Evaluate Vantage

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Snippet roundup: A new PD-L1 is born, and success for Newron at long last

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

This week, March 20 to March 24, 2017, we had thoughts on the following: avelumab crosses the finish line, but bigger market remains elusive; Newron finally wins US approval for Parkinson's project; Jazz sets the Tones with sleep apnoea data; Lilly joins battle for CDK inhibitor crown; FDA warns of Absorb risks.

These snippets were previously published daily via twitter.

Avelumab crosses the finish line, but bigger market remains elusive

March 24, 2017

Yesterday's US approval of avelumab for Merkel cell carcinoma is unlikely to trouble the competition, but it will be important for having got the Pfizer/Merck KGaA anti-PD-L1 MAb across the regulatory finish line. Indeed, Merkel cell, a rare skin cancer, is perceived as such an economically unviable proposition that, barring a couple of investigator-initiated studies, none of the leading anti-PD-1/PD-L1 projects are in trials specifically for it. An NCI-sponsored study of Keytruda generated positive data in first-line Merkel cell carcinoma at last year's AACR meeting, but despite this its maker, Merck & Co, has not picked up the gauntlet. Merkel cell is an orphan cancer with about 2,000 new US cases a year, and avelumab, now trademarked Bavencio, is being priced at $13,000 a month. For its originators this indication was always just a foot in the door to prove avelumab's safety; indeed, the safety database comprised 1,738 patients – many more than the 200 who took part in the registrational Javelin Merkel-200 trial. Bigger indications hold the key to Bavencio's success, but given the recent two-year delay to the important Javelin Lung-100 trial victory is far from assured.

Key US approvals of anti-PD-1/PD-L1 Mabs

Therapy	Indication	Notes
Bavencio (Pfizer/Merck KGaA)		
Monotherapy	2nd-line Merkel cell carcinoma	Javelin Merkel-200 study
Tecentriq (Roche)		
Monotherapy	2nd-line NSCLC	Oak study
Monotherapy	2nd-line urothelial carcinoma	Imvigor-210 study
Opdivo (Bristol-Myers Squibb/Ono)		
Monotherapy	2nd-line urothelial carcinoma	Checkmate-275 study
Monotherapy	2nd-line squamous head & neck cancer	Checkmate-141 study
Monotherapy	3rd-line classical Hodgkin lymphoma	Checkmate-205 & 039 studies
Yervoy combo	1st-line melanoma	Checkmate-067 & 069 study
Monotherapy	1st-line melanoma	Checkmate-066 study
Monotherapy	2nd-line renal cell carcinoma	First anti-PD1 to show OS benefit in renal cancer
Monotherapy	2nd-line non-squamous NSCLC	Checkmate-057 study
Keytruda (Merck & Co)		
Monotherapy	4th-line classical Hodgkin lymphoma	Keynote-087 study
Monotherapy	1st-line PD-L1-positive (>50%) NSCLC	Keynote-024 study
Monotherapy	2nd-line head & neck cancer regardless of PD-L1 status	Keynote-012 study
Monotherapy	1st-line melanoma regardless of Braf status	Keynote-006 study

Newron finally wins US approval for Parkinson's project

March 22, 2017

Almost three years after seeking US marketing approval for its add-on Parkinson's therapy Xadago (safinamide), Newron Pharmaceuticals has finally got a green light. The application was knocked back by both a refusal to file and a complete response letter, meaning the drug will reach the US market a full two years after being launched in Europe. Still, FDA approval for a small Italian drug developer remains a notable achievement, even if this is muted somewhat by the limited financial exposure Newron has to the drug. Zambon has a global licence (ex-Asia) to sell Xadago, and has sublicenced it on to US Worldmeds in the world's biggest drug market. The companies will be hoping for a bigger splash here than in Europe – Newron has received €2.2m ($2.4m) in royalties since it was launched in May 2015. Optimistic peak sales forecasts range from $450m to $750m, which would certainly yield a useful income stream for the unprofitable drug developer. However the lack of share price reaction today suggests that investors are less excited about the opportunity, and most are now focused on a potentially pivotal readout from Newron's Rett syndrome project sarizotan in

early 2018.

