PRESS RELEASE

Amphista Therapeutics announces new data demonstrating *in vivo* efficacy and CNS activity of its mechanistically differentiated targeted protein degraders

- **First demonstration of efficacy in disease-relevant *in vivo* models for an orally delivered bifunctional non-cereblon / non-VHL-based protein degrader**
- **Deep degradation of target protein is achieved in a rapid, sustained, and highly selective manner**
- **Successful achievement of efficient CNS delivery for multiple degraders and demonstration of significant degradation of target protein in the brain**

Cambridge, UK, January 24th, 2024 – Amphista Therapeutics ("the Company" or "Amphista"), a leader in next generation targeted protein degradation (TPD) approaches, today announces the achievement of two compelling new data sets with its next generation bifunctional degraders demonstrating *in vivo* efficacy and the ability to target and degrade proteins in the central nervous system (CNS).

Amphista's degraders, which leverage a novel protein degrading mechanism, with advantages beyond first generation cereblon or VHL-based approaches, have demonstrated:

- **Sustained degradation of target protein and anti-tumor efficacy**: once daily oral dosing led to statistically significant reduction in tumor burden and survival advantage in multiple *in vivo* disease models.
- **Rapid degradation of target protein:** significant levels of degradation were induced rapidly after dosing.
- **Highly selective degradation of target protein:** statistically significant degradation of target protein vs >8000 other proteins, including closely related homologs, when dosed at 100x DC50.

Amphista also discloses significant progress in the advancement of its technology for the treatment of neurodegenerative diseases, a key focus of the Company. These data show:

- Amphista degraders can be rationally designed to achieve **CNS penetrance with examples achieved across multiple targets.**
- **Rapid degradation of target protein achieved in the brain** *in vivo* (dog and non-human primate, and in multiple brain regions) when dosed intravenously.

Louise Modis, Chief Scientific Officer of Amphista Therapeutics, said: "We are delighted by the progress we have made in advancing our pipeline and demonstrating the potential of our unique TPD technology. To our knowledge, this is the first time an orally delivered bifunctional non-cereblon / non-VHL-based protein degrader has shown efficacy in disease-relevant *in vivo* models. Combined with our progress in demonstrating *in vivo* degradation of targets within the CNS, we are extremely excited to have achieved these key preclinical development milestones and we look forward to providing additional updates across our pipeline throughout the year."

Beverley Carr, Interim Chief Executive Officer of Amphista Therapeutics, said: "The last six months have been transformative for Amphista and these new compelling *in vivo* data strengthen our belief that our technology has the potential to deliver differentiated protein degrader molecules with class-leading physicochemical properties, enabling us to target a wider tissue and indication scope than traditional protein degrader approaches. These data are testament to the strength of our scientific team and we are on track with our portfolio priorities, exploring the tremendous potential of our platform across multiple indications in CNS and oncology."

About Amphista Therapeutics

Amphista Therapeutics is focused on transforming the lives of patients with severe diseases including cancer. The company is applying its proprietary Amphista degrader platform to advance new approaches in targeted protein degradation (TPD). They aim to address the challenges faced by earlier stage TPD research and to realise the full therapeutic potential of this transformational approach. Founded by Advent Life Sciences, Amphista is a spin-out of TPD expert Professor Alessio Ciulli's laboratories at the University of Dundee. The Company has raised over $60M to date and is funded by leading life science investors including Forbion, Gilde Healthcare, Novartis Venture Fund, Advent Life Sciences, Eli Lilly & Company and The Dementia Discovery Fund. For more information, please visit: www.amphista.com

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