Evaluate Vantage

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Snippet roundup: Data on Novartis's human CAR and Gilead's next-gen HIV candidate

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

This week, May 30 to June 2, 2017, we had thoughts on the following: Novo Nordisk's label comes up short in haemophilia B; Grail goes shopping; US claims massive EpiPen overpayment; Asco – Novartis makes another case for turning CARs human; Gilead scores some points against Glaxo in HIV.

These snippets were previously published daily via twitter.

Novo Nordisk's label comes up short in haemophilia B

1 June, 2017

For Novo Nordisk US approval of its haemophilia B product, Rebinyn (nonacog beta pegol), should have been a cause for celebration. Rebinyn will however be the third product to launch in the long-acting recombinant factor IX (rFIX) space, giving it more work to do in carving out sales. This job will be made even harder by the label the drug has been handed. Rebinyn has only been approved in the on-demand and pre-operative setting. Given that the drug has one of the longest half-lives of the current approved long-acting haemophilia B products, its biggest opportunity would have been in the prophylactic setting, where it is already approved in Europe. The FDA's reason for not giving the product the nod in this indication could have been due to concerns raised during the FDA panel hearing regarding the long-term use of the PEG in Rebinyn. Novo is now almost certainly going to be seeking a label extension for the prophylactic setting. But for now the uptake of the drug is likely to be a lot smaller and slower than expected.

Top 5 Marketed Haemophilia B Products

		WW sales ($m)		
Product	Company	2017	2022	Half life
Alprolix	Bioverativ/ Swedish Orphan Biovitrum	399	668	82 hours
BeneFIX	Pfizer	630	507	34 hours
Idelvion	CSL	183	249	104 hours
Rebinyn/Refixia	Novo Nordisk	9	217	111 hours
Rixubis	Shire	97	188	26 hours

Source: EvaluatePharma

Grail goes shopping

1 June, 2017

Grail has spent some of the $900m it raised in March on an acquisition that should allow it access to some interesting intellectual property. The group has bought Hong Kong's Cirina, founded by Dennis Lo, the scientist who made the discovery underlying maternal blood testing for foetal abnormalities. Cirina has kept itself quiet in the three years since it was founded, and other than that it is working on early diagnosis of cancer and other diseases – via similar liquid biopsy technology to Grail's own – little is known about the group. Financial terms of the deal were not disclosed, and the only measure of Cirina's worth seems to be its single fundraising round, a $12m series A in 2016. Grail says the purchase will allow it to expand into Asian markets, but the company ought to be wary of anything that might distract from its vast US clinical trials: one in 10,000 participants and another in 120,000 breast cancer patients.

US claims massive EpiPen overpayment

1 June, 2017

US government health programmes overpaid Mylan by $1.27bn for EpiPen over a 10-year period because of the way the speciality pharma classified the injection for anaphylaxis, according to an analysis by government auditors. For purposes of the Medicaid programme for low-income and disabled people, Mylan classified EpiPen as a generic, which received reimbursement based on a percentage of average manufacturer price. However, had it been properly classified as a branded product, the government reimbursement would have been lower because Medicaid receives a discount on the best price received in the private sector, the inspector general of

the Health and Human Services Department reported in a letter to the Senate Judiciary Committee. The $1.27bn overpayment was based on the 2006-2016 period.

Asco – Novartis makes another case for turning CARs human

31 May, 2017

As Novartis awaits FDA action on its leading CD19-directed CAR-T project, CTL019, more good news has emerged with CTL119, which also targets CD19 but uses a humanised rather than a murine binding domain. A study in chronic lymphoblastic leukaemia patients who had failed to go into remission after taking Abbvie/Johnson & Johnson's Imbruvica second line saw eight of nine evaluable subjects go negative for minimum residual disease (MRD) within three months of receiving CTL119 on top of Imbruvica. MRD-negative status is a measure of stringent complete response (CR) in the bone marrow, though radiologic responses in the spleen and lymph nodes will require longer follow-up. Full data will be revealed at Asco on Monday. An update of a separate CTL119 trial presented at the International Society for Cellular Therapy congress showed CRs in 100% of 22 CAR-naive paediatric acute lymphoblastic leukaemia subjects, and in nine of 15 patients relapsed or non-responsive to CTL019. CTL119 is one of several CAR constructs that aim to prevent potential rejection by the human immune system by avoiding use of a mouse-derived binding domain.

Anti-CD19 CARs that do not use a murine binding domain

Name	Binding domain	Developers	Study	Trial ID
			Paediatric ALL, CAR-naive & post-CTL019 subjects	NCT02228096
CTL119	Humanised	Novartis/Penn	CLL, Imbruvica combo	NCT02640209
huCD19	Fully human	Kite/NCI	B-cell leukaemia/lymphoma	NCT02659943
JCAR021	Fully human	Juno/Eureka	Data due in 2017	None found

Gilead scores some points against Glaxo in HIV

30 May, 2017

Gilead's bold move of pitting its next-generation integrase inhibitor bictegravir against Glaxosmithkline's rival product dolutegravir has paid off – partly. Four phase III trials have shown that Gilead's product is non-inferior to Glaxo's, but presumably failed to show superiority, as this was not mentioned by the company. The battle between the two drugs could now be fought on side-effect profiles – although Gilead did not give details, it said that no patients discontinued bictegravir due to renal events. Analysts have previously speculated that the suggestion of a more favourable renal safety profile could give Gilead's product an edge over dolutegravir, which is already marketed as monotherapy – known as Tivicay – and as part of a triplet, brand named Triumeq. Full data from the bictegravir phase III programme – two head-to-head and two switching studies – could give a better idea of how the agents stack up against each other. Gilead plans to file bictegravir for approval in the second quarter and could use one of its priority review vouchers to speed up the process, Leerink analysts speculate. This could help Gilead go some way to catching up with Glaxo – but superiority data would have been better.

Bictegravir vs dolutegravir

Project	Company	Status	2022e sales ($m)
Bictegravir/F/TAF	Gilead	Phase III	4,378
Triumeq (dolutegravir-based triple)	Glaxosmithkline	Marketed	5,376
Tivicay (dolutegravir monotherapy)	Glaxosmithkline	Marketed	2,600

Source: EvaluatePharma

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