Evaluate Vantage

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Snippet roundup: Tecentriq gets lung cancer win, Enbrel biosimilar patent dance intensifies

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

This week, 29 August-2 September 2016, we had thoughts on the following: Roche Oak success with Tecentriq could see Keytruda migrate to first line only; patent dance spoils the party for Sandoz's Erelzi; Clovis milestone deferral shows keenness to cut costs; Mitsubishi Tanabe tries a radical approach to ALS in the US; partial hit doesn't alter pacritinib's poor standing; Vectura's Flutiform fails to grow beyond asthma; and Moderna breaks its own funding record.

These snippets were previously published daily via twitter.

Roche Oak success with Tecentriq could see Keytruda migrate to first line only

1 September 2016

Roche's Tecentriq has beaten chemotherapy in second-line non-small lung cancer (NSCLC) by showing a statistically significant improvement in overall survival in the Oak trial. Should regulators add second-line disease to the label, it would make Tecentriq the third antibody blocking the programmed death-1 pathway to be approved in this setting. The practical effect could be to squeeze Merck & Co's competitor Keytruda out of the second-line setting – that is, if the data can be reviewed by the US FDA before an NSCLC decision deadline of October 19. This is because Tecentriq showed a significant survival benefit both in patients expressing PD-L1 and in those who do not – although whether the benefit in all-comers was driven by the high PD-L1 expressers will only become clearer with full data. The third marketed PD-1/L1 antibody, Bristol-Myers Squibb's Opdivo, has been approved for all second-line NSCLC patients, while Keytruda has approval only in patients who have tested positive for PD-L1 expression. Merck has had some good fortune, however – so far Keytruda is the only one to show positive data in front-line use, while Opdivo has stumbled.

PD-1/L1 Market

Product	Company	WW sales 2022 ($m)	Phase
Opdivo	Bristol-Myers Squibb/ Ono Pharmaceutical	14,634	Marketed
Keytruda	Merck & Co	5,959	Marketed
Tecentriq	Roche	5,331	Marketed
durvalumab	AstraZeneca/Celgene	1,911	Phase III
avelumab	Pfizer	556	Phase III
Total		**28,432**	

Patent dance spoils the party for Sandoz's Erelzi

31 August 2016

When it comes to biosimilar approvals in the US victory takes on a very different meaning. Yesterday, Novartis's Sandoz unit gained marketing authorisation for Erelzi, its biosimilar version of Enbrel, a drug that last year clocked up sales of $5.36bn. But with no sign of an end to the patent dance Erelzi will join Pfizer's Inflectra as an approved, but as yet unlaunched US biosimilar, unable to chip off any of the chunky sales of the reference product. Sandoz has vowed to bring Erelzi to market as soon as possible, but it still has to give the originator, Amgen, 180 days' notice of its intention to launch. To complicate matters further, earlier this year Amgen secured an injunction barring Sandoz from launching until five patents on the drug, extending to 2029, expire. A trial date is set for April 2018, and with Sandoz unlikely to take the brave or foolhardy step of launching at risk it will be awhile before any celebrations can start.

Clovis milestone deferral shows keenness to cut costs

31 August 2016

When a biotech company has almost $380m of net cash it seems unusual for it to renegotiate a big pharma licensing deal to defer the payment of a mere $21m milestone, but this is precisely what Clovis Oncology has done. The clue lies in the group's cash burn – an astonishing $300m or so in the past four quarters – which is largely due to a sales force it had recruited but which is now sitting idle after the severe setback to its lead project, rociletinib. This likely necessitates the elimination of any expenditure that is not strictly necessary as Clovis's attention switches to the Parp inhibitor rucaparib, whose US filing was recently accepted. Rucaparib had been licensed from Pfizer in 2011, and Clovis revealed yesterday that a fee, previously put at $21.2m to account for US filing and approval, would be deferred by 18 months in return for increased payments relating to other milestones.

Mitsubishi Tanabe tries radical approach to Lou Gehrig's disease in the US

31 August 2016

Two years after gaining approval for amyotrophic lateral sclerosis in its manufacturer's home market, Mitsubishi Tanabe Pharma's edaravone could hit the US. The FDA has accepted a filing for edaravone in the neurological disorder, with a decision on the application expected by June 16, 2017. The free radical scavenger, known as Radicut in Japan, will be sold under the name Radicava in the US by the newly formed MT Pharma America, should it gain approval. With orphan designation and competition that consists solely of riluzole, an expensive generic with limited effect, Radicava could do well. Moreover, the late-stage pipeline in ALS is thin, with the only other filed drug being YooYoung Pharmaceutical's YYB-103, awaiting approval in South Korea.

