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Go or no go? Argenx's December showdown

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2021 rounds off with key FDA decisions for Argenx, Calliditas and Merck, while Novartis will be hoping for an early Leqvio verdict.

The most valuable US approval decision left for 2021 concerns Argenx's efgartigimod in myasthenia gravis. A green light is expected, but questions remain over how broad the label might be.

Calliditas could also gain its first US approval after a three-month delay with Nefecon. Meanwhile, Merck & Co's Keytruda could bag its eighth FDA nod this year alone, this time in adjuvant melanoma.

There is also a chance that Novartis gets closure next month for Leqvio, its cholesterol-lowering project which targets PCSK9 via RNA interference. The Pdufa date is January 1, nearly a year after the project received its knockback for manufacturing inspection-related issues.

One step ahead

Argenx's efgartigimod, an anti-FcRn Ab fragment, impressed in its pivotal Adapt study in myasthenia gravis. Significantly more patients had improved symptoms than placebo, while safety looked hard to beat with similar rates of headache, stuffy nose and nausea in both arms.

Myasthenia gravis (MG) is a neurological condition that causes certain muscles to weaken progressively. For around 85% of MG patients, autoantibodies against AChR drive the disease, and it was in these patients that Adapt's primary endpoint was measured. Therefore, a restriction to the AChR-positive population could be on the label.

If given the greenlight, efgartigimod will be the first anti-FcRn agent on the market, but the space is fiercely competitive.

UCB's anti-FcRn antagonist rozanolixizumab has data in the first half of 2022, and as a subcutaneous injection it has a convenience advantage over efgartigimod's IV infusion route. Argenx's subcutaneous version is not far behind, however, and is being tested in a non-inferiority study called AdaptSC, which is due to report early next year.

Also J&J paid $6.5bn for Momenta last year, mainly for its anti-FcRn antagonist nipocalimab, although that project's phase 3 study in MG only started in July. Efgartigimod is one of the sector's most valuable unpartnered assets, according to *Evaluate Pharma*.

The wait is over

December will see a final decision on Calliditas's Nefecon in IgA nephropathy after a three-month delay. The news of the extended timeline saw shares plummet 25% in September.

Calliditas had to submit additional analysis on estimated glomerular filtration rate (eGFR). Nefecon was originally filed under the accelerated approval programme using proteinuria as a surrogate endpoint.

Despite the delay Nefecon could still become the first approved therapy for IgA nephropathy, although Travere's sparsentan is closing in. Travere plans to file for accelerated approval in the first quarter of next year based on interim data from the Protect study.

Earlier therapy

Keytruda could see its target adjuvant melanoma market doubled next month, with a decision due in stage IIB/IIC melanoma. Merck's juggernaut already has an adjuvant label in stage III disease, a setting where the cancer has spread to the lymph nodes. For stage II the current practice after surgery is observation, but high-risk patients often experience disease recurrence.

The Keynote-716 study, reported at Esmo, showed Keytruda cut the risk of disease relapse by 35% versus placebo (p=0.007). Safety will be a focus for the FDA as serious drug-related adverse events were seen in 16% of Keytruda versus 4% of placebo recipients, and the resulting discontinuation rates were 15% and 3% respectively.

If approval is granted, this would be Keytruda's fourth adjuvant setting in the US, following a green light in adjuvant renal cell cancer in mid November.

Closure?

After shelling out $9.7bn on The Medicines Company in 2019 for Leqvio, Novartis and its investors will be keen to get the asset to the US market as soon as possible. The project achieved impressive LDL cholesterol-lowering in phase 3, and safety looked clean.

Initially, Leqvio was scuppered by an unresolved facility inspection at a contractor plant in Italy, so Novartis moved the manufacturing to the company's own plant in Austria.

Encouragingly, Leqvio was approved in Europe last December, but the rollout has been slow, with Novartis reporting sales of just $8m in the first nine months of the year.

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

Notable first-time US approval decisions due in December					
Project	**Company**	**PDUFA date**	**Indication(s)**	**2026e SBI ($m)**	**Note**
LV-101	Levo	By YE	Hyperphagia and behavioural distress associated with Prader-Willi syndrome	-	Negative FDA panel meeting in November
Tadfin	Veru	Dec	Benign prostatic hyperplasia	18	Combination of tadalafil and finasteride
DARE-BV1	Dare Bioscience	Dec 7	Bacterial vaginosis	28	Bioadhesive hydrogel containing clindamycin phosphate
Nefecon	Calliditas	Dec 15	IgA nephropathy	562	See text
Brixadi	Camurus/ Braeburn	Dec 15 (resubmission)	Opioid use disorder	-	Previous CRL due to quality-related deficiencies
Efgartigimod	Argenx	Dec 17	Myasthenia gravis	2,068	See text
Libervant (diazepam) buccal film	Aquestive	Dec 23 (resubmission)	Management of seizure clusters	172	Previous CRL, additional PK modelling submitted
Illuccix	Telix	Dec 23	Prostate cancer imaging	98	Extended from September due to manufacturing-related information submitted by the company
Epsolay	Sol-Gel	YE?	Papulopustular rosacea	-	Delayed in April due to Covid-19 travel restrictions preventing a pre-approval inspection
Eohilia (TAK-721)	Takeda	YE?	Eosinophilic esophagitis	188	April Pdufa missed
AXS-05	Axsome	YE?	Major depressive disorder	893	August Pdufa delayed due to two deficiencies related to analytical methods in the CMC, no new date disclosed
Leqvio (inclisiran)	Novartis/ Alnylam	Jan 1 (could come early)	Hyperlipidaemia in adults who have elevated LDL-C while being on a maximum tolerated dose of a statin therapy	2,026	See text

SBI=sales by indication, CMC=Chemistry, manufacturing and controls. Source: Evaluate Pharma & company releases.

Advisory committee meeting in December					
Project	**Company**	**Adcom date**	**Indication**	**2026e SBI ($m)**	**Note**
Bardoxolone methyl	Reata	Dec 8	Chronic kidney disease caused by Alport syndrome	1,210	Pdufa in February
SBI=sales by indication. Source: Evaluate Pharma, FDA ad com calendar.					

Supplementary and other notable approval decisions in December			
Product	**Company**	**Indication (clinical trial)**	**Date**
CHS-1420 (Humira biosimilar)	Coherus	Plaque psoriasis, ankylosing spondylitis, ulcerative colitis, psoriatic arthritis, rheumatoid arthritis and Crohn's disease	Dec
Keytruda	Merck	Adjuvant treatment stage IIB/C melanoma following complete resection (Keynote-716)	Dec 4
Caplyta	Intra-cellular	Bipolar disorder as monotherapy and adjunctive therapy (Study 402, 404)	Dec 17
Otezla	Amgen	Mild-to-moderate plaque psoriasis (Advance)	Dec 19
Orencia	Bristol Myers Squibb	Prevention of acute graft versus host disease (aGvHD) (Ph2 ABA2)	Dec 23
Oxbryta	Global Blood Therapeutics	Sickle cell disease in children ages 4 to 11 years, age-appropriate dispersible tablet dosage form	Dec 25
Cabenuva	J&J/ Viiv/ GSK	HIV treatment for use every two months (Altas-2M)	Est Dec 24
Xeljanz	Pfizer	Ankylosing spondylitis (A3921120)	YE?
Olumiant	Lilly	Atopic dermatitis (Breeze-AD programme)	YE?
Rinvoq	Abbvie	Atopic dermatitis, psoriatic arthritis and ankylosing spondylitis	YE?
Source: Evaluate Pharma & company releases.			