Evaluate Vantage

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Snippet roundup: Biogen's chief exec choice underwhelms as a big 2016 decision is delayed to 2017

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

This week, December 19-23, 2016, we had thoughts on the following: manufacturing review delays Ocrevus launch; Japan tightens pricing screw with annual review; Bioinvent couples to year-end partnering gravy train with Pfizer deal; Bristol-Psioxus deal confirms allure of oncolytic viruses; Biogen underwhelms with CEO choice; pump trial could boost Adocia ultra-fast insulin case; US Medicare drops plan to cut physician drug price markup; Scanadu declines to honour Scout.

Manufacturing review delays Ocrevus launch

December 21, 2016

One of the biggest expected approvals of 2016 now will be pushed into 2017 with the US FDA's decision to delay the decision deadline for Roche's multiple sclerosis candidate Ocrevus. The antibody is slated to become the first drug specifically indicated for primary progressive MS, but a review of the commercial manufacturing process has not been completed, and the PDUFA date is now set for March 28, from December 28. Ocrevus is forecast as one of the two biggest commercial launches of 2017, in a neck-and-neck race with Sanofi's eczema project Dupixent in 2022 sales – Roche's project is forecast to sell $4bn and Sanofi's $4.6bn. A three-month delay in the Ocrevus decision date will probably not affect 2022 sales by much, but it now looks as though the two projects could hear an approval decision within three days of each other, as Dupixent's PDUFA is set for March 31.

Big launches of 2017

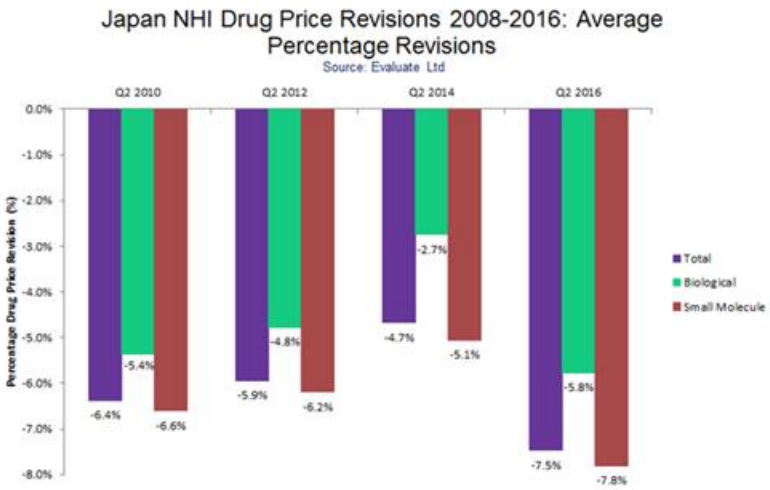
Product	Company	2022 sales WW ($bn)
Dupixent	Sanofi	4.7
Ocrevus	Roche	4.0
Durvalumab	AstraZeneca	2.3
Semaglutide	Novo Nordisk	2.2
Baricitinib	Eli Lilly	1.8

Source: EvaluatePharma

Japan tightens pricing screw with annual review

December 21, 2016

Japan will double the frequency of its drug price reviews to once a year beginning in 2018 in a bid to control rising costs, and will add all prescription drugs to its review, the government has announced. The formerly biennial review had included only those products with a big disparity between a negotiated price with the government and a lower price paid by hospitals and wholesalers. With an annual review, and more drugs included, this suggests that generics as well as branded drugs will be subject to price cuts. Reimbursed prices for drugs approved in Japan in 2016 have ranged between a 24% and 87% discount off US prices, according to *EvaluatePharma* data. The decision to go to annual reviews comes one month after the government imposed an off-cycle cut on the price of Bristol-Myers Squibb/Ono's Opdivo, which had cost more than in the US. Today, Ono issued a profit warning because of the price cut. Japan's action shows that, even in markets with more aggressive negotiation than the US, the price of drugs is under increasing scrutiny as payer budgets are stretched.



