Evaluate Vantage

December 16, 2016

Snippet roundup: generics price-fixing, Agios loses its blood drug and an approval for Intercept

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

This week, December 12-16, 2016, we had thoughts on the following: generics price-fixing suits could snowball; Agios reassurance falls flat; Ocaliva takes small step forward with EU approval; Goldfinch chirpy after $55m series A; after dispatching its first attacker, Actelion moves on to its next foe; Alexion calls in former Astrazeneca chief as senior management head for the door.

Generics price-fixing suits could snowball

December 16, 2016

Christmas has come early for the lawyers, with antitrust suits both civil and criminal alleging price-fixing against six generics companies. On Wednesday the US Justice Department charged the former chief executive and former president of Heritage Pharmaceuticals with conspiring to fix prices of the antibiotic doxycycline hyclate and the diabetes drug glyburide. Heritage had fired the executives in August and had already filed its own civil lawsuit against them alleging "an elaborate embezzlement and self-dealing scheme" through which they stole millions of dollars from the company. Fixing doxycycline's price – which allegedly rose more than 9,000% in a seven-month period – took place from as early as April 2013 until at least December 2015, prosecutors allege, and that of glyburide from April 2014 until at least December 2015. This criminal case was followed yesterday by a federal civil lawsuit against Heritage and five other companies – Teva, Mylan, Aurobindo Pharma, Citron Pharma and Mayne Pharma – filed by the attorneys general of 20 US states. This concerns the same two drugs and alleges that Heritage was "the principal architect" of a conspiracy in which pricing was coordinated directly via email and phone as well as more covertly at industry trade shows and conferences. Hints have been dropped by lawyers and politicians that this is just the beginning, perhaps making for an uneasy holiday break for other generics executives, too.

Agios reassurance falls flat

December 16, 2016

Agios Pharmaceuticals was quick to reassure investors that the discontinuation of its second back-up pyruvate kinase-R activator, AG-519, would not have a knock-on effect on its first-in-class project, AG-348. But the markets were not convinced, sending the group's shares down 19% in premarket trading today. It does not help that the discontinuation is down to safety – the FDA put AG-519 on hold after a case of drug-induced cholestatic hepatitis, so there will no doubt be fears that the similarly acting AG-348, also being developed for the ultra-rare blood disorder pyruvate kinase deficiency, will be affected. AG-348 is in a phase II study called Drive PK, and should go into phase III next year – providing it does not run into the same problems. Leerink analysts lowered their probability of success for the PKR programme from 75% to 55%, adding that the project makes up around 50% of Agios's current valuation. Jittery investors face a nervous wait.

Agios's pipeline

Product	Indication	Mechanism	Status	2022e sales ($m)
AG-221*	Acute myeloid leukaemia	Isocitrate dehydrogenase (IDH)-2 inhibitor	Phase III	39 (royalties)
AG-120	Acute myeloid leukaemia	Isocitrate dehydrogenase (IDH)-1 inhibitor	Phase II	414
AG-348	Pyruvate kinase deficiency	Pyruvate kinase R activator	Phase II	325
AG-881*	Acute myeloid leukaemia	Isocitrate dehydrogenase (IDH)-1 & 2 inhibitor	Phase I	-

**Partnered with Celgene; Source: EvaluatePharma*

Ocaliva takes small step forward with EU approval

December 15, 2016

European approval of Intercept Pharmaceuticals's Ocaliva unlocks a small revenue stream that will add to what the primary biliary cirrhosis (PBC) treatment is already earning in the US. The first new PBC treatment in 20 years, the farnesoid X receptor agonist has been approved as an add-on to ursodeoxycholic acid (UDCA) in patients with an inadequate response or as a monotherapy to patients intolerant to UDCA. Ocaliva is forecast to earn €4m ($4.2m) in Europe in 2017 and €20m in 2018, according to *EvaluatePharma*. If clinical trials in NASH are successful it could gain regulatory approval and begin reporting sales in that much bigger indication in 2019. PBC approvals do not change the outlook of Intercept, which remains firmly a developmental-stage company until NASH trials are completed. Through September 30, its R&D spending of $122.6m and overhead of $177.1m far outweigh the $4.8m it has earned from Ocaliva in the US.

