# Ustekinumab poised to enter the psoriasis market

Later this month, the US Food and Drug Administration (FDA) will decide whether a new psoriasis drug, Stelara (ustekinumab), can enter the market. The human monoclonal antibody (mAb), developed by Johnson & Johnson's subsidiary Centocor, of Horsham, Pennsylvania, was unanimously recommended for plaque psoriasis by an FDA expert panel back in June. By targeting both interleukin (IL)-12 and IL-23, Stelara is the first therapeutic that aims to stop T helper cells from producing interleukin (IL)-17 and other cytokines, which have been implicated in autoimmune responses. Together with several other IL-12/23 blockers under development, Stelara could potentially challenge the markets of tumor necrosis factor (TNF) α-inhibitors currently in use for treating psoriasis.

Expectations surrounding Stelara and other IL-12/23 inhibitors have been rising ever since late-stage human trial data were released. "These drugs produce the most spectacular results we've seen yet," says Alan Menter, chair of the Psoriasis Research Institute at Baylor University Medical Center, in Dallas. When the FDA's dermatologic and ophthalmic drugs advisory committee reviewed Stelara in June, they evaluated two multicenter, phase 3 clinical trials involving more than 2,000 patients.

The Phoenix 1 and Phoenix 2 trials show up to 76% of patients achieving at least a 75% improvement in the psoriasis area and severity index (PASI 75)—a widely used metric for assessing the extent of illness—whereas placebo-treated controls averaged 3%. On the back of these trial results published in May (*Lancet* **371**,1675–1684, 2008), the FDA advisory panel voted the following month 11–0 in favor of approving Centocor's mAb for moderate to severe plaque psoriasis. Citing amendments made to the new drug application, however, the FDA then extended Stelara's approval review period, with a PDFA date of December 29.

Psoriasis is a chronic inflammatory skin disease that affects an estimated 125 million people worldwide. Although not fatal, this incurable skin condition can have a great impact on quality of life. While mild psoriasis is conventionally treated with topical lotions, 20% of patients with moderate to severe psoriasis are prescribed TNF-α blockers, such as Enbrel (etanercept), Humira (adalimumab) and Remicade (infliximab). According to Datamonitor, psoriasis-specific sales reached $1.5 billion in 2007 for this class of drugs. But not all patients respond to TNF blockers—which can cost patients up to $15,000 a year—and those that do often relapse over time. Centocor's mAb, by targeting a different pathway involved in the disease, represents an alternative line of therapeutic attack.

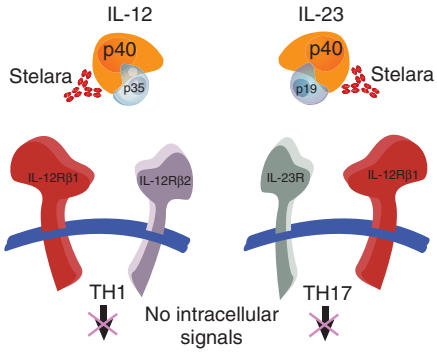


**Figure 1** Centocor's mAb Stelara is the first dual-action drug aimed at the p40 subunit of the IL-12 and IL-23 cytokines to treat severe plaque psoriasis. Growing evidence implicates IL-23 and TH17 cells in psoriasis.

Brian Kenney, Centocor's spokesperson, says Stelara delivers clinical improvements roughly comparable to TNF inhibitors. A head-to-head comparison presented at the European Academy of Dermatology and Venereology, in Paris, in September, showed that up to 76% of Stelara-treated patients improve compared with 57% with Enbrel. Centocor is also developing Stelara and other IL-12/23 blockers for Crohn's disease, ulcerative colitis, rheumatoid arthritis, and multiple sclerosis (**Table 1**).

Stelara's closest rival ABT-874 is Abbott Park, Illinois–based Abbott Laboratories' IL-12/23 candidate. This fully human mAb, isolated and characterized in collaboration with Cambridge Antibody Technologies, targets the same p40 subunit as Stelara. According to projections by New York–based Citigroup, Abbott's antibody is roughly 2 years behind Stelara in development; however, phase 2 data suggest ABT-874 may enjoy superior efficacy over Centocor's product, as 90% of patients treated with the drug achieve PASI 75.

Elsewhere, Synta Pharmaceuticals, of Lexington, Massachusetts, is developing an orally administered small molecule—apilimod (STA-5326)—targeting IL-12/23 for rheumatoid arthritis. Unlike Stelara and ABT-874, which inhibit IL-12/23 by

# IN brief

## German BioPharma awards


Protagen

Protagen of Dortmund, a joint winner with the NeuroAllianz consortium.

The German Federal Ministry of Education and Research has announced the winners of the BioPharma strategy competition. The three top picks will share a total of €100 million ($139 million) over five years for structural projects aimed at boosting the nation's biotech and pharma industries. The Ministry launched the competition to attract "entrepreneurially minded consortia" with innovative drug development projects and financing structures designed to speed up commercialization of university research. Although Germany has the most biotech companies in the European Union, few biotech-based drugs are produced in the country. "The federal government is pursuing the goal of bringing German biotech to the forefront in Europe, not only in terms of the number of companies, but also in terms of revenue and employment figures," says Viola Klamroth, from the Ministry. The strategy competition attracted small and large companies with partners from academia and clinical practice, and the winners were announced in October. One award goes to the Max Planck Innovation GmbH, the tech transfer agency of the Max Planck Society, for its novel sustainable financing model to enable high-risk, early-stage drug projects from German research institutions to reach clinical studies. Their proposed Drug Discovery and Development Centre (DDC) jointly conceived with London-based financial services firm Inventive Capital will allow private investors and pharma to become involved within the framework of a fund. Another award goes to the NEU$^2$ consortium, a project bringing together a number of northern German research institutes, biotech and pharma companies. The NEU$^2$ partnership, financed through a privately sourced fund, will use the award to develop novel therapeutic and diagnostic approaches for multiple sclerosis. The third award winner is the NeuroAllianz consortium, a strategic public partnership aimed at taking new treatments for neurodegenerative diseases from research to market. The 12 participating partners include public research institutes, biotechs and regulatory authorities. The BioPharma competition is part of Germany's new Pharmaceutical Initiative, which will spend over €800 ($1,000) million between 2007 and 2011 to restructure existing funding strategies as well as to create new ones. "With the three consortia selected in the BioPharma competition, there is a strong chance that Germany will be able to perform better as a location, and make better use of existing resources," says Klamroth. "We hope to restore the earlier tradition of being the world's pharmacy."—*Susan Aldridge*