Bioinvent couples to year-end partnering gravy train with Pfizer deal

December 21, 2016

The Swedish group Bioinvent won Pfizer as a partner for its programme to develop antibodies to combat tumour-associated myeloid cells. Pfizer made a $6m investment in Bioinvent and will spend an additional $4m in up-front licensing fees and early research funding to support the programme, which seeks to supplement the immuno-oncology approach of checkpoint inhibitors like Pfizer and Merck KGaA's avelumab. Bioinvent did not disclose the number of drug candidates that could be part of the agreement, but estimated that if five antibodies emerged from the collaboration it would be eligible for $500m in milestones. Tumour-associated myeloid cells play a role in cancer-associated inflammation, and Bioinvent is seeking to reverse their immunosuppressive properties or reduce their numbers to combat disease in patients who respond poorly to other treatments. Bioinvent shares were up 29% in mid-day trading today.

Bristol-Psioxus deal confirms allure of oncolytic viruses

December 20, 2016

The modest outlook for Amgen's Imlygic, the first approved oncolytic virus, has not discouraged big pharma from deal-making in this innovative space. Bristol-Myers Squibb today paid $50m up front to secure rights to NG-348, a preclinical "armed" oncolytic virus that aims to infect tumour cells and turn on T-cell signalling. This is the third oncolytic virus deal involving a big pharma player since early October, with Pfizer and Boehringer Ingelheim having entered the space. As with its peers, Bristol says it is most interested in seeing how this project will enhance the effectiveness of other immuno-oncology agents such as checkpoint inhibitors. Bristol will pay for clinical development and commercialisation, and provide funding for preclinical development; $886m in milestones are also included as part of the deal, as well as royalties.

Selected clinical-stage oncolytic virus projects

Project	Company	Note
Phase III		
Pexa-Vec	Transgene/Sillajen	Copenhagen strain vaccinia poxvirus, genetically modified to express GM-CSF
Reolysin	Oncolytics Biotech	Reovirus
Phase II		
G47Δ	Daiichi Sankyo	3rd-generation HSV-1
TG1042/ ASN-002	Transgene/Ascend	Adenovirus-interferon-γ
Cavatak	Viralytics	Coxsackievirus A21
GL-ONC1	Genelux	Laboratory strain GLV-1h68
Marabex	Turnstone Biologics	Bioselected from rhabdovirus isolates
ORCA-010	Orca Therapeutics/VCN Biosciences	Adenovirus serotype 5
ParvOryx	Oryx	Parvovirus H-1
LOAd703	Lokon Pharma	Adenovirus that introduces expression of CD40L & 4-1BBL
NDV-HUJ	Theravir Management	Newcastle disease virus
JX-929	Sillajen Biotherapeutics	Western Reserve strain of oncolytic vaccinia virus
PV701	Wellstat Group	Replication-competent Newcastle disease virus strain
MV-NIS	Vyriad	Edmonston strain of measles virus
ONCOS-102	Targovax	Adenovirus serotype 5
Seprehvir	Virttu Biologics (Sorrento)	HSV-1
Enadenotucirev	Psioxus	Non-naturally occurring Group B adenovirus

Biogen underwhelms with CEO choice

December 20, 2016

Biogen's announcement that it has selected its chief commercial officer, Michel Vounatsos, to replace George Scangos as chief executive has been received with muted enthusiasm by investors and analysts. As sales growth levels off, the Massachusetts-based group is in the midst of a strategic transition that includes the spin-out of its haemophilia business and rumours of a trade sale. An internal appointment from the commercial side has unnerved some investors who want the company to be acquired. That outcome cannot be expected until

intellectual property disputes involving the multiple sclerosis pill Tecfidera are resolved early next year. The company's valuation is also dependent on approval and launch of the spinal muscular atrophy drug Spinraza. The company said it would review its strategy, and investors will eagerly await an announcement of its plans in the first few months of 2017.

Top-selling Biogen products, 2022

		Annual Sales WW ($bn)		
Product	Indication	2015	2022	WW Phase
Tecfidera	Multiple sclerosis	3.6	4.4	Marketed
Aducanumab	Alzheimer's disease	-	1.5	Phase III
Tysabri	Multiple sclerosis	1.9	1.5	Marketed
Spinraza	Spinal muscular atrophy	-	1.4	Filed
Avonex	Multiple sclerosis	2.6	1.3	Marketed

