Evaluate Vantage

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Snippet roundup: Medica and Cell Medica are in the money, but Endo and Valeant feel the pain

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

This week, March 13 to March 17, 2017, we had thoughts on the following: Medica investors see value in remote radiology; it pays off for Cell Medica to put the CAR-T before the money; Opana panel reverses risk-benefit verdict; Keytruda's colorectal cancer delay spurs new PD-1 race; Ackman throws in a very expensive towel; Roche cancels patent dance on Herceptin biosimilar.

These snippets were previously published daily via twitter.

Medica investors see value in remote radiology

March 17, 2017

Medica's £121m ($150m) initial public offering is the fourth in less than a year on the London stock exchange – and also illustrates a growing appetite in the medtech world for telemedicine. Hastings-based Medica specialises in teleradiology, the electronic transmission of patient images from one location to another for diagnosis. The group, via its network of consultants, provides interpretation and reporting services to UK hospitals for imaging modalities including MRI, CT and X-ray, remotely linking hospitals with experts in other parts of the country and potentially speeding up diagnosis. Demand is obviously growing: Medica's sales increased at a compounded rate of 27% between 2013 and 2015. That a little-known UK company has managed to raise so much is impressive – it is the only medtech IPO so far this year, and would have been the largest by 2016's standards had it not been for an outlier, Convatec's huge $1.9bn float. Medica's offering is also far larger than all of the other listings on the London exchanges in the past few years, once Convatec's is excluded.

Top 10 medtech IPOs of 2016

Date	Company	Amount raised ($m)	Exchange	Offering price	Change since float
October 26	Convatec	1,947.9	LSE	£2.25	4%
October 20	Irhythm Technologies	107.0	Nasdaq	$17.00	76%
October 6	Obalon Therapeutics	75.0	Nasdaq	$15.00	(41%)
September 29	Tabula Rasa Healthcare	51.6	Nasdaq	$12.00	25%
March 18	Senseonics	45.0	NYSE	$2.85	(6%)
July 28	Tactile Medical	41.2	Nasdaq	$10.00	64%
December 9	Creo Medical	26.3	LSE	£0.76	7%
May 18	Pulse Biosciences	20.0	Nasdaq	$4.00	63%
May 18	Oncimmune	15.9	LSE	£1.30	1%
June 3	Sensus Healthcare	11.0	Nasdaq	$5.50	(5%)

Medtech IPOs in London, 2011-2016

Date	Company	Amount raised ($m)	Exchange	Offering price (£)	Change since float
December 9, 2016	Creo Medical	26.3	LSE	0.76	7%
October 26, 2016	Convatec	1,947.9	LSE	2.25	4%
May 18, 2016	Oncimmune	15.9	LSE	1.30	1%
April 18, 2013	Cambridge Cognition	10.0	AIM	0.70	(3%)
November 17, 2011	Sphere Medical	22.1	AIM	0.93	(1%)

It pays off for Cell Medica to put the CAR-T before the money

March 16, 2017

It might have come a little later than promised, but the £60m ($74m) series C raised by Cell Medica is one of the biggest by a UK company, and easily eclipses the biggest UK round so far this year, the $28.7m raised by Nerre Therapeutics in February. Many previous investors doubled down on their initial bets, with the likes of Touchstone Innovations and venture funds managed by the serial investor Neil Woodford again putting money into the London-based company. Cell Medica's recent decision to focus its portfolio on the CAR-T space, using

autologous natural killer T cells, is bound to have helped in persuading these investors to top up their original investments. Last year the UK group Autolus raised £40m solely on the strength of a preclinical CAR-T pipeline, showing the continuing appetite for immuno-oncology. Cell Medica is expected to use the money to advance key projects into phase II trials as well as complete a phase II trial for its lead asset, baltaleucel-T. In February the FDA granted baltaleucel-T fast-track designation in relapsed or refractory lymphoma.

Top 10 UK company VC rounds

Financing Date	Company	Financing Round	Investment ($m)
2015	Immunocore	Series Undisclosed	320
2015	Mereo BioPharma	Series A	119
2014	Adaptimmune	Series A	104
2010	Archimedes Pharma	Series Undisclosed	100
2016	Kymab	Series C	100
2016	MISSION Therapeutics	Series Undisclosed	86
2014	Cell Medica	Series B	80
2016	Biohaven Pharmaceutical Holding	Series A	80
2017	Cell Medica	Series C	74
2016	F2G	Series Undisclosed	60

Source: EvaluatePharma

Opana panel reverses risk-benefit verdict

March 15, 2017

The panel verdict is in, but the question of whether Endo International's Opana ER will be pulled from market is still open. An adcom yesterday voted 18 to eight, with one abstention, that the extended-release oxymorphone's benefits no longer outweigh its risks, but no vote on its removal from sale was proposed or taken. Even so, some committee members did suggest that this might be a sensible move on the FDA's part, citing Opana ER's potential for intravenous abuse, which has led to addicts contracting serious blood disorders including HIV. The FDA is not obliged to accept the panel's determination on the risk/benefit ratio, let alone take comments about market withdrawal made in the course of the discussion as instructions. But it could do this, or – perhaps more likely – make the drug's label more restrictive. Endo's shares sank late yesterday and closed off 4%, so some people are taking at least some loss of sales as a realistic possibility.

