Evaluate Vantage

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Snippet roundup: J&J shrinks, while Vernalis vanishes altogether

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

This week, March 12-16, 2018, we had thoughts on the following: J&J sheds another medtech business; Siemens Healthineers sets a record; et tu, Vernalis? UK biotech succumbs to the ides of March; right to try applies to legislation too; subpoena adds to Myriad's hereditary test pressures; Teva cull unlikely to have claimed its last victim; Astra as good as confirms that Mystic has failed; Acufocus sells its Kamra; Glaxo gets another Advair reprieve.

These snippets were previously published daily via twitter.

J&J sheds another medtech business

March 16, 2018

The statement is couched in cautious language, but it looks like Johnson & Johnson's divestment of its Lifescan diabetes unit is all but a done deal. The company – less of a conglomerate with each passing day – has received a binding offer of $2.1bn for what remains of its diabetes business from the investment group Platinum Equity, and though consultations are under way and the acceptance period for the offer lasts until June J&J appears to be shrinking further away from medtech. It has sold off or shut down seven businesses since it shook off Ortho-Clinical Diagnostics in early 2014, and four of these went for more than $1bn. If the Lifescan sale does indeed go ahead, the proportion of revenue J&J gets from medical devices will shrink from around 35% to 33%.

J&J's significant medtech divestments

Date	Unit	Technology	Buyer/partner	Deal value ($bn)
January, 2014	Ortho-Clinical Diagnostics	Blood testing	Carlyle Group	4.0
March, 2015	Cordis	Interventional cardiology	Cardinal Health	1.9
February, 2016	Janssen Betalogics	Stem cell therapy for diabetes	ViaCyte	Undisclosed
December, 2016	Cellsearch	Liquid biopsy	Menarini	Undisclosed
October, 2017	Animas*	Insulin pumps	Medtronic	Undisclosed
October, 2017	Codman Neurosurgery	Neurosurgery	Integra LifeSciences	1.0
March, 2018	Lifescan	Blood glucose testing	Platinum Equity	2.1

*Unit shut down; J&J partnered with Medtronic to continue patients' therapy

Sources: EvaluateMedTech & EvaluatePharma.

Siemens Healthineers sets a record

March 16, 2018

Having curbed the size of its IPO at the planning stage, Siemens Healthineers had to take a further haircut – or perhaps more of a trim – to get the offering away this morning. The price of €28 ($34.51) per share was just marginally below the midpoint of the preannounced range, allowing the German group to raise €4.2bn ($5.2bn) and valuing Healthineers at around €28bn. Though the deal has nearly halved in size from the initial figure bandied around – €10bn – it is still comfortably the largest healthcare IPO in history. Trading actually opened at €29.10, and had reached €29.80 at noon CET. Moving away from its parent could allow Healthineers to cut its overheads by €240m in the medium term, according to Barclays analysts; sadly the group seems to have missed a neat opportunity to change that ridiculous name.

Healthcare IPOs worth more than $1bn

Date	Company	Amount raised ($bn)	Offering price	Stock exchange
March 16, 2018	Siemens Healthineers	5.2	€28.00	Frankfurt Stock Exchange
December 15, 2010	Otsuka Holdings	2.4	¥2100	Tokyo Stock Exchange
October 26, 2016	Convatec	1.9	£2.25	London Stock Exchange
December 23, 2014	Indivior	1.4	£2.00	London Stock Exchange
July 31, 2014	Catalent Pharma Solutions	1.0	$20.50	NYSE

Source: EvaluateMedTech & EvaluatePharma.

Et tu, Vernalis? UK biotech succumbs to the ides of March

March 15, 2018

Comparisons to the fall of a Roman emperor are stretched, but confirmation that time is up for Vernalis is a major moment for UK biotech. The company was forged from successive mergers of mostly British drug developers over the past 18 years, and has survived brushes with death before: it has avoided bankruptcy at least once, entered and exited the US twice, and raised many hundreds of millions from investors to fund various corporate strategies. Its latest pivot looks to have finally done for it, however – a decision to enter the US cough and cold market with a narcotic-based product portfolio at the exact time when attitudes towards opiates were hardening was fatally mistimed. The business is up for sale and US operations are being wound down, with chief exec Ian Garland pledging to leave when the process has ended. With the company's enterprise value already half its £44m ($61m) cash balance the UK life sciences sector must brace itself for an ignominious end to one of the country's most famous names. Its end also spells yet another catastrophe for the well-known fund manager Neil Woodford – he was a vocal supporter of Mr Garland's strategy, and his funds own around 30% of Vernalis's stock.

