Evaluate Vantage

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Upcoming events – Approaching data for Ionis and decision time for Roche’s Ocrevus

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Welcome to your weekly digest of approaching regulatory and clinical readouts. Ionis expects phase III data from volanesorsen this month in a rare hereditary condition, and safety will be under scrutiny after thrombocytopenia earlier knocked investor confidence.

Also, Roche could finally see approval of its multiple sclerosis treatment Ocrevus by March 28, as a decision was delayed from the end of last year. The drug is expected to be one of the biggest launches of 2017 (see table below).

Lowering triglycerides

In the phase III Approach trial, 300mg of Ionis's volanesorsen is administered subcutaneously once-weekly for 52 weeks versus placebo in patients with familial chylomicronemia syndrome (FCS). The primary outcome is the percent change in fasting triglycerides from baseline at 13 weeks. 50 patients have been recruited and data are expected this month; regulatory submissions are set for later in the year.

FCS is a rare hereditary condition in which sufferers lack properly functioning lipoprotein lipase, an enzyme that clears triglycerides from plasma, causing repeated episodes of severe abdominal pain and pancreatitis. Standard of care is a low fat diet, but most patients find this difficult to adhere to.

Volanesorsen is designed to inhibit the production of apolipoprotein C-III (Apoc-III), a protein that plays a pivotal role in regulating plasma triglycerides.

In Compass, a previous phase III volanesorsen trial in severe hypertriglyceridemia, in a subgroup of seven FCS patients none discontinued therapy and they had a 73% mean reduction in triglycerides after 13 weeks compared with a mean increase of 70% for placebo recipients *(Compass puts Ionis back on the right track, December 20, 2016).*

Last year cases of severe thrombocytopenia were reported with a different project, IONIS-TTRRx, which was being tested in a form of amyloidosis. Ionis also saw cases with volanesorsen in FCS, but at the time did not provide further details, causing shares to fall 39% with the worry that this could be a class effect of its antisense therapies *(Ionis safety blow boosts Alnylam, May 27, 2016).*

More frequent platelet monitoring was introduced to the FCS studies. Ionis has said that FCS itself is likely a contributing factor to the side effect as patients experience substantial fluctuations in platelet counts, which could be related to high triglyceride levels. In volanesorsen-treated patients thrombocytopenia has only been seen in FCS.

An open-label study is ongoing, and a phase III trial in familial partial lipodystrophy is planned this year.

Sellside consensus from *EvaluatePharma* sees 2022 sales of volanesorsen of $490m, including partnering outside the US. No new thrombocytopenia events have been seen since the initial reports, and as volanesorsen is its biggest growth driver Ionis will be eager to keep it that way.

Valuable asset

By the end of March Roche should finally see approval of its multiple sclerosis candidate Ocrevus, which it has filed for both the relapsing and primary progressive forms of the disease. It had been due an FDA decision at the end of last year, but was delayed owing to the submission of additional data regarding commercial manufacturing.

It is set to be one of 2017’s biggest approvals in commercial terms, sitting just behind Sanofi’s Dupixent. Worldwide Ocrevus sales are forecast to reach $4bn by 2022, according to *EvaluatePharma*, and it is Roche’s second-biggest growth driver behind the oncology drug Tecentriq.

Dupixent, a monoclonal antibody for atopic dermatitis, has its own US decision a day later, on March 29.

The 5 biggest products slated for launch in 2017 (includes biologicals and small molecules)					
Project	**Therapy area**	**Pharma class**	**Company**	**Status**	**2022e global sales ($bn)**
Dupixent	Dermatitis	Anti-IL-4 & IL-13 MAb	Sanofi	Filed	4.6
Ocrevus	Relapsing and primary progressive MS	Anti-CD20 MAb	Roche	Filed	4.0
Durvalumab	Bladder cancer	Anti-PD-L1 MAb	Astrazeneca	Filed	2.3
Semaglutide	Type 2 diabetes	Once-weekly GLP-1 agonist	Novo Nordisk	Filed	2.0
Niraparib	Ovarian cancer	Parp inhibitor	Tesaro	Filed	1.8
Source:EvaluatePharma.					

Study	**Trial ID**
Compass	NCT02300233
Approach	NCT02211209
Approach open label trial	NCT02658175

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