Evaluate Vantage

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Snippet roundup: Nuplazid reviewed by FDA and Nucala reviewed by Icer

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

This week, April 23-27, 2018, we had thoughts on the following: Don't panic, it's all about the second half, says Sanofi; Abbvie sees hep C windfall, but don't get comfortable just yet; Nuplazid headache continues to bother Acadia; Glaxo still wants to be a pharma company; Amgen could give its migraine rivals a pricing headache; Icer Nucala review will hit all asthma agents; Lilly needs to bulk up in oncology; Autolus gets a me-too CAR with a feline difference.

These snippets were previously published daily via twitter.

Don't panic, it's all about the second half, says Sanofi

April 27, 2018

The ongoing decimation of Sanofi's diabetes franchise was not the only disappointing number lurking in the French pharma giant's first-quarter earnings statement today – key products also performed poorly. MS drugs Aubagio and Lemtrada were weak, with the latter hit by Roche's new star Ocrevus; heart drug Praluent is still struggling with payer restrictions; while perhaps most worrying was a weak quarter for Sanofi's biggest hope, Dupixent, which was hit by inventory stocking and higher contributions to patient assistance programmes. New and organic growth will offset declining diabetes sales and a rebound will happen in the second half, chief executive Olivier Brandicourt insisted, but for investors desperate to find out where future growth is coming from the statement painted a gloomy picture. Shares fell 2% in Paris trading, and the stock is only a touch above six-year lows. Quarterly Lantus sales fell below €1bn ($1.2bn) for the first time since 2011, so Sanofi has a huge hole to fill here. With large scale M&A off the table, a lacklustre performance from supposed growth drivers is the last thing investors want to see. The company can claim to be doing something about all this – two big acquisitions in the first quarter should provide future growth and two big C-suite departures should bring in fresh eyes, but in the meantime investors are being told to wait and see. If the second half bounce fails to materialise, Mr Brandicourt may find the merde rolls further uphill.

Abbvie sees hep C windfall, but don't get comfortable just yet

April 27, 2018

Abbvie surprised just about everybody in biopharma when it announced that its first quarter sales of hepatitis C doublet pill Mavyret nearly hit $1bn – $850m to be exact – and guided to 2018 hepatitis C sales of $3.5bn, substantially more than consensus forecasts. Biotech investors have mostly lost interest in hep C since Gilead Sciences revolutionised the space with Sovaldi and Harvoni – it turned out offering vast swathes of patients a cure is not a sustainable business model. Yet for a day investors seem to have forgotten that lesson, bidding up Abbvie shares 6%, adding $9bn in market capitalisation – the Mavyret news was emphatically positive in a quarter marked by caution on Humira ahead of European biosimilars. But lest one is left with the assumption that Mavyret will continue to outperform forecasts, part of its success was due to Japanese patients with genotype 1 who have not been cured by treatment with other direct-acting antivirals – these patients were "warehoused" and thus sought treatment as soon as it was available. The company's guidance points to a belief that demand will flatten through the remainder of 2018, so it looks like this may have been a one-time event. Nonetheless, analysts will be taking a look at their models and probably boosting Mavyret numbers. Abbvie, meanwhile, has had more than its share of wild valuation swings this year – in January, it gained 14% on news that its 2018 tax rate would drop to single digits, but tumbled 13% in March following news of a major oncology clinical setback.

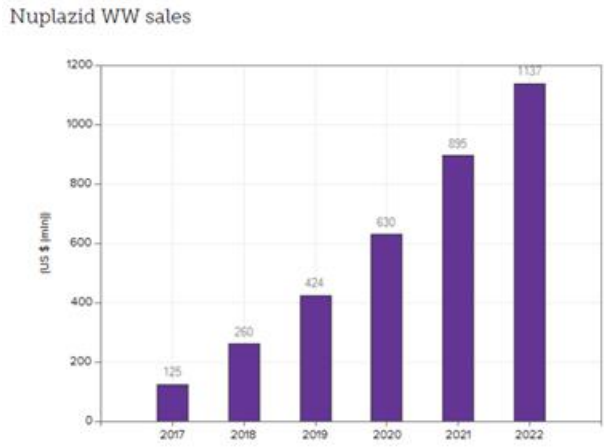
Abbvie hep C forecasts

	WW sales ($bn)		
	2018	2020	2022
EvaluatePharma consensus (pre-Q1 results)	2.6	3.1	3.1
Abbvie Q1 hep C guidance	3.5	-	-