The rise and fall of Vernalis

2000	Vanguard Medica and Cerebrus merge to form Vernalis and focus on CNS drug development
2003	British Biotech, Ribotargets and Vernalis complete a three way merger
2004	Vernalis reaquires North American rights to frovatriptan
2005	Vernalis buys Canada's Cita Neuropharmaceuticals for $30m, for access to neuropathic pain and Parkinson's disease candidates
2005	Vernalis buys Ionix Pharmaceuticals, a private UK biotech, for $13m, for a post-operative pain candidate
2007	FDA refuses to grant migraine drug Frova expanded approval in migraine prevention, shares crash 90%.
2008	Vernalis sells US operations and brings in new CEO, Ian Garland
2012	Vernalis raises £66m in equity placing and pivots to cough/cold market via Tris Pharma deal
2014	Vernalis re-opens a US office to sell cough and cold products
2015	Vernalis and Tris win US approval for Tuzistra XR
2016	Vernalis raises £44m in placing to fund US expansion
2017	Two follow-on cough/cold products get CRLs from the FDA
2018	After Tuzistra XR demand fails to meet expectations, company is put up for sale

Right to try applies to legislation too

March 14, 2018

An attempt to pass national "right-to-try" legislation in the US House of Representatives fell short yesterday, failing to draw the two-thirds vote necessary for passage under the fast-track procedure being used by the Republican leadership. With 38 states having already enacted right-to-try measures, however, the national effort might serve as a largely symbolic gesture. Nevertheless, the 259-140 US House vote suggests that the legislation has strong support and could pass with a simple majority under normal pathways that require committee hearings. Using these pathways, though, could lead to passage of the bill taking months and likely becoming part of a bigger healthcare package. Right-to-try legislation, which is designed to permit terminally ill patients to take investigational drugs without having to enrol into clinical trials, got a boost when President Donald Trump expressed support for it in his State of the Union address in January.

Subpoena adds to Myriad's hereditary test pressures

March 14, 2018

In 2011 Labcorp, its competitor Quest Diagnostics and six other diagnostics companies were found to have overcharged California's Medicaid programme; Labcorp had to pay $50m and Quest $241m to settle the case. So when Myriad Genetics quietly revealed in a Form 8-K filed late on Monday that it had received a subpoena by the US Department of Health and Human Services related to "possible false or otherwise improper claims" under Medicare and Medicaid, its shareholders reacted with horror. The subpoena requests documents relating to Myriad's core technology, hereditary cancer tests; according to William Blair analysts, doctors typically order the BRACAnalysis breast and ovarian cancer test and myRisk, which tests for eight cancers, for Medicare patients. Sales of Myriad's hereditary cancer tests are forecast to decline, from $512m in 2017 to $483m in 2022, according to *EvaluateMedTech*'s sellside consensus, and the company has been trying to diversify away from this technology. The possibility of a multimillion-dollar settlement only adds to the pressure Myriad is under, and so does yesterday's 12% share price fall.

Myriad Genetics' hereditary cancer tests

	WW sales ($m)		
Segment	2017	2022	CAGR
BRACAnalysis	49	21	-16%
BRCAnalysis CDx	13	11	-3%
Colaris & Colaris AP	8	3	-17%
MyRISK	442	449	0%
Hereditary cancer testing - total	*512*	*483*	*-1%*
MedTech sales	*722*	*863*	*4%*
Total company revenues	*770*	*920*	*4%*

