MARKET WATCH

# Upcoming catalysts in Q2 2015

Clinical data read-outs from several Phase III oncology studies that could alter the treatment paradigms for their respective diseases are expected in the second quarter of 2015. Two programmes are led by Bristol-Myers Squibb, with results expected from pivotal studies of elotuzumab for multiple myeloma, and of nivolumab (Opdivo) for non-small-cell lung cancer (NSCLC). In addition, Exelixis expects to announce top-line data from the Phase III METEOR trial of cabozantinib (Cometriq) in patients with metastatic renal cell carcinoma (RCC).

Elotuzumab targets cleavage signal 1 protein (CS1), which is a cell surface glycoprotein that is highly expressed on myeloma cells but minimally expressed on normal cells. There is currently only one other drug in clinical development that targets CS1: PVX-410, from OncoPep. In May 2014, the US Food and Drug Administration (FDA) granted elotuzumab breakthrough therapy designation for use in combination with lenalidomide and dexamethasone for the treatment of multiple myeloma in patients who have received one or more prior therapies. Elotuzumab has demonstrated promising signs of efficacy in a Phase II study of that same combination, where a 10 mg per kg dose resulted in an 84% overall response rate. Elotuzumab is currently being evaluated in two Phase III studies — known as ELOQUENT-1 and ELOQUENT-2 — with top-line data expected in early 2015. ELOQUENT-1 is evaluating the elotuzumab combination as a first-line therapy, whereas ELOQUENT-2 is assessing effects in relapsed or refractory disease. Positive results from these studies will be not only critical for elotuzumab, but also important for the validation of treatments that target CS1.

Nivolumab, an antibody that is specific for programmed cell-death protein 1 (PD1), is part of the new wave of immune checkpoint inhibitors that is generating excitement across the oncology field. The antibody was approved to treat melanoma in December 2014, and became the first PD1 inhibitor to be approved for NSCLC in March this year. The most recent approval was based on a Phase III trial in patients with advanced squamous cell NSCLC, known as CHECKMATE 063, in which the estimated overall survival rate at 1 year for patients receiving nivolumab was 41%. This is substantially higher than the historical rate of 4.5–18% for third-line therapy in this indication, and impressive for the hard-to-treat squamous cell disease, for which there are no other approved therapies. In the second quarter of 2015, Bristol-Myers Squibb expects to announce data from another Phase III trial — known as CHECKMATE 057 — in patients with non-squamous NSCLC, which could provide the basis for nivolumab to be approved to treat this larger population of NSCLC patients as well.

The Phase III METEOR trial is testing cabozantinib as a second-line treatment in patients with metastatic RCC that has progressed after a prior treatment with receptor tyrosine kinase (RTK) inhibitors that target vascular endothelial growth factor receptors. Cabozantinib also inhibits other RTKs that have been implicated in various cancers, including mast- or stem-cell growth factor (KIT), FMS-like tyrosine kinase 3 (FLT3) and the angiopoietin 1 receptor (also known as TIE2). Cabozantinib has already gained approval for thyroid cancer, which is a small market, but it suffered a major failure in its development for the much larger prostate cancer market. Thus, the success of cabozantinib in other indications, including RCC and hepatocellular carcinoma (for which Phase III trials are also in progress) will be crucial for Exelixis, which currently has no other approved drugs in its portfolio.

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