IN THE PIPELINE

Updates on Promising Agents in Development for Gastroenterology & Hepatology

Vedolizumab Biologics License Application for Ulcerative Colitis Gets Priority Review Status

Priority review status of a Biologics License Application (BLA) for the humanized monoclonal antibody vedolizumab in the treatment of moderate to severe ulcerative colitis was granted to Takeda Pharmaceuticals by the US Food and Drug Administration (FDA) in early September 2013. The BLA was submitted in June 2013 for approval of vedolizumab in the treatment of both moderate to severe active ulcerative colitis and moderate to severe active Crohn's disease. The BLA for approval of vedolizumab in Crohn's disease will be reviewed under the standard review timeline.

The BLA submission was supported by findings from a series of phase 3 clinical trials, termed GEMINI (I, II, III, and a long-term safety study). The GEMINI program investigated the efficacy and safety of vedolizumab on clinical response and remission in patients with moderately to severely active Crohn's disease and ulcerative colitis who failed at least 1 conventional therapy. For more information, see:

-Feagan BG, Rutgeerts P, Sands BE, et al. Vedolizumab as induction and maintenance therapy for ulcerative colitis. *N Engl J Med.* 2013;369(8):699-710.

-Sandborn WJ, Feagan BG, Rutgeerts P, et al. Vedolizumab as induction and maintenance therapy for Crohn's disease. *N Engl J Med.* 2013;369(8):711-721.

Eluxadoline for IBS-D Symptoms Fast-Tracked

The locally acting mu opioid receptor agonist and delta opioid receptor antagonist eluxadoline (Furiex) has received fast-track status from the FDA and just completed enrollment for 2 phase 3 pivotal trials to further investigate its efficacy and safety in the management of pain and diarrhea in irritable bowel syndrome (IBS-D). The studies are designed to capture FDA and European Medicines Agency endpoints for treatment of IBS-D. One study includes a 52-week and the other a 30-week treatment period. Both studies are placebo-controlled and investigate eluxadoline twice daily at a dose of either 75 mg or 100 mg. The FDA agreed that the composite endpoint of improvement in pain and diarrheal symptoms from the phase 2 post hoc responder analysis of eluxadoline is an acceptable primary endpoint for the phase 3 trials. The phase 3 program will also collect long-term global and IBS pain outcomes that could support the drug's registration in the European Union. For more information, see:

-Wade PR, Palmer JM, McKenney S, et al. Modulation of gastrointestinal function by MuDelta, a mixed μ opioid receptor agonist/μ opioid receptor antagonist. *Br J Pharmacol.* 2012;167(5):1111-1125.

-Dove LS, Lembo A, Randall CW, et al. Eluxadoline benefits patients with irritable bowel syndrome with diarrhea in a phase 2 study. *Gastroenterology.* 2013;145(2):329-338.e1.

Sofosbuvir Granted Priority Review Toward New Drug Application

A priority review of a New Drug Application (NDA) has been granted by the FDA to Gilead Sciences for sofosbuvir, the once-daily oral nucleotide analogue inhibitor, for the treatment of chronic hepatitis C virus (HCV) infection. The FDA's target review date is December 8, 2013.

The NDA contains information that supports the use of sofosbuvir plus ribavirin in patients with genotype 2 or 3 HCV infection (an all-oral, interferon-free regimen) and sofosbuvir in combination with ribavirin and peginterferon for treatment-naive patients with genotype 1, 4, 5, or 6 HCV infection. Data were gleaned from 4 phase 3 clinical trials in which patients were treated with sofosbuvir-based therapy for 12 or 16 weeks. For further information, see:

-Jacobson IM, Gordon SC, Kowdley KV, et al. Sofosbuvir for hepatitis C genotype 2 or 3 in patients without treatment options. *N Engl J Med.* 2013;368(20):1867-1877.

-Lawitz E, Mangia A, Wyles D, et al. Sofosbuvir for previously untreated chronic hepatitis C infection. *N Engl J Med.* 2013;368(20):1878-1887.