Evaluate Vantage

August 04, 2016

Snippet roundup: Lilly pill slips, Mek inhibitors reach limit, Myriad buys

Edwin Elmhirst

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

This week, 8-12 August 2016, we had thoughts on the following: effective new emesis products must now prove their profitability; Lilly breast cancer pill moves down a gear; Pharming goes it alone in Americas too; Array and Astra fail to expand Mek inhibitor use beyond melanoma; Abbott's Alere buy on shaky ground; Adaptimmune's clinical setback spreads; MEI Pharma gets another chance with pracinostat; GE reiterates its interest in Check-Cap; Myriad moves to neurology with Assurex purchase.

These snippets were previously published daily via twitter.

Effective new emesis products must now prove their profitability

12 August 2016

The fact that the highly genericised anti-emesis space continues to tempt small drug developers is testament to the substantial need for more effective agents. Earlier this week Heron won approval in chemotherapy-induced sickness for Sustol – the US company describes it as the first sustained-release formulation of granisetron that can keep nausea and vomiting at bay for up to five days. Working in a different class is Acacia Pharma with Baremsis, which has re-purposed the D2/D3 (dopamine) antagonist amisulpride. The private UK player said today that the agent had met the primary endpoint of a pivotal trial in treating established post-operative nausea & vomiting; previous phase III data showed the drug to be effective at preventing nausea in this setting. Last year a large phase II study in the chemotherapy patients generated highly encouraging results. The challenge for these players and others, however, will be recouping development costs in an area of medicine used to paying generic prices.

Outlook for the branded anti-emesis space - sell-side consensus

Product	Pharma Class	Company	WW sales 2022e ($m)	Phase
Sustol (granisetron)	5-HT3 antagonist	Heron Therapeutics	427	Approved
Varubi (rolapitant)	(NK-1) antagonist	TESARO	404	Marketed
Syndros (dronabinol)	Cannabinoid	Insys Therapeutics	280	Approved
Emend (aprepitant)	(NK-1) antagonist	Merck & Co/Ono	281	Marketed
HTX-019 (aprepitant)	(NK-1) antagonist	Heron Therapeutics	86	Pre-filing (generics)
Aloxi (palonosetron)	5-HT3 antagonist	Otsuka Holdings	79	Marketed
Zhiruo (palonosetron)	5-HT3 antagonist	Sino Biopharmaceutical	65	Marketed

Lilly breast cancer pill moves down a gear

10 August 2016

Hopes that Lilly's breast cancer pill abemaciclib would make a sprint for the finish were dashed today with news that the Monarch 2 trial of would continue to the final analysis. Expectations were for an early stop for efficacy, like CDK4/6 class rivals Ibrance and LEE011 before it. This will rob Lilly of confirmatory data it intended to submit to the FDA to support accelerated approval of abemaciclib on the back of a phase II study, Monarch 1. Lilly says it is working with the FDA on a possible filing, although it is unclear whether this can happen before Monarch 2 reads out. Analysts at Bernstein reckon the project still has a reasonable chance of early approval, but are keeping to their conservative sales forecasts for now. Leerink analysts are more pessimistic, saying they no longer believe a filing this year is possible. The 1% fall in Lilly's share price suggests that investors are taking a similarly cautious stance.

CDK4/6 class rivals

Product	Company	Launch	2022e sales
Ibrance	Pfizer	2015	$5.5bn
Abemaciclib	Eli Lilly	2017?	$1.6bn
LEE011	Novartis	2017?	$991m

Pharming goes it alone in Americas too

9 August 2016

Pharming wants to get back rights to its hereditary angioedema drug Ruconest in North America and has offered partner Valeant $60m up front to do so. The sticking point might be raising the cash: Pharming only had €21.7m ($24.1m) available as of June, and the deal is subject to an $80-100m financing that will include debt and new equity. The company also plans to increase the size of its US sales force, which will cost it – although it hopes that, for starters, Valeant's existing 11-strong team will accept an offer to jump ship. Pharming is already set to take on responsibility for Ruconest in 21 European, African and Middle Eastern countries from another partner, Sobi. Succeeding alone in North America will be a big ask, particularly as Pharming will be going up against the likes of Shire.

