Evaluate Vantage

April 21, 2017

Snippet roundup: Tesaro's Parp pricing stumble and Asco sneak peek

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

This week, April 17 to 21, 2017, we had thoughts on the following: Atara touts T-cell promise in multiple sclerosis; Tesaro stumbles on Zejula pricing strategy; Verily plays long game with 10,000-person trial; biotech investors get an accidental sneak preview of Asco 2017; J&J's Q1 heaps pressure on Actelion deal; Circassia throws in the towel over allergy franchise; Medtronic's top line receives Cardinal's blessing; Oncomed makes early-stage shift after latest setbacks.

These snippets were previously published daily via twitter.

Atara touts T-cell promise in multiple sclerosis

April 21, 2017

Atara highlighting an investigator-led trial of its Epstein-Barr virus (EBV)-targeting T cells in multiple sclerosis provides the first solid evidence that the company might develop its flagship technology outside cancer indications. The results, to be presented at the American Academy of Neurology meeting in Boston next week, are from just six patients in a 10-patient phase I trial of the autologous therapy, but hint at efficacy in three of the participants. Next, Atara plans a phase I study of an allogeneic version known as ATA188. EBV has been linked to the development of multiple sclerosis, and in genetically susceptible people is thought to trigger an autoimmune response that leads to the destruction of myelin on nerve cells. Therefore, eliminating EBV-positive B-cells and plasma cells could improve disease symptoms, Atara believes, although this – and safety – will need to be proved in a larger patient population. The company is also trialling EBV-targeting T cells in lymphoma and lymphoproliferative disorders, where the project is known as ATA129, and plans to start phase III trials in the second half of 2017.

Atara's pipeline

Project	Status	Indication(s)	Trial ID(s)
EBV-CTL/ATA129	Phase II	Lymphomas & lymphoproliferative disorders; nasopharyngeal carcinoma (combo with Keytruda)	NCT01498484; NCT00002663; NCT02822495
CMV-CTL/ATA230	Phase II	Cytomegalovirus infection	NCT02136797; NCT01646645
EBV-CTL/ATA188	Phase I	Multiple sclerosis	
WT1-CTL/ATA520	Phase I	Leukaemia, multiple myeloma	NCT00620633; NCT01758328
STM 434	Phase I	Ovarian cancer, solid tumours	NCT02262455

Source: Company website

Tesaro stumbles on Zejula pricing strategy

April 20, 2017

Tesaro's pricing strategy for Zejula yesterday brought it attention for all the wrong reasons, and sent its share price down 11% today. While some will argue that it was a smart move to price the most commonly used dose of Zejula lower than Clovis's rival Parp inhibitor Rubraca, this has also highlighted the fact that many patients need to titrate down from the approved 300mg to avoid side effects. Relative pricing will become more important if the other Parp inhibitors begin to get approval in earlier settings and new indications; Rubraca is due results from the Ariel3 study in first-line maintenance in mid-2017. Perhaps Tesaro has its eye on the long game. It is working on combinations of Zejula, including with Merck & Co's PD-1 inhibitor Keytruda in triple-negative breast and ovarian cancers. Some had expected data from the Topacio trial at Asco, but these were not in the list of abstracts announced today. Either way, the battle for dominance in the Parp inhibitor space looks set to continue, and could ultimately affect whether a buyer for Tesaro emerges.

Zejula vs Rubraca: selected upcoming read outs

Project	Study	Setting	ID	Data due
Rubraca	Ariel3	First-line maintenance in ovarian, primary peritoneal or fallopian tube cancers	NCT01968213	Mar-17
Zejula	Quadra	Fourth-line ovarian cancer	NCT02354586	Oct-17
	Topacio	Combo with Keytruda in triple-negative breast or ovarian cancer	NCT02657889	Mar-18
	Avanova	Combo with Avastin in platinum-sensitive epithelial ovarian cancer	NCT02354131	Nov-18

Verily plays long game with 10,000-person trial

April 20, 2017

Verily, Google's life sciences arm, is nothing if not ambitious. The company has launched a study of 10,000 healthy participants, Project Baseline, that it hopes could identify factors that predict diseases and potentially find ways to prevent them. However, the initiative, which will take several years to enrol and is set to follow subjects for four years, is a long way from reporting results. And there are also concerns about what will happen to the data once collected, with the possibility that it could be sold to pharma companies or insurance companies, for example. Participants will undergo various tests including having their genomes sequenced, will get an annual health check, and will have their heart rate and activity levels measured by a smart watch, and sleeping patterns monitored via a sensor placed under their mattress. With the project estimated to cost around $100m, it is a good job that Verily is well funded – in January it sold a minority stake to Singapore's National Wealth Fund, Temasek, for $800m. But it still must be hoping to recoup its outlay somehow.

