



## Company Profile

Crescendo Biologics is a Cambridge-based company whose aim is to deliver next-generation antibody therapeutics based on novel class-leading platforms.

The company is focussed on developing a transgenic mouse platform for *in vivo* generation of human, high-affinity, soluble, V<sub>H</sub> antibody fragments. These are the smallest fragments that retain antibody binding and have many desirable properties as potential therapeutics. Crescendo will utilise this platform for product development of in-house targets or in partnership with other companies.

Crescendo is led by a management and Board with exceptional experience in the antibody field and the biotechnology sector, backed by a syndicate of leading life science investors.

## The Opportunity

Antibody-based therapies have become a major driver for the pharmaceutical industry, addressing many medical needs and yielding \$33bn of sales in 2008 with continued annual growth predicted of >20%. This has led to an intense focus on improved platforms for the generation of antibodies, and on next generation antibody-based molecules with potentially improved, more drug-like, properties.

Antibody fragments have a key role to play. Several products based on first- or second-generation antibody fragments (for example Fab and scFv) are marketed or in clinical development. However, V<sub>H</sub> fragments are the smallest fragments that retain target binding and affinity, and therefore have significant benefits over earlier generations of antibody fragments.

## History

Crescendo Biologics was set up to commercialise a set of complementary antibody technologies spun out of the Babraham Institute in Cambridge, UK.

In April 2009 Dr Mike Romanos was appointed Chief Scientific Officer to lead Crescendo's management team and R&D. In December 2009, Clive Dix was appointed the company's non-executive Chairman. The company's operations were established on the Babraham Research Campus, enabling the company to maintain close links with its originating science base.

## Management

**Mike Romanos PhD**  
*Chief Scientific Officer*

**Amanda Bettison**  
*Head of Business Operations*

**Joyce Young PhD**  
*Head of Transgenic Platform*

**Bryan Edwards PhD**  
*Head of In Vitro Platform*

**Yumin Teng PhD**  
*Head of Molecular Biology*



## Board

**Clive Dix**  
*Chairman*

**Graziano Seghezzi**  
*Sofinnova Partners*

**David Brown**  
*Aitua*

**Alan Goodman**  
*Avlar BioVentures*

**Mike Romanos**  
*Chief Scientific Officer*



## Investment

**September 2009**  
*£4.5 million private seed funding round led by Sofinnova Partners.*



## Investors

**Sofinnova Partners**  
[www.sofinnova.fr](http://www.sofinnova.fr)

**Avlar BioVentures**  
[www.avlar.com](http://www.avlar.com)

**Aitua**  
[www.aitua.com](http://www.aitua.com)

**Rainbow Seed Fund**  
[www.rainbowseedfund.com](http://www.rainbowseedfund.com)

## V<sub>H</sub> fragments

Crescendo brings together novel technologies which will enable the company to generate diverse, stable and optimised human V<sub>H</sub> fragments, the smallest functional binding units of an antibody molecule. These fragments combine the specificity and binding affinity of antibodies with certain desirable characteristics of small molecules and offer several potential advantages as starting points for the development of novel therapeutics:

- Local, topical and inhaled administration
- Greatest molecular format flexibility, including bi-specifics
- Easy to manufacture and stable.

## Transgenic Mouse Platform

Heavy chain antibodies (HCAb, immunoglobulin lacking light chains) occur naturally in camelids and sharks, and have been developed as a source of V<sub>H</sub> fragments which are then humanised prior to therapeutic development. The Crescendo transgenic mouse carries engineered human immunoglobulin heavy chain genes (IgH), in order to produce human heavy chain antibodies in response to immunisation. Crescendo believes that this *in vivo* route will provide a faster, more predictable route to candidate-quality human V<sub>H</sub> fragments than camelid or *in vitro* technologies.

Our approach depends on generating mice devoid of endogenous murine immunoglobulin heavy and light chain expression. Crescendo's proprietary knockout mice functionally ablate the loci expressing these polypeptides through either large-scale genomic deletions or marker insertion. These mice are then crossed with transgenic mice containing a large yeast artificial chromosome (YAC) construct comprising the human immunoglobulin heavy chain (IgH) V, D and J genes linked to human or murine C genes engineered for secretion in the absence of light chains.

Crescendo is working with leading academic groups in YAC construction and transgenesis to generate a pipeline of mice towards the best-in-class human HCAb mouse. These will comprise YAC constructs with increasing numbers of human V genes linked to a murine C region.

## Ribosome Display Platform

Ribosome display technology is a superior platform for *in vitro* molecular evolution of antibody affinity. It has advantages based on the very high library diversity that can be achieved, and the fact that the entire process is performed rapidly *in vitro*. Crescendo owns IP for eukaryotic ribosome display, and has developed a robust process for optimisation of V<sub>H</sub> fragments produced from its transgenic platforms.

