Evaluate Vantage

October 14, 2016

Snippet roundup: Biomarin boosted, Synairgen stung

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

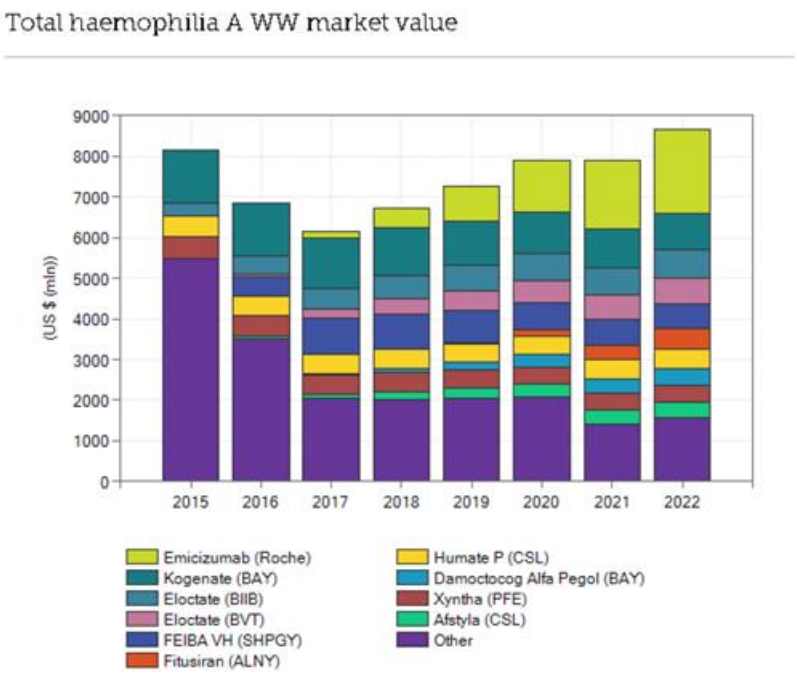
This week, October 10-14, 2016, we had thoughts on the following: Biomarin back in the haemophilia race; Regeneron to pay Ocular $10m at some point, maybe; Biomarin finds Sarepta approval appealing; Abbott adds another CDx; Januvia and Janumet join value-based pricing parade; St. Jude gives Abbott more heartache; Synairgen investors breathless after trial halt.

These snippets were previously published daily via twitter.

Biomarin back in the haemophilia race

October 14, 2016

Lifting the clinical trial hold on Biomarin's phase I/II haemophilia A gene therapy BMN270 puts the project on course for a possible pivotal phase IIb trial next year. Dosing in the study (NCT02576795) was halted in June – nine of a planned 12 patients had then been enrolled – after the third patient showed elevated levels of alanine aminotransferase, a possible marker of liver damage. After discussions with the UK's MHRA three patients will be enrolled at a new intermediate dose of 4x1,013vg/kg, and an additional three may be enrolled at either this dose or the previously tested high dose of 6x1,013vg/kg. Still, with forecast 2022 sales of $179m BMN270 will be an awfully long way behind the haemophilia A leader. Roche's bispecific antibody emicizumab is set to do more than $2bn of business, according to *EvaluatePharma*'s consensus data.



Regeneron to pay Ocular $10m at some point, maybe

October 14, 2016

Ocular Therapeutix's shares have jumped 14% after it signed a deal with Regeneron that is worth $10m up front – except it isn't. Ocular is to develop a sustained-release hydrogel depot formulation of Regeneron's wet AMD blockbuster Eylea, but the $10m only changes hands if Regeneron picks up its option to the resulting formulation. This is smart deal-making by Regeneron, which badly needs a follow-on after its last lifecycle extension plan, a combination of Eylea with rinucumab, was outperformed by Eylea alone earlier this month.

That said, Ocular Therapeutix was perhaps not in the best position to drive a bargain after the catastrophic phase III failure of Dextenza, which uses the same depot formulation technology, in ocular itching in June.

Regeneron's ophthalmology pipeline

Indication	Status	Product	Pharmacological class
Glaucoma	Phase III	Eylea	VEGFr kinase inhibitor
Wet AMD	Phase II	AVA-101	Soluble VEGFr-1 gene therapy
Cataract surgery	Phase II	Eylea	VEGFr kinase inhibitor
Macular oedema	Phase II	Nesvacumab	Anti-angiopoietin-2 MAb
Wet AMD	Phase II	Nesvacumab	Anti-angiopoietin-2 MAb
Wet AMD	Phase II	REGN2176-3	PDGF receptor beta MAb & VEGFr kinase inhibitor
Macular oedema	Phase II	REGN910-3	Anti-angiopoietin-2 MAb & VEGFr kinase inhibitor
Wet AMD	Phase II	REGN910-3	Anti-angiopoietin-2 MAb & VEGFr kinase inhibitor
Uveitis	Phase II	Sarilumab	Anti-IL-6 receptor MAb
Ocular inflammation	Phase I	Eylea	VEGFr kinase inhibitor

Source: EvaluatePharma

Biomarin finds Sarepta approval appealing

October 13, 2016

Any Biomarin bulls holding out for a change in fortune will be clinging to growing speculation that the company plans to appeal against the FDA rejection of its Duchenne muscular dystrophy project Kyndrisa. The company told JP Morgan analysts that it would decide either way by the end of the year, fanning hopes that first emerged with the approval of Sarepta's rival DMD product Exondys 51 last month. Biomarin has reportedly been cheered by the fact that the Exondys 51 label contains only dystrophin data, believing its dystrophin results to be stronger. However, it is far from clear whether this is the case. Ultimately, Biomarin might be scuppered by the fact that it carried out a larger trial than Sarepta, with equally equivocal data and the added problem of a safety signal. An appeal might also be less likely if Biomarin wants to keep on the FDA's good side with reviews of Brineura and pegvaliase coming up. But, with the Exondys 51 approval coming as a surprise to many, it would not be surprising if Biomarin tried its luck again.

