Vesper Bio announces positive Phase Ib/IIa topline results for lead candidate VES001 for frontotemporal degeneration

- Phase Ib/IIa study found VES001, the first oral therapy being tested in FTD, led to >95% mean increase in progranulin levels in CSF, compared to baseline
- Topline results indicate VES001 normalises levels of progranulin in people who have a shortage of this vital protein for genetic reasons, potentially stopping them developing symptomatic frontotemporal dementia (FTD)
- VES001 had a favourable safety and tolerability profile during the three-month daily dosing regimen, with few adverse events (AEs) reported
- Results support progressing VES001 into Phase IIb/III trials in people with FTD-GRN, the variant of FTD caused by genetically low progranulin levels

Copenhagen, Denmark, 31 October 2025 – Vesper Bio ApS ("Vesper" or "the Company"), a clinical stage biotech developing novel oral therapies for neurodegenerative and neuropsychiatric diseases, today announces positive topline results from its Phase Ib/IIa SORT-IN-2 clinical study evaluating VES001 in asymptomatic carriers with frontotemporal degeneration (FTD) caused by mutations in the progranulin gene (GRN).

Mean progranulin levels increased by more than 95% compared to baseline at the highest dose tested. As individuals with FTD-GRN typically have progranulin concentrations that are around half that of people without GRN mutations, this represents a normalising of progranulin levels. The data also showed dose-dependent increases in progranulin protein levels in both plasma and cerebrospinal fluid (CSF).

Mads Kjolby, Co-Founder and Chief Medical Officer at Vesper Bio, said: *"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 these topline Phase Ib/IIa data, we believe VES001 has the potential to normalise progranulin levels not only in asymptomatic individuals with GRN mutations, but in symptomatic people too, without affecting other sortilin functions crucial for neuronal health. We therefore think VES001 has great potential to slow or even arrest FTD-GRN disease progression."*

Jacob Falck Hansen, Chief Executive Officer at Vesper Bio, added: *"These data represent an important milestone for Vesper Bio and the FTD community. We thank all participating individuals and the dedicated staff at the clinical sites. The strong clinical results validate our targeted approach. It gives us great confidence in further developing our selective sortilin inhibitor VES001 with potential to become the first approved treatment for FTD-GRN."*

The open-label, single arm study included six individuals from the Netherlands and the UK who all carry GRN mutations, which cause them to have very low progranulin levels, but are asymptomatic. The study demonstrated that VES001 had a safe and tolerable profile. It also

confirmed target engagement took place, with significantly elevated levels of progranulin in both plasma and CSF found in the participants after treatment, compared to baseline levels of the protein for this population. The findings provide the first validation of Vesper's approach of restoring normal progranulin levels in this population by selectively inhibiting progranulin binding to the sortilin receptor without affecting sortilin levels or functions important for neuronal health. This is in contrast to antibody-mediated degradation of sortilin.

The study has been carried out at two clinical centres: the Erasmus University Medical Centre, Rotterdam, in the Netherlands, and the Leonard Wolfson Experimental Neurology Centre Clinical Research Facility at the National Hospital for Neurology and Neurosurgery, University College London, in the UK.

Professor Jonathan Rohrer, of the Dementia Research Centre, UCL Queen Square Institute of Neurology, London, UK, Principal Investigator at the trial's UK sites, said: "*This is the first oral therapy being tested in FTD. The increase of progranulin levels back to normal levels in these asymptomatic mutation carriers – who know they will develop symptoms in the next 10 to 20 years – speaks to the future potential of this treatment to prevent people ever developing symptoms of FTD.*"

Participants in the PhIb/IIa SORT-IN-2 study received daily oral doses of VES001 – first at a lower dose for 28 days, and then at a higher dose for 56 days. VES001 was well tolerated with only a few mild adverse events (AEs) reported. There were no severe adverse events (SAEs) reported, or discontinuations due to treatment-related effects.

Separately, Vesper Bio is pleased to announce that it has successfully completed its long-term, pivotal toxicology studies of VES001 in animals.

The SORT-IN-2 study is supported by the Alzheimer's Drug Discovery Foundation (ADDF) and the Association for Frontotemporal Degeneration (AFTD) through the TreatFTD programme. It will fully report in Q1 2026. Vesper Bio will then prepare to start a Phase IIb/III clinical trial to evaluate VES001's efficacy on clinical progression and biomarker endpoints in symptomatic FTD-GRN patients.

For more information about the trial (NCT06705192), please visit www.clinicaltrials.gov.

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Notes to Editors

About Vesper Bio

Vesper Bio is a clinical stage biotech and world leader in sortilin receptor biology. Vesper is developing small molecule-based selective sortilin inhibitors as novel oral therapies for neurodegenerative and neuropsychiatric diseases. VES001, its lead compound, is a patient friendly, first-in-class, brain penetrant, oral treatment which targets progranulin deficiency, a major underlying cause of a genetically driven type of frontotemporal degeneration (FTD-GRN). VES001 is a competitive sortilin inhibitor that selectively prevent degradation of progranulin while preserving sortilin levels and functions crucial for neuronal health, in contrast to antibody-mediated degradation of sortilin. With VES001, Vesper aims at normalising levels of progranulin and reducing neuroinflammation and disease progression in both asymptomatic and symptomatic FTD-GRN patients.

About frontotemporal degeneration (FTD)

Frontotemporal degeneration (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 a form of FTD caused by mutations of the progranulin gene (GRN), 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/