Evaluate Vantage

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Big pharma’s key third-quarter data

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GSK takes on arthritis and Roche aims for convenience, while Pfizer is set to report infant pneumococcal vaccine data.

Delving into big pharma’s key upcoming data sees GSK trying its luck in rheumatoid arthritis with otilimab, an anti-GM-CSF MAb; this class is littered with setbacks in the autoimmune condition.

For Roche, convenience could help crovalimab gain market share in paroxysmal nocturnal haemoglobinuria, assuming data are positive. Meanwhile Pfizer will hope to unlock the important infant market with results on its latest pneumococcal vaccine, Prevnar 20.

Vaccine dominance

The childhood market makes up around 80% of pneumococcal vaccine sales, and three global studies in infants are expected to report soon on **Prevnar 20**, **Pfizer’s** 20-valent conjugate vaccine.

There is a three-dose regimen, a four-dose regimen and a safety study that also uses four doses. All three global trials use Pfizer’s earlier 13-valent vaccine, Prevnar 13, as control. Separately, an infant study run in Japan that was pegged for data in the first half is yet to report.

Merck & Co is ahead in the infant space with its latest contender, Vaxneuvance. Though this is only a 15-valent conjugate vaccine it received an FDA approval just last week, and has provisional recommendation from the CDC's advisory committee on immunisation practices.

Others are trying to trump Pfizer’s 20-valent offering. Merck itself has a 21-valent vaccine, V116, which is expected to start phase 3 in adults soon, while GSK and Vaxcyte both have 24-valent contenders in phase 1/2, the former via its recent purchase of Affinivax. For now Pfizer’s dominance looks set to continue, with the sellside expecting the company to have the top-selling vaccine franchise in 2028.

Pfizer's dominance in pneumococcal vaccines				
			Annual sales ($m)	
Product	**Company**	**Type**	**2022e**	**2028e**
Prevnar franchise	Pfizer	Prevnar 13: 13-valent conjugate vaccine Prevnar 20: 20-valent conjugate vaccine	5,509	6,752
Vaxneuvance	Merck & Co	15-valent conjugate vaccine	199	1,341
Pneumovax	Merck & Co	23-valent polysaccharide vaccine*	853	762
**Polysaccharide vaccines, first approved in 1983, are less immunogenic than conjugate vaccines. Source: Evaluate Pharma, June 23.*				

Right target?

GSK's otilimab has already been discontinued in Covid, and next up is its test in rheumatoid arthritis.

Three phase 3 trials in moderate-to-severe disease are due to yield data: Contrast 1, 2 and 3 . These 52-week studies will compare 90mg and 150mg of subcutaneous otilimab against placebo, the Jak inhibitor Xeljanz, or the anti-IL-6 MAb Kevzara.

All are given in combination with methotrexate or other DMARDs. The primary endpoint for all the studies is the proportion of patients achieving a 20% improvement in American College of Rheumatology criteria (ACR20) at week 12 versus placebo.

The earlier phase 2 Baroque study missed its primary endpoint, remission defined as a disease activity score (DAS28(CRP)) of less than 2.6 at week 24. At the time the company called this an "unusual endpoint to be used in phase 2" and blamed underpowering.

However, GSK did claim a benefit on ACR20, and pointed to a placebo-adjusted 40.5% response rate at the highest dose, 180mg – which is not being tested in phase 3.

Still, this result compares favourably against Abbvie's Rinvoq, which showed a placebo-adjusted ACR20 of 28-37% across three studies.

The rheumatoid arthritis market is incredibly crowded, and several companies that once pursued anti-GM-CSF MAbs are no longer doing so: Humanigen's lenzilumab, Roivant's namilumab and gimsilumab (via its Kinevant business), and Kiniksa's mavrilimumab all look to have been discontinued.

Aiming for convenience

Meanwhile, **Roche** hopes to challenge Astrazeneca's dominance of the paroxysmal nocturnal haemoglobinuria market with **crovalimab**, which is given subcutaneously, rather than intravenously like Astra's Ultomiris and Soliris.

Data are due from three pivotal crovalimab trials. Commodore-1 is in treatment-experienced PNH patients, testing non-inferiority versus Soliris. The primary measure is mean percentage change in lactate dehydrogenase (LDH) levels, a measure of haemolysis, at weeks 21, 23 and 25.

Commodore-2 is also a non-inferiority study but in treatment-naïve patients. Here the primary measures are the percentage of participants who achieve transfusion avoidance, and those with haemolysis control at week 25. Lastly, Commodore-3 is a single-arm study in naïve patients in China. All three studies use an intravenous loading dose followed by a subcutaneous maintenance phase.

