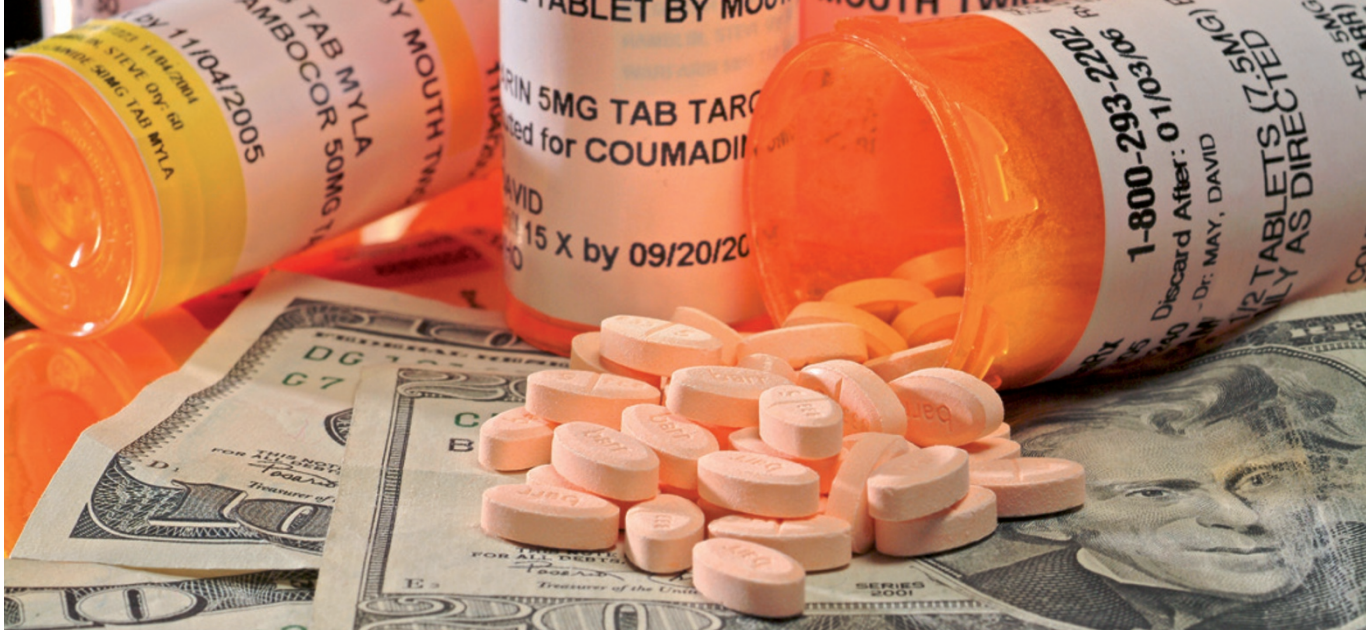

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BIOBUSINESS BRIEFS

MARKET WATCH

Upcoming market catalysts in Q3 2013

Notable market catalysts expected in the third quarter of 2013 include the first Phase III data for Regeneron's proprotein convertase subtilisin kexin 9 (PCSK9) inhibitor REGN727. In addition, decisions from the US Food and Drug Administration (FDA) are expected in July on the potential approvals of suvorexant (developed by Merck for insomnia) and afatinib (developed by Boehringer Ingelheim for non-small-cell lung cancer (NSCLC)).

PCSK9 inhibitors, which are an experimental class of drugs to lower levels of low-density lipoprotein cholesterol (LDL-C) to reduce the risk of cardiovascular disease, have shown highly promising results in Phase I and II trials. REGN727 (developed by Regeneron) and AMG145 (developed by Amgen) are the most advanced in development, with Phase III programmes initiated recently, whereas RN316 (developed by Pfizer) and RG7652 (developed by Roche) are closely behind in Phase II development. REGN727 and AMG 145, which are monoclonal antibodies, are given every 2–4 weeks via intravenous or subcutaneous injections, and so would primarily be used in higher-risk patients who do not reach LDL-C reduction goals with oral drugs such as statins and statin-intolerant patients.

In a Phase II trial, patients taking 300 mg REGN727 showed an ~43% reduction in LDL-C levels from the baseline after 12 weeks, whereas in a similar trial patients taking 420 mg AMG145 showed an ~55% reduction in LDL-C levels from the baseline after 12 weeks. Whether AMG145 actually has a higher efficacy will be clarified by the Phase III programmes, but a potential key difference between the two drugs is their dosing; REGN727 will probably be dosed every 2 weeks, whereas AMG145 may be dosed every 2 weeks or every 4 weeks, based on its Phase III programme. The top-line data from Regeneron's Phase III programme, known as ODYSSEY, which is evaluating the percentage change in LDL-C levels with REGN727 both alone and in combination with statins over 24 weeks, should shed some light on whether REGN727 could have any competitive advantages in efficacy or side effect profile.

Suvorexant, an orexin A and orexin B receptor antagonist developed by Merck, is under review by the FDA for the treatment of insomnia characterized by difficulties with sleep onset and/or maintenance. On 22 May, an FDA advisory committee met to discuss the efficacy, dosing and safety of suvorexant. The FDA was surprisingly critical of the safety of suvorexant in its review documents presented at the meeting, with the primary concern being next-day somnolence and impaired driving ability in patients who take higher doses of the drug. However, the committee voted positively on safety issues around drowsiness, as the effects of suvorexant were comparable to already approved insomnia medications. The committee votes were also strongly supportive of the efficacy of suvorexant, as well as its novel mechanism, which means that it lacks the addictive potential of established drugs that affect GABA (γ-aminobutyric acid) signalling. The Prescription Drug User Fee Act (PDUFA) date for suvorexant is anticipated to be in July; based on the generally positive view of the drug by the committee, it seems likely to be approved.

Boehringer Ingelheim has developed afatinib, an oral small-molecule inhibitor of epidermal growth factor receptor (EFGR) and human epidermal growth factor receptor 2 (HER2; also known as ERBB2), for the treatment of NSCLC. Boehringer Ingelheim announced positive Phase III results from its pivotal trial at the American Society for Clinical Oncology (ASCO) meeting in 2012; patients treated with afatinib had a median progression-free survival (PFS) of 11.1 months, compared to 6.9 months for patients who were treated with a combination of pemetrexed and cisplatin. Notably, patients in the trial who had the common 19Del/L858R activating mutation in EGFR had a greater PFS benefit than the overall population. One major concern about the drug is the high incidence of adverse events, particularly diarrhoea and rash, which were observed in 95% and 62% of patients, respectively, in the two trial arms. Boehringer Ingelheim filed its new drug application (NDA) for afatinib in November 2012 and, having received a priority review, a decision on its approval from the FDA is expected in July.

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The author declares no competing financial interests.