Vesper Bio initiates Phase Ib/IIa proof of concept study of VES001 in asymptomatic patients with gene mutations that cause frontotemporal dementia (FTD)

- *Dosing of VES001 has commenced in patients with causal gene mutations for FTD(GRN), a type of frontotemporal dementia which is invariably fatal*
- *This follows Vesper having received clinical trial authorisation from the Netherlands and the United Kingdom to initiate its Phase Ib/IIa "SORT-IN-2" trial*
- *VES001 is a first-in-class, potentially disease-modifying, orally-dosed, brain-penetrant treatment for FTD(GRN), which elevates progranulin levels, a protein vital for neuronal health and for which FTD(GRN) patients are deficient*
- *Vesper expects to complete dosing of all participants by mid-2025*

Copenhagen, Denmark, 7 January 2024 – Vesper Bio ApS ("Vesper" or "the Company"), a clinical stage biotech and world leader in sortilin receptor biology, today announces the initiation of a Phase Ib/IIa Proof of Concept (POC) study of its lead candidate VES001 for frontotemporal dementia. The SORT-IN-2 study will evaluate VES001 in patients with mutations in their progranulin-coding gene (GRN), which are causal for FTD(GRN). FTD(GRN) is an early onset degenerative brain disease which is invariably fatal.

SORT-IN-2 is an open-label, dual centre study assessing the clinical efficacy of VES001 in patients with GRN mutations who are currently asymptomatic. It will be performed at one clinical centre in the Netherlands and another in the United Kingdom. The first patient has now been enrolled and Vesper expects to have completed enrolment and dosing by mid-2025.

Mads Fuglsang Kjølby, Co-Founder and interim Chief Medical Officer at Vesper Bio, said: "*The aim of this study is to further demonstrate the safety and tolerability of VES001 and confirm whether VES001 has a positive effect on progranulin levels in the cerebrospinal fluid and blood plasma of these patients. Progranulin is vital for maintaining neuronal health, however, progranulin levels in asymptomatic people with GRN mutations are typically half that of people without such mutations. Based on the data from our successful First-in-Human trial, we believe VES001 will normalise progranulin levels, and thus has great potential to slow or even arrest FTD(GRN) disease progression.*"

Paul Little, Chief Executive Officer at Vesper Bio, added: "*It is an incredible achievement by the Vesper team that we have been able to progress VES001 so quickly into this next clinical trial phase. We are committed to bringing this important new oral treatment option to families living with FTD, where there is no approved therapy available today. We are all striving for a future free from FTD for patients and their families.*"

The SORT-IN-2 study will be conducted at Erasmus University Medical Centre, Rotterdam, the Netherlands, under Principal Investigator (PI) Professor Harro Seelaar; and the Leonard Wolfson Experimental Neurology Centre, CRF National Hospital for

Neurology and Neurosurgery, University College London, UK, under PI Professor Jonathan Rohrer.

The clinicaltrials.gov identifier for SORT-IN-2 is NCT06705192.

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Notes to Editors

About VES001

VES001 targets sortilin, a neuronal surface receptor that 'competes' with other receptors to bind progranulin. When bound by sortilin, progranulin is degraded through a specific internalisation process, which also leads to further reductions in extracellular free progranulin. VES001 is designed to protect cells by normalising and maintaining progranulin levels. With its unique mode of action and convenient oral daily dosing, VES001 promises to be an ideal, patient-friendly treatment option.

In early September, Vesper reported positive clinical data from a Phase Ia study of VES001 in healthy volunteers. High levels of safety and tolerability of VES001 were observed and there were no serious or treatment-emergent adverse events. The data also showed orally-administered VES001 exhibited excellent pharmacokinetic properties, distributed well to both plasma and CNS compartments, and resulted in strong target engagement – as evidenced by an increased level of progranulin in both compartments.

About Vesper Bio
Vesper Bio is a clinical stage biotech and world leader in sortilin receptor biology. Its lead program uses a rationally-designed small molecule sortilin inhibitor to rebalance levels of progranulin in patients where the sortilin receptor would otherwise reduce circulating and extracellular progranulin, contributing to disease. Progranulin is a protein that the body uses to regulate cell growth, survival, repair and attenuate inflammation. Low progranulin levels are believed to be a factor in cell dysfunction and damage in a range of neurodegenerative disorders. By normalising progranulin levels, Vesper believes its compounds will have a disease-modifying effect, protecting and preserving the remaining neurons.

Its lead compound, VES001, is a patient friendly, first-in-class, brain penetrant, oral treatment which targets progranulin deficiency, a major underlying cause of frontotemporal dementia (FTD). As an orally delivered small molecule, VES001 is able to cross the blood-brain barrier and is an ideal dosing method among these patients due to their rapidly declining mental state.

About frontotemporal dementia (FTD)

Frontotemporal dementia (FTD), also known as frontotemporal lobar degeneration (FTLD), is a group of brain disorders that cause degeneration in the frontal and temporal lobes of the brain. FTD impacts a person's behaviour, judgement, communication and ability to participate in all activities of daily living. It is the most common cause of dementia in people under the age of 60 and is often misdiagnosed as Alzheimer's Disease. FTD(GRN) is an inherited form of FTD caused by mutations of the progranulin gene (GRN), resulting in approximately 50 per cent reduction in progranulin levels. FTD(GRN) accounts for up to 12% of all FTD cases. There are thought to be around 17,400 patients with FTD(GRN) in the seven major markets, and roughly 140,000 carriers at risk who will go on to develop FTD(GRN).

For further information please visit, https://www.vesperbio.com/