Evaluate Vantage

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# Go or no go? Key FDA decisions for Argenx and Regeneron

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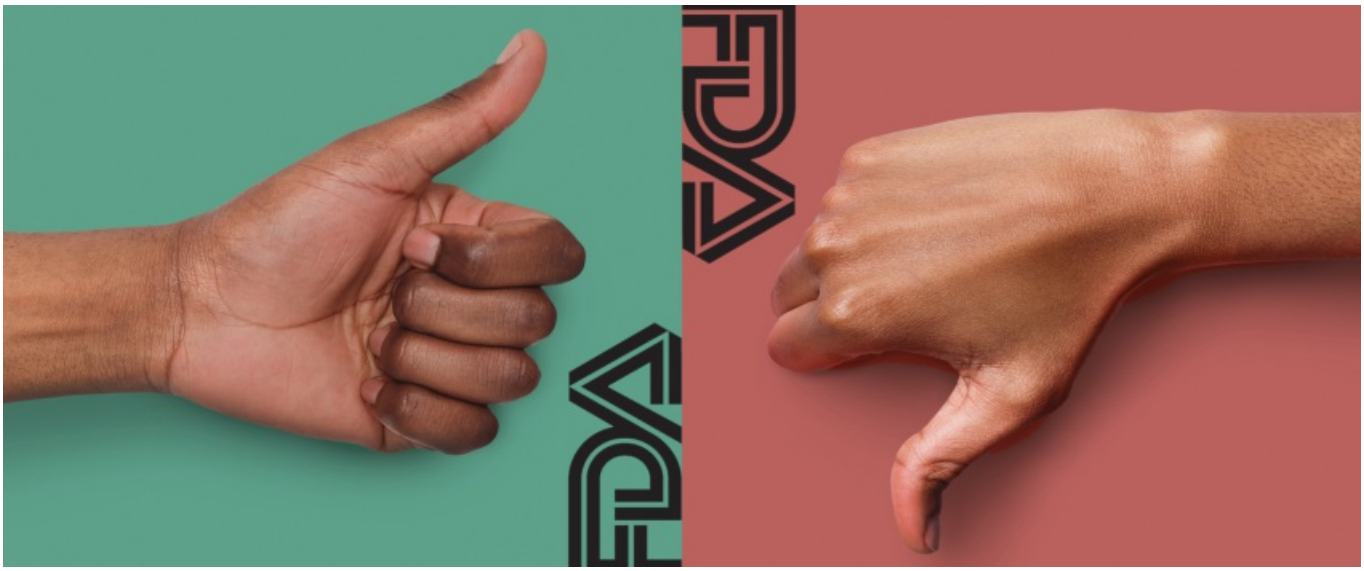


## Pdufa dates are also set for Sarepta and UCB, and panels will discuss Leqembi and Beyfortus.

The first month of summer brings with it several key Pdufa decisions, including one for Argenx, which is going for convenience with its subcutaneous version of Vyvgart in generalised myasthenia gravis. UCB's competing project rozanolixizumab is also due a decision soon, but that agent needs to be infused, and has a poor side effect profile.

Sarepta will finally see an outcome for its Duchenne muscular gene therapy SRP-9001, and accelerated approval is on the cards, albeit with a likely age restriction. Regeneron has a Pdufa date for high-dose Eylea, a product that represents the company's defence against increasing competition. Lastly, panels are set for Eisai's Alzheimer's agent Leqembi, to discuss full approval, and Astrazeneca/Sanofi's Beyfortus, a respiratory syncytial virus antibody for young children.

### Convenience win

Argenx's intravenous efgartigimod, branded Vyvgart, became the first FcRn antagonist approved a couple of years ago, and now the company hopes to launch the first subcutaneous version.

Subcutaneous efgartigimod met its primary endpoint in the Adapt-SC study in generalised myasthenia gravis. The project was non-inferior to Vyvgart on mean total IgG reduction from baseline at day 29, with comparable performances on measures of clinical efficacy, which were secondary endpoints.

There were issues with injection site reactions with the subcutaneous product, and more patients in the subcutaneous arm experienced a rebound in generalised myasthenia gravis symptoms, although these cases typically happened towards the end of the follow-up period. A long-term safety study called Adapt-SC+ is ongoing and looks at repeat dosing on an as-needed basis.

Hot on Argenx's heels is UCB's rozanolixizumab with a Pdufa set for the second quarter. The project is also a subcutaneous FcRn antagonist but needs to be infused over 30 minutes.

Rozanolixizumab looks to have the poorest side effect profile of the FcRn class. Headache was the most frequently reported adverse event in its MycarinG study, with diarrhoea, pyrexia and nausea also problematic. Berenberg analysts have suggested that rozanolixizumab might be positioned in the acute refractory setting.

