying phase III trials of cebranopadol "in light of the changing opioid landscape", with phase III trials now expected to begin in late 2018.

Depomed sales decline

Product	Q1 2017 ($m)	Q1 2016 ($m)
Nucynta	60.7	69.4
Gralise	18.6	19.0
All products	90.4	104.8

Soon-Shiong adds patent loss to his woes

9 May

Patrick Soon-Shiong's complex network of Nanthealth companies and subsidiaries has already come under fire over allegations of improper use of philanthropic funding and the departure of a senior executive. As of yesterday it has a new problem: a US court has upheld a District Court's rejection of an appeal brought by Nantkwest, the NK cell-focused company, which claims to own rights to the NK-92 cell line. In a brief mention slipped into Nantkwest's quarterly filing with the US SEC the group says this upholds the rejection of a key patent application covering use of the cell line, although other claims were allowed. NK-92 is a continuously growing line of NK (natural killer) cells identified in 1992, which Nantkwest plans to use for its CAR-NK constructs. In the same filing the group insists: "We believe that we have worldwide commercial rights to the NK-92 cell line and we believe that we control commercial use of our aNK, haNK, and taNK cells in key territories." However, first-in-human clinical trials of Her2 and CD19-directed CAR-NK cells, promised last year, have still not begun.

Rex goes down under

8 May

Rex Bionics is to abandon London for sunnier climes. The powered exoskeleton developer has been unable to raise the money it needs on the AIM exchange, and – if shareholders approve its plans – will instead spin off its assets into a private Australian company, also called Rex Bionics, which will receive Aus$7.5m (US $5.5m) of funding from a Melbourne-based investor, Bioscience Managers. In exchange, Bioscience Managers gets control: it will own 64% of the new company, with Rex's current shareholders keeping the rest. Rex will also form a two-year development partnership with McLaren Applied Technologies, a unit of the car company McLaren Group, to design the next generation of the Rex exoskeleton. McLaren would be issued warrants under the deal, which could dilute existing Rex shareholders down to 29%. This might not sound too enticing to shareholders, but Rex says it will go bust if the deal does not go ahead; investors might have to choose between dilution and outright loss of their investment. Then again, few Rex shareholders will be in the black anyway. The company floated at £1.80 per share three years ago, and its shares are currently worth just 6.5p.

The expected leaves Active shareholders nursing surprising losses

8 May

If a largely expected event can wipe two thirds off the value of your shares, then investors in Active Biotech might have cause to wonder what an unexpected event might have done. The Swedish company is down 67%, but possibly not out, on yet another major setback for its multiple sclerosis project laquinimod. Its partner Teva appeared to throw Active yet another lifeline when it said that, while development would be discontinued in relapsing and remitting MS, it would continue in primary progressive MS and Huntington's disease. Active had previously seen its shares plummet when a safety scare caused development with the highest doses of laquinimod to be scrapped, leaving only the lower 0.6mg dose in play. Two previous failures in RRMS at this dose had (theoretically) lowered expectations. On Friday that failure rate rose to three. Given laquinimod's less than stellar performance in RRMS it is sensible to focus on other indications, but even the most optimistic investor must doubt the chances of success for Active's most advanced asset.

Stockholm ACTI