Evaluate Vantage

May 11, 2018

Snippet roundup: Pivotal fluffs from Faron and Fasenra

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

This week, May 7-11, 2018, we had thoughts on the following: ARDS approval far off for Faron; Sirtex mulls $1.4bn counteroffer; Akili attracts corporates for ADHD game; Fasenra lacks puff beyond asthma; volanesorsen set to receive US blessing, setting up bigger problems.

These snippets were previously published daily via twitter.

Volanesorsen set to receive US blessing, setting up bigger problems

May 11, 2018

Despite the closeness of yesterday's US adcom vote Ionis's volanesorsen looks likely to receive FDA approval by its August 30 action date. Patient need in its target indication of familial chylomicronemia syndrome, cited frequently at the panel meeting, and the FDA's positive stance to rare diseases likely assure a regulatory green light in spite of the safety concerns that led to eight of the 20 panellists voting against. If volanesorsen is approved it will be marketed by Ionis's Akcea subsidiary under the trade name Waylivra, and attention will turn to how it can be made economically viable. Already there must be doubts as to whether the market will bear an orphan price given questions over Waylivra's dosing regimen and high rate of patient discontinuations due to treatment-related thrombocytopenia and clinical bleeding. Sellside consensus is for 2024 sales of $506m, according to *EvaluatePharma*, but yesterday Stifel analysts issued a savage forecast cut, halving peak revenue expectations to $200m to account for patient discontinuations and dose reductions. Nevertheless, Ionis and Akcea had absorbed much of the downside earlier in the week, and both stocks were up in today's premarket.

Fasenra lacks puff beyond asthma

May 11, 2018

Astrazeneca's anti-IL-5 antibody Fasenra already looked like it would struggle commercially in its approved use of severe eosinophilic asthma, and it now seems unlikely to get a helping hand from a second indication. Today's failure of the pivotal Galathea trial, in chronic obstructive pulmonary disease, leaves Astra dependent on a second phase III study, Terranova, for hints of a path forward in this use. True, sellside consensus does not factor COPD as a contributor to 2024 sales, which stand at $1bn, but some had expected more; Bernstein, for instance, cited Astra's hope of activity in COPD patients with a history of exacerbations, a disease type thought to have an inflammatory component targeted by Fasenra. Galathea and Terranova are bigger than competitors' pivotal studies, and both were enriched for subjects with high eosinophil levels. The fact that this did not yield a positive result in Galathea warrants further investigation, especially given Fasenra's approved use specifically in asthma with the eosinophilic phenotype. Astra's biggest focus now will be carving out a niche for Fasenra in asthma against IL-5 competition from Teva's Cinqair and especially Glaxosmithkline's Nucala.

Fasenra's pivotal programme in COPD

Study	Population studied	Design	Primary endpoint	Trial ID
Galathea	1,656 moderate to v severe COPD pts with exacerbations history, stratified by eosinophil levels	2 active arms vs placebo	56-wk effect on exacerbations	NCT02138916
Terranova	2,255 moderate to v severe COPD pts with exacerbations history, stratified by eosinophil levels	3 active arms vs placebo	56-wk effect on exacerbations	NCT02155660

Source: Clinicaltrials.gov

Akili attracts corporates for ADHD game

May 10, 2018

The fourth-biggest series C round for a medtech company this year has gone to fund what is intended to be the first prescription computer game. Akili Interactive has raised $55m from investors including Temasek, Singapore's National Wealth Fund, Amgen Ventures, and M Ventures, the VC arm of Merck KGaA, and will put the funds towards securing FDA clearance of AKL-T01, a computer game designed to treat ADHD in children and adolescents. The product's US pivotal trial was a hit, with data released in December showing that children playing the game showed significant improvement on measures of attention and focus compared with a control group that played a different game. A filing is expected in the coming months. The VC cash will also go towards

developing Akili's other products: data from a pilot trial of its programme for high-functioning children with autism spectrum disorders, AKL-T02, are to be presented this month, and AKL-T03 is in both a phase II study in cognitive dysfunction in adults with depression, set to report this year, and a pilot study in cognitive dysfunction in multiple sclerosis.