Source: EvaluatePharma

Pump trial could boost Adocia ultra-fast insulin case

December 19, 2016

Adocia's ultra-rapid-acting version of Humalog has shown that it can outperform the Lilly flagship insulin in a pump test, although the results could have investigators closely examining the data to see whether to move into advanced testing. The phase I test in type 1 diabetics consisted of two parts. The first used Roche's Accu-Chek Spirit to deliver first one insulin, then the other, to 36 patients. The second consisted of a crossover design in which 44 patients received first one insulin, then the other, via the Roche pump, and subsequently one insulin after the other via Medtronic's Paradigm Veo pump. Syringe delivery was used as a control. In the first part of the trial, Adocia's BioChaperone lispro U100 did not show a benefit over Humalog. In the second part, the Adocia insulin demonstrated a statistically significant increase in insulin exposure over the first 30 minutes compared with Humalog in both of the two pumps tested – by 33% in the Roche pump and by 54% in the Medtronic pump. Lilly, which has licensed in the Adocia project, now must consider whether to advance this or its own internal ultra-rapid insulin. Novo Nordisk, meanwhile, has filed its ultra-fast version of NovoRapid, now called Fiasp, in both the US and Europe. It has received a complete response letter from the FDA and a positive recommendation from the European Medicines Agency.

Selected insulin candidates in the R&D pipeline

			WW Sales ($)		
	Product	Company	2018	2020	2022
Filed	Fiasp	Novo Nordisk	244	487	702
Phase III	SAR342434 (biosimilar Humalog)	Sanofi	27	97	158
Phase II	BioChaperone Lispro U100	Adocia/Eli Lilly	-	41	115
	Ultra Rapid Insulin	Eli Lilly	-	-	-
	HinsBet U100	Adocia	-	-	-

Source: EvaluatePharma

US Medicare drops plan to cut physician drug price markup

December 19, 2016

The US Centers for Medicare and Medicaid Services has binned its plan to cut prices on the most expensive biological drugs administered in physicians' offices. The demonstration plan, which was meant already to have begun, would have limited the markup for the most expensive drugs in some, but not all, physician practices to evaluate how changing reimbursement affected utilisation. Some practices would have retained the current payment of the average selling price (ASP) plus 4.5%, while others would have been reimbursed at ASP plus 2.5%, plus a flat fee of $16.80. The latter payment method would increase reimbursement for the cheapest drugs and cut it for the most expensive. CMS had also planned to experiment with some value-based pricing principles as part of this demonstration.

Most expensive drugs sold in the US

		Cost per Patient per Year ($)	
Product	Company	2014	2015
Soliris	Alexion Pharmaceuticals	549,806	582,253
Naglazyme	BioMarin Pharmaceutical	486,452	493,544
Cerezyme	Sanofi	458,700	458,517
Eloctate	Biogen	442,427	446,589
Cinryze	Shire	504,391	416,029
NovoSeven	Novo Nordisk	338,564	387,256
Advate	Baxalta	368,576	378,262
Fabrazyme	Sanofi	280,289	357,875
BeneFIX	Pfizer	331,396	336,479
Aldurazyme	Sanofi	310,682	311,365

Source: EvaluatePharma

Scanadu declines to honour Scout

December 19, 2016

Scanadu branded its Scout diagnostic device as similar to Star Trek's tricorder, but the reality has turned out a little more dystopian. In a cautionary tale for the users of crowdfunding sites the company is to stop supporting the Scout next May, leaving those who had contributed to its record-breaking $1.6m fund-raising at Indiegogo in the lurch. The Scout, which has until now been given to Indiegogo contributors as part of a pivotal US study, measures body temperature, respiration, oximetry, ECG and systolic and diastolic blood pressure with just 10 seconds of contact with the forehead. But it has failed to win FDA approval, and Scanadu says that FDA regulations require that the study cease and the devices be deactivated. Its crowdfunders, who have spent at least $149 each and in some cases much more, are now left with technology that will slowly become obsolete. And Scanadu has investors beyond its Indiegogo contributors. Its $35m series B was the eighth largest medtech VC round of 2015, and those backers too will have been looking forward to FDA approval.

Scanadu's investment to date

Date	Round	Investment ($m)	Investors
April 27, 2015	Series B	35	Fosun Pharma, Tencent Holdings, Ame Cloud Ventures, Broe Group, China Broadband Capital, iGlobe Partners, Redmile Group, Relay Ventures
November 12, 2013	Series A	10.5	Relay Ventures, Ame Cloud Ventures, Broe Group, Mindful Investors, Redmile Group, VegasTechFund
June 9, 2013	Seed Capital	0.8	Undisclosed
July 20, 2013	Indiegogo crowdfunding	1.6	Undisclosed
November 8, 2011	Seed Capital	4.0	Undisclosed
	Total	**51.9**	

Source: EvaluateMedtech

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