New data demonstrate that Humabodies® are highly effective in generating monospecific and bispecific CAR-T cells to target solid tumours

Cambridge, UK, 16 April 2021 – Crescendo Biologics Ltd (Crescendo), a clinical stage immuno-oncology company developing novel, targeted T cell enhancing therapeutics, today announces the publication of new preclinical data demonstrating that its Humabody® V_H domains can be used to generate highly effective chimeric antigen receptor (CAR) molecules, and that redirected Humabody CAR-T cells elicit potent killing activity in solid tumours.

These data have been published in the *Journal for ImmunoTherapy of Cancer*, and the full paper by Wang *et al* can be accessed online HERE.

The study was conducted by Gianpietro Dotti, MD, and colleagues at the University of North Carolina (UNC) at Chapel Hill and used Humabody V_H domains targeting prostate-specific membrane antigen (PSMA) and mesothelin (MSLN) sequences to redirect T cells with V_H-based CARs. The preclinical antitumour activity and mode of action of these PSMA V_H and MSLN V_H CARs were evaluated *in vitro* and *in vivo* compared with traditional single-chain fragment variable (scFv)-based CARs.

Humabodies are small, *in vivo* matured human V_H domain building blocks that can be easily configured into multifunctional biotherapeutics, and these new results suggest that Humabody V_H domain-based CARs targeting PSMA and MSLN are stable and functional both *in vitro* and *in vivo*. Furthermore, these Humabody CARs bind their targets with similar affinities in both monospecific and bispecific formats, and redirected T cells elicit antitumoural responses in solid tumours at least as well as conventional scFv-based CARs.

Dr Gianpietro Dotti, Professor of Microbiology and Immunology at the University of North Carolina, said: "The antigen-binding moiety of chimeric antigen receptors is a critical component of these artificial molecules and has major implications for the functionality of the CAR-T cells. In collaboration with Crescendo, we demonstrated that fully-human V_H can be effectively used as the antigen-binding moiety in CAR molecules and provide potent antitumour effects. Furthermore, this work shows that at least two V_H can be assembled to generate dual specific CAR-T cells."

Dr Colette Johnston, Senior Director of Research at Crescendo Biologics, commented: "These findings are an exciting step forward in the continued development of safe and effective CAR-T cell therapies, and the data also demonstrate the broad applicability of our Humabody platform. Our collaboration with Dr Dotti's team has combined the strengths of Crescendo's V_H platform with the CAR-T technology from UNC's Department of Microbiology and Immunology, and we are delighted with its success."

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About Crescendo Biologics

Crescendo Biologics is a clinical stage immuno-oncology company developing novel, targeted T cell enhancing Humabody® therapeutics.

Leading its proprietary pipeline, Crescendo Biologics has developed CB307, a novel half-life extended CD137 x PSMA Humabody® for the selective activation of tumour-specific T cells exclusively within the tumour microenvironment. CB307 is designed to achieve a longer lasting anticancer effect whilst avoiding systemic toxicity.

The Company's ability to develop multi-functional Humabody® therapeutics is based on its unique, patent protected, transgenic mouse platform generating 100% human V_H domain building blocks (Humabody® V_H). These robust molecules can be configured to engage therapeutic targets in such a way that they deliver novel biology and superior bio-distribution. This results in larger therapeutic windows compared to conventional IgG approaches. Humabody®-based formats can also be applied across a range of non-cancer indications.

Crescendo Biologics is located in Cambridge, UK, and is backed by blue-chip investors including Sofinnova Partners, Andera Partners, IP Group, Takeda Ventures, Quan Capital and Astellas.

For more information, please visit www.crescendobiologics.com and follow @HUMABODY.