Evaluate Vantage

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Go or no go? Lecanemab’s destiny approaches

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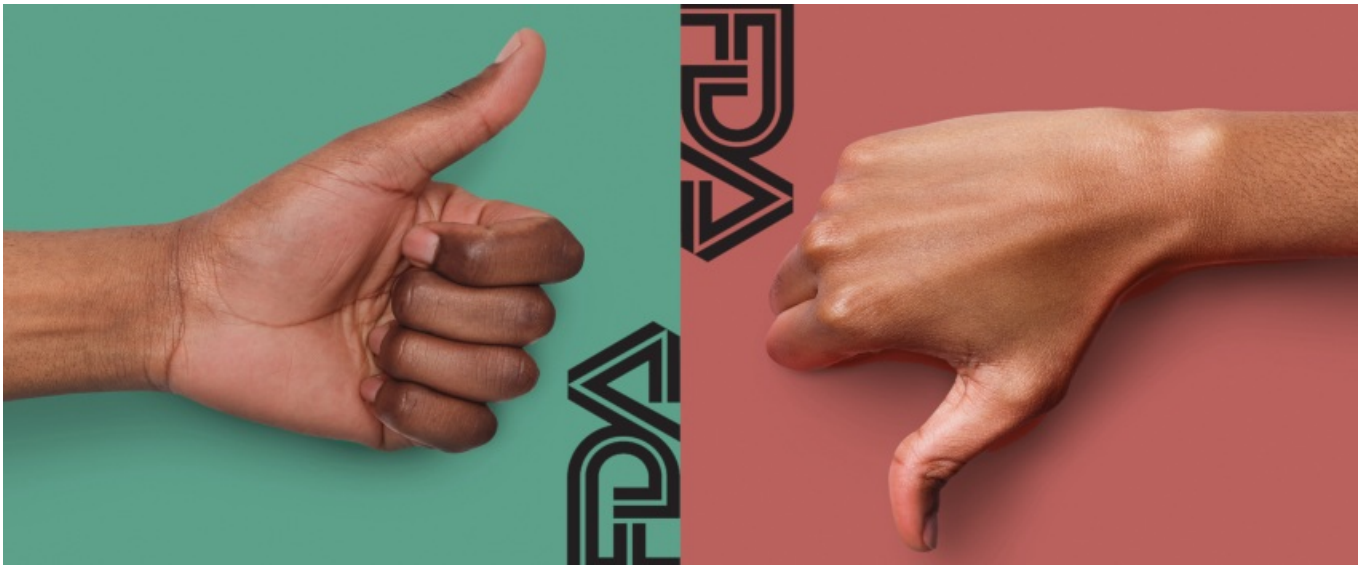

2023 begins with FDA decisions for Eisai’s Alzheimer’s project and Pfizer’s zavegepant, with an adcom for Cidara’s rezafungin.

2023 could start off with a bang, with a potential accelerated approval for Eisai's lecanemab in Alzheimer’s disease. The project looks to have a manageable safety profile, but efficacy remains modest, and the FDA will want to tread carefully after controversially approving Biogen's Aduhelm.

The first intranasal CGRP receptor antagonist, Pfizer’s zavegepant, looks likely to be approved next month for acute migraine, and the FDA will discuss Cidara’s rezafungin, a next-generation antifungal for certain hospital-acquired infections.

Alzheimer’s next MAb?

The keenly awaited US approval decision for lecanemab is due early next month. The amyloid-beta MAb was filed under the accelerated approval pathway with data from the phase 2b Study 201, alongside safety data from an open-label extension and blinded safety data from the phase 3 Clarity AD trial.

Clarity AD will act as the confirmatory study, which statements from November suggested Eisai would submit by the end of March for traditional approval.

However, what the FDA will do is anyone's guess. Accelerated approval, perhaps early, is one possibility, as is a delay to carry out full review of Clarity AD for a potential formal green light. The bull case is that the FDA has already seen Clarity AD data and might give lecanenamab full formal approval early.

Clarity AD, which yielded detailed data in November, showed a manageable Aria-E rate of 12.5%, well below the 35% seen with Biogen’s Aduhelm. The study met its primary endpoint, the effect on CDR-SB at 18 months, as well as key secondaries, although efficacy on a prospective basis looks not that different from the dataset cherrypicked for Aduhelm.

Aduhelm has had one of the worst drug launches in biopharma history, and after controversially being granted accelerated FDA approval on inconclusive data the CMS then refused to reimburse it. The CMS called for a meaningful benefit on cognition and function, rather than biomarkers, setting the bar for all amyloid-beta MAbs.

The next MAb on the horizon is Lilly’s donanemab; it has an accelerated filing with a decision potentially in February, with pivotal data due by mid-2023.

