Modular Antibody Technology

COMPANY:
f-star Biotechnologische Forschungs- und Entwicklungsges.m.b.H.

LOCATION:
Vienna, Austria
Cambridge, UK

COMPANY FOCUS:
Discovery and development of improved antibodies and antibody fragments with new functionalities and pharmacologic properties

TECHNOLOGY PLATFORM:
Modular Antibody Technology

PRODUCT:
Fcab™: antigen binding Fc
mAb²: bispecific antibody

LEAD INVESTORS:
Atlas Venture
Aescap Venture
Novo A/S

ADVISORY BOARD:
Sir Gregory Winter, UK
Sir Ravinder Maini, UK
Prof. Anthony Rees, Sweden

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COMPANY

f-star is an antibody engineering company developing improved therapeutic antibodies and antibody fragments based on its Modular Antibody Technology, which allows the introduction of additional binding sites into antibodies and antibody fragments by engineering the non-CDR loops of constant or variable domains. Using Modular Antibody Technology, antibody fragments with antibody functionality and long half-life but much smaller size (Fcab™) or full antibodies with additional functionality (mAb²) can be created.

f-star was founded by a team of experienced antibody engineering and biotech executives in 2006. Seed-financed by Austrian government agencies and Atlas Venture, the company recently closed a Series A financing round with Aescap Venture, Atlas Venture and Novo A/S and has raised EUR 13.0m in total so far. In its advisory board, the company is supported by pioneers in the field of monoclonal antibodies. f-star has 20 employees at its headquarter and research sites in Vienna, Austria and Cambridge, UK.

OVERVIEW OF MODULAR ANTIBODY TECHNOLOGY

Nature uses the highly variable CDR-loops (Complementarity Determining Regions) in the variable domains of an antibody to form antigen binding sites. Modular Antibody Technology extends this principle to the non-CDR loops of constant as well as variable domains to engineer additional binding sites. Non-CDR loops are randomized, libraries of antibody fragments are created via standard techniques such as phage display and molecules with desired binding properties are selected from these libraries.

Modular Antibody Technology allows building additional functionality into therapeutic antibodies or antibody fragments of any size without changing the basic molecular structure of the respective starting molecule. Molecules that can be engineered include full antibodies (e.g. IgG), immunoglobulin constant regions (Fc), antigen binding fragments (Fab) and single chain antibodies (scFv) as well as diabodies, unibodies, single domain antibodies and other antibody formats. Binding sites can be engineered against a broad range of therapeutically useful targets.

PRODUCTS

f-star will apply its unique Modular Antibody Technology to develop its own proprietary pipeline of therapeutic product candidates. The company is in the process of evaluating a number of different product candidates in the field of oncology and inflammatory disease. f-star currently focuses on two highly promising molecular formats: Fcab™ antigen binding Fc, and mAb² bispecific / multivalent antibody.

INTELLECTUAL PROPERTY

The technology is protected by a comprehensive IP portfolio owned by f-star, including a basic international patent application and a series of further applications claiming Modular Antibodies, libraries, products, methods and certain applications to develop product candidates. See first published patent application WO06072620A1: Synthetic immunoglobulin domains with binding properties eingineered in regions of the molecule different from the complementarity determining regions.

BUSINESS DEVELOPMENT

f-star is open to partner its Modular Antibody Technology with pharma and biotech companies who seek to improve their product candidates with f-star's technology. In this regard, f-star is currently engaging in a limited number of feasibility studies, in which the starting molecule provided by the partner will be engineered to display the desired additional properties. With this approach f-star intends to broaden the scope of its technology exploitation and add value to developers of antibody based therapeutics.

f-star modular antibodies

www.f-star.com

Fcab™: an antibody "compressed" into a much smaller format

Modular Antibody Technology is absolutely unique in delivering an alternative scaffold with full antibody properties and small size. Fcab™ (antigen binding Fc) is a highly innovative yet conservative protein engineering scaffold. It consists of the CH2 and CH3 domains of an antibody, naturally folded as a homodimer with a size of approximately 50kDa, with two identical antigen binding sites engineered into the CH3 domains.