Endo's top five drugs in 2022

Product	Therapeutic Subcategory	WW sales ($m) 2016	2022	CAGR
Xiaflex	Other musculoskeletal agents	189.7	339.4	10%
Opana ER	Narcotic analgesics	158.9	124.0	-4%
Percocet	Narcotic analgesics	139.2	110.2	-4%
Supprelin LA	Female sex hormones	78.6	96.4	3%
Vasostrict	Pituitary & Hypothalamic hormones	217.0	87.7	-14%
	Total company sales:	**4,010**	**4,489**	**2%**

Source: EvaluatePharma

Keytruda's colorectal cancer delay spurs new PD-1 race

March 15, 2017

Merck & Co's Keytruda has won FDA approval in another new indication, Hodgkin lymphoma, but will have to wait a while longer for the go-ahead in solid tumours with a microsatellite instability-high phenotype, including colorectal cancer. A decision in the latter indication had been due this month, but has now been pushed back to June 9 after Merck submitted additional data and analyses to the FDA. Patients with high microsatellite instability (MSI) account for around 15% of early-stage metastatic colorectal cancer, and specialists had expected Keytruda to become the new standard in this subgroup. However, as ever in the PD-1/PD-L1 space, competition is fierce, with both Bristol-Myers Squibb and Roche already studying their products in broader colorectal cancer populations. The former is testing Opdivo, either alone or in various combinations depending on MSI status, in the Checkmate-142 trial. And Roche is evaluating a combination of Tecentriq and Cotellic in MSI-stable patients in the Cotezo study. Merck had hoped that its headstart would allow it to carve out a niche in colorectal cancer, but the latest delay could give momentum back to its rivals.

Key checkpoint inhibitor studies in CRC

Drug	Name	Design	Line	NCT ID	Data
Keytruda	Keynote-164	Keytruda monotherapy (single arm)	3rd, MMR-d or MSI high	NCT02460198	July 2018
Keytruda	Keynote-177	Keytruda vs standard therapy	1st, MMR-d or MSI-high	NCT02563002	Aug 2019
Opdivo in combination	Checkmate-142	Opdivo +/-Yervoy (+/-Cotellic), Darzalex and BMS-986016	Allocated according to MSI-H status	NCT02060188	Jul 2017
Tecentriq/Cotellig	Cotezo	Tecentriq +/- Cotelliq vs Stivarga	>3rd	NCT02788279	Apr 2019

Ackman throws in a very expensive towel

March 14, 2017

The jig is up. After hanging on to its stake in Valeant for more than two years, Bill Ackman's hedge fund Pershing Square has finally sold up, in the process making a loss measured in the billions. Pershing initially bought into Valeant in February 2015 when the stock was trading at $160, and the bet looked good for a while, with shares up to nearly $260 in late July. Then, when the slide began thanks to Valeant's price hikes and other controversial business practices Pershing doubled down, buying even more shares that October at $108 apiece. This started to look like good money after bad almost immediately, but Mr Ackman held on like grim death, certain that a turnaround was coming. No such luck: yesterday Pershing said it had sold its entire stake, 27 million shares and options, for just $306m. At its peak, Pershing's stake was worth around $4bn; Mr Ackman has paid for his stubbornness. Many of Valeant's other shareholders have taken the hint, pushing its shares down 11% in early trading.

NYSE: VRX 2 year share price

Roche cancels patent dance on Herceptin biosimilar

March 13, 2017

Roche has decided that the decision on when a Herceptin biosimilar will be launched will not be left to the courts and regulators. The Swiss group and its rival Mylan announced a global agreement under which Roche will license out the right to market trastuzumab in all markets except for Japan, Brazil and Mexico. The launch dates of the Mylan biosimilar, called Canmab or Hertraz in the markets where it is already marketed, are confidential under the agreement – the US FDA has set a September 3 deadline for regulatory approval. Mylan says it expects to be the first company to launch a US Herceptin biosimilar. In return for the licence, Mylan has dropped inter partes review challenges against two Herceptin patents. The agreement averts further litigation costs, including those over the exchange of intellectual property following approval known as the "patent dance". Sales of Herceptin peaked at $6.9bn in 2016, and are expected to shrink to $3.5bn in 2022.

Herceptin and its rivals: The outlook

		WW sales ($m)*							
Product	Company	2016	2017	2018	2019	2020	2021	2022	WW Phase
NME									
Herceptin	Roche	6,884	6,806	6,436	5,822	4,957	4,179	3,506	Marketed
Biosimilar									
PF-05280014	Pfizer	-	-	-	105	205	271	336	Phase III
Herzuma	Celltrion	-	-	-	96	144	211	267	Approved
ABP 980	Amgen	-	12	37	56	81	97	106	Phase III
SB3	Merck & Co	-	-	7	27	47	67	83	Filed
Herzuma	Teva Pharmaceutical Industries	-	-	-	4	10	16	23	Phase III
CANMAb/Hertraz	Mylan	-	-	2	7	12	16	20	Marketed

** Forecasts made pre-announcement so subject to revision; Source: EvaluatePharma*

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