Evaluate Vantage

June 24, 2020

Important catalysts approach for smaller biotechs

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Crucial clinical data are expected in the third quarter for small to mid-sized players including Beigene, Turning Point, Intra-cellular and Immunovant.

With the third quarter nearly upon us *Evaluate Vantage* has looked at important events approaching for the smaller players – those with a market cap between $1.5bn and $14bn. While the filing for Biogen's controversial Alzheimer's project dominated the catalysts for the larger drug makers, here nearly half of upcoming data reveals are oncology-related.

One such event is **Beigene's** Sequoia trial of **Brukinsa**, a BTK inhibitor, in treatment-naive chronic or small lymphocytic lymphoma. The expected data are from cohort one, made up of 420 subjects without the difficult-to-treat 17p deletion. Here Brukinsa is up against Treanda plus Rituxan, and the primary endpoint is progression-free survival.

Data released at Ash on 109 patients with the 17p deletion showed that Brukinsa monotherapy, at a median follow-up of 10 months, yielded an overall response rate of 93%, including a complete remission rate of 1.9%. 36.7% of patients experienced a serious adverse event, the most common being neutropenia, pneumonia and hypertension. There was also one treatment-related death.

Brukinsa is approved for relapsed/refractory mantle cell lymphoma, but CLL is a bigger opportunity. However, the market is dominated by Abbvie and J&J's BTK inhibitor Imbruvica. Leerink analysts reckon that, if Brukinsa can confirm better safety than Imbruvica on atrial fibrilliation and major haemorrhage, Beigene could start to take market share.

Notably Alpine, a head-to-head study against Imbruvica, should read out next year, this time in relapsed/refractory CLL.

Sticking with oncology, **Turning Point's** selective kinase inhibitor **repotrectinib** is in a registrational phase II study, Trident-1, in advanced solid tumours harbouring Ros1, NTRK or ALK rearrangements, including subjects who have failed prior therapies. The third quarter will see preliminary data from 30-40 patients across multiple cohorts.

In the trial's phase I portion there was a 91% overall response rate in tyrosine kinase inhibitor-naive Ros1-positive NSCLC. The ORR was 36% for pretreated patients.

Treatments are needed for patients failing front-line drugs like Pfizer's Xalkori. However, repotrectinib has exhibited some worrying toxicities, the earlier data showing that around half of patients experienced dizziness. A case of sudden death has also been judged possibly related to treatment.

Other therapy areas

Elsewhere, Study 402 tests **Intra-cellular's Caplyta** as an adjunctive treatment in depressive episodes associated with bipolar-I or bipolar-II disorder. 520 patients are enrolled and are taking the mood stabilisers lithium or valproate.

The drug already has one positive global trial, study 404, in the bag, but a US trial, study 401, failed. Both tested Caplyta monotherapy; the 401 failure was said to be due to a high placebo response.

Intra-cellular hopes to file on a single positive trial, possibly with supportive data, so even if the latest study, 402, misses statistical significance the idea is that it could still provide the support. Caplyta is approved in schizophrenia, but bipolar is a bigger opportunity; if the label only permits adjunct use this would limit its market.

Immunovant's IMVT-1401 is an anti-FcRn MAb being tested in myasthenia gravis, an IgG-driven autoimmune condition. Immunovant could have the edge over competitors as its project is subcutaneous and so far other groups have only released data from intravenous therapies.

Immunovant's phase II Ascend-MG trial has given 21 patients once-weekly 340mg or 680mg IMVT-1401 versus placebo for six weeks. The primary outcome measure includes safety and changes in baseline IgG levels. MG-ADL, a change on symptom scale, is a secondary endpoint.

Competing trials have shown placebo-adjusted response rates on MG-ADL of 40% for Argenx's efgartigimod, and 36.5% for Momenta's nipocalimab. Both have subcutaneous versions in earlier development, while UCB's own version, rozanolixizumab, has phase III data due next year.

The following table notes additional third-quarter events for mid-sized groups. *Evaluate Vantage* has separately assessed expected catalysts for larger drug makers, and a further analysis covering companies with a market cap below $1.5bn will follow.

Q3 clinical catalysts (excludes Covid-19 data) for companies with market cap $1.5-14bn*					
Project	**Company**	**Therapy area**	**2026e indication sales ($m)**	**Q3 clinical catalyst**	**Vantage note/*story* link**
Trodelvy	Immunomedics	Breast cancer	2,154	Topline from confirmatory Ascent trial	Ascent terminated early for efficacy; Trodelvy gained accelerated approval
LN-144 (lifileucel)	Iovance	Melanoma	1,473	Pivotal phase II NCT02360579	Primary endpoint disclosure from cohort 4, which Iovance expects to support US filing
Caplyta (lumateperone)	Intra-Cellular Therapies	Bipolar depression adjunct	1,086	Phase III study 402	See text
Brukinsa (zanubrutinib)	Beigene	1L CLL	1,018	Topline results from cohort 1 of Sequoia	See text
Sage-217 (zuranolone)	Sage	Major depressive disorder	1,012	Topline from phase III Shoreline study	Mountain study failed; Shoreline studies zuranolone as needed retreatment
				6mth data from	Positive data from four-week

Q3 clinical catalysts (excludes Covid-19 data) for companies with market cap $1.5-14bn*

Trans[illegible]	[illegible]	[illegible]	[illegible]	[illegible] open-label extension of Path forward trial	[illegible] portion; ph3 starts in Q4
Repotrectinib	Turning Point	Solid tumours	795	Phase II portion of pivotal Trident-1 study in ROS1+ NSCLC	See text
Nuplazid (pimavanserin)	Acadia	Major depressive disorder adjunct	766	Combination of Clarity-2 and Clarity-3, with pre-specified analyses	If positive company will submit sNDA with phase II Clarity-1 study, if negative another ph3 starts in H2
Zepzelca (lurbinectedin)	Jazz/ Pharmamar	2L SCLC	399	Confirmatory ph3 Atlantis (doxorubicin combo)	Accelerated approval as monotherapy based on a single-arm study
Ublituximab	TG	Relapsing-remitting MS	239	Phase III Ultimate I and II trials, data H2	Pivotal data
Voclosporin Ophthalmic Solution	Aurinia	Dry eye syndrome	223	Phase II/III Audrey, dose ranging trial	Previous phase II showed superiority vs Restasis
IMVT-1401	Immunovant	Myasthenia gravis	222	Phase IIa Ascend-MG	See text
Vynpenta (avacopan)	Chemocentryx/ Vifor	Hidradenitis suppurativa	72	Phase IIb Aurora	Filing expected mid-year; Inflarx's similarly acting IFX-1 failed last year
Cabometyx	Exelixis	Thyroid cancer	-	Pivotal phase III Cosmic-311 trial, H2	Interim ORR and PFS data due for first 100 subjects

**Market cap date June 22, 2020. Sources: EvaluatePharma sales by indication data, company releases, analyst notes & clinicaltrials.gov.*