Evaluate Vantage

August 09, 2019

Upcoming events – United seeks a Distinct hit, and Biogen nears a rare catalyst

Jacob Plieth

A low-key lung cancer readout approaches for United Therapeutics' Unituxin, while Biogen hopes to buck the tau trend.

Welcome to your weekly roundup of approaching clinical readouts. While investors tracking clinical trials in small-cell lung cancer are focusing on pivotal data from front-line studies of Keytruda and Zepsyre, due in 2019/early 2020, and the September presentation of data from Astrazeneca's Caspian trial of Imfinzi, one project remains a completely unknown quantity in this setting.

This is United Therapeutics' dinutuximab, an NCI-originated anti-GD2 MAb that, excluding Abbvie's ill-fated Rova-T, is the only industry asset in an active phase III SCLC study.

The trial, named Distinct, has overall survival as its primary endpoint, while safety and other measures of efficacy such as PFS and remission rate, are secondaries. It adds dinutuximab on top of irinotecan in 485 second-line subjects, and is due to read out in November, according to clinicaltrials.gov.

It seems strange that United, a company focused on pulmonary arterial hypertension, should be developing a project like dinutuximab. But the drug is in fact already approved, under the trade name Unituxin for the second-line treatment of children with high-risk neuroblastoma.

The rationale for testing it in lung cancer hinges on the theory that GD2 is expressed on SCLC tumours. But there is virtually no clinical data available to back its efficacy, and Distinct does not seem to have GD2-positivity as an inclusion criterion. The drug is known to be rather toxic, and one of its few published datasets concerns a safety study in 12 SCLC subjects.

On its second-quarter earnings call last week United said it hoped to hit the necessary final number of events in Distinct sometime later this year, and the trial not having already been stopped for futility at one of its interim analyses is some comfort.

EvaluatePharma sellside consensus shows no Unituxin sales forecasts from SCLC, which likely reflects both the intractability of the disease and the fact that the drug remains under the radar of most of the company's followers.

Study	Design	Trial ID
Distinct	Dinutuximab + irinotecan vs irinotecan in 485 2nd-line SCLC subjects	NCT03098030

Tau time for Biogen

Biogen, meanwhile, is approaching the readout of a phase II trial of its tau MAb BIIB092 in progressive supranuclear palsy (PSP) in the full knowledge that the market's expectations of success have been significantly reduced since the failure in July of Abbvie's tau antibody ABBV-8E12 in the same indication.

If BIIB092 is also a dud Biogen's shares, already weakened by the failure of the group's Alzheimer's candidate aducanumab, could be in further trouble. With growth in the core business slowing, the BIIB092 readout represents one of the few big catalysts for Biogen's stock ahead of the critical inter partes review ruling for its multiple sclerosis blockbuster Tecfidera in 2020.

PSP is a neurodegenerative disease characterised by tau accumulation in the brain. The 459-patient, placebo-controlled Passport study, due to report this half, has co-primary endpoints of change from baseline in the PSP rating scale at week 52, and the proportion of patients who die or suffer serious adverse events.

What might give some investors hope, despite ABBV-8E12's failure, is that BIIB092 has shown a dose-dependent increase in N-terminal tau suppression in a previous phase I study. Still, according to Stifel analysts it is an open question whether antibodies like BIIB092 can clear tau from the brain, as the protein largely accumulates inside neurons.

If Passport does succeed against the odds the data could support a regulatory filing, Biogen stated during its most recent earnings call. And a win could also bode well in Alzheimer's, where BIIB092 is being tested in the phase II Tango trial.

However, given the numerous failures in Alzheimer's, the chances of success here look even slimmer than in PSP. The current consensus forecast for BIIB092's 2024 sales is just $63m, according to *EvaluatePharma*.