Evaluate Vantage

June 22, 2020

Third-quarter events to watch for large drug makers

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Biogen's aducanumab filing is keenly awaited, as are clinical data from Sanofi, Bristol Myers Squibb, Lilly and others.

As the second quarter comes to a close *Evaluate Vantage* delves into non-Covid-19-related catalysts due next quarter for large drug makers. One of the most keenly awaited events is not clinical data but a filing for **Biogen's** Alzheimer's projecr **aducanumab.** Biogen had previously guided to a submission earlier in the year, but a delay announced in April saw shares fall over 9%.

The submission will be based on the Emerge and Engage studies whose reanalysis claimed to have teased out an efficacy signal if dosing was high enough for long enough. An advisory committee will no doubt be called, to scrutinise the statistical rigour of the analysis and aducanumab's toxicity profile, although first the FDA must accept the filing.

Just last week Biogen lost a patent dispute with Mylan over its multiple sclerosis drug Tecfidera, making it even more reliant on aducanumab.

The company, which has been criticised for its thin pipeline, also expects a readout on a mid-stage Parkinson's candidate in the second half. **BIIB054,** an anti-alpha synuclein MAb, is in the phase II Spark study whose primary measure is safety. Key secondary measures are geared towards the pharmacodynamic effects of BIIB054 on dopaminergic nerves, as well as pharmacokinetics and immunogenicity.

Another anti-alpha synuclein MAb, Roche/Prothena's prasinezumab, has previously reported mixed results. The ongoing phase II Pasadena study failed to meet the primary endpoint of change in MDS-UPDRS after 52 weeks, but did show signs of efficacy in secondary and exploratory endpoints looking at cognitive and other markers of disease. The 52-week blinded extension is ongoing.

Oncology

A test of **Sanofi's** $2.3bn Synthorx acquisition is expected in the second half of the year, with data from **Thor-707** in the phase I/II Hammer trial. As a non-alpha IL-2, Thor-707 should avoid triggering vascular leak syndrome, a serious side effect that has been attached to IL-2 therapies, and the Hammer study primarily looks at toxicities.

Thor-707 is being investigated as a single agent and in combination with an unspecified PD-(L)1 agent in solid tumours; a combination with Sanofi's own Libtayo is likely. Libtayo was approved in 2018, making it a late

entrant to a very competitive market, so a combination with Thor-707 could differentiate it. Combining IL-2 treatment with PD-(L)1 inhibition is thought to enhance CD8+ T-cell responses, giving greater antitumour effects than checkpoint blockade alone.

In first-line liver cancer **Astrazeneca's** Himalaya trial is expected to report soon. The study tests **Imfinzi** as a monotherapy, or in two combinations with the anti-CTLA-4 agent **tremelimumab**, against Nexavar; the primary outcome is overall survival.

Earlier this month the first immunotherapy was approved in a front-line liver cancer setting − Roche's Tecentriq/Avastin combo, backed by the Imbrave-150 study. The combination reduced risk of death by 42% (p=0.0006) and cut risk of disease worsening or death by 41% (p<0.0001) versus Nexavar.

Fibrosis

Bristol Myers Squibb's turn in Nash is with the FGF21 stimulant **pegbelfermin**. The phase IIb Falcon 1 study could report in the second half, while a second, longer-term study has a primary completion date in September.

Falcon 1 is testing three doses and is a 24-week trial. The primary endpoints include ≥1 stage improvement in fibrosis without worsening of Nash, and Nash improvement with no worsening of fibrosis as determined by liver biopsy. Fibrosis and activity scores are two further primary measures.

In a phase IIa study once-weekly pegbelfermin at 20mg reduced hepatic fat fraction by a placebo-adjusted 3.9 percentage points (p=0·008).

Akero is developing a similar agent, AKR-001, and in April reported impressive MRI data. The relative reductions in liver fat were 63% to 72% versus baseline for the three AKR-001 doses tested. Biopsy data were pegged for the second quarter, so could come any day now.

The table below shows additional third-quarter events for large drug makers. A look at catalysts for smaller companies will be published in the coming days.

Selected Q3 clinical catalysts (excludes Covid-19 data)					
Project	**Company**	**Therapy area**	**2026e indication sales ($m)**	**Q3 event**	**Evaluate Vantage note/*story link***
Aducanumab	Biogen/Eisai	Alzheimer's disease	2,987	Expected to complete filing in Q3, based on Engage and Emerge data	See text
Ide-cel	Bristol Myers Squibb/Bluebird	Multiple myeloma	1,452	Filing will be resubmitted by the end of July (part of the Celgene CVR)	RTF letter received in May (*Another knock for the Celgene contingent value right*)
Yescarta	Gilead	Diiffuse large B-cell lymphoma	1,331	Zuma-7, versus SOC, data H2	Seeks to expand Yescarta's lymphoma use from third to second line
Bimekizumab	UCB	Psoriasis	947	Be Radiant phase III head-to-head vs Cosentyx	*UCB's growth driver squares up against the competition*
Imfinzi + tremelimumab	Astrazeneca	1L liver cancer	124	Himalaya, H2	See text
BIIB054 (cinpanemab)	Biogen	Parkinson's disease	26	Phase II Spark, H2	See text
Thor-707	Sanofi	Solid tumours	11	PhI/II Hammer, H2	See text
Pegbelfermin	Bristol Myers Squibb/Ambrx	Nash	7	Falcon 1 study, primary completion was April (Falcon 2 primary completion September)	See text
Mevidalen/LY3154207 (D1 PAM)	Lilly	Lewy Body Dementia	5	Phase II Presence, primary completion July	Dopamine D1 positive allosteric modulator, 340 patient trial with three doses vs placebo

EvaluatePharma sales by indication data. Source: company releases, analyst notes & clinicaltrials.gov.