Welcome to your weekly digest of approaching regulatory and clinical readouts. In the next few weeks Synergy Pharmaceuticals is slated to release results from a phase IIb trial of its lead project, the constipation therapy plecanatide, in patients with irritable bowel syndrome, helping to determine how effectively it will be able to compete in the market.

A couple of closely watched US approvals are also on the horizon. GlaxoSmithKline is due to hear the FDA’s verdict on its once-weekly type II diabetes therapy Eperzan by April 15, while Lilly is awaiting the regulator’s opinion on ramucirumab, which has been filed as a second-line treatment for gastric cancer.

Second use
Synergy recruited 350 patients with constipation-associated irritable bowel syndrome (IBS-C) for the phase IIb trial; the placebo-controlled study is testing four doses of plecanatide and will measure the change in the mean number of complete spontaneous bowel movements over 12 weeks. Secondary endpoints include abdominal pain and stool consistency.

The agent has previously been successful in a large phase IIb study in chronic idiopathic constipation (CIC) and belongs to the same class as Ironwood’s Linzess (linaclatide), which is approved to treat both CIC and IBS-C. As such, the study is widely expected to generate positive results (Phase III data position plecanatide for grudge match with Linzess, January 3, 2013).

Synergy is hoping to establish that plecanatide works as well as Linzess with a more benign tolerability profile in terms of causing less abdominal pain and fewer cases of diarrhoea. In pivotal trials of Linzess, 20% of patients experienced diarrhoea – 2% had severe diarrhoea – and 7% experienced pain, so showing an improvement in these measures is crucial.

The company started two large pivotal studies of plecanatide in CIC late last year, and results should start to emerge late this year. If the programme is successful the project will become the second guanylate cyclase type-C receptor agonist to reach the market. Linzess, licensed to Forest Labs in the US, generated $167m last year and analysts expect sales of $798m in 2018, according to consensus data from EvaluatePharma.

Synergy ended 2013 with $68m in cash, and will need to raise further funds before the year is out. It will be hoping that positive data in IBS-C provide a strong enough story to persuade investors to top up its coffers, or tempt a partner on board.

US approvals
The FDA has already delayed its decision on Glaxo’s Eperzan by three months, so the UK drug maker will be hoping for a green light this time around. European regulators sanctioned its approval last month. Generically known as albiglutide, this project would be the second once-weekly GLP-1 agonist to reach the US market after Bydureon, now owned by AstraZeneca, and the third in its class.

It would be the first to reach the US without an advisory committee review, however. Intense scrutiny of the safety of these medicines over the past few years has not confirmed the worst fears – predominantly concerning cancer and cardiovascular risks – and the agency has apparently felt comfortable reviewing Eperzan without input from its external experts. This also bodes well for a positive outcome.

Either way, Eperzan is not considered a big future product for Glaxo. It offers little differentiation versus other entrenched drugs in its class, and analysts expect Novo Nordisk’s once-daily GLP-1 agonist Victoza to continue to dominate this space; consensus for Eperzan sales in 2018 sits at $418m, against Victoza’s $4bn.

It is less clear when Lilly might hear the FDA’s verdict on ramucirumab as a PDUFA date has not been confirmed, but again a positive outcome is expected. Last October the company said the agency had granted priority review as a single-agent treatment for advanced gastric cancer following disease progression after
chemotherapy. No other treatment is approved in this setting.

The filing was based on the 355-patient Regard trial, which generated a significant 37% increase in median overall survival over placebo at 5.2 months. Analysts forecast sales of $764m for the drug in 2018, according to EvaluatePharma.

A recent win in lung cancer means hopes for ramucirumab are rising, however (Lilly revels in ramu lung cancer win, February 19, 2014). As such, getting it on the market will represent a big win for Lilly, which has not had a novel therapeutic approved by the FDA since Effient in 2009.

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