Source: EvaluateMedTech

Teva cull unlikely to have claimed its last victim

March 13, 2018

The good news for Sosei is that Teva's canning of a deal with its UK subsidiary Heptares is unlikely to reflect doubts about the early-stage oral antimigraine assets in question. Rather, it looks like yet another effort to shore up the Israeli company's precarious financial position and focus on paying down debt. Teva's chief executive, Kåre Schultz, recently boasted of having culled 25 speciality R&D projects, saying: "Teva has been

very successful on taking good ideas within neurology and CNS into its pipeline from other research organisations ... whereas it has not been our strength to do the basic research." This will be little solace to investors in the remaining biotech companies with which Teva still has deals in place, and many might well wonder for how long the Israeli group will continue with such companies as Erytech, whose Graspa recently failed in AML, or Galena, now that this struggling group has been taken over by Sellas. At the JP Morgan healthcare conference Mr Schultz said Teva was focusing on key assets only, and the Sosei setback shows that even its core area of neurology is not safe.

The fate of selected Teva deals

Project	Deal year	Deal source	Current status
Bendeka (bendamustine)	2015	Eagle Pharmaceuticals	Marketed
Belviq	2015	Arena Pharmaceuticals	Marketed
Veregen	2010	Medigene	Marketed
Sprix (ketorolac)	2015	Egalet	Filed
Fasinumab	2016	Regeneron Pharmaceuticals	Phase III
NeuVax (nelipepimut-s)	2012	Galena (Sellas Life Sciences)	Phase III
Graspa ((L)-asparaginase)	2011	Erytech Pharma	Phase III
Metadoxine XR	2011	Alcobra	Phase III
Several, incl HTL0022562	2015	Heptares (Sosei)	Teva returned rights to Sosei in Mar 2018
DNA damage response project	2013	Cancer Research Technology	Teva returned portfolio in May 2015 to focus on market-ready assets
Adasuve (loxapine)	2013	Alexza Pharmaceuticals	Alexza reacquired rights in Feb 2016
Funapide Topical	2012	Xenon Pharmaceuticals	Deal terminated in Mar 2018
Sitavig (acyclovir)	2012	Onxeo	Teva seems to have abandoned this deal
Hepatitis C research programme	2012	Cocrystal Pharma	Abandoned
INN-202 (larazotide)	2011 (via Cephalon)	Alba Therapeutics	Deal terminated in Feb 2014
OpRegen	2010	Biotime	Unexercised option to Teva expired in Feb 2015
Several, incl MPC-150-IM	2010 (via Cephalon)	Mesoblast	Teva returned rights to Mesoblast in Feb 2017

Source: EvaluatePharma.

Astra as good as confirms that Mystic has failed

March 12, 2018

Investors can take today's six-month delay to final readout of Astrazeneca's Mystic trial as further confirmation that Imfinzi is a bust in first-line metastatic lung cancer. Still, given Astra's success in getting Imfinzi approved for earlier first-line use – in stage III, non-metastatic disease, based on the Pacific study – Mystic is largely irrelevant; this likely explains why Astra's stock did not react to this morning's revelation that the trial would now read out in the second rather than the first half of this year. A delay to an event-driven study like Mystic results from subjects across the trial living longer than expected, which in Mystic's case is likely due to progressing patients crossing over to other treatments, including rival anti-PD-(L)1 agents, and wiping out a relative benefit. Mystic had already failed to show a progression-free survival benefit at its first readout last year. The first-line NSCLC market now looks like being split between Keytruda and Tecentriq in the stage IV setting, with Imfinzi having stage III disease to itself.

The new timeline for Astra's Mystic

Study arm	Primary endpoint	PD-L1 expression*	Note
Not disclosed	Interim OS	Not disclosed	Now seem unlikely to be disclosed
H2 2018 events			
Imfinzi + tremelimumab, >25% PD-L1	OS	>25%	Stratification level; first hierarchical analysis
Imfinzi + tremelimumab, <25% PD-L1	OS	>5%	Capable of showing significance if >25% level is positive
Imfinzi + tremelimumab, <25% PD-L1	OS	>1%	Capable of showing significance if >5% level is positive
Imfinzi + tremelimumab, <25% PD-L1	OS	All-comers	Capable of showing significance if >1% level is positive
Imfinzi monotherapy, >25%**	OS	>25%	Design specifies "PD-L1 expressing tumours" only

*Note: *not disclosed formally; **for Imfinzi monotherapy PFS is a secondary endpoint only.*