Due to the localization of essential functional sites of antibodies in the CH2 and CH3 domains, this molecule has the potential to offer antibody functionality:

- Biological half-life comparable to full length IgG
- Effector functions
- Protein A binding
- Two antigen-binding sites

In addition to antibody functionality,
Fcab™ potentially offers the following advantages over antibodies: Fcab™

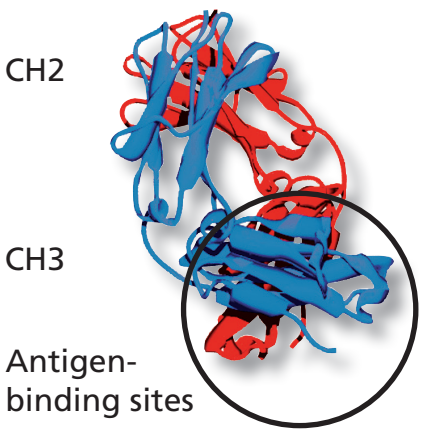
- has a size of 50kDa (compared to 150kDa of a full length antibody) which promises
  > improved tissue penetration > better efficacy on a molar basis and therefore
  > reduced side effect potential as well as > ease of manufacture
- can be produced in E.coli, yeast as well as mammalian cells depending on desired properties and
- its effector functions may be tuned by a number of techniques, even be switched off by expression in a non-glycosylation production system such as E.coli.
- may offer significant IP advantages in many cases by lacking variable regions, which may be claimed by third party antibody patents.

mAb²: an antibody with inbuilt additional functions

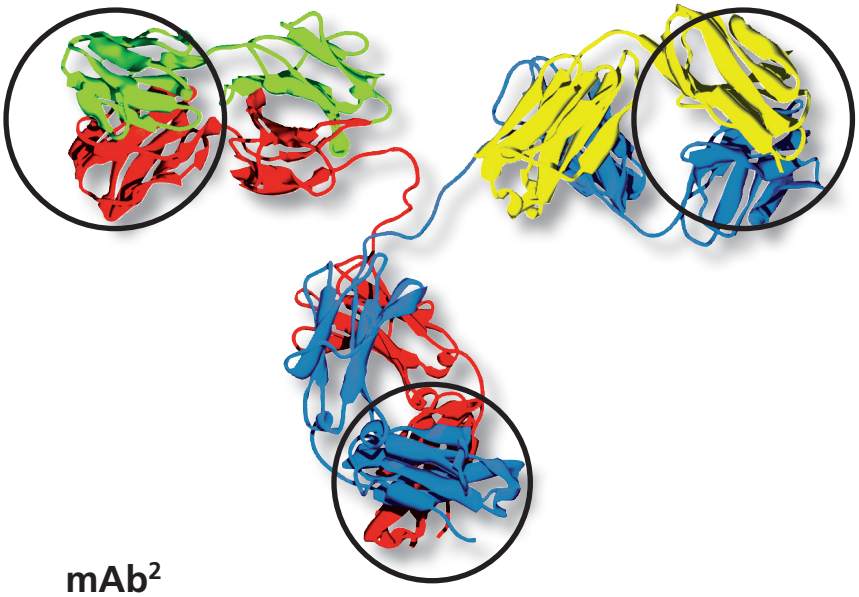
mAb² antibodies are full IgG length antibodies with two additional binding sites engineered into the CH3 domains. Depending on the type of additional binding sites assigned to the CH3 domains of the IgG molecule, a number of exciting and completely new therapeutic applications become possible. Examples include oligovalence (additional binding sites to the same disease antigen), dual targeting (additional binding sites to a second disease antigen, all within one single IgG molecule) or tissue targeting (additional binding site to tissue-specific markers, enriching the antibody at the site of action). All these applications have one objective: making therapeutic antibodies even more effective in treating patients with high unmet medical need.

- mAb² antibodies are antibodies with additional binding sites capable of performing a therapeutically useful tasks. Modular Antibody Technology is absolutely unique in delivering such innovative therapeutic approaches of an antibody with only minimal changes in the molecular structure and production processes.

Modular Antibody Technology allows introduction of additional binding sites by randomization of non-CDRloops



Fcab™
antigen binding Fc



mAb²
multispecific / multivalent antibody