BIOBUSINESS BRIEFS

REGULATORY WATCH

First drug for idiopathic pulmonary fibrosis approved in Japan

Shionogi and InterMune have announced the marketing approval of pirfenidone (Pirespa) for the treatment of idiopathic pulmonary fibrosis (IPF) in Japan, making it the first approved therapy for IPF in a major market. Shionogi developed pirfenidone in Japan and has rights in Japan, Taiwan and South Korea, and InterMune is currently conducting a Phase III programme known as CAPACITY to support approval in other markets.

IPF is characterized by worsening pulmonary function, dyspnoea and cough. The precise aetiology of IPF is unknown, but lung injury and excessive pulmonary deposition of fibrotic tissue have a key role in disease pathogenesis. There are presently no drugs approved specifically for IPF by the FDA or the EMEA, and standard therapy based on corticosteroids and immunosuppressants has shown only very limited benefit in reducing disease progression in patients with IPF.

However, several types of novel therapies are being investigated (*Curr. Opin. Pharmacol.* 6, 284–292; 2006), including anti-inflammatory agents, antifibrotics and immune modulators (TABLE 1). Pirfenidone seems capable of tackling some IPF characteristics through inhibition of collagen synthesis, downregulation of profibrotic cytokine production and blockade of fibroblast proliferation. Importantly, pirfenidone met the primary end point of reducing decline in vital capacity (VC) in Shionogi's Phase III trials. "The key challenges in drug development for IPF are to identify agents that will reverse the fibrosing disease process and are safe to use," says Ron du Bois, National Jewish Health, Denver, Colorado, USA, who is also a co-chair for the CAPACITY trials steering committee. "But, until these drugs are found, novel treatments are not expected to achieve much more than improving the rate of decline in lung function, and in this context, the Shionogi findings, as yet unpublished in a peer-reviewed journal, may represent a significant breakthrough."

Oxidative stress is also implicated in IPF, and like *N*-acetyl cysteine — which slowed the rate of lung function decline when added to a traditional immunosuppressive drug regimen in a Phase III trial (*N. Engl. J. Med.* 353, 2229–2242; 2005) — pirfenidone has anti-oxidant activity, notes Victor Thannickal, University of Michigan Medical Centre, USA. "It is intriguing that two different small molecules with anti-oxidant activity have shown the greatest promise so far in the treatment of IPF, and hopefully, more effective anti-oxidant strategies for IPF will be designed," he says. "Since the clinical syndrome of IPF may result from the activation of different biological pathways, identification of patients most likely to benefit from targeting these pathways may allow for the development of more effective, patient-specific drug therapies. Identification of patients with early disease and of biomarkers that reliably predict meaningful clinical end points represent additional future challenges."

InterMune have also released a progress report on the CAPACITY trials (http://www.capacitytrials.com/wt/page/index). So far, patient visits at week 72 of the trial, at which the primary end point forced VC is measured, have been completed for 97% of enrolled patients. "If the CAPACITY studies produce similar findings to that of the Shionogi studies, this will be good news for patients with IPF," says du Bois. InterMune is hoping to announce top-line results early next year, and if data are positive, is on track for submission of a new drug application to the FDA in mid-2009.

Table 1 | **Current development status of therapies for idiopathic pulmonary fibrosis***

Drug (company)	Properties	Development status
PRX-08066 (EPIX Pharmaceuticals)	5-HT_{2B} receptor antagonist	Discovery
Cintredekin besudotox (NeoPharm)‡	Chimeric human IL13 conjugated to a genetically engineered *Pseudomonas* exotoxin	Discovery
Roflumilast (Nycomed)§	PDE4 inhibitor	Preclinical
FG-3019 (Fibrogen)	Anti-connective tissue growth factor human mAb	Phase I
GC-1008 (Genzyme/MedImmune)	TGF-β human mAb	Phase I
Treprostinil (United Therapeutics/ Aradigm)	Prostacyclin analogue	Phase I
BIBF-1120 (Boehringer Ingelheim)	VEGF, FGF and PDGF receptor inhibitor	Phase II
Interferon-α (Amarillo Biosciences)	Interferon-α ligand	Phase II
Tetrathiomolybdate (Adeona Pharmaceuticals)‖	Copper chelating agent	Phase II
QAX-576 (Novartis)	IL13 modulator	Phase II

*Information was obtained from the Investigational Drugs Database from Thompson Reuters. ‡Under license from the National Institutes of Health. §Acquired ALTANA Pharma in 2006. ‖Under license from the University of Michigan, USA. 5-HT_{2B}, 5-hydroxytryptamine 2B; FGF, fibroblast growth factor; IL13, interleukin 13; mAb, monoclonal antibody; PDE4, phosphodiesterase 4; PDGF, platelet-derived growth factor; TGF-β, transforming growth factor-β; VEGF, vascular endothelial growth factor.