Vesper Bio announces successful Phase I study for potentially disease-modifying treatment for frontotemporal dementia

- *VES001 is a first-in-class oral, brain penetrant, small molecule sortilin inhibitor for treatment of FTD(GRN)*
- *Data demonstrate excellent safety, tolerability profile, dose-proportionality and target engagement with elevations in progranulin in both plasma and CNS*
- *CTA filed for Phase IIa study, first dose targeted for Q4 2024*

Copenhagen, Denmark, 04 September 2024 – Vesper Bio ApS ("Vesper" or "the Company"), a clinical stage biotech and world leader in sortilin receptor biology, today announces the successful completion of the Phase I study for its lead candidate, VES001, a potentially disease-modifying treatment for frontotemporal dementia patients with mutations in the progranulin gene (FTD(GRN)).

Frontotemporal dementia is the most common cause of dementia in people under the age of 60. FTD(GRN), which is estimated to account for a quarter of familial FTD cases, is a form of FTD caused by mutations of the progranulin gene (PGRN), a protein responsible for the regulation of cell growth, survival, and repair. Low levels of progranulin are associated with cellular dysfunction, neuroinflammation and neuronal damage across a variety of neurological indications.

VES001 is a first-in-class oral, brain-penetrant, small molecule sortilin inhibitor rationally designed as a potentially disease-modifying treatment for FTD(GRN). Sortilin is a receptor found on the surface of neurons that competes with progranulin receptors for progranulin binding. Progranulin is degraded when binding to sortilin through an internalization process, leading to further reductions in free progranulin and subsequent neuronal damage and cell death. VES001 is designed to cross the blood brain barrier and inhibit this process, binding to the sortilin receptor and stopping progranulin from binding, thereby helping to maintain and normalize progranulin levels. With its unique mode of action and convenient oral daily dosing, VES001 is an ideal, patient-friendly treatment option.

The Phase I study was a two-part trial in 78 healthy volunteers investigating safety, tolerability, pharmacokinetics and pharmacodynamic target engagement endpoints across a range of separate dose levels. All endpoints were successfully met, with the top line data from the 7-day multiple ascending dose (MAD) stage re-affirming the findings seen in the single ascending dose (SAD) stage, announced in May 2024.

High levels of safety and tolerability of VES001 were observed across the doses tested, with no serious or treatment-emergent adverse events reported. The data demonstrate that following oral dosing, VES001 exhibits excellent pharmacokinetics and distribution to plasma and the targeted Central Nervous System compartment. Furthermore, VES001 showed strong target engagement evidenced by an increased and accumulating level of progranulin in the volunteers dosed once or twice daily in the MAD stage. Data from this study will be published in due course and when modelled on to the target population, represent a substantial normalization of progranulin concentration after 7 days of dosing.

Vesper Bio has completed a clinical trial application (CTA) seeking to progress VES001 into a Phase IIa proof-of-concept study in a relevant patient population, with dosing expected to start in Q4 2024.

Mads Fuglsang Kjølby, Chief Medical Officer at Vesper Bio, commented: *"Vesper Bio is proud of its status as a world leader in sortilin biology. The data generated in our Phase I trial of VES001 demonstrate the potential of sortilin inhibition as a therapeutic approach to the treatment of frontotemporal dementia, and potentially other neurodegenerative diseases."*

Paul Little, Chief Executive Officer at Vesper Bio, added: *"At Vesper, we are motivated by our patients and their relatives, who inspire our mission to develop innovative therapies that can help fight this awful disease. These promising clinical data coupled with VES001's patient friendly profile bring us one step closer to transforming patient outcomes in frontotemporal dementia."*

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Notes to Editors

About Vesper Bio
Vesper is a clinical stage biotech and world leader in sortilin receptor biology. Its lead program uses a 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 avoid inflammation. Low progranulin levels are believed to be a factor in cell dysfunction and damage in a range of indications across neurology. By normalizing progranulin levels, Vesper believes its compounds will have a disease modifying effect, protecting and preserving the remaining cells.

Its lead compound, VES001, is a patient friendly, first-in-class, brain penetrant, oral treatment which targets progranulin deficiency, a major underlying cause of fronto-temporal 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 behavior, 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 a form of FTD caused by mutations of the progranulin gene (PGRN), resulting in low progranulin levels. FTD(GRN) is thought to account for a quarter of familial FTD cases.

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