Nuplazid headache continues to bother Acadia

April 26, 2018

Acadia's stock had slid 23% early this month when CNN broke news of 700 deaths in patients taking its Parkinson's disease drug Nuplazid, and the shares lost another 22% yesterday when the US FDA confirmed that it was reviewing the product's safety. Nuplazid had been launched two years ago and is an important growth driver for Acadia, the sellside expecting revenues to breach the blockbuster barrier in 2022, according to consensus collected by *EvaluatePharma*. But it has underperformed: 2017 sales of $125m came at the low end of expectations, with Leerink bemoaning low demand and the group blaming low awareness of the drug among patients and doctors. While the company could thus do without the added problem of safety fears investors should bear in mind that the CNN's totals are derived from FAERS, the FDA's adverse events reporting database; unless properly curated FAERS data are notoriously unreliable, potentially including duplicate reports and making no association between an adverse report and its direct link with the drug in question.



Source: EvaluatePharma

Glaxo still wants to be a pharma company

April 25, 2018

Anyone thinking that Glaxo's recent moves in consumer health will mean a diminished focus on its pharma business should think again, according to its chief executive, Emma Walmsley. She said during an earnings call today that Glaxo's $13bn buyout of Novartis's consumer joint venture stake in March would merely free up the UK company to allocate cash to its number-one priority; namely, strengthening its pharma pipeline. This could include M&A – Ms Walmsley said Glaxo was interested in early-stage assets and technology platforms, but ruled out any big acquisitions including a move for Shire. Analysts speculated that oncology could be a focus for the new-look Glaxo, given the recent appointment of Kevin Sin from Roche as head of business development, and Ms Walmsley did not disabuse them of this notion. However, she would not be drawn further, saying that the company would give a more detailed update on its pharma R&D priorities alongside its second-quarter earnings. Still, Glaxo has a long way to go to reinvent itself: shares were down 4% today after a disappointing quarter for Advair, whose US sales declined 32% on pricing pressure even though a generic has yet to hit the market.

Amgen could give its migraine rivals a pricing headache

April 25, 2018

The migraine market could soon become crowded, and Amgen wants to make its likely first-mover advantage count. The company hinted yesterday that it plans to set a competitive price for its anti-CRGP MAb, Aimovig, with Tony Hooper, head of commercial operations, saying the $8,500-per-year price tag recently suggested by the Institute for Clinical and Economic Review (Icer) was "reasonable". He also said on yesterday's earnings call that Amgen would look "very carefully" at value-based pricing for Aimovig, which is partnered with Novartis. If Amgen does go in hard on price it would be bad news for its closest anti-CGRP rivals, Lilly and Teva, which are lagging behind in the race to approval. Lilly executives claimed yesterday that a three to four month delay would not be a big deal for its candidate, galcanezumab – but that a 12-18 month wait would be more detrimental. This appeared to be a dig at Teva whose project, fremanezumab, has been stalled by an FDA warning letter. Frema had been due an FDA approval decision in June, but Teva might now have to wait until mid-2019 to get the go-ahead, Leerink analysts estimate.

The battle of the anti-CGRP MAbs

Project	Company	Status	Approval decision due...	2022e sales ($m)
Aimovig	Amgen/Novartis	Filed	May 17, 2018	1,265
Galcanezumab	Eli Lilly	Filed	October 11, 2018	664
Fremanezumab	Teva	FDA warning letter Jan 2018	Mid-2019?	607
Eptinezumab	Alder Biopharmaceuticals	BLA submission due H2 2018	2019	387

Source: EvaluatePharma

Icer Nucala review will hit all asthma agents

April 25, 2018

More than two years ago, the Institute for Clinical and Economic Review (Icer) hit Glaxosmithkline's Nucala for its high price, saying a 63% discount off its $32,500 annual list price would be necessary to meet cost-effectiveness standards. It has had little effect, as the annual Medicaid-published price remains at about $32,000, according to *EvaluatePharma*. Now Icer is having a second look at Nucala, along with four fellow biological agents: Sanofi and Regeneron's Dupixent, Roche and Novartis's Xolair, Teva's Cinqair, and Astrazeneca's Fasenra. With the exception of Xolair and Dupixent, the asthma drugs all have been launched in the last three years for severe asthma patients with an eosinophilic phenotype – Dupixent is due an approval in eosinophilic asthma in October, while Xolair has been on the market since 2003 for patients with persistent allergy-related asthma. Competition should have an effect on moderating prices – however, a side-by-side assessment of cost-effectiveness that includes clinical data should help payers, physicians and patients make more informed choices. A draft assessment is due from Icer in September.

