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MARKET WATCH

Upcoming market catalysts in Q2 2018

Potential market catalysts in the second quarter of 2018 include top-line clinical trial results for NEOD001 (developed by Prothena) for light-chain (AL) amyloidosis and ALXN1210 (developed by Alexion) for paroxysmal nocturnal haemoglobinuria (PNH), as well as an FDA advisory committee meeting on volanesorsen (developed by Akcea Therapeutics) for familial chylomicronaemia syndrome (FCS).

Prothena expects top-line results from the phase IIb PRONTO study of its lead product, NEOD001, in AL amyloidosis — a haematological disease in which amyloid deposits formed from misfolded light-chain proteins produced by plasma cells accumulate in tissues and organs. NEOD001 is a monoclonal antibody (mAb) with the potential to be the first therapy approved for AL amyloidosis that neutralizes and clears misfolded light-chain aggregates and deposits. Other drugs in phase III development for AL amyloidosis target plasma cells to reduce aberrant light-chain production, which is currently treated by various off-label chemotherapeutic regimens or haematopoietic cell transplantation. It is possible that these two approaches could be used together or in different stages of treatment. The expected phase IIb results for NEOD001 will provide information on the drug's effect as a monotherapy in patients previously treated with therapies that target plasma cells. Results from a phase I/II study showed positive responses in cardiac (N-terminal pro-brain natriuretic peptide; NT-proBNP), renal (proteinuria) and neuropathy (Neuropathy Impairment Score of the Lower Limb; NIS-LL) biomarkers. If positive, the phase IIb results would help increase investor confidence in NEOD001 before results are reported from the pivotal phase III VITAL study in treatment-naive patients, which are expected in the second half of 2019.

Alexion plans to release data from the phase III - 302 (SWITCH) study, in which patients with PNH receiving its blockbuster therapy eculizumab (Soliris) either switched to the company's longer-acting ALXN1210 or remained on Soliris. These results are expected to bolster those recently released for the pivotal phase III - 301 (Naïve) study, in which the two drugs were compared in newly treated patients. PNH is a rare blood disease caused by the inability to synthesize a glycolipid that anchors many proteins to the cell surface, including some proteins that protect cells from destruction by the complement pathway. Like Soliris, ALXN1210 is a humanized mAb that inhibits complement-mediated intravascular haemolysis by binding specifically to complement protein C5. ALXN1210 has the advantage of dosing every eight weeks instead of every two with Soliris. Results from the Naïve study validated non-inferiority to Soliris on both co-primary endpoints of transfusion avoidance and normalization of lactate dehydrogenase levels as well as all four key secondary endpoints. The SWITCH study has the potential to further confirm non-inferiority and support regulatory submissions for ALXN1210 in the United States, Europe and Japan in the second half of 2018. Approval of ALXN1210 could help fend off competition from eculizumab biosimilars, which are expected to enter the market in 2021, as well as competitor drugs in development with preferential routes of administration, thereby solidifying Alexion's market dominance in PNH.

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Lastly, Akcea Therapeutics (an affiliate of Ionis Pharmaceuticals) announced that the FDA's Division of Metabolism and Endocrinology Products will hold an advisory committee meeting on 10 May 2018 to review data supporting the new drug application (NDA) for volanesorsen for the treatment of FCS. Volanesorsen is an antisense drug designed to lower triglycerides by inhibiting the production of apolipoprotein C-III, and is currently under regulatory review in the United States, Europe and Canada, with approval decisions expected by 30 August 2018, the second half of 2018 and late 2018 to early 2019, respectively. The NDA submission is based on data from the phase III APPROACH and COMPASS studies, which both met the primary end point of a mean reduction in triglycerides from baseline after 3 months and demonstrated a reduction in on-study pancreatitis attacks. One safety concern is the serious reduction in platelet count, and Akcea has implemented a monitoring system to mitigate this risk during treatment. This upcoming advisory committee meeting will help to elucidate the FDA's thoughts on the platelet issue being controllable, the potential need for further prospective data and, ultimately, the approval decision.

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Competing interests
The author declares no competing interests.