Biotech investors get an accidental sneak preview of Asco 2017

April 20, 2017

Embargo breaches are common in the real-time publishing environment, but it is still rare for a medical conference to break its own rules. Yet this is what appears to have happened yesterday when Asco briefly put up on its website all the abstract titles for its 2017 meeting. These are formally to be unveiled this afternoon, so what was revealed is subject to change. But the sneak preview suggests that among the late-breakers Roche's keenly awaited Aphinity trial will play a starring role. Just like AACR, Asco promises to be an important meeting for IDO inhibition and for various novel immuno-oncology combinations. The accidental unveiling prompted Abbvie to rush out a statement yesterday about the failure of veliparib, and the positive Olympiad trial of its rival Parp inhibitor, Astrazeneca's Lynparza, features in a late-breaker. There are also numerous CAR-T abstracts, the most prominent of which details Bluebird's highly promising bb2121. While the Transcend trial of Juno's JCAR017 will invite comparisons with Kite's Zuma-1 data of KTE-C19, Novartis's own lymphoma study of CTL019, Juliet, does not appear to have made it into Asco.

Selected provisional Asco 2017 abstracts

Project(s)	Companies	Detail	Asco abstract
Perjeta + Herceptin	Roche (relevant for Puma)	Aphinity study, late-breaker	LBA500
bb2121	Bluebird Bio (relevant for Kite, Novartis, Juno etc)	Anti-BCMA CAR, late-breaker	LBA3001
Larotrectinib	Loxo (relevant for Ignyta)	Anti-NTRK, late-breaker	LBA2501
Opdivo + Yervoy	Bristol-Myers Squibb	Mesothelioma, late-breaker	LBA8507
Lynparza	Astrazeneca (relevant for Clovis, Tesaro etc)	Olympiad study, late-breaker	LBA4
Veliparib	Abbvie (relevant for Tesaro, Clovis etc)	Failure in TNBC	520
BGB-A317 + BGB-290	Beigene	PARP + PD-1	3013
Epacadostat + Keytruda	Incyte (relevant for Newlink)	Keynote-037, IDO + PL-1	9014 & others
GDC-0919 + Tecentriq	Newlink, Roche (relevant for Incyte)	IDO + PD-L1	105
BMS-986156	Bristol-Myers Squibb	GITR agonist + Opdivo	104
BMS-986016	Bristol-Myers Squibb	Anti-Lag3 + Opdivo	9520
CPI-444	Corvus (relevant for Novartis & Astrazeneca)	A2a antagonist + PD-1/PD-L1	3004
CB-1158	Incyte/Calithera	Arginase inhibitor + PD-1	3005
JTX-2011	Jounce	Anti-Icos + Opdivo	3033
Anti-CEA bispecific	Roche	Anti-CEA + Tecentriq	3002
MSB0011359C	Merck KGaA	Anti-PD-L1/TGFb fusion protein	3006
Varilumab	Celldex	Anti-CD27 + Opdivo	3007
JCAR017	Juno (relevant for Kite & Novartis)	Transcend (DLBCL) study	7513
Anti-Her2 CAR-T	Undisclosed (relevant for Leucid Bio)	Sarcoma study after lymphodepletion	10508
Anti-GPC3 CAR	Undisclosed Chinese company		3049
Anti-CD133 CAR	Chinese PLA General Hospital		3042
Cabiralizumab	Bristol-Myers Squibb/Five Prime	Anti-CSF1R MAb	11078
LY3022855	Lilly	Anti-CSF1R MAb	2523
REGN2810	Regeneron/Sanofi	Anti-PD-L1	9503
ABT-414	Abbvie	Anti-EGFR ADC + Temodar	2003