Late-stage ALS pipeline

Phase	Product	Company
Filed (South Korea)	YYB-103	YooYoung Pharmaceutical
Phase III	Tirasemtiv	Cytokinetics
Phase III	Masican	AB Science
Phase III	Amyotrophic Lateral Sclerosis Research Program	ICON
Phase III	Arimoclomol Citrate	Orphazyme
Phase III	HYNR-CS	Corestem

Partial hit doesn't alter pacritinib's poor standing

30 August 2016

CTI Biopharma's ailing Jak2/FLT3 inhibitor pacritinib was already a highly doubtful competitor to Incyte's marketed Jakafi, and yesterday's data from the Persist-2 trial are unlikely to change this view. True, the trial in 311 high-risk myelofibrosis patients met one co-primary endpoint – spleen volume reduction versus best available therapy including Jakafi – but it missed the other, 50% reduction in total symptom score. CTI stock rallied 15% yesterday, but this was from an extremely low base, and the group is capitalised at little over $100m. It still faces much bigger problems than inconclusive clinical data, such as the US clinical hold under which pacritinib was placed in February after deaths and other adverse events were seen in the Persist-1 trial. CTI completed a rolling US filing for pacritinib in January, but there is still no sign when the hold might be lifted.

Vectura's Flutiform fails to grow beyond asthma

30 August 2016

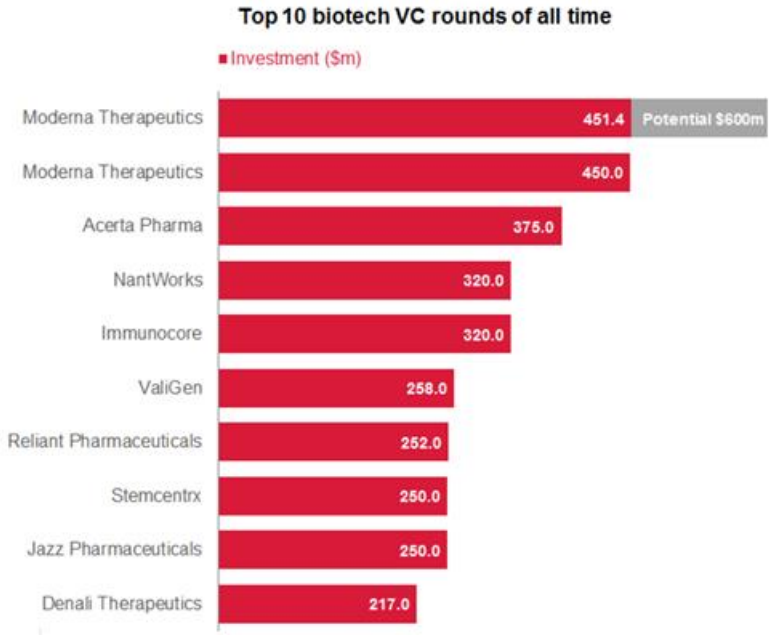
Expanding Vectura's beta-agonist/steroid combination Flutiform beyond asthma into COPD was always a long shot, but it would have been a big win had it worked. Today the base-case scenario played out, with Vectura's partner Mundipharma confirming that Flutiform had failed to reduce COPD exacerbations in a 1,767-patient trial versus beta-agonist monotherapy. Edison analysts had not considered COPD in their valuation of Flutiform, while Numis today wrote that off-label use was still likely but a COPD label was key to the drug reaching $500m in peak sales. Vectura was off 6% this morning, less than three months after it completed the acquisition of Flutiform through its £441m ($578m) takeover of Skyepharma.

Moderna breaks its own funding record

30 August 2016

If a US regulatory filing slipped out last week refers to a new financing round then the mRNA specialist Moderna Therapeutics looks to have broken its own record for a private fund raising. According to a Form D filed with the SEC the group has raised $451m of a planned $600m, beating the record-setting $450m series D

round it closed in May 2015. It also catapults Moderna well past $1bn in cumulative private cash raised; the $950m of venture capital the group had received to date was already a record, and in addition to this $240m had come from AstraZeneca up front under a 2013 deal. Perhaps the most incredible aspect of Moderna's financing success is that it only has two clinical trials under way, and nothing is known about them.



Moderna's reported clinical pipeline

Project	Target	Status	Trial ID
mRNA 1440	Undisclosed infectious disease	Phase I in EU	None found in EU Clinical Trials Register
mRNA 1851	Undisclosed infectious disease	Phase I in US	None found in Clinicaltrials.gov
AZD8601	VEGF-A	Application submitted to start phase I	–

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