Ocaliva EU sales forecast (€m)

2017	2018	2019	2020	2021	2022
4	20	53	174	242	413

Source: EvaluatePharma

Goldfinch chirpy after $55m series A

December 15, 2016

At $55m, the investment with which Third Rock Ventures yesterday launched Goldfinch Bio just squeaks into the top 10 series A rounds this year. Goldfinch says it can integrate genetic, genomic and biological tools to pinpoint drug targets and genetically stratify patient groups. It will initially focus on conditions including focal segmental glomerulosclerosis and polycystic kidney disease, orphan indications for which no FDA-approved therapies exist. Goldfinch's interim chief executive will be Abbie Celniker, who joined Third Rock as a partner in October. Goldfinch is the third entrant in the table to be there by the grace of Third Rock: Relay Therapeutics' $57m and Fulcrum Therapeutics' $55m also came from the investment group. And they won't be the last – in the autumn Third Rock raised $616m for its fourth fund, which will go towards healthcare startups.

Top 10 series A rounds of 2016 to date

Date	Company	Investment ($m)	Profile
August 16	Tioma Therapeutics	86.0	Anti-CD47 antibodies for solid and haematologic cancers
February 24	Forty Seven	75.0	Therapies targeting cancer immune evasion pathways
January 7	C4 Therapeutics	73.0	Targeted protein degradation therapeutics
January 6	NextCure	67.0	Immuno-oncology products
May 10	Aptinyx	65.0	Therapeutics for disorders of the brain and nervous system
January 8	Zymeworks	61.5	Antibodies and other protein-based therapeutics
July 19	Oncorus	57.0	Oncolytic viruses for cancers including glioblastoma multiforme
September 14	Relay Therapeutics	57.0	Drug discovery platform centred on protein motion
July 19	Fulcrum Therapeutics	55.0	Modulating gene regulation
December 14	Goldfinch Bio	55.0	Precision therapies for kidney disease

Source: EvaluatePharma

After dispatching its first attacker Actelion moves on to its next foe

December 14, 2016

Having had years of practice fending off takeover approaches – if the rumours are true – and with a management team fiercely set on independence, Actelion was always going to be a tough negotiator. Too tough for Johnson & Johnson, which has walked away from bid talks over what seems to be a disagreement over price. If the Swiss drug developer is really determined to see a deal structured whereby its founder and chief executive, Jean-Paul Clozel, retains control and the acquirer takes some sort of strategic stake, then the exit of J&J should be considered disappointing – the US conglomerate is comfortable with such transactions and has successfully pursed them in the past with companies like Crucell, a Dutch vaccines maker. Not so the remaining bidder, said to be Sanofi, which according to the *Wall Street Journal* is considering a $30bn offer. This sounds much more like a straightforward knockout bid, representing a huge premium to Actelion's $20bn market cap, and should be plenty to persuade Mr Clozel to hand over the keys to his office. However the 2.2% drop in Sanofi shares this morning reveals understandable alarm at such a price tag. The 8% slide in Actelion can perhaps provide comfort to worried investors, as it points to diminishing belief in a deal actually getting done.

Mind the gap... the valuations of Actelion

Valuer	NPV ($bn)
Marketed drugs	*6.6*
R&D drugs	*0.7*
Consensus sellside valuation*	7.3
Current market valuation	20.3
J&J bid**	26
Sanofi bid**	30

** Source: EvaluatePharma*
*** Unconfirmed*

Alexion calls in former Astrazeneca chief as senior management head for the door

December 12, 2016

First came the whistleblowing scandal and today come board changes to add to Alexion Pharmaceuticals' bad news haul. The rare diseases company announced that it was parting company with not only its chief executive, but also its chief financial officer, in a boardroom clean sweep. Bounding to the rescue is internal hero – David Brennan, former Astrazeneca chief executive officer and current Alexion board member. His elevation came after the company announced that David Hallal, chief executive, had resigned for "personal reasons". Meanwhile, Vikas Sinha, chief financial officer, was reported to be vacating his office "to pursue other opportunities". Mr Brennan is bound to be seen as a safe pair of hands to guide Alexion through the search for a new chief executive – and as it completes its own internal investigation into claims about sales practices for lead drug Soliris. The company was, however, keen to point out that so far the audit had not turned up anything that could cause it to restate any historical results and that its delayed third quarter 10-Q would be will be filed in January 2017, or earlier. If this changes then it could become an even harder task to find someone prepared to take on a company that has seen its shares fall 41% since the start of the year – unless Mr Brennan decides he likes the view from his new office.

These snippets were previously published daily via twitter.

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