Evaluate Vantage

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Snippet roundup: Moderna gets richer than ever but Amazon causes a slump

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

This week, January 29 - February 2, 2018, we had thoughts on the following: Moderna becomes an ubercorn; Vertex closes in on cystic fibrosis triplet; when it rains it pours as big pharma shares tumble; Mylan's window of opportunity narrows for Copaxone generic; back of the GEP-NET for Lutathera.

These snippets were previously published daily via twitter.

Moderna becomes an ubercorn

February 2, 2018

Anyone waiting for Moderna to go public will have to wait a bit longer. The company just raised another huge private round – this one worth $500m – giving it a staggering valuation of $7bn and making it the biggest unicorn on the block. Roivant Sciences pulled in a bigger round but, cumulatively, Moderna has raised more. The group's ability to reel in the big bucks continues to raise eyebrows as its many mRNA assets are still far away from the market. The most advanced, the Astrazeneca-partnered cardiovascular project mRNA AZD-8601, should start phase II development soon. Still, Moderna has picked up the pace – since unveiling its first clinical candidates just over a year ago it now has 10 projects in human trials, with new entrants including a personalised cancer vaccine partnered with Merck & Co. Moderna has a long way to go, but with $1.4bn in cash it should not have any problem funding its trials. The trouble will come if any of these studies disappoint.

Top VC rounds of the last decade

Financing Date	Company	Investment ($m)	Financing Round
Aug 2017	Roivant Sciences	1,100	Series A
Feb 2018	Moderna Therapeutics	500	Series G
Aug 2016	Moderna Therapeutics	451	Series Undisclosed
Jan 2015	Moderna Therapeutics	450	Series D
May 2015	Acerta Pharma	375	Series Undisclosed
Oct 2016	Cheplapharm Arzneimittel	374	Series Undisclosed
Oct 2017	Vir Biotechnology	350	Series A
Jul 2015	Immunocore	320	Series Undisclosed
Oct 2014	Nantworks	320	Series B
Jan 2018	Biontech	270	Series A

Source: EvaluatePharma

Vertex closes in on cystic fibrosis triplet

February 1, 2018

Vertex has confirmed which next-gen correctors it will take forward in its cystic fibrosis triplets – but the question of how much triple therapy will cost still hangs over the company. The triplets are designed to treat 90% of cystic fibrosis patients, including the currently untreatable F508del/Min population. Vertex has selected VX-659 and VX-445, the latest of its four candidates to report phase II results, and a glance at the phase II data suggests a reason why (see table): these projects produced a greater benefit in ppFEV1, a measure of lung function, than the other two contenders, VX-440 and VX-152. VX-152 has also previously been linked with gastrointestinal side effects. The group will now start phase III trials of two different triplet regimens, putting it well ahead of its closest competitor, Galapagos. But, even if Vertex succeeds in bringing a triplet to the market, its cost could be a problem in the current climate. Analysts expect a price tag lower than that for Vertex's marketed doublet Orkambi, but with the latter costing $270,000 per year in the US this might not be much comfort. In spite of the high prices, Vertex managed to grow its cystic fibrosis sales by 29% in 2017.

Vertex's next-gen correctors

Project	Dosing	Biggest change in ppFEV1 in phase II vs baseline*	Phase III details
Selected			
VX-659	Once-daily	13.3 percentage points (400mg)	VX-659 + tezacaftor + ivacaftor in F508del/Min and F508del/F508del
VX-445	Once-daily	13.8 percentage points (200mg)	VX-445 + tezacaftor + VX-561 in F508del/Min and F508del/F508del
Not selected			
VX-440	Twice-daily	12.0 percentage points (600mg)	N/A
VX-152	Twice-daily	9.7 percentage points (200mg)	N/A