The table below contains a list of upcoming catalysts with consensus forecasts from *Evaluate Pharma.*

Clinical catalysts in Q3 2022					
Product	**Company**	**Therapy area**	**Catalyst**	**2028e indication sales ($m)**	**Note/Vantage coverage**
Prevnar 20	Pfizer	Pneumococcal infection (vaccine)	Three ph3 global studies, H2 (see text for trials)	6,752 (Prevnar franchise)	See text

Clinical catalysts in Q3 2022					
Tecentriq	Roche	Neoadjuvant NSCLC (stage II-IIIb)	Ph3 Impower-030 data	4,906*	*Bristol leapfrogs Roche in lung cancer*
Donanemab	Lilly	Early symptomatic Alzheimer's disease	Topline from Trailblazer-Alz 4, vs Aduhelm, H2	2,586	Trailblazer-Alz 2 ph3 data '23, Biogen's lecanemab data Q3, and Roche's gantenerumab Q4
Lumakras	Amgen	NSCLC with Kras G12C mutation after at least one systemic therapy	Ph3 Codebreak-200 (confirmatory study)	2,003*	Gained accelerated approval in '21; Mirati's adagrasib has a Dec Pdufa date & confirmatory data '23
RSVpreF (PF-06928316)	Pfizer	RSV (vaccine)	Ph3 maternal protection trial, ph3 Renoir in adults ≥60	640	Delayed from H1, GSK has claimed a win in adults, J&J data also H2 (*Outstanding questions overshadow GSK's RSV virus win*)
Otilimab	GSK	RA	Ph3 Contrast 1, 2 + 3	541	See text
Jemperli	GSK	2L and 1L endometrial cancer	Ph3 Garnet for conversion to full approval, Ruby in 1L disease	402*	Accelerated approval in '21 in 2L MMRd endometrial cancer
Camizestrant	Astrazeneca	2L+ ER+ Her2- breast cancer	Serena-2 H2 (30-40% of patients are expected to be ESR1-positive)	351	Oral Serd, enriching for ESR1 mutation could be key (*Close encounters of the Serd kind*)
Capivasertib	Astrazeneca	Locally advanced/metastatic HR+/HER2 breast cancer	Ph3 CAPItello-291	316	Concerns following failure of Roche's Akt inhibitor ipatasertib (*Why ipatasertib is not the Akt Astra wants to follow*)
Insulin icodec/ LAI287	Novo Nordisk	Type 2 diabetes	Ph3a Onwards 3 (vs degludec), 4 (vs glargine + aspart), 5 (insulin naïve using app-based dosing recommendations)	186	Once weekly, Onwards 1, 2 & 6 met primary endpoints but icodec has shown high rates of hypoglycaemia; Lilly's LY3209590 (BIF) has started ph3

Clinical catalysts in Q3 2022					
					GSK claimed a win with its vaccine in adults; Pfizer data also H2 (*Outstanding questions overshadow GSK's RSV virus win*)
Ad26.RSV.preF (VAC18193)	Johnson & Johnson	RSV (vaccine)	Ph3 Evergreen H2 in adults ≥60	109	
PF-06480605	Pfizer	Moderate-to-severe UC	Ph2 Tuscany-2	12	TLA1 MAb
Tiragolumab + Tecentriq	Roche	2L+ PD-L1+ cervical cancer, 1L oesophageal cancer	Ph3 Skyscraper-04 (cervical), Skyscraper-08 (oesophageal), H2	-	Two Skyscraper studies failed (*Looking beyond Roche's Tigit bombshell*)
Cagrilintide + semaglutide (Cagrisema)	Novo Nordisk	Type 2 diabetes	Ph2	-	Cagrilintide is an amylin receptor agonist (Cagrisema ph3 expected to start in obesity in Q4)
Crovalimab	Roche	PNH	Ph3 Commodore 1 (treatment experienced, H2H vs Soliris & switching study), 2 (treatment naive, vs Soliris), 3 (treatment naive, China only)	-	See text
Iptacopan (LNP023)	Novartis	PNH	Ph3 Apply-PNH H2	-	Oral complement factor B inhibitor, Biocryst's BCX9930 on pause due to adverse events
Lumakras	Amgen	Advanced solid tumours with KRAS p.G12C mutation	Ph1/2 Codebreak-101, + Keytruda or + RMC-4630 (SHP2), expected late summer, possibly at World Lung	-	Will determine whether Lumakras has potential beyond its current label
Elranatamab (PF-06863135)	Pfizer	Triple class refractory multiple myeloma	Pivotal MagnetisMM-3, H2	-	BCMAxCD3 bispecific; ph1 MagnetisMM-1 showed ORR of 75% & CR of 30% at top 2 dose levels
Talzenna + Xtandi vs Xtandi	Pfizer	1L all comers, metastatic CRPC	Pivotal Talapro-2	-	Parp inhibitor (*Asco-GU – prostate cancer Parps move to the front line*)

**Already on the market in different settings. Source: clinicaltrials.gov, company releases & Evaluate Pharma 23 June*

23 June.

Clinical catalysts in Q3 2023

Check out our podcast discussing third quarter catalysts here.