Evaluate Vantage

October 26, 2017

Upcoming events – Adcom for Indivior and Haven 3 data for Roche

Joanne Fagg

Welcome to your weekly digest of approaching regulatory and clinical readouts. On October 31 a US FDA advisory committee will scrutinise Indivior's RBP-6000, a project for treating opioid addiction. It is a longer-acting follow-on to Suboxone, the company's current money maker, which could face generics shortly.

Also, Roche is expecting data with its haemophilia MAb emicizumab by the fourth quarter, this time in the key non-inhibitor population. These patients are fairly well served by factor replacement therapies, but if emicizumab can show similar efficacy to existing treatments its convenience could help market penetration.

Trick or treat for Indivior

RBP-6000 is an injectable monthly depot formulation of buprenorphine facing a decision on approvability by November 30.

In its phase III trial subcutaneous injections of RBP-6000 were given as six once-monthly 300mg doses, or two months of 300mg followed by four months of 100mg, versus placebo. Patients on both dosing schedules showed statistically better abstinence from opioids, measured via urine samples, versus those given placebo. Significantly more subjects in both dosing cohorts completed the study than those in the placebo group.

Briefing documents released today suggest that the agency is concerned about higher rates of adverse events with the higher dose regimen of RBP-6000, as well as the risk of patients administering the product intravenously, which could be life-threatening. RBP-6000 is intended to be given in a clinical setting by a healthcare provider.

RBP-6000 is a follow-on to Suboxone film, a sublingual once-daily combination of buprenorphine and naloxone that Indivior needs to replace, given the expected entry of generics. The company's shares plummeted 36% last month when a US court decided that the Indian generics company Dr Reddy's could make its own version. Indivior is planning to appeal *(Snippet Roundup: PI3Ks not dead, but PD(L)-1 multiple myeloma hopes falter, September 08, 2017).*

Last year Indivior reported sales of $933m for Suboxone film, accounting for 88% of total revenues, but this is expected to drop to $209m by 2022, according to *EvaluatePharma* consensus. RBP-6000, on the other hand, is forecast to hit $782m that year.

On the competitor front, Camurus and Braeburn Pharmaceuticals' own buprenorphine project CAM2038 will go before the panel a day later, on November 1. These companies have filed both weekly and monthly formulations, which have a PDUFA date in January. Stifel analysts believe that RBP-6000 will gain 30% share of the US market, versus 20% for CAM2038, by 2021.

Given the ongoing US opioid crisis and the promotion of addiction treatment by the FDA positive results at the committee meetings look likely.

Safe Haven?

Roche's emicizumab is a bispecific monoclonal antibody that binds factors IX and X and mimics the function of factor VIII. The Haven 3 trial, set to report in the fourth quarter, tests it in patients without inhibitors against factor VIII.

The phase III study, in 145 participants, has four treatment arms: emicizumab once weekly or once every two weeks in patients already on episodic treatment with factor VIII; an active comparator group that continues to use episodic factor VIII with a switch to emicizumab prophylaxis possible after 24 weeks; and emicizumab once a week in patients who had been on factor VIII prophylaxis before the study.

The primary endpoint measures number of bleeds over 24 weeks. Secondary endpoints include a quality of life questionnaire and the percentage of patients with anti-emicizumab antibodies at two years.

Emicizumab already has an approval action date of February 23 for patients who have developed inhibitors to factor VIII, though here too an adcom could be scheduled. This population has limited treatment options, but safety issues with emicizumab have caused concern *(The risks keep rising for Roche's haemophilia hope, February 23, 2017)*.

Non-inhibitor patients are already effectively treated by factor-replacement therapy, including Shire's market leader, Advate. All else being equal, convenience will be key: emicizumab is a once-weekly subcutaneous injection while prophylactic factor VIII therapy is given intravenously several times a week.

Uptake in the non-inhibitor population will also depend on how Roche chooses to price the product. On the company's third-quarter call its R&D chief, Daniel O'Day, said the group would target the entire market: "We want pricing to be set at a level that allows patients in both the inhibitor and non-inhibitor setting to be able to access to our medicine."

Consensus forecasts peg Advate still ahead of emicizumab by 2022. This is a notoriously conservative segment and switching could be an uphill battle, but impressive data could help Roche close the gap.

Top five haemophilia projects by 2022

			Global indication sales ($m)				
Product	**Company**	**Pharma class**	**2016**	**2018e**	**2020e**	**2022e**	**Indication status**
Advate/Adynovate	Shire	Factor VIII	1,519	2,562	2,514	2,378	Marketed
Emicizumab	Roche/Chugai	Anti-factor IXa/X bispecific MAb	-	199	1,092	1,828	Filed
Eloctate	Bioverativ/Swedish Orphan Biovitrum	Factor VIII	544	977	1,243	1,470	Marketed
Kogenate	Bayer	Factor VIII	1,290	1,159	995	843	Marketed
NovoSeven	Novo Nordisk	Factor VII	1,167	993	763	630	Marketed

Source: EvaluatePharma.

To contact the writer of this story email Joanne Fagg in London at joannef@epvantage.com or follow @ByJoFagg on Twitter