

PA401

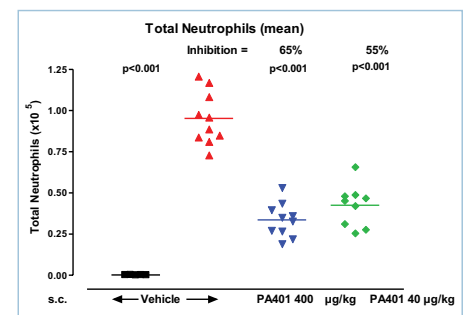
product profile



PA401 is a glycan-binding decoy protein based on IL-8 and it is ProtAffin's most advanced product candidate. The Company's proprietary CellJammer® discovery platform was used to modify wild-type human IL-8 (CXCL8) so that it acts as a targeted anti-inflammatory product. The novel mechanism of action of PA401 has been thoroughly characterised *in vitro*, using cell-based assays, *in ex vivo* models and in preclinical disease models. PA401 shows an increased binding affinity to glycans driving inflammatory processes and does not bind to CXCR1 and CXCR2, the GPCR receptors for IL-8 found on human neutrophils. PA401 can be cost-effectively manufactured by *E.coli* fermentation. PA401 is in preclinical development, with Phase 1 trials planned for early 2012.

IL-8 and COPD

Chronic obstructive pulmonary disease (COPD) is a common, chronic inflammatory disease of the airways and lung parenchyma, largely caused by smoking and atmospheric pollution. The inflammation is characterised by increased numbers of neutrophils, CD8+ T lymphocytes and macrophages and associated cytokines, chemokines and proteases, particularly during exacerbations. IL-8 (CXCL8), is one of the best characterised members of the chemokine family of proteins and is one of the most important neutrophil chemoattractants and activators in man. It recruits neutrophils to sites of bacterial infection and tissue injury by interacting with GAGs on endothelial cells and guides neutrophils into the underlying lung tissue. If this recruitment is not kept in check then inflammation progresses and further lung damage results (eg small airway obstruction, fibrosis and emphysema). As IL-8 is known to play a central role in the chronic neutrophilic inflammation seen in COPD patient's lungs, the glycan-binding decoy protein PA401 represents a potential therapeutic breakthrough in tackling this severe unmet medical need. Other pharmaceutical companies such as GSK and Merck have small molecule antagonists of the IL-8 receptor CXCR2 in clinical development for COPD and related conditions.



Activity of PA401 in gold-standard preclinical model of COPD

	Neutrophils	Lymphocytes	Macrophages	Epithelial cells
PA401 (400µg/kg daily)	65%	67%	37%	67%
p value	<0.001	<0.001	<0.01	<0.001
Roflumilast (5mg/kg daily)	73%	71%	56%	46%
p value	<0.001	<0.001	<0.001	ns
SCH527123 (10mg/kg twice a day)	45%	33%	41%	26%
p value	<0.001	ns	<0.001	ns

Broad anti-inflammatory activity of PA401 compared to other benchmark compounds.

Future development

PA401 is currently in preclinical development for treatment of COPD and related conditions. In July 2010, the Company announced a manufacturing agreement with CMC Biologics A/S, Copenhagen for the manufacture of PA401 for early clinical development. The Company will carry out registrational toxicology in 2011 and will initiate clinical development of PA401 early in 2012. ProtAffin will generate clinical data on PA401 prior to considering partnering discussions.

In vivo efficacy

The Company has demonstrated impressive efficacy data for PA401 in gold-standard preclinical models of COPD. The activity of PA401 was benchmarked against other relevant treatment modalities including the PDE4 inhibitor roflumilast and the CXCR2 antagonist SCH527123. These studies showed that PA401 has strong and broad anti-inflammatory activity, while also reducing the levels of several inflammatory biomarkers. PA401 is active when administered by numerous routes including; i.v., s.c. and inhalation. The differentiated pharmacology of PA401 compared to other treatment modalities suggests that this novel first-in-class product has the potential to bring specific benefits to certain populations of COPD patients. PA401 also hold promise for chronic neutrophilic lung inflammation that is prevalent in other severe diseases, such as cystic fibrosis and steroid-resistant asthma.

Development

Phase 1 scheduled for early 2012

Manufacture

Non-glycosylated protein produced by *E.coli* fermentation

Partnering

PA401 funded to clinical milestones

Management

Jason Slingsby, CEO
Andreas Kungl, CSO