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Go or no go? J&J’s bispecific FDA first

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Pdufa decisions also beckon for Amicus, Acadia and Bluebird.

Next month is expected to be relatively quiet on the US regulatory front. Nevertheless, Amicus’s Pompe disease candidate AT-GAA will come under scrutiny after a three-month delay, while Johnson & Johnson’s teclistamab could become the first FDA-approved BCMA-targeting bispecific.

As summer gets into full swing no FDA adcoms are scheduled, but both Acadia and Bluebird will get final decisions for projects that have previously gone through panels.

Teclistamab is filed for relapsed/refractory multiple myeloma; no Pdufa date has been disclosed, but analysts expect a late August decision. The project, a T-cell recruiter, was recently recommended for conditional approval in the EU, where it is branded Tecvayli, and a confirmatory study is under way.

EMA and FDA filings were both based on data from teclistamab’s phase 1/2 MajesTEC-1 studies, with the bispecific showing a 63% ORR and 39% CR in heavily pretreated patients. Safety issues were evident, with cytokine release syndrome occurring in 72% of patients. In addition, 45% of patients experienced grade 3 or 4 infections.

While J&J looks like it will be first to the US market with teclistamab, the BCMA T-cell engager space is crowded. Pfizer’s elranatamab looks next in line with a final analysis from the pivotal MagnetisMM-3 expected in the second half, while ABBV-383, REGN5458 and AMG 701 are all in studies.

Of course other anti-BCMA treatments are already available, comprising Car-T and GSK's antibody-drug conjugate Blenrep. J&J itself sells the Car-T therapy Carvykti, and it is easy to see teclistamab and Carvykti cannibalising each other.

Two-parter

After a three-month delay miglustat, one part of Amicus’s Pompe disease therapy AT-GAA, is due its approval decision. Miglustat acts to stabilise the second component, cipaglucosidase alfa, a recombinant acid alpha-glucosidase enzyme, which has its own Pdufa set for October. Although the Pdufas are split, Amicus and Stifel analysts expect the FDA to decide on the two components at the same time.

Pompe disease is caused by a deficiency of acid alpha-glucosidase, which leads to severe muscle weakness. The current standard of care is Sanofi's enzyme-replacement Lumizyme, also known as Myozyme.

Amicus had hoped that AT-GAA would prove more effective than Lumizyme, but this was not borne out by the

pivotal Propel study, which failed to show superiority on the six-minute walk test versus Sanofi's incumbent.

At the time of the Propel results Amicus pointed to “clinically significant” improvements on other measures such as forced vital capacity (FVC), a lung function test – it was effectiveness on this endpoint that won Lumizyme approval.

FVC was also the primary endpoint for Sanofi’s follow-on Nexviazyme, which gained FDA approval last August; that product also failed to show superiority to Lumizyme.

Combined Lumizyme/Myozyme and Nexviazyme forecasts sit at $1.7bn by 2028, according to *Evaluate Pharma*, while AT-GAA is just $266m.

Adcom outcomes

For Acadia, expanding Nuplazid’s label into Alzheimer’s disease psychosis looks dead in the water after a negative panel in June. A complete response letter is likely, which would be the second for the project after it failed to expand into dementia-related psychosis last year.

Nuplazid will likely have to stick with its approved Parkinson’s disease psychosis label for now, with studies in schizophrenia expected to yield data next year.

Meanwhile, things look rosier for Bluebird’s beti-cel for transfusion dependent beta-thalassaemia, which received a unanimous recommendation from its panel meeting. Approval would give the group a priority review voucher to sell, providing a much-needed cash injection.

The bigger task for the group will be making the gene therapy a commercial success. In Europe, Bluebird tried to enter the market with a $1.8m price tag but failed to strike deals with payers there.

In the US, a favourable assessment by Icer could sway decisions. The pricing watchdog recently modelled beti-cel cost effective at a cumulative price of $2.1 million, subject to an 80% payback option for patients who do not achieve and maintain transfusion independence over a five-year period.

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

Notable first-time US approval decisions due in August					
Project	**Company**	**Pdufa date**	**Indication(s)**	**2028e sales by indication ($m)**	**Note**
Betibeglogene autotemcel (Zynteglo, beti-cel)	Bluebird	Aug 19	Beta-thalassaemia (requiring regular red blood cell transfusions)	120	Positive adcom, see text
Miglustat for AT-GAA	Amicus	Aug 29	Pompe disease	266*	Delayed from May, part of two-component therapy with cipaglucosidase's Pdufa in Oct, see text
Teclistamab	Johnson & Johnson	Est Aug 29	R/R multiple myeloma	264	Bispecific T-cell engager targeting BCMA and CD3, see text
AXS-05	Axsome	Q2	Major depressive disorder	787	Received proposed labelling from the FDA at the end of June
Annik (penpulimab)	Akeso/Sino	Pending	3L nasopharyngeal carcinoma	-	*China-backed US approvals continue to hang in the balance*
**Forecast for AT-GAA. Source: company releases & Evaluate Pharma.*					

Private companies with pending FDA approvals			
Project	**Company**	**Indication(s)**	**Filing date**
SH-111	Shorla Oncology	Undisclosed project for T-cell leukaemia	Apr 2021
Spesolimab	Boehringer Ingelheim	Generalised pustular psoriasis	Dec 2021
Source: company releases & Evaluate Pharma.			

Supplementary and other notable approval decisions due in August			
Product	**Company**	**Indication (clinical trial)**	**Date**
Nuplazid	Acadia	Hallucinations and delusions associated with Alzheimer's disease psychosis	Aug 4 (negative adcom in June)
Myfembree	Pfizer/ Myovant	Moderate to severe pain associated with endometriosis (Spirit 1, Spirit 2)	Aug 6 (delayed from May)
Imfinzi + chemo	Astrazeneca	1L biliary tract cancer (Topaz-1)	Q3
Enhertu	Astra/Daiichi Sankyo	2L Her2-positive NSCLC (Destiny-Lung01)	Q3
CHS-201/ FYB201 (Lucentis biosimilar)	Teva/Bioeq/ Formycon/Coherus	Ophthalmologic indications	Q3
Orkambi	Vertex	Patients with cystic fibrosis aged 12mth to <24mth	H2
Actemra	Roche	Hospitalised Covid patients (EUA in Jun 2021) (Empacta, Covacta, Remdacta, Recovery)	H2
Source: company releases & Evaluate Pharma.			