Evaluate Vantage

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Go or no go? Apellis and Heron head for the finish line

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May will see US FDA decisions for Apellis, Heron and Bristol Myers Squibb, while Provention Bio is set for a panel meeting.

Next month, Apellis's rare severe anaemia treatment pegcetacoplan is expected to be approved, but it could have a hard time competing in a crowded market. Meanwhile, Heron will have another crack at the US after two previous knockbacks for its post-operative pain therapy HTX-011.

Other highlights include Bristol Myers Squibb finding out whether it will get an extension for Zeposia in ulcerative colitis, and a panel discussing Provention's troubled type 1 diabetes asset teplizumab, which was originally cast off by Lilly over a decade ago.

Second-line use?

Apellis's lead project, a systemic formulation of pegcetacoplan, is awaiting a decision in paroxysmal nocturnal haemoglobinuria (PNH), with a Pdufa date on May 14.

The PNH market is dominated by Astrazeneca's intravenous anti-C5 antibodies Ultomiris and Soliris. Apellis's pegcetacoplan works by inhibiting a different complement factor called C3, and is given subcutaneously twice a week.

Combined sales of Soliris and Ultomiris are set to reach $1.4bn by 2026, according to *Evaluate Pharma*. Pegcetacoplan forecasts are much lower at $273m as analysts expect Apellis's treatment to initially receive a second-line label from regulators.

Apellis's filing was based on the Pegasus study, in which pegcetacoplan improved haemoglobin levels versus Soliris in PNH patients who had previously been treated with Soliris.

A treatment-naive study called Prince is ongoing, with data expected in the second quarter. However, competition is set to increase, with several oral projects in late-stage development *(Biocryst joins the push against Soliris, March 22, 2021).*

Third time lucky?

Heron Therapeutics' non-opioid-based pain therapy HTX-011 is once again before the US regulators. Last June the agency knocked back the project a second time, requesting additional non-clinical information. The

asset had received its first CRL in 2019 over manufacturing issues.

In Europe the drug received approval last September and is known as Zynrelef, though launch is not expected until 2022, with the company awaiting a US green light and the potential for worldwide licensing opportunities.

HTX-011 is an extended-release formulation of bupivacaine combined with the anti-inflammatory meloxicam. It was filed for use as post-operative pain management, with phase 3 studies showing sustained pain relief after bunionectomies or hernia repair and a decreased need for opioids *(Heron wades into crowded pain-relief waters, March 19, 2018).*

Despite HTX-011 being superior to Pacira's Exparel on efficacy, and having comparable safety, Heron might need to be aggressive on price to gain market share. A survey by SVB Leerink found that 75% of current users of Exparel, a liposomal form of bupivacaine, indicated that HTX-011 would need to be priced at a discount to switch.

Consensus forecasts by *Evaluate Pharma* see little growth for Exparel over the next five years, with 2026 sales of $514m. HTX-011 forecasts sit at $448m the same year.

Valuable indication

Bristol's Zeposia, an S1P receptor modulator, is awaiting an extension into ulcerative colitis, an indication worth $1.4bn to the company in 2026, according to *Evaluate Pharma*, nearly three times greater than the figure in MS, Zeposia's currently approved use.

The filing in ulcerative colitis is based on the True North study that showed highly statistically significant results in clinical remission in the induction phase at week 10, as well as in maintenance at week 52.

Arena's similarly acting etrasimod is expected to yield data from two phase 3 studies in ulcerative colitis in the first quarter of 2022.

Provention's woes

Lastly, a panel meeting is set for May 27 for Provention Bio's teplizumab, a project with ongoing regulatory issues.

The anti-CD3 MAb had originally been filed for the delay or prevention of type 1 diabetes in at-risk individuals, but earlier this week the FDA recommended the removal of the word "prevention" for the drug's proposed indication.

The FDA also identified deficiencies in the group's filing, noting pharmacokinetic inconsistencies between Provention's project and that used historically in clinical trials and manufactured by Lilly *(Delays look like the best-case scenario for teplizumab, April 9, 2021).* Lilly cast off teplizumab after it flunked a pivotal type 1 diabetes trial in 2010.

Provention has been keen to point out that the focus of the upcoming panel will be efficacy and safety, but the regulator has said that it plans to mention its PK comparability review in the briefing documents.

A potential solution could be to give the FDA PK/PD data from the ongoing phase 3 Protect study in newly diagnosed type 1 diabetes patients. An action date had originally been set for July, but a delay of up to a year has been pegged by some analysts.

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

Notable first-time US approval decisions due in May				
Project	**Company**	**Pdufa date**	**2026e sales by indication ($m)**	**Note**
Zynrelef (HTX-011)	Heron Therapeutics	May 12 (resubmission)	448	See text
Pegcetacoplan (APL-2)	Apellis	May 14	273	See text
Camcevi	Foresee Pharmaceuticals	May 27	-	Used 505(b)(2) pathway
PyL	Lantheus Holdings	May 28	233	Prostate cancer diagnostic imaging agent
Dehydrated alcohol injection (DS-100)	Eton	May 27	-	Treatment of methanol poisoning
Zonisamide oral suspension	Eton/Azurity Pharmaceuticals	May 29	-	Treatment of partial seizures in patients with epilepsy
Tralokinumab	Leo Pharma	Q2	-	Anti-IL-13 for moderate to severe atopic dermatitis
Source: Evaluate Pharma & company releases.				

Advisory committee meetings in May				
Project	**Company**	**Adcom date**	**2026e sales by indication ($m)**	**Note**
Vynpenta (avacopan)	Chemocentryx	May 6	348	Anti-neutrophil cytoplasmic antibody-associated vasculitis, Pdufa date in July *(Chemocentryx soars on superior avacopan)*
Teplizumab	Provention Bio	May 27	-	Delay of clinical type 1 diabetes in at-risk individuals, deficiencies identified in filing in April *(Delays look like the best-case scenario for teplizumab)*
Source: Evaluate Pharma & FDA adcom calendar.				

Supplementary and other notable approval decisions in May			
Product	**Company**	**Indication (clinical trial)**	**Date**
MSB11455 (Neulasta biosimilar)	Fresenius	Reduce the incidence of infection associated with febrile neutropenia	Estimated May
Esbriet	Roche	Unclassifiable interstitial lung disease (NCT03099187)	May
Aubagio	Sanofi	Paediatric relapsing MS (Terikids)	May 2
Opdivo	Bristol Myers Squibb	Adjuvant therapy resected esophageal or gastroesophageal junction cancer (Checkmate-577)	May 20
Zeposia	Bristol Myers Squibb	Ulcerative colitis (True North)	May 30
Alecensa	Roche	First-line Alk-positive NSCLC (Bfast)	Q2
Nurtec ODT	Biohaven	Prevention of migraine (Study 305, 201)	Q2
Farxiga	Astrazeneca	CKD with or without type 2 diabetes (Dapa-CKD)	Q2
Source: Evaluate Pharma & company releases.			