Evaluate Vantage

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# Go or no go? Seagen's Padcev eyes FDA approval

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## Seres and Pfizer are also set for upcoming FDA Pdufa decisions, and a panel is scheduled for Astrazeneca and Merck’s Lynparza.

Having caught the eye of Pfizer, Seagen has a crucial accelerated approval decision due next month. The FDA is set to come to a conclusion on Padcev's combination with Keytruda in first line metastatic urothelial cancer, a big commercial opportunity.

Elsewhere Seres is coming after Ferring with its more convenient microbiome product, SER-109, and Pfizer will see whether its Jak3/Tec inhibitor ritlecitinib can get a clean label in alopecia. Lastly Astra and Merck’s Lynparza will be before a panel with the discussion likely to centre on whether the Parp inhibitor can get a broad label in first line castration-resistant prostate cancer.

**Padcev’s opportunity**

The immediate focus for Seagen, and soon to be Pfizer, is Padcev’s 21 April Pdufa in first line metastatic urothelial cancer. The accelerated decision is based on cohorts A and K of the EV-103/Keynote-869 trial, where Padcev was given in combination with Keytruda in cisplatin-ineligible patients.

A thumbs-up is largely expected. If it comes it will open a key commercial opportunity for the anti-nectin-4 antibody-drug conjugate. Evercore ISI analysts have said that the first-line opportunity could account for over $1bn of sales for Padcev. According to *Evaluate Pharma* consensus 2028 forecasts are close to $5bn. Padcev is currently approved in certain second- and third-line patients.

In Keynote-869's cohort K the combination of Padcev plus Keytruda yielded a 65% overall remission rate, in cohort A, the uncontrolled combo yielded a 73% ORR, including 85% in PD-L1-high and 67% in PD-L1-low patients.

The confirmatory study, the open-label EV-302, is expected to report by year end and is in the broader cisplatin-eligible setting.

**Microbiome battle**

The private group Ferring may already have the first faecal transplant product approved, but Seres and its partner Nestlé are gunning for convenience with its rival therapy SER-109, which is likely to get a favourable decision next month.

SER-109 is an oral therapy made up of firmicutes spores from healthy donors and is designed to inhibit the

growth of *Clostridioides difficile*. Ferring's Rebyota gained approval last November in adults following antibiotic treatment for recurrent *C difficile* infection. The crux here is that the therapy, a one-time dose, is given rectally via an enema. SER-109 on the other hand is given as a capsule four times daily for three days.

On a cross-trial basis it looks like SER-109 produced a greater treatment effect than Rebyota, albeit in a more refractory population.

For SER-109 TD Cowen analysts are modelling $750m in peak US sales in patients after two or more infection recurrences, but they expect upside should the therapy be granted a broad label to include patients with one or more recurrences.

**Pfizer's turn in alopecia**

Pfizer's Jak3/Tec inhibitor ritlecitinib is up for approval in individuals aged 12 and older with alopecia. The filing is based on the phase 2b/3 Allegro study and the ongoing long-term phase 3 Allegro-LT trial. An approval decision is expected in the second quarter.

In the Allegro study, when compared to placebo, a statistically significant higher proportion of patients given ritlecitinib achieved an absolute severity of alopecia tool score of 20 after 24 weeks of treatment, the primary endpoint.

Given the safety track record of Jaks the adverse event profile of ritlecitinib will be closely scrutinised. In Allegro there were no major adverse cardiac events but there was one case of pulmonary embolism, and two cases of breast cancer.

Pfizer's efficacy data looks in line with Lilly and Incyte's Olumiant on a cross trial basis. Olumiant, a Jak 1 & 2 inhibitor, gained US approval last year in adult alopecia patients, an older population than the one Pfizer's ritlecitinib is aiming for.

Olumiant was first approved in rheumatoid arthritis and its label comes with a black box warning for serious infections, malignancies, cardiovascular events and thromboses, a fate ritlecitinib will want to avoid.

**Can Lynparza propel?**

Astrazeneca and Merck's Lynparza will be discussed at a panel next month. The groups are hoping that the Parp inhibitor, in combination with Zytiga, can make its mark in first line castration-resistant prostate cancer.

The discussion will likely centre on whether data from Lynparza's Propel study support an approval in an all-comer population versus a homologous recombination repair (HRR)-deficient population only.

On Propel's primary endpoint of radiological progression-free survival, Lynparza showed a benefit in all comers, though this was clearly driven by HRR-deficient patients. On overall survival, a secondary endpoint, the combo was nominally positive for HRR-deficient patients while in the HRR-proficient subgroup there was no benefit.

Mizuho analysts note that an all-comer approval could translate to ~15,000 addressable patients, whereas the HRR-deficient-only scenario would result in just ~3,000 patients.