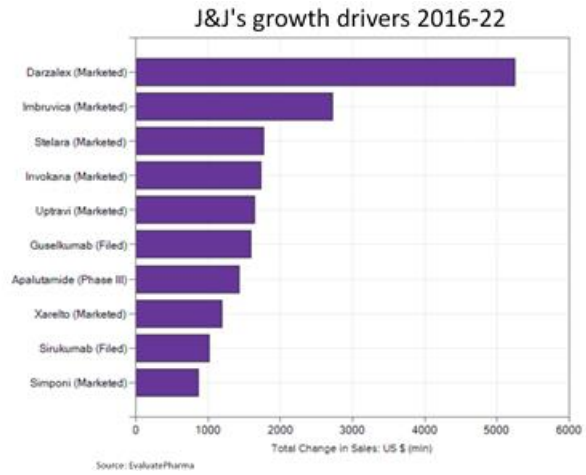
Note: revealed by Asco accidentally yesterday, so subject to change.

J&J's Q1 heaps pressure on Actelion deal

April 19, 2017

The good times are over for Johnson & Johnson's pharma division. With sales of Xarelto down 10% in the first quarter and its diabetes therapy Invokana also struggling with US pricing pressure, investors sent its stock down 3% yesterday on concerns about the next phase of growth. Fortunately J&J's purchase of Actelion, which is expected to close in June, shows that the group was already looking to the future before these disappointing results. But with a $30bn price tag J&J will need Actelion's top products, Uptravi and Opsumit, to outstrip current consensus forecasts if this investment is to pay off. Uptravi is set to become J&J's fifth-biggest growth driver, according to *EvaluatePharma* – with the caveat that this is based on forecasts by analysts covering Actelion before the deal was announced. As for its other bright hopes, if these are to live up to expectations Darzalex must break into front-line multiple myeloma and Invokana needs a hit in the Canvas cardiovascular outcomes study, due to report at the ADA meeting in June. With the impact of Remicade biosimilars yet to hit

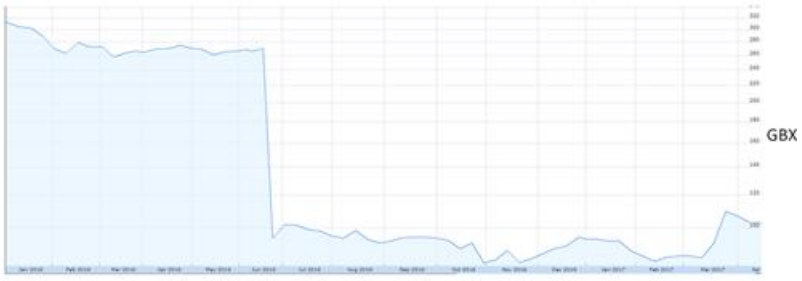
in the US, J&J still has a job to do to turn things around – but, unlike some, at least it has made a decisive move.



Circassia throws in the towel over allergy franchise

April 18, 2017

With a wave of a sneeze-filled hanky Circassia is saying goodbye to all its ambitions in allergy after today's phase II flop in house dust mite allergy. The news follows the catastrophic failure last year of its cat allergy product, which wiped out two thirds of its market value. Like its feline friend, the house dust mite treatment failed to show any benefits above placebo, and it came after an earlier bomb in ragweed. One mark of the exceptionally low expectations around the tail end of the allergy franchise was the 3% share price fall, leaving the stock more than 60% below its float price. Now a long way from its IPO promises, the focus for the British biotech is respiratory. The group has an asthma diagnosis business, and more recently announced a strategic collaboration with Astrazeneca to develop and commercialise two COPD products. Few forecasts are available for the respiratory franchise, but investors will hope that Circassia can make a better go of things in this very crowded and increasingly genericised market than it did in allergy.