Outlook for asthma biological agents

		WW sales ($m)		
Product	Company	2018	2020	2022
Xolair	Roche/Novartis	2,920	3,089	2,785
Dupixent	Sanofi	120	734	1,546
Nucala	Glaxosmithkline	711	1,015	1,284
Fasenra	Astrazeneca	148	447	734
Cinqair	Teva	46	63	76

Source: EvaluatePharma

Lilly needs to bulk up in oncology

April 24, 2018

It would be fair to say that Lilly has missed the immuno-oncology boat. But with the company stressing today that oncology was its "number-one priority" for business development, and highlighting IO as a particular area of interest, it might be attempting to catch up. Some significant acquisitions or partnerships will probably be needed if Lilly truly wants to revamp its oncology offering – the company's cancer pipeline is looking sparse. Highlights picked out by executives today included two phase I projects: a "potentially best-in-class" Tim-3 monoclonal antibody and an IDO inhibitor. Hopes for the latter cannot be high in light of the failure of Incyte's epacadostat earlier this month, perhaps demonstrating how desperate Lilly is. The company also said it was excited about a partnership with Curevac on RNA-based anticancer vaccines, and bispecific antibodies, where it has a number of assets with different targets that should be moving into the clinic soon. In bispecifics, Lilly is collaborating with companies including Zymeworks and Innovent Biologics. Still, bigger deals might be needed if Lilly is to regain ground on its immuno-oncology rivals.

Lilly's oncology pipeline

Project/mechanism	Lead indication(s)	2022e sales ($m)
Phase II		
Prexasertib (Chk 1 inhibitor)	SCLC, ovarian cancer	52
Merestinib (c-Met kinase inhibitor)	NSCLC, solid tumours, biliary cancer	31
LY3023414 (PI3K & mTOR inhibitor)	NSCLC, pancreatic, endometrial, prostate cancers	13
Phase I		
TIM-3 MAb	General oncology	-
IDO1 inhibitor	General oncology	-
CSF-1R MAb	General oncology	-
ERK inhibitor	General oncology	-
TGF-beta receptor I kinase inhibitor	General oncology	-
PD-L1 + LY combo	General oncology	-

Source: Company presentation, EvaluatePharma.

Autolus gets a me-too CAR with a feline difference

April 23, 2018

Clinicaltrials.gov lists 161 individual studies of CD19-directed CAR-T projects, but the UK's Autolus still sees an opportunity here. Today's agreement with University College London brings into its pipeline Auto1, an anti-CD19 project developed by a group that includes the company's own chief scientific officer, Martin Pule. While the marketed anti-CD19 therapies Kymriah and Yescarta use murine-derived binding domains, Auto1 employs a cat-derived binder specifically designed to have lower affinity, the idea being that this could provide more physiological T-cell signalling and cause less toxicity. At Ash last year UCL's Dr Sara Ghorashian reported nine

complete remissions in 10 evaluable paediatric ALL subjects in a phase I trial of Auto1, though there were four remissions (all through antigen loss), and one CD19-positive child did not respond. Importantly, there were no cases of grade 3-5 cytokine storm or neurotoxicity. Autolus, whose last raise valued it at £231m ($321m), last month filed a confidential document with the US SEC for a proposed IPO, and Auto1 and the recently disclosed anti-GD2 neuroblastoma asset Auto6 give it four clinical-stage assets with which to hit the markets.

Autolus R&D pipeline

Project	Target	Indication	Trial ID
Phase I			
Auto1	CD19 (feline binder)	ALL	NCT02443831 (Carpall)
Auto2	BCMA & Taci (via April ligand)	Multiple myeloma	NCT03287804 (April)
Auto3	CD19 & CD22 dual CAR (humanised binder)	DLBCL (with Keytruda) ALL	NCT03287817 (Alexander) NCT03289455 (Amelia)
Auto6	GD2	Neuroblastoma	NCT02761915
Preclinical			
Auto4	TRBC1 (via Jovi-1 ligand)	T-cell lymphoma	Starting late 2017
Auto5	TRBC2 (via Jovi-1 ligand)	T-cell lymphoma	Starting 2019
Auto7	Undisclosed AND/OR/NOT gated CARs	Solid tumours	NA

Source: Company disclosures, presentations at scientific meetings.

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