**Sarepta again**

A modest Pdufa delay hit Sarepta's Duchenne muscular dystrophy gene therapy in May after a positive, albeit close, adcom vote. The decision is now set for 22 June.

SRP-9001 is expected to gain an accelerated approval in ambulant patients who have a confirmed DMD gene mutation but only in ages 4-5 years, a narrower population than Sarepta had initially proposed. Embark, the confirmatory study, is due to readout in the fourth quarter and could lead to an expansion into other age groups.

**Eylea's defence**

Approval is likely for Regeneron's high dose Eylea, off the back of the Pulsar and Photon studies in wet AMD and diabetic macular oedema, respectively. The data showed that the high dose version, given at four-monthly intervals, worked as well as the original formulation dosed every two months.

High dose Eylea is key to fending off biosimilars, which are expected to launch next year, and help defend against Roche's bispecific Vabysmo, which is also available at long dosing intervals.

Regeneron is already feeling the pinch with Eylea first quarter US sales at $1.43bn, missing expectations, and 6% lower than the same period last year. Vabysmo, meanwhile, was Roche's pharmaceuticals division's biggest growth driver, with SFr360m ($404m) in US sales beating expectations.

**Panels**

Eisai's Alzheimer's therapy Leqembi, which has already bagged an accelerated approval, will likely gain a positive panel vote for full approval next month. The confirmatory Clarity-AD study read out positively last year and a Pdufa is set for July.

On the competition front Eli Lilly's donanemab, which was turned down for accelerated approval, can now boast success in phase 3. On the surface donanemab looks similar to Leqembi, although with more toxicity. More details from donanemab's Trailblazer-Alz 2 study are expected at the Alzheimer's Association International Conference in July and a filing is expected soon.

Astrazeneca and Sanofi's Beyfortus will also go before a panel next month. The antibody is filed to prevent respiratory syncytial virus (RSV) disease in neonates and infants; a decision is due in the third quarter.

Beyfortus cut cases of medically attended RSV compared with placebo in the Melody study, which was part of the US filing, but there was no impact on hospitalisation rates. Recently a European study reported a significant decrease in RSV-related hospitalisations, but it is unclear whether that data will make it onto the US label.

Competition will come from Pfizer's RSV vaccine Abrysvo, which gained a positive adcom in May in pregnant individuals to protect infants from disease. The committee voted unanimously on effectiveness, with a narrower 10-4 vote on safety. An imbalance of pre-term births was seen in Pfizer's studies. Abrysvo's Pdufa is scheduled for August.

On a cross-trial basis Abrysvo has shown less impressive reductions than Beyfortus on both medically attended RSV infections and hospitalisations.

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 June 2023 | | | | | |
|---|---|---|---|---|---|
| **Project** | **Company** | **Pdufa date** | **Indication(s)** | **2028e SBI ($m)** | **Note** |
| Epinephrine nasal spray (Neffy) | ARS Pharmaceuticals | Mid year | Emergency treatment of allergic reactions (type I) including anaphylaxis | - | Favourable adcom in May |
| CyclASol (cyclosporine ophthalmic solution) | Novaliq (subsidiary of Geuder Group) | 8 June | Dry eye disease | - | Bausch + Lomb's Miebo (NOV03) was recently approved (has strategic collaboration with Novaliq) |

| Notable first-time US approval decisions due in June 2023 | | | | | |
|---|---|---|---|---|---|
| Momelotinib | GSK | 16 June | Myelofibrosis with anaemia | 320 | Via GSK's buyout of Sierra Oncology for $1.9bn |
| Olorofim | F2G (private)/ Shionogi | 17 June | Invasive fungal infections in patients who have limited or no treatment options | 35 | *Full steam ahead at F2G* |
| Vyvgart SC (subcutaneous efgartigimod) | Argenx | 20 June | Generalised myasthenia gravis | - (IV forecasts 2,981) | Delayed from March due to major amendment, SC FcRN MAb, see text |
| ADX-2191 (methotrexate injection) | Aldeyra | 21 June | Primary vitreoretinal lymphoma | 9 | - |
| Ocaliva (obeticholic acid) | Intercept | 22 June | Pre-cirrhotic liver fibrosis due to Nash | 663* | Negative adcom (*Intercept's Nash exit feels inevitable*) |
| SRP-9001 (delandistrogene moxeparvovec) | Sarepta | 22 June | Ambulatory patients with Duchenne muscular dystrophy with a confirmed DMD gene mutation | 2,770* | See text, delayed from May |
| Travivo (Exxua) | Fabre-Kramer Pharmaceuticals/ Bristol | 23 June (resubmitted) | Major depressive disorder | - | Submitted amendment in Dec 2022 |
| Dehydrated alcohol injection (DS-100) | Eton | 27 June (resubmitted) | Methanol poisoning | - | Previous CRL due to pre-approval inspection of contract manufacturer |
| Valrox (Roctavian) | Biomarin | 30 June | Haemophilia A gene therapy | 1,430 | Delayed from March due to submission of three-year data from the GENEr8-1 study |
| IPX203 | Amneal | 30 June | Parkinson's disease | - | Oral formulation of carbidopa/levodopa extended-release capsules |
| Glofitamab (Columvi) | Roche | 1 July (Saturday) | Relapsed/refractory large B-cell lymphoma after ≥2 lines lines of systemic therapy | 763 | CD20xCD3 T-cell engaging bispecific antibody, Abbvie and Genmab's Epkinly received approval in May |
| Rozanolixizumab | UCB | Q2 2023 | Generalised myasthenia gravis | 331 | SC FcRN MAb, see text |
| Ritlecitinib | Pfizer | Q2 2023 | Alopecia (aged 12 and older) | 502 | See *Go or no go? Seagen's Padcev eyes FDA approval* |
| Bimzelx | UCB | Q2 2023 | Plaque psoriasis | 718 | FDA recently issued a Form 438 relating to |

