Evaluate Vantage

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Go or no go? Vaccines and neurology up for discussion

Joanne Fagg

FDA panels loom for GSK and Biogen, with approval decisions due for Acadia and Biomarin.

Several FDA advisory committee hearings are set for March, including one for GSK's adult respiratory syncytial virus (RSV) vaccine Arexvy, following today's panel on Pfizer's rival candidate. Both jabs are expected to get positive recommendations. Biogen's ALS project tofersen will also come in front of an adcom later in the month to determine whether it warrants accelerated approval.

Regarding approval decisions, Acadia's trofinetide will likely become the first therapy for Rett syndrome, although tolerability issues remain. Elsewhere, Biomarin's haemophilia A gene therapy contender Roctavian is due a verdict next month, though a delay is possible as the company recently submitted three-year data that the FDA had requested.

RSV vaccine contenders

There has been a lot of activity of late in RSV, and the next big events are adcoms for the lead adult vaccine projects, aimed at people aged 60 or over. Pfizer's bivalent jab Abrysvo is up before a panel today, while GSK's adjuvanted shot Arexvy will face the experts on 1 March; analysts think both will receive a positive vote following robust data.

Assuming all goes well, and both vaccines get approved by their May Pdufa dates, the next hurdle will be the CDC's Advisory Committee on Immunisation Practices (ACIP), which recommends vaccines for routine immunisation programmes in the US. In a recent work group discussion, ACIP members supported both vaccines in adults aged 65 and over, but did not recommend them for adults aged 60-64.

The committee will reconvene in June and cast a vote on the vaccines. By then, there should also be two-season data, which could start to answer questions about durability. Some believe that GSK's Arexvy might be longer lasting because it is adjuvanted.

Up next in ALS

Following last year's green light for Amylyx's Relyvrio in ALS, Biogen and Ionis are up next with tofersen, with an FDA panel set for next month.

Tofersen, which is expected to be branded Qalsody, is designed for patients with a *Sod1* gene mutation, who

account for around 2% of the ALS population. Amylyx's Relyvrio is approved in the broader sporadic or familial ALS setting.

Biogen and Ionis are going for an accelerated approval, using neurofilament light chain (NfL) as a surrogate marker. The project's phase 3 Valor study failed to meet the primary functional endpoint, ALSFRS-R, at six months, but did show a reduction in NfL. Because NfL has been linked with neuronal damage tofersen might slow neurodegeneration, the partners argue. However, NfL is a controversial biomarker, and its utility will likely a big topic for the panel.

Biogen also filed 12-month data from Valor and an open-label extension study, showing that earlier initiation with tofersen, compared with delayed initiation, slowed the declines in clinical function. There were also sustained reductions in total Sod1 protein and NfL.

Another phase 3, the Atlas study, is enrolling presymptomatic subjects with Sod1 mutations and elevated levels of NfL, and will presumably serve as the confirmatory trial. Its primary endpoint is the percentage of participants with emergence of clinically manifest ALS within 12 months of randomisation, and the primary completion date is in 2026.

Rett decision

Meanwhile, Acadia is seeking the go-ahead for its IGF1 regulator trofinetide in Rett syndrome, a rare genetic neurological disorder that almost exclusively affects girls.

The project's phase 3 Lavender study met its co-primary endpoints, change from baseline in RSBQ and CGI-I, two common Rett scores, at week 12. Analysts questioned how clinically meaningful the data were, but given the unmet need approval is expected.

There was a higher incidence of diarrhoea with trofinetide versus placebo that contributed to dropouts, but most cases were mild to moderate. Previously, Acadia has said that diarrhoea could be addressed by patients discontinuing drugs to treat constipation, a common problem in Rett syndrome.

A disease-modifying approach using gene therapy would be the ultimate treatment goal for Rett syndrome. According to *Evaluate Pharma* the most advanced is Taysha and Astellas's TSHA-102; initial data from a phase 1/2 study are due in the first half.