Jazz sets the Tones with sleep apnoea data

March 21, 2017

Jazz's efforts to reduce its reliance on Xyrem are beginning to pay off, with phase III success for its new stimulant JZP-110 in excessive sleepiness associated with obstructive sleep apnoea (OSA). This was expected to be the trickier indication for the project, which is also in a pivotal trial for narcolepsy, so should increase its overall chances of approval. Two phase III trials of JZP-110 in OSA met their co-primary endpoints, with the 12-week Tones 3 study doing so at all four doses – it had only been powered to detect differences between placebo and the higher 300mg and 150mg dose arms. Jazz did not give more detailed data, and plans to present the full results in June at the American Academy of Sleep meeting in Boston. Safety will also be paramount, given the abuse potential of stimulants. On this point, Jazz would only say that adverse events were consistent with those seen in phase II studies of JZP-110, but these were low compared with other stimulants studied for excessive daytime sleepiness, Leerink analysts noted. Data from the phase III trial in narcolepsy are due mid-year and the company plans to file JZP-110 in late 2017. Jazz's share price closed up 7% on March 20.

Jazz Pharmaceuticals' top products in 2022

			WW annual sales ($m)	
Product	Therapeutic subcategory	Status	2016	2022
Xyrem	Psychostimulants	Marketed	1,108	1,476
Defitelio	Cerebral & peripheral vasotherapeutics	Marketed	109	330
Vyxeos	Other cytostatics	Phase III	-	292
Erwinaze	Other cytostatics	Marketed	201	254
JZP-110	Psychostimulants	Phase III	-	170

Source: EvaluatePharma

Lilly joins battle for CDK inhibitor crown

March 21, 2017

Lilly's abemaciclib has prevailed in phase III, setting it up to become the third approved CDK4/6 inhibitor behind Pfizer's Ibrance and Novartis's Kisqali. But how Lilly's agent stacks up against its rivals in terms of efficacy and safety is still unknown – the company has not given any more details from the Monarch 2 trial in second-line breast cancer, apart from saying it met its primary endpoint of progression-free survival. Investors will want to know if abemaciclib has matched Ibrance, which posted a median PFS of 9.2 months in combination with fulvestrant in the Paloma-3 trial – the same combination studied in Monarch 2. Safety will also be closely watched, as this is one way that abemaciclib could set itself apart from the competition. Lilly's project has shown lower rates of neutropenia that could negate the need for a drug "holiday", but has been linked with high rates of diarrhoea. The company would only say that adverse events were "consistent with previous studies of abemaciclib". Lilly plans a second-quarter filing based on the Monarch 1 trial, with an additional submission for Monarch 2 due in the third quarter. It also expects data from the first-line Monarch 3 study by the end of the year, but it still has some way to go to catch up with Pfizer.

Top CDK 4/6 inhibitor products by 2022

		WW annual sales ($m)			
Product	Company	2016	2022	Phase	First Launch WW
Ibrance	Pfizer/Amgen	2,135	6,014	Marketed	Feb-15
Abemaciclib	Eli Lilly	-	1,559	Phase III	Dec-18
Kisqali/LEE011/ribociclib	Novartis/Otsuka	-	1,543	Approved	Sep-17

Source: EvaluatePharma

FDA warns of Absorb risks

March 20, 2017

Once the subject of a great deal of excitement, the first dissolving drug-eluting stent has been rather a disappointment on the commercial front. Now it looks to be a dismal prospect from clinical and regulatory standpoints too, with the FDA stating that it is investigating Abbott's Absorb after trial data showing a worryingly high risk of serious adverse events at two years. Absorb was approved in the US last summer on one-year results from the Absorb III trial, showing it to be non-inferior to Abbott's market-leading DES, Xience. Two-year results from this same trial showed that 10.9% of Absorb-treated patients had target lesion failure compared with 7.9% of Xience recipients. Heart attack was also more common with Absorb, at 7.3% compared with 4.9% with Xience. A change in guidelines means that in 19% of patients Absorb was implanted in arteries that are now considered too small; excluding those patients, the difference between the two stents was not statistically significant. The FDA has said it is conducting more analyses, and these might yet vindicate Absorb – but for a device whose raison d'être is its long-term safety and efficacy this is a poor show.

Drug-eluting stents

		WW annual sales ($m)		
Company	Product(s)	2016	2022	CAGR
Medtronic	Endeavor/Resolute	974	983	0%
Abbott Laboratories	Absorb	247	657	18%
Boston Scientific	Promus Element	762	628	-3%
Abbott Laboratories	Xience	978	605	-8%
Boston Scientific	Synergy	476	591	4%
Biosensors International	Biomatrix/Axxess/Excel	250	332	5%
Terumo	Ultimaster	176	226	4%
Reva Medical	Fantom	-	103	N/A
Microport Scientific	Firehawk/Firebird 2/Waltz	23	51	14%
Terumo	Nobori	20	7	-16%

Source: EvaluateMedtech

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