



Crescendo Biologics Announces First 'Triple Knockout' Mouse

Mice lacking endogenous antibody polypeptides offer powerful new tool for antibody fragment development

Cambridge, UK. 29 September 2010 – Crescendo Biologics Limited (Crescendo) today announces it has established a colony of engineered mice completely devoid of endogenous antibody polypeptides. The proprietary 'triple knockout' mice are believed to be unique and have the immunoglobulin heavy chain (IgH), kappa light chain and lambda light chain loci all functionally silenced by large-scale genomic deletion.

This is a significant advance over previous knockout mice which retain intact lambda light chain. While lambda light chain accounts for at most 10% of the light chains in mouse antibodies, Crescendo believes that knockout of all light chain expression is critical for the efficient generation of human heavy chain antibodies in transgenic mice. The new knockout mouse thus offers an enhanced background for the generation of new antibody therapeutics and is a key step in the establishment of Crescendo's world-leading V_H antibody fragment platform. V_H fragments are the smallest fragments that retain antibody binding, and have many desirable properties as potential therapeutics.

In a parallel development, Crescendo has also demonstrated the potential of its first generation yeast artificial chromosome (YAC) with the successful expression of human antibodies. Working with Professor Lluís Montoliu at the Centro Nacional de Biotecnología (a centre belonging to the Spanish National Research Council, CSIC) in Madrid, transgenic mice have been generated by oocyte microinjection with a first YAC comprising several human V genes, all human D and J genes and a C region engineered for expression in the absence of light chains. This YAC has been shown to rearrange and express human antibodies in wild type mice.

"Today's announcement marks an important milestone in the development of our highly innovative antibody fragment technology," said Mike Romanos, CSO of Crescendo Biologics. "We have successfully delivered what we believe to be a unique asset in our triple knockout mice, and have also made significant steps in the generation of YACs which direct the production of human heavy chain antibodies. When combined, and with further developments in our YAC technology, we believe we will have the strongest platform for the generation of new V_H fragment therapeutics and can harness the great benefits they will bring as therapeutics."

The Crescendo approach is aimed at bringing together two highly desirable characteristics of antibody platforms — human origin and *in vivo* maturation — to allow rapid creation of high affinity fragments. The company intends to progress at least one V_H-based product to the clinic.

Crescendo is now working to generate mice that combine its newly developed YAC and the triple knockout mouse, in order to generate a first generation Crescendo mouse platform. In addition, Crescendo is generating additional YAC transgenics to progress towards the best in class mouse.



Contacts

Mike Romanos/Amanda Bettison
Crescendo Biologics
Tel: +44 (0) 1223 497140
Email: mromanos/abettison@crescendobiologics.com

Chris Gardner
Citigate Dewe Rogerson
Tel: +44 (0)207 638 9571
Email: chris.gardner@citigatedr.co.uk

About Crescendo Biologics Ltd

Crescendo Biologics will apply highly innovative antibody fragment technologies to the development of new targeted therapeutics. The Crescendo transgenic mouse platform under development has the potential to rapidly and predictably generate high-affinity human heavy chain antibodies that readily yield V_H fragments that have no requirement for humanisation. This is combined with a powerful *in vitro* ribosome display technology which offers significant advantages over existing approaches in antibody optimisation. V_H fragments provide great flexibility as a starting point for the development of new targeted therapeutics combining the specificity and binding affinity of antibodies with certain desirable characteristics of small molecules.

Crescendo's technologies were invented by scientists at the Babraham Institute, Cambridge (UK). The Company has raised £4.5 million in seed funding from leading life sciences investors, Sofinnova Partners with Aitua, Avlar BioVentures and the Rainbow Seed Fund also participating. www.crescendobiologics.com