Evaluate Vantage

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Snippet roundup: Opdivo's first-line lung combo delay and Colucid's Lilly windfall

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

This week, January 16-20, 2017, we had thoughts on the following: Keytruda continues its first-line lung cancer rout of Opdivo; Colucid gets payday thanks to Lilly; Pulmatrix is QIDPs in; Hutchison Chi-Med widens oncology assault; a bump in the road for Lilly's top pipeline asset.

These snippets were previously published daily via twitter.

Keytruda continues its first-line lung cancer rout of Opdivo

January 20, 2017

Investors' ears pricked up last week when Bristol-Myers Squibb told the JP Morgan conference not to expect data this year from Checkmate-568, its first-line lung cancer trial of Opdivo plus Yervoy. Yesterday the markets found out why when the group threw in the towel and abandoned an "accelerated regulatory pathway" for the combo in this setting – a plan the group was saying last week was still in place. Analysts had hoped that Checkmate-568 and 012, both uncontrolled trials, might have allowed for early filing after the failure of Checkmate-026 last year, but Bristol now seems to have resigned itself to awaiting readout from Checkmate-227, a phase III study that should yield progression-free survival data next year. Checkmate-568 had been significantly expanded, and the worry now is that its results, which Bristol could already have in house, are weak. This represents another coup for Merck & Co's rival, Keytruda, which could still stumble if the US FDA rejects its audacious first-line filing as a chemo combo. For now the markets are pretty convinced – Merck today opened up 4% while Bristol crashed 10%.

Selected immuno-oncology trials in 1st-line NSCLC

Study	Company	Notes	Trial ID
Impower-150	Roche	Tecentriq + chemo combo; PFS data in 2017	NCT02366143
Keynote-189	Merck & Co	To serve as confirmatory trial for ORR benefit seen in Keynote-021 Keytruda + chemo combo arm; PFS data H2 2017	NCT02578680
Mystic	Astrazeneca	Now to look at OS & PFS in PD-L1-high & all-comer patients given durvalumab + tremelimumab combo, and PFS & OS in PD-L1-high patients on durvalumab monotherapy; PFS data H2 2017, OS in 2018 "at the latest"; undisclosed interim OS analyses	NCT02453282
Pearl	Astrazeneca	New study with durvalumab monotherapy in Asia, measuring PFS & OS in PD-L1-high patients	NCT03003962
Checkmate-568	Bristol-Myers Squibb	Uncontrolled, expanded study of Opdivo + Yervoy. ORR data likely in house soon, but not being announced	NCT02659059
Checkmate-227	Bristol-Myers Squibb	Opdivo +/- Yervoy; PFS data due 2018	NCT02477826
Javelin Lung 100	Merck KGaA & Pfizer	Avelumab monotherapy, but design being changed; PFS data no longer expected in H2 2017	NCT02576574

Colucid gets payday thanks to Lilly

January 18, 2017

Investors in Colucid Pharmaceuticals have been rewarded for their patience: 12 years after the company licensed the migraine candidate lasmiditan from Lilly for $1m up front its originator has bought it back for $960m. In the interim Colucid has invested in getting lasmiditan to phase III, with an accumulated deficit of $129m as of September 2016 – still giving it a tidy profit. Meanwhile, Lilly gets an asset that, if approved, looks likely to be positioned between the now-generic triptans and the upcoming prophylactic anti-CGRP MAbs. Several of the latter are in phase III development, including Lilly's galcanezumab, so the company could soon have much of the migraine spectrum covered. Lasmiditan, an oral serotonin agonist, will need to confirm its benign cardiovascular safety profile in its second pivotal study, Spartan – if this is similar to that seen in the previous phase III Samurai trial the product could be used in migraine patients with cardiovascular problems who therefore cannot take triptans.

