Evaluate Vantage

April 29, 2022

Go or no go? Lilly’s valuable diabetes contender

Joanne Fagg

Tirzepatide heads for its first FDA approval and Enhertu eyes an earlier setting, as Verrica and Axsome keep their fingers crossed.

May could see one of the most valuable approvals of the year: that of Lilly’s tirzepatide in diabetes. A precise Pdufa date has not been disclosed but the deadline is looming, and Lilly is gunning for a slice of Novo Nordisk’s share of this market.

Elsewhere, Astrazeneca and Daiichi Sankyo’s Enhertu looks set to move into second-line breast cancer. And Verrica and Axsome are hoping for better outcomes after previous setbacks for VP-102 and AXS-05 respectively.

Big bucks

Approval is expected for Lilly’s tirzepatide in type 2 diabetes, after the GLP-1/GIP dual agonist scored in five pivotal trials showing statistically significant HbA1c (blood sugar) reductions and weight loss.

The project has also demonstrated cardiovascular safety – a meta-analysis of the Surpass programme found a 19% relative risk reduction in major cardiovascular events with tirzepatide versus pooled comparator data. A large cardiovascular outcome trial versus Lilly’s own Trulicity is ongoing.

Cross-trial comparisons point to fierce competition for Novo Nordisk's flagship GLP-1, Ozempic, with tirzepatide displaying stronger efficacy and little additional toxicity. Still, Novo's lead is important, with Ozempic set to remain the market leader in type 2 diabetes by 2026, according to *Evaluate Pharma*'s sellside numbers.

Diabetes is only the beginning of the road for tirzepatide, which scored in obesity this week, while trials in Nash and heart failure with preserved ejection fraction are ongoing.

Novo leads in type 2 diabetes					
Product	**Company**	**Mechanism of action**	**Admin route**	**Indication sales ($bn)**	
				2022e	**2026e**
Ozempic (semaglutide)	Novo Nordisk	GLP-1 receptor agonist	Injection	6.4	9.0
Trulicity	Lilly	GLP-1 receptor agonist	Injection	7.2	6.2
Tirzepatide	Lilly	GLP-1/GIP dual agonist	Injection	0.1	5.4
Rybelsus (semaglutide)	Novo Nordisk	GLP-1 receptor agonist	Oral	1.5	4.9
Jardiance	Boehringer Ingelheim	SGLT2 inhibitor	Oral	3.6	4.9
Source: Evaluate Pharma.					

Label expansion

Astra and Daiichi's Enhertu looks set for approval in second-line Her2-positive breast cancer. Data at last year's Esmo showed a highly significant 72% reduction in risk of progression versus Roche's rival antibody-drug conjugate Kadcyla in the Destiny-Breast03 study.

The partners need Enhertu's well-known toxicity, interstitial lung disease (ILD), to be kept under control if the drug is to sell well in early treatment lines. Education of physicians is ongoing, and rates of ILD seem to be coming down in clinical trials. In Destiny-Breast03 ILD was seen in 10.5% of patients given Enhertu, versus 1.9% with Kadcyla. This was an improvement on earlier studies, with most of the Enhertu cases grade 1 or 2.

Enhertu is approved in third-line disease under the accelerated pathway, and the confirmatory study Destiny-Breast02 is to report in the second half of the year. Subsequent approvals this year could come in Her2-low breast cancer, following success in Destiny-Breast04, on which filings are due before mid-year, and in Her2-mutated lung cancer, which is already under review.

And finally

Two decisions expected soon come after prior setbacks, namely those for Verrica's VP-102 and Axsome's AXS-05.

The latter, for major depressive disorder, missed its Pdufa date last August after the FDA issued a CMC-related deficiency letter, causing Axsome's shares to plummet 46%. And the company announced this week it is expecting a knockback for another of its products, AXS-07 for migraine, also on CMC problems.

Hopefully the AXS-05 issues are over. Axsome announced earlier this month that it had received and agreed to post-marketing requirements for the depression therapy, with FDA action now anticipated this quarter.

For Verrica it will need to be third time lucky for VP-102, after two previous knockbacks.

Initially the product, which will be called Ycanth if approved, received a CRL in 2020 owing to CMC-related requests. The second knockback a year later was due to quality issues at a contract manufacturer.

VP-102, a formulation of cantharidin delivered via a single-use applicator, is intended to treat molluscum contagiosum, a common infectious skin disease, and VP-102 is Verrica's lead product. Verrica desperately needs a win as it is light on cash. The company says its current reserves of just $70m are enough to support operations into the third quarter.

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

Notable first-time US approval decisions due in May					
Project	**Company**	**Pdufa date**	**Indication(s)**	**2026e sales by indication (SBI) ($m)**	**Note**
Vonoprazan (dual and triple therapy)	Phathom	May 3	Adults with *H pylori* infection	-	Phathom in-licensed US, European, and Canadian rights to vonoprazan (Takecab) from Takeda
MT-1186 (oral edaravone)	Mitsubishi Tanabe	May 12	ALS	-	Oral version of Radicava (intravenous infusion)
VP-102	Verrica	May 24	Molluscum contagiosum	251	See text
Miglustat	Amicus	May 29	Pompe disease	169*	Part of AT-GAA a two-component therapy with cipaglucosidase, Pdufa for second part in July
Tirzepatide	Lilly	Q2	Type 2 diabetes	5,441	See text
Tapinarof	Dermavant	Q2	Plaque psoriasis	-	-
AXS-05	Axsome	Q2	Major depressive disorder	582	See text
Bimzelx	UCB	H1	Plaque psoriasis	953	Decision delayed in Oct owing to Covid travel restrictions
Annik (penpulimab)	Akeso/Sino	Est H1	3L nasopharyngeal carcinoma	-	*Go or no go? Bristol's first-in-class hopes*
**Forecasts for AT-GAA. Source: Evaluate Pharma & company releases.*					

Supplementary and other notable approval decisions due in May			
Product	**Company**	**Indication (clinical trial)**	**Date**
Tyvaso DPI	Mannkind/ United Therapeutics	PAH and pulmonary hypertension associated interstitial lung disease	May (resubmitted, previous CRL)
Myfembree	Pfizer/ Myovant	Moderate to severe pain associated with endometriosis (Spirit 1, Spirit 2)	May 6 (delay likely as deficiencies noted)
Evrysdi	Roche/ PTC	Pre-symptomatic infants under 2 months old with spinal muscular atrophy (Rainbowfish)	Estimated May 25
Opdivo + Yervoy, Opdivo + chemo	Bristol Myers Squibb	1L unresected advanced, recurrent or metastatic oesophageal squamous cell carcinoma (Checkmate-648)	May 28
Enhertu	Astra/Daiichi	Her2+ve breast cancer after anti-Her2-therapy (Destiny-Breast 03)	Q2
Olumiant	Lilly	Treatment of certain hospitalized patients with Covid	Q2 (already has EUA)
Kymriah	Novartis	3L FL (Ph2 Elara)	Pending
Source: Evaluate Pharma & company releases.			

More from Evaluate Vantage

Evaluate HQ
44-(0)20-7377-0800

Evaluate Americas
+1-617-573-9450

Evaluate APAC
+81-(0)80-1164-4754