MARKET WATCH

Upcoming market catalysts in Q1 2012

Important catalysts for the first quarter of 2012 include approval decisions on vismodegib for the treatment of adults with advanced basal cell carcinoma (BCC), and on peginesatide for anaemia associated with chronic kidney disease (CKD). Top-line Phase III data are also expected for tivozanib for the treatment of advanced renal cell carcinoma (RCC).

The US Food and Drug Administration (FDA) is expected to make a decision by 8 March 2012 regarding the accelerated approval of vismodegib for adults with advanced BCC for whom surgery is not appropriate. In this patient population there are limited treatment options with no standard of care. Vismodegib (developed by Genentech) is a first-in-class oral Hedgehog signalling pathway inhibitor. The single-arm Phase II ERIVANCE BCC study demonstrated substantial overall response rates and median duration of response in patients with advanced BCC. Serious adverse events were observed, but no fatal events were treatment-related. Given the increased scrutiny of the accelerated approval process (*Nature Rev. Drug Discov.* **10**, 797–798; 2011) and recent guidelines from the Oncologic Drugs Advisory Committee (ODAC), the FDA may require an additional randomized study to confirm the benefit–risk profile of vismodegib.


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The Prescription Drug User Fee Act (PDUFA) date for the FDA to make a decision on the approval of peginesatide, a pegylated synthetic peptide erythropoiesis-stimulating agent (developed by Affymax), is 27 March 2012. The Phase III programme for peginesatide consisted of four trials: two in dialysis patients (EMERALD 1 and 2), and two in non-dialysis patients (PEARL 1 and 2). Results from all Phase III trials showed that peginesatide had similar efficacy in maintaining haemoglobin levels within the target range using a once-monthly dosing regimen compared to a thrice-weekly regimen of epoetin. There was an observed increase in cardiovascular events in non-dialysis patients that may be explained by increased heterogeneity in non-dialysis patients with CKD and a higher baseline cardiovascular risk allowed in the PEARL trials. However, Affymax is only seeking approval for the dialysis patient population. If approved, peginesatide will be the first available once-monthly anaemia medication for patients with CKD and will substantially reduce the number of hospital visits needed for anaemia treatment. An ODAC panel voted strongly in favour (15–1 with one abstention) that both the clinical and quality-of-life benefits of peginesatide outweigh potential cardiovascular risks.

The top-line Phase III TIVO-1 results of tivozanib (developed by Aveo) for first- or second-line treatment of advanced RCC are also expected in the first quarter of 2012. Tivozanib is an oral inhibitor targeting all three vascular endothelial growth factor (VEGF) receptors. In a Phase II study, tivozanib treatment resulted in an 11.7-month progression-free survival (PFS) in all patients with advanced RCC, and a 14.8-month PFS in patients with clear-cell RCC who had undergone nephrectomy. The current first-line therapy, sunitinib malate (Sutent; Pfizer), has demonstrated an 11-month PFS in previously untreated patients with clear-cell RCC. The reported safety profile for tivozanib shows a reduction in off-target toxicities compared with other VEGF-targeted therapies. The anticipated Phase III results could support the filing of a new drug application in 2012.

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