Top 5 series C rounds of 2018

Date	Company	MedTech Focus	Investment ($m)	Investors
April 4	Reflexion Medical	Radiology	100	GT Healthcare; Johnson & Johnson Development Corporation; KCK Group; Pfizer Venture Investments; Sofinnova Partners; T. Rowe Price; TPG Growth; Venrock
April 26	V-Wave	Cardiology	70	Aperture Venture Partners; BioStar Ventures; BRM Group; Deerfield Management; Edward Lifesciences; Endeavour
January 8	Metavention	Diabetic Care	65	Horowitz Group; New Enterprise Associates; Richard King Mellon Foundation; Sanderling Ventures; Versant Ventures
May 9	Akili Interactive	Neurology	55	Temasek; Baillie Gifford; Amgen Ventures; M Ventures; Jazz Venture Partners; Canepa Advanced Healthcare Fund; Brooklands Capital Strategies
January 10	Stimwave Technologies	Neurology	50	Undisclosed

Source: EvaluateMedTech

Sirtex mulls $1.4bn counteroffer

May 8, 2018

What do you do when you've already said yes to one offer, only to receive a better one at the very last minute? In January Sirtex Medical agreed a takeover by Varian Medical Systems at A$28 per share, but has now received an unsolicited bid worth $33.60 per share from the Chinese asset manager CDH Investments. The Varian bid was to go to a shareholder vote yesterday morning, but this has now been delayed to allow Sirtex to consider CDH's offer. Given that this clocks in at US$1.4bn in total, versus US$1.2bn for Varian's bid, there is always a chance CDH will carry the day. But Sirtex's management is playing this possibility down, stating that Varian's offer is in shareholders' best interests. Shareholders themselves seem unsure – the stock sits at A$28.94, more than Varian's offer but nowhere near CDH's. While Sirtex mulls its options, two further questions remain. Why has CDH lobbed its offer now, rather than when Sirtex was seeking acquirers at the end of last year? And why are two buyers duking it out over a company whose microsphere technology, despite being approved in Europe and the US in 2002, has repeatedly failed to improve survival over standard cancer therapy?

Phase III trials of Sirtex's SIR-Spheres

Name	Number of patients	Results	Trial ID
Sirflox	518 patients with liver mets from colorectal cancer	Miss. PFS with SIR-Spheres plus chemo 10.7mth vs 10.2mth with chemo alone	NCT00724503
Foxfire	360 patients with liver mets from colorectal cancer	Miss. OS with SIR-Spheres plus chemo 22.6mth vs 23.3mth with chemo alone	-
Sarah	495 hepatocellular carcinoma patients	Miss. Intent-to-treat OS with SIR-Spheres 8.0mth vs 9.9mth with Nexavar; per-protocol OS with SIR-Spheres 9.9mth vs 9. 9mth with Nexavar	NCT01482442

Source: Company website

ARDS approval far off for Faron

May 8, 2018

Faron Pharmaceuticals' Traumakine has failed the phase III Interest study in acute respiratory distress syndrome (ARDS), leaving the company with almost bare cupboards, a share price down 85%, and not a great deal of hope for the future. At the 28-day primary endpoint cut-off, patients given Traumakine had had a median of 10 ventilator-free days, compared with 8.5 in the placebo group; all-cause mortality was 26.4% for Traumakine and 23.0% for placebo. Neither difference was statistically significant. There was no difference in mortality at 90 days either, with the figures being 32.6% with Traumakine and 31.6% with placebo. Interest had been expected to succeed – the US FDA had suggested that Faron file a BLA using data from Interest, despite this being a European trial. Perhaps data from a Japanese ARDS trial, expected in the third quarter, will allow something to be salvaged from the wreckage. If not, a phase II study of Traumakine for the prevention of organ failure in patients with a ruptured abdominal aortic aneurysm is due to report next spring. Failing that, things look pretty dire: Faron's next candidate is Clevegen, an anti-Clever-1 antibody intended for solid tumours that has not yet entered the clinic.

Faron's pipeline

Product	Mechanism of action	Indication	Indication status
Traumakine	Interferon beta 1a regulator	Respiratory distress syndrome	Phase III Interest trial (NCT02622724) failed; phase III Japanese trial (JapicCTI-163320) due to report Q3 2018
		Abdominal aortic aneurysm	Phase II InforAAA trial (NCT03119701) due to report H2 2019
		Traumatic brain injury	Preclinical
		Spinal cord injury	Preclinical
Clevegen	Clever-1 antibody	Hepatoma, liver cancer	Preclinical
		Melanoma	Preclinical
		Pancreatic cancer	Preclinical
		Ovarian cancer	Preclinical
CIRT Program	Clever-1 antibody	General inflammatory disorders	Preclinical
VRET Program	Clever-1 antibody	General inflammatory disorders	Preclinical

Source: EvaluatePharma, clinicaltrials.gov

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