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 April 2023 | | | | | |
|---|---|---|---|---|---|
| **Project** | **Company** | **Pdufa date** | **Indication(s)** | **2028e SBI ($m)** | **Note** |
| LetibotulinumtoxinA/ Botulax/ Letybo | Hugel | 6 Apr (resubmitted) | Glabellar lines | 276 | Previous CRL, owing to documentation |
| Quizartinib (Vanflyta) + standard cytarabine and anthracycline induction | Daiichi Sankyo | 24 Apr | Newly diagnosed FLT3-ITD +ve AML | 114 | Previous CRL as monotherapy in relapsed/refractory disease |
| Tofersen | Biogen/Ionis | 25 Apr | ALS associated with a mutation in the Sod1 gene | 10 | Adcom voted in favour of using biomarker to predict a clinical benefit in accelerated approval decision |
| SER-109 | Seres | 26 Apr | *Clostridioides difficile* infection | - | See text |
| Aripiprazole 2-month | Otsuka/ Lundbeck | 27 Apr | Treatment of schizophrenia and the maintenance treatment of bipolar I disorder | - | Abilify Maintena is the one month version |
| TransCon PTH | Ascendis | 30 Apr | Adult patients with hypoparathyroidism | 1,214 | Takeda's Natpara, a hormone-replacement therapy for hypoparathyroidism, was pulled from the US market in 2019 owing to manufacturing contamination |
| Ritlecitinib | Pfizer | Q2 2023 | 12 yrs+ with alopecia | 479 | See text |
| Rozanolixizumab | UCB | Q2 2023 | generalised myasthenia gravis | 144 | Subcutaneous FcRN MAb, the Pdufa for Argenx's subQ version of Vyvgart was delayed until 20 June |
| Bimzelx | UCB | Q2 2023 (resubmission) | Plaque psoriasis | 877 | Previous CRL due to pre-approval inspections |
| Mirikizumab | Eli Lilly | H1 2023 (filed Q1 2022) | Ulcerative colitis | 617 | Anti-IL-23 MAb |
| Qdenga (TAK-003) | Takeda | H1 2023 (filed Nov 2022) | Dengue vaccine (4-60 years of age) | 574 | Approved in Europe |
| Concizumab | Novo Nordisk | H1 2023 | Haemophilia A and B With Inhibitors | 120 | Once-daily subcutaneous project, tissue factor pathway inhibitor |
| *SBI: sales by indication. Sources: Evaluate Pharma & company releases.* | | | | | |

| Advisory committee meetings due in April 2023 | | | | | |
|---|---|---|---|---|---|
| **Project** | **Company** | **Adcom date** | **Indication** | **2028e SBI ($m)** | **Note** |
| Rexulti | Otsuka/ Lundbeck | 14 Apr | Agitation associated with Alzheimer's dementia | 783 | Pdufa 10 May, approved in major depressive disorder (adjunctive), and schizophrenia |
| Sulbactam-durlobactam for injection (Sul-Dur) | Innoviva (Entasis) | 17 Apr | Hospital-acquired and ventilator-associated bacterial pneumonia caused by *Acinetobacter baumannii-calcoaceticus* complex in adults | 82 | Pdufa 29 May, β-lactam-β-lactamase inhibitor combination |
| NDAs for extended-release and long-acting opioid analgesics | - | 19 Apr | Discussion will focus on a clinical trial designed to address long-term efficacy of opioid analgesics and the risk of opioid-induced hyperalgesia | - | Postmarketing requirement |
| Lynparza + Zytiga + prednisone/prednisolone | Astrazeneca/ Merck & Co | 28 Apr | 1st-line castration-resistant prostate cancer | 1,389* | See text, Pdufa date TBC, had been expected Q1 2023 |

**Already on the market in different treatment line. Sources: Evaluate Pharma, FDA adcom calendar & company releases.*

| Supplementary and other notable approval decisions due in April 2023 | | | |
|---|---|---|---|
| **Product** | **Company** | **Indication (clinical trial)** | **Date** |
| Polivy + Rituxan + R-CHP | Roche | Previously untreated DLBCL (Polarix) | 2 Apr (positive adcom, although briefing docs were largely negative) |
| AVT02 | Alvotech | Humira biosimilar interchangibility | 13 Apr (previous CRL due to manufacturing deficiencies) |
| Padcev + Keytruda | Astellas/Seagen | 1L urothelial cancer patients cisplatin ineligible, (Ph1b/2 EV-103/Keynote-869 cohort A and cohort K) | 21 Apr (accelerated) |
| Trikafta | Vertex | Cystic fibrosis in children 2 to 5 years of age | 28 Apr |
| Prevnar20 | Pfizer | Pneumococcal vaccine in infants and children 6 weeks through 17 years of age (Ph3 NCT04382326, NCT04546425, NCT04379713, Ph2) | Apr 2023 |
| Farxiga | Astrazeneca | Heart failure with preserved ejection fraction (Deliver) | H1 2023 |
| Qulipta | Abbvie | Preventative treatment of chronic migraine (Progress) | Estimated H1 2023 |
| Sogroya | Novo Nordisk | Growth hormone deficiency in children up to 11 years old (Real4) | H1 2023 |
| Abrilada (Humira biosimilar) | Pfizer | Interchangibility | Estimated H1 2023 |
| *Sources: Evaluate Pharma & company releases.* | | | |

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