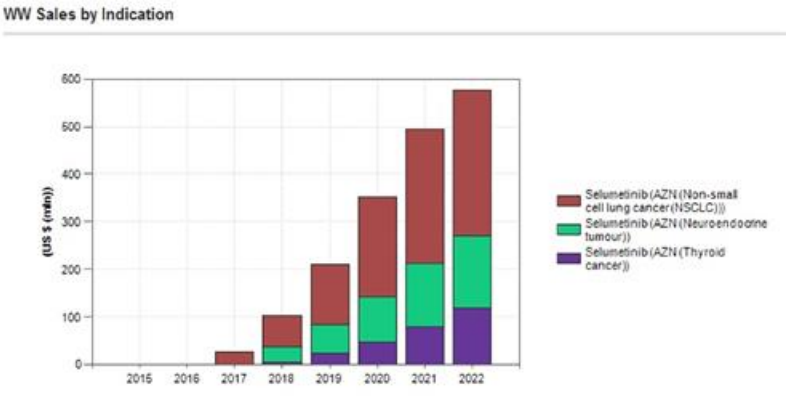
Top-five hereditary angioedema drugs in 2022

Product	Company	Status	2022e sales ($m)
Lanadelumab	Shire	Phase III	1043
Cinryze	Shire	Marketed	615
Firazyr	Shire	Marketed	315
Avoralstat	BioCryst Pharmaceuticals	Phase III	98
Kalbitor	Shire	Marketed	80

Array and Astra fail to expand Mek inhibitor use beyond melanoma

9 August 2016

It is remarkable how much value had been baked into Array/AstraZeneca's Mek inhibitor selumetinib in second-line lung cancer, a setting in which the project flunked a phase III study today. *EvaluatePharma*'s sales by indication suggested that over 50% of 2022 sales of $576m would come in lung cancer, and the rest in neuroendocrine tumours and thyroid cancer, despite the fact that the advent of immuno-therapy is causing a tectonic shift in the second-line NSCLC setting (*Growth of anti-PD1 therapy threatens traditional second line chemo in NSCLC, April 22, 2015*). Array stock fell 20% in the pre-market, before opening off 13%. Select-1 had recruited 510 patients with Kras-positive tumours. Array has another Mek inhibitor, binimetinib, awaiting approval for melanoma – an indication where several other similarly acting agents are already available. The odds of successfully expanding this class into lung cancer just widened considerably.



Abbott's Alere buy on shaky ground

9 August 2016

Abbott has already tried to back out of its $5.8bn purchase of Alere, and the relationship now looks even rockier after the diagnostics specialist submitted its delayed financials. Alere has restated its results for 2013, 2014 and the first three quarters of 2015 after finding "immaterial errors" caused by "material weaknesses" in how it recognised revenue and accounted for income taxes. Abbott, which in April offered Alere up to $50m to terminate the deal, is not impressed, saying the filing does not eliminate its concerns over Alere's business practices "given the litany of issues that have come to light since our agreement was announced". The latest development comes on top of a US Department of Justice investigation into Alere's sales practices in Africa, Asia and South America, and a subpoena seeking billing records for patient samples tested at its Texas pain

management lab. Alere plans to reports its first-quarter results by August 18, and second-quarter numbers “as soon as practicable”. It had better hope for no more nasty surprises.

Impact of revisions on Alere’s financial results

	Q1-3 2015	FY 2014	FY 2013
Previous net revenue	$1,839m	$2,589m	$2,616m
Revision adjustment	$1m	($13m)	($8m)
Revised net revenue	$1,840m	$2,575m	$2,609m
Previous GAAP EPS	$2.53	($0.71)	($1.15)
Revision adjustment	($0.14)	$0.05	($0.03)
Revised GAAP EPS	$2.39	($0.66)	($1.18)

Adaptimmune’s clinical setback spreads

8 August 2016

Adaptimmune did a good job of containing the fallout from last week’s US hold on its NY-ESO-targeting engineered T-cell receptor project in a yet to be initiated trial in myxoid round cell liposarcoma. The second time around the group might not be so lucky, having today revealed that a pivotal trial of the project in synovial sarcoma will not start until mid-2017, and that slow enrolment into lung cancer trials for this and a Mage-A10 TCR project has pushed expected data readouts for these into next year. Adaptimmune blames the US hold on switching from academic to commercial manufacturing, and intends to respond to the FDA shortly. Investors were less convinced, and the stock opened off 4% this morning.