First-line lung cancer PD-(L)1 players

Project	Company	Setting	Status
Keytruda + chemo	Merck & Co	Metastatic/stage IV, non-squamous	Accelerated approval, confirmatory Keynote-189 succeeded
Imfinzi	Astrazeneca	Stage III, non-metastatic	Approved on Pacific trial
Tecentriq + chemo + Avastin	Roche	Metastatic/stage IV, non-squamous	Impower-150 succeeded
Opdivo + Yervoy	Bristol-Myers Squibb	Metastatic/stage IV	Checkmate-227 benefit claimed in TMB-high subgroup
Imfinzi + tremelimumab	Astrazeneca	Metastatic/stage IV	Mystic trial failed on PFS; OS data due H2 2018
Bavencio	Pfizer/Merck KGaA	Metastatic/stage IV, PD-L1+ve	Data mid-2019; 2nd-line study failed to extend OS

Acufocus sells its Kamra

March 12, 2018

It took Acufocus four years from foundation to get its corneal implant Kamra CE marked and a further 10 to gain US approval. The company has now decided not to enjoy the fruit of its labours, and has sold the device to Sightlife Surgical, a Seattle-based group that processes and sells corneal transplant tissue. The sum for which the device – the first such implant to be approved by the FDA for the surgical correction of presbyopia, and the leader of the market, according to Acufocus – changed hands has not been disclosed. Acufocus says the divestment frees it up to concentrate on development and US approval of its IC-8 intraocular lens. The deal is likely to come as a disappointment for Acufocus's venture investors, who have ponied up the best part of $200m over the past 16 years and were doubtless hoping for an exit in the form of an acquisition ever since Kamra reached the US in 2015. That those investors include Medtronic and Bausch & Lomb only makes the lack of a trade sale all the more disappointing.

Acufocus's venture funding

Date	Round	Investment ($m)	Investors
September 9, 2016	Series H	66.0	KKR & Co
September 3, 2014	Series G	21.0	Accuitive Medical Ventures, Carlyle Venture Partners, HealthCare Royalty Partners, Medtronic, SV Life Sciences, Versant Ventures
November 29, 2011	Series F	65.0	Cowen Healthcare Royalty Partner, Accuitive Medical Ventures, Bausch & Lomb, Carlyle Venture Partners, Medtronic, SV Life Sciences, Versant Ventures
December 23, 2008	Series E	6.0	Undisclosed
June 16, 2007	Series D	18.0	Undisclosed
June 28, 2004	Series B	1.0	Undisclosed
March 9, 2004	Series B	0.2	Undisclosed
June 17, 2003	Series B	0.0	Undisclosed
November 6, 2002	Series B	9.0	Undisclosed
Total		**186.2**	

Source: EvaluateMedTech.

Glaxo gets another Advair reprieve

March 12, 2018

Glaxosmithkline's worst-case scenario – that substitutable generic versions of Advair would be launched in the US by mid-2018 – now appears even less likely after another knockback for Hikma and Vectura. The FDA's decision to uphold a previous complete response letter leaves Mylan's contender as the only copycat that could realistically mount a challenge this year – Mylan expects FDA action on a response to its own complete response letter in June. Glaxo previously said that, should a substitutable Advair generic be launched by mid-2018, US sales from its top product would more than halve to £750m ($1bn). Meanwhile, even with no substitutable generic this year, US Advair sales would still drop 20-25%, the company predicted, and this now looks like the most likely scenario. Hikma and Vectura are now out of the running for at least a year – the FDA has requested a new clinical study, which Hikma plans to start in the coming weeks, and submit to the agency "as early as possible in 2019". Hikma's stock was down 3% this morning, while Vectura fell 5%.

US generic versions of Advair

Company	Status	Note
Teva	Airduo Respiclick approved	Not substitutable
Mylan	Complete response letter Mar 2017	FDA action on Mylan's response expected Jun 2018
Sandoz (Novartis)	Complete response letter Feb 2018	No reasons disclosed
Hikma/Vectura	Mar 2018: FDA upholds previous rejection	Hikma plans to submit response with new clinical data in 2019

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