

FXT's mission is to advance to clinical proof of concept a portfolio of proprietary, first in class therapeutics in the area of inflammation, by leveraging FXT's competencies in early stage development of drugs acting on the immune system and in functional based discovery

SOMATOTAXINS

They are a new class of anti-inflammatory small molecules that exploit a new pathway discovered by FXT. This pathway is acting through the type-2 somatostatin receptor (sstr2), which has previously been associated with significant anti-inflammatory activity in various clinical and non-clinical studies using somatostatin and its analogues. The major limitation for the clinical use of these compounds in inflammation however has been their potent endocrine effects. FXT has discovered a second class of natural ligands at sstr2, which offer a solution to this problem and involve various mechanisms, including the sequential action of arginase-2 and proteases (such as thrombin) on peptide substrates, to generate a novel post-translational modification of a C-terminal lactam. These C-terminal lactam peptides (CTLPs) are specific ligands at sstr2 and mediate anti-inflammatory effects through sstr2, but without agonist activity on endocrine markers at the dose levels required for anti-inflammatory activity. The importance of this pathway is revealed by genetic studies conducted by FXT, which showed that variation at the sstr2 locus is associated with chronic inflammatory conditions, and also by studies of IGF-1 levels which are depressed during chronic inflammation due to the low levels of CTLPs that normally compete with somatostatin binding at sstr2. This novel pathway is therefore disrupted in chronic inflammatory diseases including asthma and rheumatoid arthritis.

Somatotaxins are synthetic ligands that bind to the 'CTLP site' on sstr2. They are the first drugs to target the CTLP pathway and therefore mimic the anti-inflammatory effects of natural CTLPs implicated in the physiological resolution of inflammation while they are devoid of endocrine effects. Somatotaxins are characterized in vitro by the ability to inhibit leukocyte chemotaxis at sub-nanomolar concentrations, an activity entirely dependent on sstr2. Since the activity of somatotaxins depends on cell surface sstr2, their effects are focusing on cells involved in the inflammatory response (that have up-regulated sstr2), while avoiding undesirable immunosuppressive effects on cells of the adaptive immune system (that generally lack sstr2). FXT's portfolio of somatotaxins includes different compounds optimized for topical, parenteral and oral delivery. The lead somatotaxin (FX125L) is ready for Phase II studies in major inflammatory conditions.

OTHER PROPRIETARY TECHNOLOGIES

G-PROTEIN COUPLED RECEPTORS AGONIST-ENRICHED LIBRARIES (GAEL)

FXT developed a technology (called GAEL) to generate proprietary libraries of novel small molecules which are enriched in agonists at a wide range of different G-protein coupled receptors (GPCRs). This technology is based on a cutting-edge multivariate QSAR study to identify the structural motifs that uniquely distinguish GPCR agonists from antagonists irrespective of the receptor being targeted. The libraries then present these motifs on scaffolds that have low intrinsic toxicity and excellent PK/PD properties. Further development of this technology will be pursued through the licensing-out to a suitable partner.

FXT'S OPERATIONAL MODEL

FXT's research facilities are based in Cambridge (UK), while the development work is managed centrally but conducted internationally through Contract Research Organizations and a network of expert advisors in each operational area.

FXT operates a very capital efficient, virtual organisation structure. The company is financially robust through to the completion of clinical proof of concept studies in various inflammation indications, scheduled to start in 1H2011.

COMMENCED OPERATIONS

January 2007

LOCATION

Cambridge, UK

FOCUS

Novel anti-inflammatory therapies

TECHNOLOGIES

- Somatotaxins
- GAEL

PIPELINE

- **FX125L**
(Oral administration, Completed Phase I)
- **FX141L**
(Back up molecule, Preclinical)
- **FX87L**
(Topical administration, Preclinical)

