Crescendo Biologics

Crescendo Biologics Announces the Crescendo Mouse

Breakthrough technology generates superior human single domain antibody V_H fragments in a transgenic mouse

Cambridge, UK. 16th January 2013 – Crescendo Biologics Limited (Crescendo) today announces the Crescendo Mouse, a breakthrough in antibody fragment technology which allows the efficient generation of high-quality fully human single domain antibody V_H fragments from a transgenic mouse.

V_H fragments are next-generation antibody-based therapeutic proteins that have exciting applications beyond the scope of full length antibodies. They are the smallest antibody fragments that retain the ability to bind antigens specifically and with high affinity and, when generated in the Crescendo Mouse, human V_H have superior biophysical properties that make them highly attractive drug products. V_H fragments can be formulated for topical delivery, are highly amenable to modular engineering of bispecific and multivalent products, have superior tissue penetration characteristics, and are simple to manufacture in microbial systems.

Mike Romanos, CEO of Crescendo, said, “The majority of recent approvals for monoclonal antibody therapeutics have been fully human and derived from transgenic mice. Transgenic mice are highly valued for their ability to generate fully human antibodies that develop *in vivo*, through the natural process of B cell maturation, and require little or no further manipulation to create highly potent therapeutics. The Crescendo Mouse combines all the benefits of transgenic mouse technology with the excellent drug qualities of single domain V_H fragments. We believe this will enable rapid generation of superior therapeutic products, and fully realise the potential of human V_H fragments in the development of our pipeline and that of future partners.”

Key to generation of V_H fragments in the mouse is Crescendo’s proprietary triple knock out (TKO) background, which is completely devoid of all endogenous immunoglobulin chains, and therefore enables *in vivo* maturation of human V_H single domains uncontaminated by association with any light chains. B cell development within the Crescendo Mouse is driven from a construct introduced into the TKO background that combines human V- D- and J-

genes, together with murine constant and regulatory regions, to generate heavy chain only antibodies. The power of the mouse immune system is consequently fully harnessed to drive B cell development and maturation, leading to a diverse repertoire of fully-human V_H domains with superior stability and solubility.

The Crescendo Mouse responds robustly to immunisation with target proteins and *in vivo* B cell maturation yields diverse human V_H domains, from all V_H families, which have also undergone somatic hypermutation. Because the antibody response following immunisation is entirely encompassed within the V_H domain, Crescendo has been able to develop a fully integrated discovery process utilising *in vitro* display to comprehensively mine and rapidly identify V_H drug candidates directly from immunised mice. Purified V_H fragments have been shown to bind immunogen with high affinity, exhibit very high thermostability and have excellent expression levels. These data indicate that B cell maturation in the Crescendo Mouse is driving selection and optimisation of matured human V_H domains, with all of the properties that make them highly potent, drug quality antibody-based therapeutics.

Crescendo has commenced discovery for its own pipeline of therapeutic products, and is in discussion with pharmaceutical companies interested in accessing the Crescendo Mouse.

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About Crescendo Biologics Ltd

Crescendo Biologics is building a pipeline of novel medicines based on its highly innovative V_H antibody fragment platform through both in-house development and strategic partnerships. Crescendo's proprietary V_H technology produces human heavy chain-only antibodies in the transgenic Crescendo Mouse providing a unique source of fully human V_H fragments that have matured *in vivo* to have high affinity, stability and solubility. V_H fragments are the smallest antibody fragments that retain binding affinity and specificity offering the potential to generate novel products with improved drug-like properties and able to address unmet medical needs.

Crescendo's technologies originated from discoveries by scientists at the Babraham Institute, Cambridge (UK). The company has raised funding totalling £7.7 million from an investment consortium led by Sofinnova Partners with Avlar BioVentures, Babraham Bioscience Technologies, and the Rainbow Seed Fund.

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