Vesper Bio doses first volunteer in Phase I study of first-in-class oral treatment for Frontotemporal Dementia (FTD)

- *Vesper Bio, backed by* Lundbeckfonden BioCapital*, initiates a Phase I study to evaluate its lead asset VES001, for the treatment of FTD (GRN mutation), addressing a critical unmet medical need*
- *VES001 is a product designed with the needs of the patients and their care givers in mind*
- *The Phase I study will assess safety, tolerability and pharmacokinetics and target engagement biomarkers across a range of single and multiple doses, moving on to a Phase Ib/c Proof of Concept*

Copenhagen, Denmark, 7th December 2023 – Vesper Bio ApS ("Vesper" or "the Company"), a clinical stage biotech and world leader in sortilin receptor biology, today announces that the first volunteer has been dosed with its lead compound VES001, a patient friendly, first-in-class, brain penetrant, oral treatment, that could bring a meaningful disease-modifying benefit to patients suffering from Frontotemporal Dementia harbouring loss of function mutations in the progranulin gene (FTD)(GRN). VES001 aims to rebalance circulating progranulin in life changing diseases.

Vesper has successfully initiated a randomised, double-blind, single and multiple ascending dose Phase I study in healthy volunteers. The study will assess safety, tolerability and pharmacokinetics and target engagement biomarkers across a range of single and multiple doses of this new treatment in healthy volunteers before continuing to proof of concept in asymptomatic GRN mutation carriers. As a small molecule, VES001 is ideal for convenient oral daily dosing and is designed to cross the blood brain barrier. There are currently no approved disease-modifying treatments for FTD(GRN) with current standard of care treatments only able to address symptoms of the disease, such as anxiety, depression and agitation.

Paul Little, PhD, Chief Executive Officer of Vesper Bio, said: *"We have taken a significant step forward in bringing VES001 closer to treating patients suffering from FTD(GRN). This is a devasting disease for both patients and their families and we hope to show that this is a potentially game-changing treatment. The role of progranulin is becoming better understood, with clinical validation using antibody approaches, and pre-clinical trials with our small molecule, VES001, have shown the effectiveness of targeting the uptake of progranulin in this way. I am grateful to the Vesper team, scientific advisors and patient groups who have been involved in bringing Vesper Bio to this important moment, as we transition to a clinical stage company.*

"FTD is a disease that hits very hard and affects the lives of patients and their families in profound ways, making normal life all but impossible. We are striving to bring a product forward with the aim of halting this terrible disease."

Anders Nykjaer, MD, PhD Chief Scientific Officer of Vesper Bio, commented: "*The ultimate goal for every scientist in biomedical research is to make an observation that may enable the development of a treatment against a devastating or fatal disorder. I have been privileged to experience such a journey. Starting many years ago, when we identified the Vps10p-domain receptor sortilin, and later demonstrating that it may represent an attractive target to normalize progranulin levels that are commonly too low in FTD(GRN), we have today dosed the first human subjects with the first orally*

available sortilin antagonist. This has truly been one of the greatest experiences of my professional life."

About FTD(GRN)

FTD(GRN) is a genetic disease, where family history accounts for between 20%-40% of all FTD cases. The GRN mutation in FTD patients is one of several mutations and is associated with a 50% reduction in circulating progranulin compared to healthy individuals. There are c.17,400 patients with FTD(GRN) in the seven major markets and c.140,000 carriers at risk who will go on to develop FTD. With no disease-modifying treatments available, there is a clear, critical unmet need.

VES001 Mode of Action

Patients suffering from FTD(GRN) have lower circulating levels of progranulin in their blood plasma and central nervous system (CNS). By blocking the uptake of progranulin into cells via the sortilin receptor, VES001 returns progranulin in blood and CNS to normal levels, protecting neurons from further damage.

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 in neurology. By normalizing progranulin levels, Vesper believes its compound will have a disease-modifying effect, protecting and preserving remaining cells. The company intends to demonstrate this through clinical trials in various indications, starting with Fronto-Temporal Dementia where there are genetically defined patient populations with progranulin deficiency FTD(GRN).

Vesper is currently expediting the development of VES001 for FTD(GRN) through the ongoing Phase I study followed by a Phase Ib Proof-of Concept study in GRN mutation carriers in advance of potentially registrational Phase II/III trials, and for Phase I readiness of VES002, a treatment focused on a second central nervous system indication.

About the trial

- Phase 1 single ascending dose: 48 healthy subjects, six cohorts of eight subjects each randomized in a 6:2 ratio.
- Phase 1 multiple ascending dose: 30 healthy subjects, three cohorts of 10 subjects each randomized in an 8:2 ratio.

About Vesper

Founded by Dr. Mads Kjolby, CMO, and Professor Anders Nykjaer, CSO, Vesper are pioneers in sortilin biology, with a strong background in biopharma, backed by an exceptional multi-national scientific advisory board, consisting of leading FTD KOLs. Anders Nykjaer discovered with his colleagues the Vps10p-domain receptor sortilin and its interaction with progranulin, and the team draw on the groundbreaking knowledge of sortilin biology generated at Aarhus University, Denmark.

Research at Aarhus University has been supported for many years by the Lundbeck Foundation, an enterprise foundation encompassing a comprehensive range of enterprise and philanthropic activities. The Foundation's philanthropic grants amount to more than DKK 500m annually, primarily focusing on the brain – including the world's largest personal prize for neuroscience: The Brain Prize.

Vesper has received financial and operational backing from Lundbeckfonden BioCapital, the investment arm of The Lundbeck Foundation, for a number of years, bringing exciting basic science to clinical stage biotech programmes at the frontier of its field.

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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 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.

FTD(GRN) is a genetic disease, where family history accounts for between 20%-40% of all FTD cases. The GRN mutation in FTD patients, for example, is one of several mutations and is associated with a 50% reduction in circulating progranulin compared to normal. There are c.17,400 patients with mutated GRN in seven major markets symptomatic at any one time and c.140.000 carriers at risk who will go on to develop FTD. With no treatments available, there is a clear, critical unmet need.

Vesper is currently expediting the development of VES001 for FTD(GRN) through ongoing Phase I studies that will include a Phase Ib Proof-of Concept in GRN mutation carriers in advance of potentially registrational Phase II/III trials, and for Phase I readiness of VES002, a treatment focused on a second central nervous system indication. For further information please visit, https://www.vesperbio.com/.

About Lundbeckfonden BioCapital

Lundbeckfonden BioCapital is a leading Danish biotech investor and currently has investments of over DKK 2 billion in 21 Danish and international companies. Lundbeckfonden BioCapital focuses its new investments primarily on Danish-based biotech companies and the local ecosystem with the purpose of bringing discoveries to the benefit of patients worldwide.

Read more: www.lundbeckfonden.com/business-activities/lundbeckfonden-biocapital

About the Lundbeck Foundation

The Lundbeck Foundation is an enterprise foundation encompassing a comprehensive range of enterprise and philanthropic activities – all united by its strong purpose; Bringing Discoveries to Lives. The Foundation is the long-term and engaged owner of several international healthcare companies – Lundbeck, Falck, ALK, Ellab, and Ferrosan Medical Devices – and an active investor in business, science, and people through its commercial investments in the financial markets; in biotech companies based on Danish research and through philanthropic grants to science talents and programs in Danish universities. The Foundation's philanthropic grants amount to more than DKK 500m annually primarily focusing on the brain – including the world's largest personal prize for neuroscience: The Brain Prize.

Read more: www.lundbeckfonden.com