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FX125L

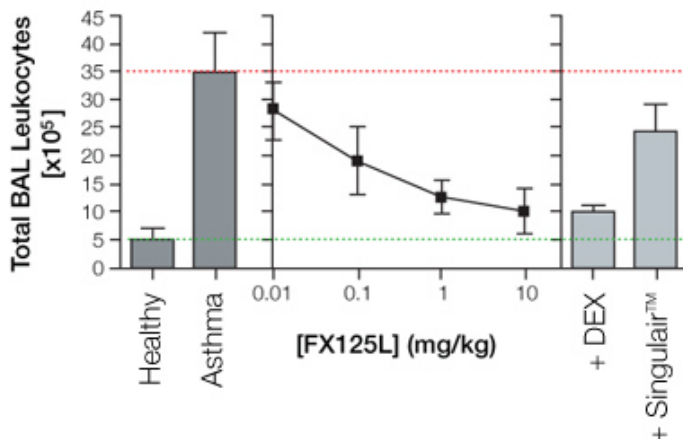
FX125L is the lead, orally available somatotaxin, with completed Phase I clinical trials (single and multiple ascending dose studies) conducted in the US, involving over 100 healthy subjects.

The potent anti-inflammatory activity of FX125L following oral administration has been clearly demonstrated in a wide range of animal models of disease in vivo, including rodent models of allergic asthma, RA, diabetic nephropathy and surgical adhesions, suggesting therapeutic doses in man in the range of 10mg-100mg once a daily and that FX125L may have in the clinic similar efficacy but better safety than corticosteroids and superior efficacy than montelukast.

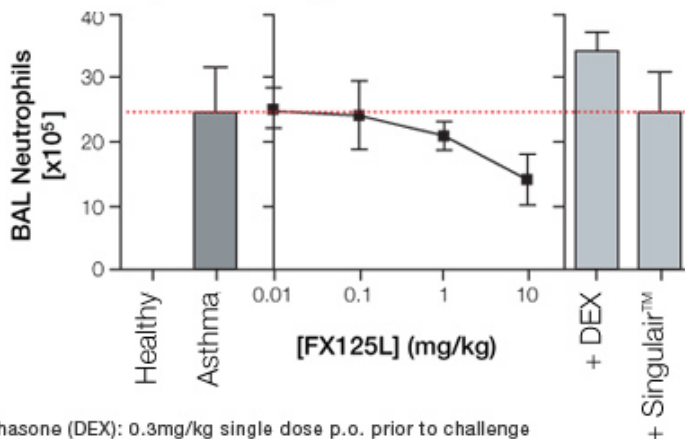
The regulatory preclinical studies (including 90-days regulatory tox studies) with FX125L suggested a very favourable safety profile and a wide therapeutic range. FX125L has optimal CMC characteristics and is obtained by a straightforward 3-step chemical synthesis with an extremely low cost of goods. GMP production has been established as well as the development and stability data of a capsule formulation to be used in Phase II trials.

FX125L showed excellent safety, was well tolerated in doses up to 30-fold the presumed therapeutic dose in man and its pharmacokinetics were linear with an elimination half life of about 25h. Exploratory pharmacodynamic data suggest that FX125L has a biological activity in man that is consistent with a broad anti-inflammatory profile. The clinical indications targeted with FX125L include respiratory disorders such as asthma and COPD, and other major inflammatory conditions such as RA, IBD, psoriasis or acne.

FX125L attenuates neutrophil accumulation in a model of allergic asthma



.... and exhibits a superior efficacy profile to dexamethasone or Singulair™



Dexamethasone (DEX): 0.3mg/kg single dose p.o. prior to challenge

Singulair™: 20mg/kg twice daily p.o. for 14 days

FX125L: Once daily p.o. for 14 days

Endotoxin-free ovalbumin (<20 EU/mg) plus 1µg LPS were used as challenges

Data shown at 24hrs after the final (third) challenge

Averaged data from six different experiments (not all treatment conditions in every experiment)

BUSINESS DEVELOPMENT

FXT will partner with inflammation disease franchise leaders to accelerate late stage clinical development and launch of its products into patient markets.

To learn more about partnering opportunities with FXT, please contact info@funxionaltherapeutics.com.



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