The tables below list first-time and supplementary US approval decisions, as well as advisory committee meetings, due next month, with consensus forecasts from *Evaluate Pharma*.

Notable first-time US approval decisions due in March 2023

Project	Company	Pdufa date	Indication(s)	2028e SBI ($m)	Note
Trofinetide	Acadia	12 Mar	Rett syndrome	273	See text
Rezafungin	Cidara/ Melinta/ Mundipharma	22 Mar	Candidemia and invasive candidiasis	348	Positive adcom for patients with no alternative treatment options
Leniolisib	Pharming/ Novartis	29 Mar	Activated phosphoinositide 3-kinase delta syndrome	189	Oral PI3Kδ inhibitor
Valrox (Roctavian)	Biomarin	31 Mar	Haemophilia A gene therapy	1,420	See text, could be delayed
Zavegepant	Pfizer (ex Biohaven)	Q1 2023	Acute treatment of migraine	562	See *Go or no go? Lecanemab's destiny approaches*

SBI: sales by indication. Source: Evaluate Pharma & company releases.

Advisory committee meetings due in March 2023					
Project	**Company**	**Adcom date**	**Indication**	**2028e SBI ($m)**	**Note**
Arexvy (RSVPreF3 OA)	GSK	1 Mar	Prevention of lower respiratory tract disease caused by RSV-A & RSV-B in adults ≥60 years	1,814	See text; Pdufa date 3 May
Polivy	Roche	9 Mar	In combo with a rituximab product, cyclophosphamide, doxorubicin and prednisone for adults with previously untreated diffuse DLBCL	1,993	Has accelerated approval in r/r DLBCL after at least two prior therapies; confirmatory study Polarix (Pdufa 2 Apr)
Paxlovid	Pfizer	16 Mar	Mild-to-moderate coronavirus disease in adults at high risk of progression to severe Covid-19, incl hospitalisation or death	4,867	Received EUA in 2021; additional analyses from Epic-HR and Epic-SR studies submitted Dec 2022 as part of NDA
Naloxone hydrochloride nasal spray, 3mg/0.1ml (Rivive)	Harm Reduction Therapeutics	20 Mar	Nonprescription use as an opioid-reversal agent in the emergency treatment of opioid overdose	-	Emergent's Narcan nasal spray had positive adcom last month
Tofersen	Biogen/Ionis	22 Mar	ALS associated with a mutation in the *Sod1* gene	10	See text; Pdufa date 25 Apr, had been delayed from Jan
Influenza strain selection adcom occurring on 7 Mar. Source: Evaluate Pharma, FDA adcom calendar & company releases.					

Supplementary and other notable approval decisions due in March 2023			
Product	**Company**	**Indication (clinical trial)**	**Date**
Empaveli injector	Apellis	PNH (on-body drug delivery system that would enable patients to self-administer pegcetacoplan through SC infusion)	15 Mar
Once-daily ruxolitinib (Jakafi) extended-release formulation	Incyte	Myelofibrosis, polycythemia vera and GvHD	23 Mar
Narcan nasal spray (4mg/0.1ml)	Emergent Biosolutions	OTC emergency treatment for known or suspected opioid overdose	29 Mar
Evkeeza	Regeneron	Adjunct to other lipid-lowering therapies to treat children aged 5-11 with homozygous familial hypercholesterolemia (NCT04233918)	30 Mar
Hyrimoz (high concentration formulation of 100mg/ml) (Humira biosimilar)	Novartis	Includes the indications of the reference medicine Humira	Estimated as March
Lynparza + Zytiga + prednisone/prednisolone	Astrazeneca	1st-line castration-resistant prostate cancer (Propel)	End of Q1 2023 (delayed from Dec 2022)
Farxiga	Astrazeneca	Heart failure with preserved ejection fraction (HFpEF) (Deliver)	H1 2023
Source: Evaluate Pharma & company releases.			