Selected Adaptimmune studies

Project	Study detail	Trial ID	Note
NY-ESO1 TCR	Pivotal trial in synovial sarcoma	–	Start delayed until mid-2017
NY-ESO1 TCR	Study in myxoid round cell liposarcoma	–	On US clinical hold
NY-ESO1 TCR	10 advanced NSCLC pts	NCT02588612	Slow recruitment; readout delayed to 2017
Mage-A10 TCR	32 advanced NSCLC pts	NCT02592577	Slow recruitment; readout delayed to 2017

MEI Pharma gets another chance with pracinostat

8 August 2016

MEI Pharma’s licensing deal with Helsinn will allow it to progress its lead candidate pracinostat into phase III. The asset had looked destined for the scrap heap after failure in myelodysplastic syndrome over a year ago, so it is no wonder that the company’s stock climbed around 50% in premarket trading today, albeit from a low base. Helsinn, which wants to move beyond cancer supportive care products into oncology therapeutics, is taking a risk, but at only $20m up front it is obviously cautious. The deal is heavily backend-loaded, with the Swiss group on the hook for up to $444m in milestones if it does succeed. The companies will initially target acute myeloid leukaemia but plan to look at other indications including high-risk MDS – where they intend to define an optimal dosing regimen for pracinostat in combination with azacitidine, the same combo that failed in phase II (*MEI would be pushing its luck to plough on with pracinostat, March 24, 2015*).

GE reiterates its interest in Check-Cap

8 August 2016

Swallowable imaging technologies, once seen as pretty out-there, were validated to some degree when Covidien bought Given Imaging, developer of the PillCam, in 2013. Now GE Healthcare has signed a deal with Check-Cap, which, like Given, is developing an ingestible capsule for colorectal screening. GE is to help Check-Cap integrate X-ray source production and assembly into its X-ray Radar capsule, which is currently in a feasibility trial and will be filed for European approval early next year. GE has long been interested in the company. Before Check-Cap floated last April GE put up venture cash in 2012 and again in 2014, though the amounts it invested were undisclosed. The latest deal caused Check-Cap’s shares to rise 76% to $2.44, perhaps because shareholders took it as a sign that GE was marking the capsule maker for acquisition.

Myriad moves to neurology with Assurex purchase

8 August 2016

Mental illness has always been common but awareness initiatives mean it has never been more visible. This is surely part of the reason that the GeneSight DNA test developed by Assurex Health is “one of the fastest growing new diagnostic tests ever”, according to the chief executive of Myriad Genetics, which has just bought Assurex for $225m up front. The test is used to guide drug therapy for patients with disorders including depression, anxiety, bipolar disease and schizophrenia. Assurex has other diagnostics to guide the use of

painkillers, ADHD drugs and folic acid. The deal is an exit for the group's VC investors, but there are so many of them – 18 separate named backers plus more that remain undisclosed – that the $225m, plus a potential $185m in milestones, might not go very far.

Assurex Health's VC backers

Date	Round	Investment ($m)	Investor
21-Dec-15	Series D (second close)	15	Cincinnati Childrens Hospital Medical Center, Claremont Creek Ventures, Cross Creek Capital, Mayo Medical Ventures, Sequoia Capital
23-Dec-14	Series D	30	Allos Ventures, American Financial Group, Cincinnati Childrens Hospital Medical Center, CincyTech, Claremont Creek Ventures, Cross Creek Capital, Danmar Capital, Mayo Medical Ventures, Sequoia
21-May-14	Series C (second close)	7	Allos Ventures, Cincinnati Childrens Hospital Medical Center, CincyTech, Claremont Creek Ventures, Danmar Capital, Four Rivers Group, JVEN Capital, Mayo Medical Ventures, Sequoia Capital
30-May-12	Series C	12.5	Claremont Creek Ventures, Four Rivers Group, Sequoia Capital, Alafi Capital, Allos Ventures, Cincinnati Childrens Hospital Medical Center, CincyTech, JVEN Capital, Mayo Medical Ventures, YA Global
28-Mar-11	Series B	11	Claremont Creek Ventures, Sequoia Capital, Allos Ventures, CincyTech
11-Jan-11	Series A (second close)	8	Undisclosed
1-Mar-08	Series A	1	Queen City Angels, Blue Chip Venture Company, Cincinnati Childrens Hospital Medical Center,
-	Series Undisclosed	-	North Coast Angel Fund, Ohio Tech Angels
Total		84.5	

To contact the writers of this story email news@epvantage.com or follow @EPVantage on Twitter