The Duchenne muscular dystrophy pipeline

Company	Project	Amenable subset	Status
PTC Therapeutics	Translarna	Nonsensemutation	Approved EU
Sarepta	Exondys 51	Exon 51 skipping	Approved US
Marathon	Deflazacort	All	Filed US
Santhera	Raxone	All	Filed EU
Sarepta	SRP-4045/SPR-4053	Exon 45 & 53 skipping	Phase III
Italfarmaco	Givinostat	All	Phase III
Otsuka	TAS-205	All	Phase II
Nippon Shinyaku	NS-065	Exon 53 skipping	Phase II
Summit/Sarepta	Ezutromid	All	Phase II
Pfizer	Domagrozumab	All	Phase II
Fibrogen	Pamrevlumab	All	Phase II
Catabasis	Edasalonexent	All	Phase I/II
Capricor	CAP-1002	All	Phase I/II
Daiichi Sankyo	DS-5141	All	Phase I/II
Bristol-MyersSquibb	Myostatin adnectin	All	Phase I/II

Source: EvaluatePharma

Abbott adds another CDx

October 13, 2016

Abbott has only three companion diagnostics approved by the FDA, but is working hard to increase this number. Agreements signed yesterday with Celgene and Agios Pharmaceuticals will see the group develop tests for isocitrate dehydrogenase mutations in patients with acute myeloid leukaemia to identify responders to the companies' new projects for the disease, enasidenib (AG-221) and AG-120. The tests will run on Abbott's m2000 RealTime System, and have already been used to stratify patients in clinical trials. The group already has pacts to develop companion tests with companies including GlaxoSmithKline, AstraZeneca, Idera Pharmaceuticals, Biocartis, Epizyme and Merck & Co. Still, it has some way to go before it equals Dako: the Danish group has seven FDA-approved tests.

Groups with FDA-approved CDx

Company	No of CDx
Dako	7
Roche Molecular Systems	6
Ventana Medical Systems	5
Abbott Molecular	3
Qiagen Manchester	3
ARUP Laboratories	2
Biogenex Laboratories	1
bioMérieux	1
Leica Biosystems	1
Life Technologies	1
Myriad Genetics	1
Resonance Health	1

Source: FDA

Januvia and Janumet join value-based pricing parade

October 12, 2016

The agreement between Aetna and Merck & Co for value-based payments related to use of the DPP-IV inhibitor Januvia and its metformin combination pill Janumet is yet another sign of how 2016 has marked a dramatic shift in favour of payers in the drug-pricing game. The agreement will base Aetna's rebates for Januvia and Janumet on how well the two drugs help Aetna enrolees with diabetes achieve treatment objectives. On average, Januvia's US costs last year were about $5,200 per patient and Janumet's $4,300, representing 47% and 46% rebates, according to *EvaluatePharma*. Aetna, meanwhile, has joined CVS and Express Scripts in trying to squeeze savings out of the diabetes category, and this arrangement should in particular see other DPP-IV inhibitors like Boehringer Ingelheim's Tradjenta, Novartis's Galvus and AstraZeneca's Onglyza come under similar pressure.

Merck Januvia franchise US sales forecast ($m)

Product	2016	2018	2020	2022
Januvia	2387.0	2397	2422	1,339
Janumet	1026.0	1019	1022	797
Total	*3413.0*	*3416*	*3,444*	*2,136*

Source: EvaluatePharma

St. Jude gives Abbott more heartache

October 12, 2016

Fresh from its cyberattack scandal, St. Jude Medical now has to contend with a potentially fatal battery issue with its implanted cardiac devices. The news not only dragged down its stock, but also that of buyer Abbott, which nevertheless said it still expected to close the deal by the end of the year. St. Jude was keen to point out that, although two patients died after "premature battery depletion", the risk of the problem was low and most patients would not need to have their devices replaced. The recall also only affects devices manufactured before May 2015. Wells Fargo analysts estimate that the issue will hit St. Jude's 2018 sales and operating income by $143m and $71m respectively, but this will soon be Abbott's problem. M&A has not gone well for the company this year, with its $5.8bn purchase of Alere running into trouble after question marks over Alere's business practices. Now the St. Jude deal is also looking a lot less rosy.

Synairgen investors breathless after trial halt

October 12, 2016

Synairgen plunged 34% in London today on news that its partner AstraZeneca had terminated a trial of AZD9412 for an unusual reason: the asthma patients enrolled in the study were not experiencing enough exacerbations to detect a difference between the active and control arms. The agent, an inhaled form of interferon beta, is intended to prevent asthma exacerbations resulting from infections with common cold viruses – it was thought to offer antiviral protection because lung cells from asthmatics produced lower amounts of the cytokine and made them more vulnerable to the virus. Astra's decision to cease the phase IIa

test came after an interim analysis. Synairgen said Astra would now analyse data from secondary endpoints "that are most predictive of disease worsening to exacerbation" to determine a path forward, although that would surely be yet another early phase II trial. With little progress since Astra licensed in AZD9412, also known as SG001, in 2014, it is hard to see the UK big pharma continuing with this project.

Synairgen pipeline

	Product	Pharmacological Class	Indication	Trial ID
Phase II	AZD9412 (SNG001)	Interferon beta	Asthma	NCT02491684
			COPD	-
Pre-clinical	Fibrosis research project	Lysyl oxidase-like-2 (LOXL2) inhibitor	Idiopathic pulmonary fibrosis	-

Source: EvaluatePharma

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