Evaluate Vantage

July 29, 2020

Go or no go? Valuable drugs set for FDA decisions

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Upcoming US approval verdicts include inclisiran, valrox and risdiplam, but toxicity issues could scupper filgotinib.

Though August might normally be classed as a quiet month for the sector, this time around it holds some valuable US approval decisions. Five of the projects due to be assessed have blockbuster potential, with 2026 forecasts over $1bn, according to *EvaluatePharma* consensus.

The most valuable **Novartis's inclisiran**; its Pdufa date has not been disclosed, but has been guided to the second half of the year. The project is a small interfering RNA designed to target PCSK9 and lower LDL cholesterol.

Inclisiran looks to be as effective as the marketed anti-PCSK9 MAbs, Amgen/Astellas's Repatha and Sanofi/Regeneron's Praluent. The MAbs have, however, proved disappointing commercially, having once carried huge sales forecasts that have since been slashed.

Inclisiran's main advantage seems to be convenience as it can be injected twice yearly versus every two weeks or monthly for the MAbs. Still, it remains risky commercially, and a key factor will be how Novartis prices it.

In the money

Another expected big money spinner due a decision is **Biomarin's valrox** for haemophilia A. The gene therapy is ahead of rivals, but its durability is a lingering red flag; four-year data showed that treated patients' clotting factor continued to fade over time.

Valrox looks approvable, but there is room for improvement. Pfizer and Sangamo's offering, giroctocogene fitelparvovec, has produced encouraging, albeit early, results so far, but if it can prove durable Biomarin will have a fight on its hands.

Three days later, on August 24, the FDA will discuss **Roche's risdiplam** for spinal muscular atrophy. This SMN2 splicing modifier is filed for use in infants with type 1 disease, and patients two to 25 years old with less severe disease known as types 2 and 3.

Risdiplam has shown encouraging efficacy and a clean safety profile, and as an oral agent it threatens Biogen's Spinraza, which has to be delivered intrathecally. The sellside agrees: risdiplam forecasts look set to overtake Spinraza in 2026, according to *EvaluatePharma*.

Toxicity issues

Glaxosmithkline's belantamab mafodotin is an anti-BCMA antibody-drug conjugate that received a positive adcom vote for multiple myeloma earlier this month despite its underwhelming efficacy and serious ocular toxicities.

If it is approved its label will include a black box warning, and a risk-mitigation programme will be implemented. Whether patients are willing to accept the side-effect profile will be key to 2026 forecasts being met.

Another project with adverse event implications is **Gilead and Galapagos's filgotinib**, filed for use in rheumatoid arthritis. The Jak1 inhibitor, now called Jyseleca, received EU backing last week for both its 100mg and 200mg doses.

Several questions remain over the FDA decision, expected in the second half of the year. A black box warning is likely for thrombosis, as was the case for Abbvie's Rinvoq when this was approved for arthritis last year. A second worry is that the FDA could take a conservative approach and approve only the lower dose, as adverse events appear to be dose dependent.

Lastly is the potential for a warning for risk of testicular toxicity, a signal picked up in animal models. There have not been any specific cases in clinical trials, but two safety studies called Manta and Manta-Ray are being conducted. These are expected to read out early next year.

Stifel thinks it unlikely that the FDA will need the safety data before approving filgotinib in RA, but this is a possibility. The agency could add toxicity wording to the label before the studies read out, leading to slow early uptake until the studies report.

For now the FDA seems largely on track with approval decisions, but with little sign of the Covid-19 pandemic abating the real impact on timelines could become significant in the coming months *(Go or no go? Pandemic looms over FDA timelines, July 1, 2020).*

The tables below list first-time and supplementary FDA approvals due in August, with consensus forecasts from *EvaluatePharma.*

Notable first-time US regulatory verdicts due in August				
Project	**Company**	**Pdufa date**	**Sales by indication ($m)**	**Note**
Belantamab mafodotin	GSK/Seattle Genetics	Aug	1,251	See text
Viaskin Peanut	DBV	Aug 5	695	FDA asked for more data in March and cancelled May's adcom
Olinvo/ IV oliceridine	Trevena	Aug 7 (resubmitted)	226	Previous CRL
EM-100 (Ketotifen PF Ophthalmic Solution)	Eton	Aug 10 (resubmitted)	-	Previous CRL
Pedmark	Fennec	Aug 10	243	-
Valoctocogene roxaparvovec	Biomarin	Aug 21	1,283	See text
Veverimer	Tricida	Aug 22	-	In July FDA identified deficiencies in its review of the filing
Risdiplam	Roche/PTC	Aug 24	1,437	See text
Xaracoll	Innocoll	Aug 26 (resubmitted)	-	RTF letter in 2016
Winlevi (clascoterone cream 1%)	Cassiopea	Aug 27	406	Topical acne treatment
Tlando	Lipocine	Aug 28 (resubmitted)	-	Three previous CRLs
Tafasitamab (Revlimid combo)	Morphosys	Aug 30	846	Anti-CD19 MAb for use in late-line DLBCL, more important B-Mind bendamustine combo study against Rituxan due to report 2022
Ryoncil (remestemcel-L)	Mesoblast	Sep	274	Ad com Aug 13; steroid-refractory acute GvHD in paediatric patients
Somapacitan/ NN8640	Novo Nordisk	Q3	318	Once-weekly long-acting recombinant growth hormone in adult-onset growth hormone deficiency
Dostarlimab	GSK/ Anaptysbio	H2	512	Anti-PD-1 filed in endometrial cancer
Filgotinib	Gilead/Galapagos	H2	1,255	See text
Inclisiran	Novartis/Alnylam	H2	2,010	See text
Viltepso (viltolarsen)	Nippon Shinyaku	H2	689	Exon 53 skipping antisense for DMD, marketed in Japan
Sources: EvaluatePharma & company releases.				

Supplementary and other notable approval decisions in August			
Product	**Company**	**Indication (clinical trial)**	**Date**
Stelara	BMS/J&J	Paediatric patients with moderate to severe plaque psoriasis (Cadmus Jr)	Aug 7
Dovato	GSK/Shionogi	HIV-1 in virologically suppressed adults (Tango)	Aug 17
Spravato	Johnson & Johnson	Major depressive disorder with active suicidal ideation with intent (Aspire I and II)	H2
Trelegy Ellipta	GSK	Asthma (Captain)	H2 (Apr adcom postponed)
Xolair	Novartis	Nasal polyps (Polyp 1 and 2)	H2
Sources: EvaluatePharma & company releases.			