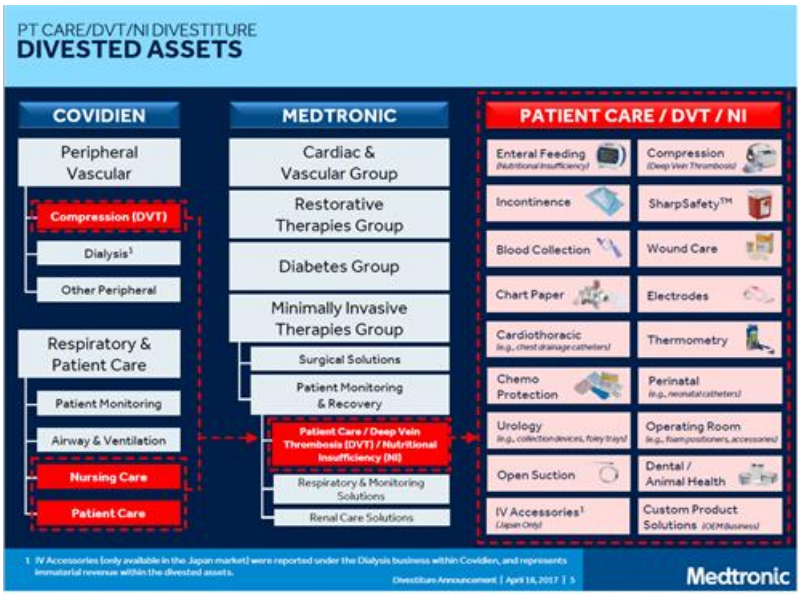


Circassia share price

Medtronic's top line receives Cardinal's blessing

April 18, 2017

Medtronic is to rid itself of the medical supplies business it obtained from Covidien in a $6.1bn cash transaction. The buyer is, as expected, Cardinal Health, which is active in the less innovative, more commoditised end of the medtech market, and therefore makes a good fit. Cardinal makes products such as wound dressings, gloves and surgical apparel, and the devices Medtronic is selling includes products for deep vein thrombosis and malnutrition, such as enteral feeding technologies, catheters, electrodes and compression products for deep vein thrombosis. Medtronic says the assets brought it $2.4bn in revenue over the last four reported quarters, but that this had declined at a rate in "the low single digits". Medtronic intends to use the proceeds for a $1bn stock buyback and to pay down debt, and says its revenue growth will see an improvement of 0.5% when the deal is closed; its shares are up 2% pre-market. Cardinal's stock is down 11%, perhaps because its medical division segment has been performing well, with second quarter operating income of $159m, a 50% increase year on year, and shareholders fear the Medtronic products will slow it down.



Oncomed makes early-stage shift after latest setbacks

April 18, 2017

Oncomed is looking ever more reliant on its early-stage pipeline after two more setbacks. Its second-most advanced candidate, tarextumab, has failed in a phase II study in small-cell lung cancer, while high rates of diarrhoea seen with bronticuzumab have effectively spelled the end of that project. True, Oncomed does still have some hope to cling to with demcizumab despite last week's pancreatic cancer setback – the Denali trial in NSCLC is due to yield data soon, and there should also be interim results this year in combination with Merck & Co's Keytruda in solid tumours. However, with $157m in the bank – enough to last until the third quarter of 2018 – the group will need something to go right soon or it will have a hard time raising cash. With most of its remaining projects still having a long development path ahead, it was little wonder that the group's shares, already down 36% on last week's news, fell another 17% yesterday.

Oncomed's pipeline

Project	Description	Notes	Trial ID
Demcizumab	Anti-DLL4 MAb	Phase II Yosemite trial in pancreatic cancer failed	NCT02289898
		Phase II Denali trial in NSCLC completes May '17	NCT02259582
		Interim data from phase I combo study with Keytruda due H1 '17	NCT02722954
Tarextumab	Anti-Notch2/3 MAb	Phase II Pinnacle trial in SCLC failed	NCT01859741
Vantictumab	Wnt inhibitor	Bayer returned rights	-
Ipafricept	Wnt inhibitor	Bayer returned rights	-
Bronticuzumab	Anti-Notch1 MAb	Phase I trial in 3L CRC discontinued on adverse events	NCT03031691
OMP-131R10	Anti-RSPO3	Phase I trial in solid tumours & metastatic CRC ongoing	NCT02482441
Navicixizumab	Anti-DLL4/VEGF bispecific	Phase I trials in metastatic CRC, ovarian cancer & solid tumours ongoing	NCT03035253 NCT03030287 NCT02298387
-	Anti-TIGIT	Phase I trial to start "soon"	-
-	GITRL-Fc trimer	IND filing due H1 '17	-

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