Evaluate Vantage

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Go or no go? Sarepta’s gene therapy faces scrutiny

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SRP-9001 heads for its month of regulatory probing, as vaccines from GSK and Pfizer, and Genmab and Abbvie’s bispecific, await FDA approval decisions.

One of biopharma's most eagerly awaited approval processes of the year comes to a conclusion next month, when the fate of Sarepta’s Duchenne muscular dystrophy gene therapy will be determined. SRP-9001, partnered with Roche, has both an FDA panel and Pdufa date scheduled.

Elsewhere, two respiratory syncytial virus vaccines, Arexvy from GSK and Pfizer's Abrysvo, are expected to receive approvals in older adults. Pfizer’s candidate will also go before a panel in the infant setting. And Genmab and Abbvie’s epcoritamab, which boasts best-in-class potential in B-cell lymphoma, is looking good for an accelerated thumbs up.

Sarepta’s next act

Next month is big for Sarepta and its followers, starting on 12 May when an FDA panel will discuss SRP-9001, followed just over two weeks later by the project’s Pdufa date. Such a tight turnaround could delay the agency's verdict, although analysts at SVB Securities reckon the deadline could be met, pointing to the precedent of Amylyx's Relyvrio, which received a green light three weeks after its adcom.

Still, a smooth passage is not guaranteed. SRP-9001 is the first gene therapy to seek an accelerated approval based on a biomarker surrogate endpoint: in this case, microdystrophin expression. A key topic for the panel will be the evidence behind the biomarker's ability to predict a clinical benefit.

The project's filing, in ambulatory patients, was based on study 101 in just four individuals, the open-label 103 testing commercial grade product, and the phase 2 study 102 in 41 boys aged four to seven.

Functional data seen so far have been mixed. Part one of study 102 failed to show a difference between SRP-9001 and placebo on the North Star Ambulatory Assessment (NSAA) score at 48 weeks.

Part two of the same trial fared better on the functional endpoint, although the data were compared against an external control cohort. Crossover patients showed a 1.3-point improvement in NSAA score from baseline, versus a 0.7-point decline with the external controls, which Sarepta claimed as statistically significant.

SRP-9001's confirmatory study, Embark, reads out by the end of the year, and the agency could choose to wait to see this before making a decision. However, pressure from patient advocates and even FDA officials could

play a part in the process, as was seen with Sarepta's exon skipper Exondys 51 in 2016, which was controversially approved after a negative adcom.

Exondys 51 has yet to generate confirmatory data, just like the rest of Sarepta's approved therapies.

Just like buses

Two vaccines for respiratory syncytial virus (RSV) are expected to be given a greenlight next month. GSK could come first with Arexvy on 3 May, with Pfizer also guiding to May for a decision on its candidate, Abrysvo. Both are aiming for adults aged 60 and over.

Both vaccines come with positive panel votes, with GSK's looking more favourable after gaining a unanimous decision. For both vaccines there were questions over safety, in particular Guillain-Barré syndrome, with the FDA requesting a postmarketing study for Pfizer's Abrysvo. GSK has not been asked for a postmarketing study but has agreed to monitor the syndrome as part of pharmacovigilance efforts.

Following approval, the next challenge will be convincing the CDC's Advisory Committee on Immunisation Practices (ACIP). A meeting is set for June to vote on the vaccines. In an earlier work group discussion, ACIP members supported both vaccines in adults aged 65 and over but did not recommend them for adults aged 60-64.

Separately, Pfizer's Abrysvo has an adcom to discuss the vaccine's use in pregnant individuals to protect infants from disease. The Matisse study met one of its two co-primary endpoints, evaluating severe medically attended lower respiratory tract illness, failing on less severe illness.

Abrysvo is the first vaccine filed in this patient group. GSK discontinued its own project GSK3888550A after safety issues. The competition for Pfizer here lies with Astrazeneca and Sanofi's antibody Beyfortus, which has a Pdufa in the third quarter. On a cross-trial basis Beyfortus has shown an efficacy edge over Abrysvo.

Best in class?

Epcoritamab, Abbvie and Genmab's anti-CD20 bispecific, is gunning for an initial approval in third-line or later large B-cell lymphoma.

The accelerated decision will be based on the phase 1/2 Epcore NHL-1 study in which epcoritamab monotherapy showed 63% ORR. Cytokine release syndrome was the most common adverse event at 50%, with 2.5% incidence at grade 3. A study called Epcore DLBCL-1 could provide confirmatory data, with results expected later this year.

On a cross-trial basis epcoritamab looks as good as Car-T, and better than other anti-CD20 bispecifics in similar populations, including Roche's glofitamab, which has a Pdufa in July.

Epcoritamab also looks favourable against Roche's Polivy, an antibody-drug conjugate that recently gained a first-line label in combination with a Rituxan-containing chemo regimen.

