MARKET WATCH

Upcoming market catalysts in Q3 2012

In the next 3 months, initial trial data are due to be reported for three drugs that are designed around unproven molecular targets and that have faced substantial challenges in development. A positive trial result could drastically alter the outlook for these drugs as well as similar drugs in their novel target classes.

First, data are expected from two pivotal Phase III studies of bapineuzumab, an antibody that binds to and clears amyloid-β, which is being developed for the treatment of Alzheimer's disease by Johnson & Johnson and Pfizer. Although the accumulation of amyloid-β plaques is a hallmark of Alzheimer's disease, the causative role of plaque accumulation in disease development is not well established, and it is not clear whether reduction of amyloid-β can reverse the course of the disease. Indeed, decades of research surrounding this potential target has so far failed to result in any effective therapeutics.

Perhaps not surprisingly then, previous data from several Phase II trials evaluating bapineuzumab have been relatively weak, revealing some improvements in protein markers of disease progression (such as levels of phosphorylated tau) but no significant improvements in cognitive measures. Nevertheless, the pivotal Phase III studies (known as 301 and 302) are near completion, and the first data releases are expected in the third quarter of this year. Any positive efficacy signals would be a remarkable development in the treatment of Alzheimer's disease.

Second, initial data are expected from a Phase IIb study (known as SUSTAIN) of Resverlogix's RVX-208 for the treatment of atherosclerosis. RVX-208 is Resverlogix's only drug in clinical development and inhibits BET bromodomains, which leads to increased production of apolipoprotein A1 (APOA1), a key component of high-density lipoprotein (HDL) cholesterol (also known as 'good' cholesterol), that could ultimately result in reductions in low-density lipoprotein (LDL) cholesterol (also known as 'bad' cholesterol). Results from a dose-ranging study known as ASSERT were generally mixed, with modest increases in APOA1 and HDL cholesterol observed in some dosing arms, but much less so than observed with cholesteryl ester transfer protein (CETP) inhibitors — another unproven drug class in development. Importantly, no significant reductions in LDL cholesterol were observed, and some liver toxicity was reported. However, the SUSTAIN study enrolled patients with lower baseline HDL cholesterol levels, which may allow for a greater detection of any efficacy signal. Another Phase IIb study, ASSURE, is ongoing but data are not expected until the first quarter of 2013.

Last, preliminary data are expected from a Phase II combination study of Array BioPharma's ARRY-520. ARRY-520 inhibits kinesin spindle protein (KSP), which has a crucial role in proper mitotic spindle assembly during cell division and is thus a potential therapeutic target for a range of cancers. An earlier effort by Cytokinetics to develop the KSP inhibitor ispinesib failed owing to little evidence of activity for several solid tumour types. Array is focusing its efforts in multiple myeloma, where some preliminary evidence of single-agent activity was identified in a Phase I/II study. The ongoing Phase II study is evaluating ARRY-520 in combination with dexamethasone in patients who are refractory to bortezomib and immunomodulatory drugs.

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