NPV of Lilly's migraine pipeline

Product	WW 2022 sales ($m)	NPV ($m)
Lasmiditan	437	969
Galcanezumab	788	2,981

Source: EvaluatePharma

Pulmatrix is QIDPs in

January 18, 2017

At the beginning of the week Pulmatrix's PUR1900 was an unloved preclinical-stage asset at the tail end of its pipeline, but yesterday the US FDA designated the inhaled itraconazole formulation a qualified infectious disease product (QIDP), driving the company's shares up 128%. Though PUR1900 is intended to treat fungal lung infections in patients with cystic fibrosis, the QIDP status specifically refers to Aspergillus infections. QIDP status confers an expedited regulatory review process and, added to the orphan drug status PUR1900 has already secured, will grant the product 12 years of market exclusivity. That, of course, relies on it obtaining US approval – by no means assured for a preclinical asset, despite the new shareholders' enthusiasm.

Pulmatrix's R&D pipeline

Product	Pharmacological class	Indication	Status
PUR003	Cationic airway lining modulator	Asthma	Phase I
PUR118	Cationic airway lining modulator	COAD/COPD and Cystic fibrosis	Phase I
CM-YJH01	Respiratory agent	Pulmonary fibrosis, idiopathic	Pre-clinical
PUR0400	Fluoroquinolone	Cystic fibrosis	Pre-clinical
PUR0700	Long-acting beta 2 adrenoreceptor agonist (LABA)	Asthma and COAD/COPD	Pre-clinical
PUR0600	Corticosteroid	Asthma and COAD/COPD	Pre-clinical
PUR1900	Triazole	Cystic fibrosis	Pre-clinical

Source: EvaluatePharma

Hutchison Chi-Med widens oncology assault

January 16, 2017

Not content to test its leading kinase inhibitors in late-line disease, Hutchison China Meditech has initiated new phase II trials of fruquintinib and sulfatinib in earlier stages of lung and gastrointestinal cancers. Fruquintinib is being tested in first-line non-small cell lung cancer in combination with Iressa, while sulfatinib's new trial is in second-line biliary tract cancer as a monotherapy. Both are currently in phase III trials – fruquintinib is in third-line non-small lung and colorectal cancers, sulfatinib in second or third-line neuroendocrine tumours. Lilly has partnered fruquinitinib for China, but sulfatinib remains unpartnered, so positive data from this project could generate more interest. The London-listed, Hong Kong-based company has licensed a third kinase inhibitor, savolitinib, to Astrazeneca for all markets outside China, so its global ambitions are clear. Hutchison Chi-Med has seven clinical-stage projects, six in oncology and HMPL-523 in autoimmune disease.

Hutchison Chi-Med pipeline

		WW sales ($m)		
Product	Generic Name	2018	2020	2022
Phase III				
Sulfatinib	sulfatinib	-	73.69	163.57
Fruquintinib	fruquintinib	18.68	67.67	131.95
Phase II				
Savolitinib	savolitinib	-	-	-
Phase I				
Epitinib	epitinib	-	-	-
Theliatinib	theliatinib	-	-	-
HMPL-523	-	-	-	-
HMPL-689	-	-	-	-

Source: EvaluatePharma

A bump in the road for Lilly's top pipeline asset

January 16, 2017

Given how vital baricitinib is to Lilly's future, the fact that the three-month delay to its US review does not look especially sinister could come as cold comfort. The company, along with baricitinib's originator, Incyte, said the US FDA had delayed its decision on the Jak inhibitor's use in rheumatoid arthritis by three months, having determined that requested additional data analyses provided by Lilly amounted to a "major amendment" to the NDA. The new PDUFA date is therefore April 19, 2017, and this also means that Incyte's potential $100m approval milestone has been similarly delayed. Still, according to the NPV of sellside consensus forecasts, as computed by *EvaluatePharma*, baricitinib is Lilly's most valuable pipeline asset, and oral dosing and a win against Abbvie's Humira head to head are reasons enough for investors to remain optimistic.

Lilly's top 5 pipeline assets

Project	Pharma class	Therapy area	2022e sales ($m)	Status
Baricitinib	JAK-1/2 inhibitor	Rheumatoid arthritis	1,827	Filed
Abemaciclib	CDK 4 & 6 inhibitor	Oncology	1,618	Phase III
Galcanezumab	Anti-CGRP MAb	Migraine	788	Phase III
BioChaperone Lispro U100	Insulin analogue	Diabetes	144	Phase II
LY2510924	CXCR4 peptide inhibitor	Oncology	59	Phase II

Source: EvaluatePharma

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