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 May 2023					
Project	**Company**	**Pdufa date**	**Indication(s)**	**2028e SBI ($m)**	**Note**
Sotagliflozin (Zynquista)	Lexicon	May (resubmitted)	Heart failure	333	Technical issue led to the re-filing, going for broad label, not just restricted to diabetes patients
Abrysvo	Pfizer	May	Prevention of acute respiratory disease and lower respiratory tract disease caused by RSV in adults ≥60 years old	1,306*	See text
Arexvy	GSK	3 May	Prevention of lower respiratory tract disease caused by RSV-A and RSV-B	1,742	See text

Notable first-time US approval decisions due in May 2023					
			in adults ≥60 years old		
Mydcombi	Eyenovia	8 May	Drug-device combination for in-office pupil dilation (mydriasis)	54	Combination of tropicamide & phenylephrine administered via Optejet drug delivery
Pegunigalsidase alfa (PRX-102/Elfabrio)	Chiesi/Protalix	9 May (resubmitted)	Fabry disease	-	Previous CRL due to manufacturing inspection
Trastuzumab duocarmazine (SYD985)	Byondis	12 May	Her2+ve unresectable breast cancer	-	Antibody drug conjugate
B-Vec (beremagene geperpavec)	Krystal	19 May	Dystrophic epidermolysis bullosa	636	Extended from February pending manufacturing information
Epcoritamab (DuoBody-CD3xCD20)	Genmab/Abbvie	21 May (accelerated)	Relapsed/refractory large B-cell lymphoma after ≥2 lines of systemic therapy	1,168	See text
Fezolinetant	Astellas	22 May	Moderate to severe vasomotor symptoms associated with menopause	1,939	Extended from February
Brixadi	Camurus	23 May (resubmitted)	Opioid use disorder	-	Had two previous CRLs due to quality/manufacturing issues
Anktiva (N-803)	Immunitybio	23 May	BCG-unresponsive non-muscle-invasive bladder cancer	-	Antibody cytokine fusion protein
Sulbactam-durlobactam (Sul-Dur)	Innoviva (Entasis)	29 May	Hospital-acquired and ventilator-associated bacterial pneumonia caused by *Acinetobacter baumannii-calcoaceticus* complex in adults	82	Positive adcom
SRP-9001 (delandistrogene moxeparvovec)	Sarepta	29 May (accelerated)	Ambulatory patients with Duchenne muscular dystrophy with a confirmed mutation in the DMD gene	2,036	See text
Ritlecitinib	Pfizer	Q2 2023	12 yrs+ with alopecia	502	See *Go or no go? Seagen's Padcev eyes FDA approval*
Rozanolixizumab	UCB	Q2 2023	Generalised myasthenia gravis	144	Subcutaneous FcRN MAb, Pdufa for Argenx's SC Vyvgart was delayed until 20 June
Bimzelx	UCB	Q2 2023 (resubmission)	Plaque psoriasis	877	Previous CRL due to pre-approval

Notable first-time US approval decisions due in May 2023					
					inspections
Qdenga (TAK-003)	Takeda	H1 2023 (filed Nov 2022)	Dengue vaccine (4-60 years of age)	574	Approved in Europe
Concizumab (Alhemo)	Novo Nordisk	H1 2023	Haemophilia A and B with Inhibitors	-	Once-daily SC project, tissue factor pathway inhibitor
**Older adults and maternal setting not split out. SBI: sales by indication. Sources: Evaluate Pharma & company releases.*					

Advisory committee meetings due in May 2023					
Project	**Company**	**Adcom date**	**Indication**	**2028e SBI ($m)**	**Note**
Epinephrine nasal spray (Neffy)	ARS Pharmaceuticals	11 May	Emergency treatment of allergic reactions (type I) including anaphylaxis in adults and children ≥30kg	-	-
SRP-9001 (delandistrogene moxeparvovec)	Sarepta	12 May	Ambulatory patients with Duchenne muscular dystrophy with a confirmed mutation in the DMD gene	2,036	See text
Abrysvo	Pfizer	18 May	Prevention of lower respiratory tract disease and severe disease caused by RSV in infants from birth through 6 months of age by active immunisation of pregnant individuals	1,306*	See text, Pdufa August 2023
Ocaliva (obeticholic acid)	Intercept	19 May	Pre-cirrhotic liver fibrosis due to Nash	663	Previous CRL, completed a new analysis of Regenerate study
**Older adults and maternal setting not split out. SBI: sales by indication. Sources: FDA adcom calendar, Evaluate Pharma & company releases.*					

Supplementary and other notable approval decisions due in May 2023			
Product	**Company**	**Indication (clinical trial)**	**Date**
Kalydeco	Vertex	Cystic fibrosis in children from 1 month to <4 months of age	3 May
Paxlovid	Pfizer	Patients who are at high risk of progression to severe disease from Covid-19 (additional analyses of Epic-HR and Epic-SR trials)	5 May (positive adcom)
Rexulti	Otsuka/ Lundbeck	Agitation associated with Alzheimer's dementia	10 May (positive adcom)
Ayvakit	Blueprint	Indolent systemic mastocytosis (Pioneer)	22 May
OPNT003 nasal nalmefene	Opiant	Opioid overdose (NCT04759768, NCT05219669, NCT04828005)	22 May
Rinvoq	Abbvie	Adult patients with moderately to severely active Crohn's disease (U-Exceed, U-Excel, U-Endure)	Estimated 26 May
MSB11456 (Actemra biosimilar)	Fresenius	Autoimmune conditions	Estimated Q2
BIIB800/ BAT1806 (Actemra biosimiar) Biogen	Biogen/ Bio-Thera Solutions	Autoimmune conditions	Estimated Q2
mdc-IRM (Uzedy) (risperidone extended-release)	Teva/Medincell	Maintenance treatment of schizophrenia	H1 (resubmission)
Farxiga	Astrazeneca	Heart failure with preserved ejection fraction (Deliver)	H1 2023
Sogroya	Novo Nordisk	Growth hormone deficiency in children up to 11 years old (Real4)	H1 2023
Abrilada (Humira biosimilar)	Pfizer	Interchangeability	Estimated H1 2023
Source: Evaluate Pharma & company releases.			