**Phase II data from studies in F508del/Min patients. Source: Company releases.*

When it rains it pours as big pharma shares tumble

January 31, 2018

The Abbvie miracle is a tough act to follow. After the Illinois-based group jumped last week on forecasting a single-digit income tax rate for 2018, Pfizer and Lilly this week have disappointed investors with news that their rates would decline only modestly. These were only two in a series of ominous news events that have served to drag down big biopharma shares this week. President Donald Trump's first state of the union speech once again raised the spectre of drug price controls, while an as-yet vague health initiative from Amazon, Berkshire Hathaway and JP Morgan has rattled the sector as big players in the economy seek to restrain cost growth. This week's slump comes after a three-month rally in big cap shares, so investors might have decided that it is time to take profits. Of course, Pfizer and Lilly have given their investors specific reasons beyond taxes to sell: the former gave little guidance on its M&A plans, while the latter is facing pressure due to its underperforming animal health division.

Big cap biopharma's tax guidance and previous year effective rates

	Annual guidance				
Company	2018	2017	2016	2015	2014
Abbvie	9%	19%	24%	23%	25%
Johnson & Johnson	17%	17%	17%	20%	21%
Pfizer	17%	20%	13%	22%	26%
Celgene	18%	16%	16%	21%	14%
Eli Lilly	18%	21%	19%	14%	20%
Biogen	24%	25%	25%	24%	25%

Source: Company annual reports and year-end earnings releases

Mylan's window of opportunity narrows for Copaxone generic

January 31, 2018

It looks like Mylan will soon be fighting unwanted company in the market for generic versions of Copaxone. Pfizer confirmed yesterday that a manufacturing plant that has been under FDA special measures should soon be up and running, paving the way for a green light for Momenta and Sandoz's 40mg dose of the Teva blockbuster. Problems at the plant had been delaying final approval of the multiple sclerosis medicine. Mylan launched its substitutable version of the 40mg shot in October and has been enjoying the generic market alone since then; the company was hoping to remain the sole generic provider for a while longer. However, Momenta said yesterday that the FDA's review of its Glatopa 40mg ANDA could be completed "at any time". Mylan reports fourth-quarter numbers next week, when it should reveal exactly how lucrative the opportunity has been – analysts' estimates range from $100m to $192m. Another kid on the block will inevitably mean more price competition, so both Mylan and Teva will be hoping that the FDA drags it feet for a little longer.

Back of the GEP-NET for Lutathera

January 29, 2018

US approval for Advanced Accelerator Applications' radiopharmaceutical Lutathera has come with a more generous label than was granted by European regulators back in September. The product, a somatostatin analogue labelled with lutetium-177, is indicated for gastroenteropancreatic neuroendocrine tumours (GEP-NETs), but in the US it has escaped the restriction on hindgut tumours present on the European label. This could permit it to outsell Bayer's Xofigo, a prostate cancer therapy that came with Bayer's $2.9bn acquisition of Algeta in 2013. Xofigo is forecast to have 2022 worldwide sales of $850m, according to *EvaluatePharma*'s

sellside consensus. But some analysts put Lutathera's 2022 sales as high as $1.1bn, rising to $1.8bn in 2025. Should Lutathera's sales turn out to hit this kind of figure it will neatly justify the $3.9bn Novartis paid for Advanced Accelerator Applications last autumn, and make this appear to be a better deal than the one Bayer struck for Algeta.

Radiopharmaceuticals: Lutathera's competition

			Annual sales WW ($m)		
Product	Generic Name	Company	2016	2022	CAGR
Xofigo	radium Ra-223 dichloride	Bayer	366	850	15%
Azedra	iobenguane I-131	Progenics Pharmaceuticals	-	191	N/A
OncoSeeds	iodine I-125	General Electric	33	18	-10%
Metastron	strontium chloride Sr-89	Nippon Kayaku/General Electric	24	31	4%
Quadramet	samarium Sm-153 lexidronam pentasodium	Lantheus Holdings	7	7	0%

Source: EvaluatePharma

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