Evaluate Vantage

March 09, 2017

Upcoming events – Teva’s chorea approval and osteoporosis data for Amgen

Joanne Fagg

Welcome to your weekly digest of approaching regulatory and clinical readouts. Teva expects a US decision on SD-809, its possible treatment for Huntington’s chorea, at the beginning of April. This is the company’s biggest growth driver, though most forecast sales are assigned to its second indication, tardive dyskinesia, for which it will go in front of regulators later this year.

Meanwhile, initial data are expected in the second quarter for Amgen’s osteoporosis antibody romosozumab. The focus here will be reduction of non-vertebral fractures, an endpoint that was missed in prior trials and which could be commercially important (see table below).

Involuntary movements

SD-809’s filing in chorea was based on results from two phase III studies, First-HD and Arc-HD. In Huntington’s disease patients it showed a significant improvement over placebo in change in chorea score, and produced positive results from a switching study showing that patients could safely move to SD-809 overnight and maintain control of their chorea *(Auspex ends the year on a high note, December 17, 2014).*

SD-809’s PDUFA date in this indication is set for April 3, and the application was made via the abbreviated 505(b)(2) pathway. The project is a deuterated version of the VMAT-2 inhibitor tetrabenazine, sold by Lundbeck as Xenazine since 2008 for Huntington’s chorea, though it has a black box warning for depression and suicidal thoughts. It can only be dosed up to 50mg a day before patients must be genotyped for the drug-metabolising enzyme CYP2D6.

Xenazine’s patent expired in 2015, and generics are on the market in the US and Europe. Worldwide sales of Xenazine are forecast to drop from its 2015 peak of $327m to $33m by 2022, according to *EvaluatePharma's* sellside consensus.

Safety needs to be SD-809’s key differentiator. In phase III there were few notable imbalances in psychiatric measures and nervous system disorders, and more than 90% of patients chose to roll over into the longer-term safety study.

Given SD-809's similarity to Xenazine the FDA has been cautious: last May it slapped it with a complete response letter. New trials were not required, but the agency called for examination of blood metabolites. At the time the company said the metabolites were the same seen in subjects who take tetrabenazine or deutetrabenazine, and the resubmission was accepted in October.

SD-809 sales are forecast to reach $1bn by 2022, with 25% of this assigned to Huntington’s chorea. It has an NPV of $3.5bn, or 10% of Teva's market cap.

Investors will likely focus on whether Teva prices SD-809 to maximise the value for Huntingdon’s chorea, an orphan indication. Given the entry of Xenazine generics a premium price is unlikely.

Fractures

Amgen and UCB’s romosozumab, trademarked Evenity, is being tested in over 4,000 postmenopausal women with osteoporosis. The phase III Arch trial is a long-term project: it will see subcutaneous Evenity plus oral alendronate, a bisphosphate, given to patients for 12 months followed by alendronate alone for at least another 12 months. A separate arm uses alendronate as an active comparator.

Primary endpoints include the incidence of clinical fracture, including non-vertebral and vertebral fractures, and incidence of new vertebral fractures, both measured after the two-year treatment schedule. Initial results are expected in the second quarter, with trial completion due in November.

Top five osteoporosis drugs in 2022					
			Global sales (indication; $m)		
Product	**Company**	**Pharma class**	**2016**	**2022e**	**Status**
Prolia	Amgen	Anti-RANKL MAb	1,635	2,723	Marketed
Evenity	Amgen/UCB	Anti-sclerostin MAb	-	743	Filed
Abaloparatide SC and TD	Radius Health/undisclosed partner sales (ex US)	Parathyroid hormone	-	735	Filed (subcutaneous); phase II (transdermal)
Forteo	Lilly	Parathyroid hormone	1,500	563	Marketed
Viviant	Pfizer	Selective oestrogen receptor modulator	133	489	Marketed
Source:EvaluatePharma.					

Last year the Frame study met both its co-primary endpoints, reducing vertebral fractures at one and two years, but secondary non-vertebral fracture endpoints were missed, and there were two cases of osteonecrosis of the jaw in the treated group. Evenity was given as a one-year course followed by Prolia *(Romo in the approval Frame, but franchise won't be built in a day, February 22, 2016)*.

The PDUFA date for Evenity is July 19. The non-vertebral fracture data are important commercially because a competing project, abaloparatide, did hit this endpoint in phase III and avoided osteonecrosis. A subcutaneously delivered parathyroid hormone-related protein analogue made by Radius, abaloparatide, has a US approval decision due on March 30. A transdermal version is also in development *(Event – Radius hopes for big break with abaloparatide, September 13, 2016)*.

The space is crowded, but Evenity clings to second place in terms of 2022 forecast sales. And while Radius can claim compelling data it will need a partner to take on the might of Amgen.

Project	Company	Trials	PDUFA date
SD-809	Teva	NCT01795859 (First-HD) NCT01897896 (Arc-HD)	April 3 (chorea)
Evenity	Amgen/UCB	NCT01575834 (Frame) NCT01631214 (Arch)	July 19 (osteoporosis)
Abaloparatide SC	Radius Health	-	March 30 (osteoporosis)

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