Spur Therapeutics Presents Promising New Data from its GBA1 Parkinson's Disease Research Program

Rationally engineered GCase85 enzyme reduces α-Synuclein accumulation, which plays a key role in the development and progression of Parkinson's, in neuronal cells more effectively than wildtype GCase

GCase85 also shows greater exposure and distribution in the brain than wildtype GCase in in vitro and in vivo studies

Data support opportunity to leverage GCase85 for development of a potentially best-in-class gene therapy candidate for Parkinson's disease patients with GBA1 mutations

LONDON, July 1, 2024 – Spur Therapeutics, formerly Freeline Therapeutics, today announced new data from its GBA1 Parkinson's disease research program demonstrating that its rationally engineered GCase85 enzyme reduces the accumulation of α-Synuclein, a protein that plays a significant role in the development and progression of Parkinson's disease, more effectively than wildtype glucocerebrosidase (GCase) in *in vitro* studies. These data were presented at the inaugural GBA1 meeting, hosted by the Montreal Neurological Institute-Hospital at McGill University and sponsored by The Michael J. Fox Foundation, Parkinson Canada, The Silverstein Foundation, the Hilary & Galen Weston Foundation and Cure Parkinson's with the aim of advancing the understanding and treatment of GBA1-associated neurodegenerative diseases.

"There is a rapidly growing body of evidence that *GBA1* mutations and the resulting deficiency of the GCase enzyme play a significant role in driving neurodegenerative processes in Parkinson's disease as well as certain forms of dementia," said Henning Stennicke, PhD, Chief Scientific Officer of Spur Therapeutics. "We're pleased to share data from our GBA1 Parkinson's research program, demonstrating that our rationally engineered GCase85 enzyme results in more robust exposure than wildtype GCase and broader distribution in the brain in both *in vitro* and *in vivo* models of disease, as well as greater reduction of the α-Synuclein accumulation that is a hallmark of Parkinson's disease. We believe the enhanced stability of GCase85 provides the opportunity to develop a potentially best-in-class gene therapy for Parkinson's disease patients with GBA1 mutations."

Spur's research program in Parkinson's disease builds on its work in Gaucher disease and is focused on a subset of Parkinson's disease patients with mutations in the *GBA1* gene, the same gene implicated in Gaucher disease. In both Gaucher and Parkinson's, *GBA1* mutations lead to a deficiency of the GCase enzyme and the accumulation of harmful substrates. *GBA1* mutations greatly increase the risk of developing Parkinson's disease and are associated with earlier onset of disease, more severe symptoms and increased likelihood of progression to dementia.

Spur scientists originally designed the GBA1-85 transgene to deliver GCase85, a rationally engineered version of GCase with enhanced stability over wildtype, as part of its work on FLT201, the company's clinical-stage gene therapy program in Type 1 Gaucher's disease. Early data from the ongoing Phase 1/2 clinical trial of FLT201 has shown significant reductions in accumulated substrate and compelling signs of clinical benefit as well as a favorable safety and tolerability profile. Leveraging the same transgene, Spur

now aims to develop a potentially life-changing gene therapy candidate for Parkinson's disease patients with *GBA1* mutations.

The data presented at the GBA1 Meeting show:

- GCase85 results in an order of magnitude higher GCase activity compared to wildtype *in vitro* and *in vivo*.
- GCase85 is more efficient at reducing α-Synuclein accumulation compared to wildtype in neuronal cells *in vitro*.
- Direct injection into the caudate putamen region of the brain using an AAV9 vector results in efficient distribution to the target cells within the substantia nigra, which is a key area of the brain affected by Parkinson's disease.
- An AAV9-GBA1-85 construct results in stronger expression and broader GCase distribution in the brain than a wildtype AAV9-GBA1 construct when directly injected into the brain in mice.

Spur is working to further optimize GCase85 for expression in the brain and identify the best capsid and route of administration for delivery of its proprietary GBA1-85 transgene to key areas of the brain affected by Parkinson's disease. The company expects to select a development candidate in the second half of 2024 to progress into preclinical studies designed to support the program's advancement into clinical trials.

About GBA1 Parkinson's Disease

Parkinson's disease (PD) is a progressive neurodegenerative disorder that results in tremors, muscle rigidity, difficulty walking, anxiety, depression and cognitive impairments. Approximately 5-15% of PD patients have mutations in the *GBA1* gene, which encodes for the glucocerebrosidase (GCase) enzyme. The most common genetic risk factor for PD, *GBA1* mutations significantly increase the risk of developing PD and are associated with earlier onset and more severe disease. There are no approved disease-modifying therapies for PD, and current treatments, which focus on managing symptoms, become less effective over time. Spur estimates GBA1 PD affects approximately 190,000 patients in the United States, United Kingdom, France, Germany, Spain and Italy.

About Spur Therapeutics

Spur Therapeutics is a clinical-stage biotechnology company focused on developing life-changing gene therapies for debilitating chronic conditions. By optimizing every component of its product candidates, Spur aims to unlock the true potential of gene therapy to realize outsized clinical results. Spur is advancing a breakthrough gene therapy candidate for Gaucher disease and a potential first-in-class gene therapy candidate for adrenomyeloneuropathy, as well as a research strategy to move gene therapy into more prevalent diseases, including forms of Parkinson's, dementia, and cardiovascular disease. Expanding our impact, and advancing the practice of genetic medicine.

Toward life-changing therapies, and brighter futures. Toward More™

For more information, visit www.spurtherapeutics.com or connect with Spur on LinkedIn and X.

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