Evaluate Vantage

September 28, 2020

Fourth-quarter events to watch for big pharma

Joanne Fagg

Oncology dominates upcoming catalysts, while results elsewhere are expected in Alzheimer's, psoriasis and diabetes.

Heading towards the end of 2020, a year dominated by Covid-19, *Evaluate Vantage* has delved into data releases expected from big pharma in the fourth quarter. Excluding readouts expected from coronavirus therapies and vaccines, oncology looks to dominate with Astrazeneca, Gilead, Takeda and Glaxosmithkline all due to unveil important updates.

Elsewhere Alzheimer's comes into play for Roche, while both Bristol Myers Squibb and Pfizer have Tyk2 inhibitors in development for psoriasis, on which the first data are pending. The first look at Lilly's GIP/GLP-1 agonist tirzepatide should also emerge.

Astrazeneca's immunotherapy **Imfinzi** is well established in stage III NSCLC, but only after chemoradiotherapy (CRT). Data are expected from Pacific-2 in an earlier setting − Imfinzi will be given with CRT versus CRT alone. The primary endpoint is PFS.

The hope is that Pacific-2 can help defend against competitors aiming to beat the efficacy achievable with Imfinzi after CRT, as well as those targeting the earlier population. Data at Asco from Merck & Co's Keytruda showed a 56.6% remission rate, and six-month overall survival of 94.8%, in the Keynote-799 study where Keytruda was given with CRT, though this was an uncontrolled study.

Data are also expected from **Imfinzi** in first-line liver cancer. The Himalaya trial tests Imfinzi as a monotherapy, or in two combinations with the anti-CTLA-4 agent tremelimumab, against Nexavar; the primary outcome is overall survival.

The readout will draw comparisons with Imbrave-150, which led to the approval of Roche's Tecentriq plus Avastin as a first-line treatment, which reduced risk of death by 42% (p=0.0006) and cut the risk of disease worsening or death by 41% (p<0.0001) versus Nexavar.

Jefferies analysts note that Imfinzi monotherapy could beat Nexavar, but it will be difficult to beat Tecentriq's combination results. Prior failures with Imfinzi plus tremelimumab in various cancer settings mean that expectations are low for the Astra combination.

Elsewhere in cancer

Takeda's pevonedistat, a first-in-class NEDD8-activating enzyme (NAE) inhibitor, should yield phase III data soon. The aim is to improve on the chemotherapy drug Vidaza, with pevonedistat given in combination versus

Vidaza alone.

The Panther study is in 454 patients with high-risk myelodysplastic syndromes (MDS), chronic myelomonocytic leukaemia, or low-blast AML. The primary endpoint is event-free survival, with OS a secondary measure.

Phase II data were reported at this year's Asco, and showed benefit particularly in 67 patients in the high-risk MDS subgroup in terms of event-free survival, the primary endpoint. The results were 20.2 months versus 14.8 months, but in the intent-to-treat population the difference in event-free survival was not statistically significant.

Gilead's anti-CD47 MAb **magrolimab** has shown impressive response data in MDS in a phase Ib study. MDS is the project's most advanced indication, with the phase III Enhance trial under way, but DLBCL data are expected in the fourth quarter. The results, likely at the Ash conference in December, will come from a phase I/II study testing magrolimab in combination with Rituxan.

Magrolimab was gained through Gilead's $4.9bn acquisition of Forty Seven; two months after that deal **Gilead** bought a stake in Arcus Biosciences to gain access to the biotech's cancer pipeline, data from which are expected next quarter.

Arc-7 is a phase II study in PD-L1-positive NSCLC patients. The trial has three arms: monotherapy with the checkpoint inhibitor **zimberelimab**, zimberelimab plus the anti-Tigit MAb **AB154**, and lastly both plus **AB928**, an adenosine A2B receptor antagonist. Arcus intends to disclose data for half of the patients, approximately 25 in each arm.