| Notable first-time US approval decisions due in June 2023 | | | | | |
|---|---|---|---|---|---|
| Bimzelx | UCB | (resubmission) | Plaque psoriasis | 718 | relating to manufacturing deficiencies |
| Qdenga (TAK-003) | Takeda | H1 2023 (filed Nov 2022) | Dengue vaccine (4-60 years of age) | 934 | Approved in Europe |
| **Forecasts prior to adcoms. SBI: sales by indication; SC: subcutaneous. Sources: Evaluate Pharma & company releases.* | | | | | |

**Advisory committee meetings due in June 2023**

| Project | Company | Adcom date | Indication | 2028e SBI ($m) | Note |
|---|---|---|---|---|---|
| Beyfortus (nirsevimab) | Astrazeneca/Sanofi/Sobi | 8 June | Prevent RSV lower respiratory tract disease in neonates and infants | 1,728 | See text, Pdufa Q3 (approved in Europe) |
| Leqembi | Eisai/Biogen | 9 June | Alzheimer's disease (confirmatory study) | 4,551 | See text, Pdufa 6 July |
| - | - | 15 June | Covid-19 (vaccine composition) | - | Recommendations on the selection of strains to be included in vaccines for 2023/24 |
| Sohonos (palovarotene capsules) | Ipsen | 28 June | Prevention of heterotopic ossification in adults and children (females aged 8 years and above and males 10 years and above) with fibrodysplasia ossificans progressiva | - | Received CRL in Dec 2022, submitted additional analyses from clinical trial data, Pdufa 16 Aug |
| *RSV: respiratory syncytial virus. Sources: FDA ad com calendar, Evaluate Pharma & company releases.* | | | | | |

| Supplementary and other notable approval decisions due in June 2023 | | | |
|---|---|---|---|
| **Product** | **Company** | **Indication (clinical trial)** | **Date** |
| Lynparza + Zytiga + prednisone/prednisolone | Astrazeneca/Merck & Co | 1st-line castration-resistant prostate cancer (Propel) | June? (adcom in April voted to restrict label to Brca+ve patients) |
| Prevymis | Merck | Prophylaxis of CMV disease in adult kidney transplant recipients at high risk (NCT03443869) | 5 June |
| Linzess | Ironwood | Children and adolecents 6-17 years old with functional constipation (NCT04026113) | 14 June |
| Bylvay (odevixibat) | Albireo | Alagille syndrome (Assert) | 15 June |
| Camzyos (mavacamten) | Bristol Myers Squibb | Reduce the need for septal reduction therapy in adults with symptomatic obstructive hypertrophic cardiomyopathy (Valor-HCM) | 16 June |
| Eylea 8mg | Regeneron/Bayer | Wet age-related macular degeneration and diabetic macular oedema (Pulsar, Photon) | 27 June |
| AVT02 (Humira biosimilar) | Alvotech/Teva | Interchangeability | 28 June (received CRL in April for biosimilarity BLA due to inspection deficiencies) |
| MSB11456 (Actemra biosimilar) | Fresenius | Auto-immune conditions | Estimated Q2 |
| BIIB800/ BAT1806 (Actemra biosimiar) Biogen | Biogen/ Bio-Thera Solutions | Auto-immune conditions | Estimated Q2 |
| Abrilada (Humira biosimilar) | Pfizer | Interchangeability | Estimated H1 2023 |
| Ultomiris | Astrazeneca | Neuromyelitis optica (Champion-NMOSD) | H1 |
| *Source: Evaluate Pharma & company releases.* | | | |

*This article has been edited to amend the infusion time of UCB's rozanolixizumab to 30 minutes.*