By the nose

With its $11.6bn buyout of Biohaven Pfizer gained several CGRP receptor antagonists, including zavegepant. The project, an intranasal spray intended as an acute treatment of migraine, has a Pdufa date in the first quarter, and could become the only US-approved intranasal CGRP receptor antagonist.

The CGRP market is crowded with oral and injectable projects, the leader of which is Nurtec ODT, another Biohaven-originated drug. The orally disintegrating tablet is sold for acute treatment and prevention.

In two phase 3 trials zavegepant was statistically superior to placebo on the co-primary endpoints of superiority at two hours for pain freedom, and freedom from the migraine-associated most bothersome symptom.

Zavegepant also met several secondary measures, including multiple ultra-rapid onset endpoints, and Biohaven highlighted pain relief in as little as 15 minutes and lasting 48 hours after a single dose.

The drug's nasal route could provide an alternative option for patients who suffer from nausea and vomiting when having a migraine.

FDA discussion

Three adcoms are set for next month, including one for Cidara's antifungal rezafungin. This novel echinocandin, which comes with an extended half-life, aims to treat candidaemia and invasive candidiasis, common hospital-acquired infections.

Echinocandins are the recommended first-line therapy but are only available as daily intravenous infusions in the hospital setting. Once patients are well enough to be discharged they are frequently placed on an oral azole. The CDC estimates that each case of candidaemia results in an additional three to 13 days' hospitalisation.

Cidara's rezafungin comes with once-weekly dosing. In the phase 3 Restore study rezafungin was non-inferior on the FDA endpoint of all-cause mortality at day 30 to caspofungin, the standard of care dosed once daily. The duration of ICU stay was lower for rezafungin, though this was just an exploratory endpoint.

According to Cidara no new therapies for candidaemia and invasive candidiasis have been approved in over a decade, and after the upcoming panel meeting a Pdufa for rezafungin is set for March. Cidara has rights in Japan and has licensed the commercial rights to Melinta in the US and Mundipharma outside the US and Japan.

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 January					
Project	**Company**	**Pdufa date**	**Indication(s)**	**2028e SBI ($m)**	**Note**
Nexobrid	Mediwound/Vericel/ Kaken	Jan 1 (resubmission)	Eschar removal in adults with deep partial-thickness and/or full-thickness thermal burns	78	Previous CRL due to CMC
Lecanemab	Eisai/Biogen	Jan 6 (accelerated approval)	Alzheimer's disease	1,779	See text
ACER-001	Acer	Jan 15 (resubmission)	Urea cycle disorder	109	Previous CRL due to facility inspection
Zavegepant	Pfizer (Biohaven)	Q1	Acute treatment of migraine	743	See text
Velmanase alfa (Lamzede)	Chiesi	H1	Alpha-mannosidosis	-	Enzyme-replacement therapy
Botulax (LetibotulinumtoxinA)	Hugel America	H1 (resubmission)	Moderate to severe glabellar lines	277	Previous CRL due to documentation
AT-GAA (cipaglucosidase + miglustat)	Amicus	Had several delays, could come H1	Pompe disease	266	Type A meeting expected before YE to discuss plans for manufacturing inspection
SBI: sales by indication. Source: Evaluate Pharma & company releases.					

Advisory committee meetings due in January					
Project	**Company**	**Adcom date**	**Indication**	**2028e SBI ($m)**	**Note**
Eylea	Regeneron	Jan 9	Retinopathy of prematurity in preterm infants	-	Data from Firefleye and Butterfleye studies, Pdufa in February
Rezafungin	Cidara/Melinta/ Mundipharma	Jan 24	Candidemia and invasive candidiasis in adults	348	See text
-	-	Jan 26	Future Covid-19 vaccination regimens	-	Consideration of the composition and schedule of the primary series and booster vaccinations
Source: Evaluate Pharma, company releases & FDA adcom calendar.					

Supplementary and other notable approval decisions due in January			
Product	**Company**	**Indication (clinical trial)**	**Date**
Vonaprazan (Takecab)	Phathom	Erosive esophagitis (Phalcon-ee)	Jan 11
Tukysa + Herceptin	Seagen	Adult patients with Her2-positive colorectal cancer who have received at least 1 prior treatment regimen for unresectable or metastatic disease (Ph2 Mountaineer)	Jan 19
Brukinsa	Beigene	Adults with CLL or SLL (Alpine, Sequoia)	Jan 20
Keytruda	Merck & Co	Adjuvant therapy for stage IB-IIIA NSCLC (Pearls/Keynote-091)	Jan 29
Myfembree	Pfizer/Myovant	Update to prescribing information (heavy menstrual bleeding associated with uterine fibroids; Liberty randomized-withdrawal study)	Jan 29
Source: Evaluate Pharma & company releases.			