The Tigit mechanism has generated interest from Merck and Roche, with the latter having the most advanced candidate, tiragolumab. As a benchmark for Arcus's upcoming data Roche's Cityscape trial showed the highest overall remission rate in PD-L1 high (≥50%) patients in combination with Tecentriq − 55.2% versus Tecentriq's 17.2%. There was no clinical benefit in PD-L1-low patients.

Through the Arcus deal Gilead gained immediate rights to zimberelimab, but should the Arc-7 data prove competitive Mizuho analysts see Gilead exercising opt-in rights for AB154, with a broader development strategy following shortly.

Oncology aside there are several readouts due from **Roche's** beta-amyloid MAbs in Alzheimer's; last week the company's anti-tau MAb semorinemab failed in phase II. Elsewhere two Tyk2 inhibitors will generate data, with **Bristol Myers Squibb** leading the pack here and **Pfizer** following in psoriasis.

Check out the table below for a full list of upcoming catalysts with consensus forecasts from *EvaluatePharma.*

A look at catalysts for biotech and the smallest companies have also been published.

Selected Q4 clinical catalysts (excludes Covid-19 data)

Product	Company	Therapy area	Q4 catalyst	2026e indication sales ($m)	Note/Vantage coverage
Imfinzi + platinum-based CRT	Astrazeneca	Stage III NSCLC	Pacific-2	3,296	See text
Skyrizi (risankizumab)	Abbvie	Crohn's disease and psoriatic arthritis	Ph3: crohn's disease induction (Motivate), psoriatic arthritis (Keepsake2)	2,440	Crohn's disease forecasts make up over a third of Skyrizi's 2026 sales
Tirzepatide	Lilly	Type 2 diabetes	Surpass-1 (first of five trials from Surpass program)	2,202	*Tirzepatide's time to shine for Lilly*
BMS-986165	Bristol Myers Squibb	Psoriasis	Ph3, Poetyk-PSO-1, vs placebo & vs Otezla	1,810	*Bristol hopes to Tyk the psoriasis box*
Blenrep (+ two		2L multiple			Approved in later setting with black

Selected Q4 clinical catalysts (excludes Covid-19 data)					
SOC regimens)	Glaxosmithkline	[illegible] myeloma	Ph2 Dreamm-6	1,213	box warning and REMS programme
Tezepelumab	Astrazeneca/ Amgen	Severe non-eosinophilic asthma	Ph3 Navigator	1,021	Previous failure in atopic dermatitis, *Amgen and Astra hope to carve out a place in asthma*
Pevonedistat (TAK-924) +/- azacitidine	Takeda	Higher-risk myelodysplastic syndromes	Ph3 Panther	634	See text
Faricimab	Roche	Diabetic macular edema	Ph3 Yosemite, Rhine, vs Eylea	610	Showed improvement over Lucentis in Ph2, tougher test against Eylea
AB154 + zimberelimab +/- AB928	Gilead/Arcus	1L NSCLC	Ph2 Arc-7	460	See text
Omecamtiv mecarbil + SOC	Amgen/ Cytokinetics	Chronic heart failure with reduced ejection fraction	Ph3 vs SOC; data at AHA (Nov 14-16)	422	>8,000-patient trial, primary endpoint time to CV death or first heart failure event
Imfinzi +/- tremelimumab	Astrazeneca	1L liver cancer	Himalaya	129	See text
Magrolimab + Rituxan	Gilead	DLBCL	Ph1/2 data likely at Ash (Dec 5-8)	72	See text
Gantenerumab	Roche	Alzheimer's disease (prodromal)	Ph3 Scarlet Road	72	*Alzheimer's catalysts round off a year dominated by Biogen*
Gantenerumab (brain shuttle) / RG6102	Roche	Healthy volunteers	Ph1	-	
PF-06826647	Pfizer	Psoriasis	Ph2 proof-of-concept	-	Tyk2 inhibitor, ~2yrs behind BMS-986165
Pentraxin-2 (RG6354, PRM-151)	Roche	Myelofibrosis	Ph2	-	1st-in-class rhPTX-2, has BTD in for IPF with ph3 to start Q4

Sources: Evaluatepharma, clinicaltrials.gov, company releases & analyst notes.