Seelos Therapeutics Announces Data Demonstrating Downregulation of Alpha Synuclein in an In Vivo Gene Therapy Study of SLS-004 Utilizing CRISPR-dCas9 in Parkinson's Disease

-A single dose of SLS-004 produced a substantial increase in recovery of tyrosine hydroxylase-positive (TH+) dopaminergic neurons that are known to degenerate in patients with Parkinson's disease

-Degeneration of TH+ midbrain dopaminergic neurons in patients with Parkinson's disease is attributed to lead to the cardinal Parkinsonian symptoms of tremor, rigidity, bradykinesia and postural disturbances

-Seelos management will discuss additional information about this study during the Research and Development Update Conference Call and Webcast today, December 15th at 1pm ET

NEW YORK, Dec. 15, 2022 /PRNewswire/ -- Seelos Therapeutics, Inc. (Nasdaq: SEEL), a clinical-stage biopharmaceutical company focused on the development of therapies for central nervous system disorders and rare diseases, today announced in vivo data demonstrating that a single dose of SLS-004 downregulated the production of alpha-synuclein (α-synuclein). This reduction of α-synuclein by SLS-004 in an established α-synuclein overexpressing animal model of Parkinson's disease (PD) resulted in substantial increase and recovery of degeneration in tyrosine hydroxylase positive (TH+) dopaminergic neurons. TH+ dopaminergic neurons in the midbrain region, called substantia nigra pars compacta (SNpc), are known to degenerate in patients with PD. This degeneration is attributed to lead to the cardinal Parkinsonian symptoms of tremor, rigidity, bradykinesia, and postural disturbances.

"These data suggest that SLS-004 may have substantial potential for a disease-modifying gene therapy in Parkinson's disease."

These findings observed in an in vivo PD model validate and extend prior findings from in vitro data using SLS-004. SLS-004 demonstrated therapeutically desirable reduction in SNCA mRNA (α-synuclein messenger RNA) which led to reduced α-synuclein protein expression.

"Increasing the recovery of TH+ dopaminergic neurons after a single administration of SLS-004 is a significant achievement, and this in vivo study validates and extends our prior findings," said Raj Mehra, Ph.D., Chairman and CEO of Seelos. "These data suggest that SLS-004 may have substantial potential for a disease-modifying gene therapy in Parkinson's disease."

PD is the second most common neurodegenerative disorder in the world and currently, there is no effective treatment to prevent PD or to halt its progression. Mutations in the SNCA gene, which provides the genetic code for the production of α-synuclein protein, are widely accepted as a therapeutic target to treat PD. In addition, accumulating evidence has suggested that elevated levels of α-synuclein are causative in the pathogenesis of PD. Patients with impaired regulation of the SNCA gene show as high as 200% expression of α-synuclein protein. A reduction of 25%-50% in SNCA mRNA and protein expression is believed to be sufficient to restore normal physiological levels of α-synuclein.

Preliminary Findings of In Vivo Study

The goal of this in vivo study was to validate and extend the findings in an established animal model of PD based on prior in vitro results that were described in human-induced pluripotent stem cells (hiPSC) derived neuronal system from well-characterized Parkinson's patients with triplication of the SNCA locus (SNCA-Tri hiPSC-derived system).

The human A53T α-synuclein viral vector that expresses human A53T α-synuclein to model PD in animals was used in this study with the addition of human intron 1. The human A53T α-synuclein viral vector has been characterized in the mouse, rat and non-human primate models for its ability to: express human A53T α-synuclein, induce nigrostriatal degeneration, and model PD pathology when administered in the substantia nigra pars compacta (SNpc). The SNpc is an area in the brain that is known to degenerate in PD and is believed to be the causative factor for the cardinal signs of the disease such as tremor, rigidity, bradykinesia, and postural disturbances. The administration of the disease inducing vector in the SNpc leads to increased production of α-synuclein protein that leads to nigrostriatal degeneration and thus reduces the number of TH+ midbrain dopaminergic neurons in the SNpc. In this study, the disease inducing vector was injected into the SNpc along with either the test article SLS-004 or control article in the other hemisphere and brain tissues were evaluated at the end of the study.

The preliminary findings indicate that a single dose of SLS-004 administered in the SNpc of the test hemisphere in the brain produced a substantial increase in and recovery of degenerating TH+ dopaminergic neurons compared to the administration of the control vector in the SNpc of the other hemisphere. The nigrostriatal degeneration of TH+ midbrain dopaminergic neurons in the SNpc is implicated in PD pathology and attributed to the cardinal signs of parkinsonian symptoms.

In July 2021, Seelos announced positive in vivo data demonstrating down-regulation of SNCA mRNA and protein expression from a study of SLS-004 in an in vivo rodent model utilizing CRISPR-dCas9 gene therapy technology. A single dose of SLS-004 produced a therapeutically desirable 27% reduction in SNCA mRNA and a 40% reduction in SNCA protein expression.

Seelos plans to advance the study of SLS-004 in PD and in August 2022, Seelos was selected to receive a grant from The Michael J. Fox Foundation for Parkinson's Research to advance preclinical research and development for the SLS-004 program.

Also, In June 2022, Seelos released statistically significant data in an in vitro gene therapy study of SLS-004 utilizing CRISPR-dCas9 in dementia with Lewy bodies.

Registration for today's conference call and webcast is available at: **https://lifescievents.com/event/seelos-therapeutics-kol-event/** and **https://seelostherapeutics.com/registration-for-12-15-rd-update-webcast/**.

About SLS-004

SLS-004 is a novel epigenome-editing approach to modulate expression of α-synuclein protein through the SNCA gene. This approach is mediated by hyper methylation of the SNCA genetic code that ultimately leads to a controlled and regulated decrease in α-synuclein production. SLS-004 utilizes an all-in-one lentiviral vector harboring dCas9-DNA methyltransferase 3A (DNMT3A) to enrich DNA-methylation within CpGs (cytosine-phosphate-guanine site) island at the SNCA intron 1 region. The system resulted in a precise and fine-tuned downregulation (30%) of SNCA overexpression in hiPSC-derived dopaminergic neurons from a PD patient with the triplication of the SNCA locus (SNCA-Tri). Most importantly, the reduction of SNCA expression mediated by the developed system was sufficient to ameliorate PD related cellular phenotypes. The in vitro studies achieved several key milestones, including the establishment that DNA hyper-methylation at SNCA intron 1 allows for an effective and sufficiently tight downregulation of SNCA expression levels. These data suggest the potential of SLS-004, a CRISPR-dCas9 technology, as a novel epigenetic-based therapeutic approach for PD.

About Seelos Therapeutics

Seelos Therapeutics, Inc. is a clinical-stage biopharmaceutical company focused on the development and advancement of novel therapeutics to address unmet medical needs for the benefit of patients with central nervous system (CNS) disorders and other rare diseases. The Company's robust portfolio includes several late-stage clinical assets targeting indications including Acute Suicidal Ideation and Behavior (ASIB) in Major Depressive Disorder (MDD), amyotrophic lateral sclerosis (ALS) and spinocerebellar ataxia (SCA), as well as early-stage programs in Huntington's disease, Alzheimer's disease, and Parkinson's disease.

For more information, please visit our website: **https://seelostherapeutics.com**, the content of which is not incorporated herein by reference.

Forward Looking Statements

Statements made in this press release, which are not historical in nature, constitute forward-looking statements for purposes of the safe harbor provided by the Private Securities Litigation Reform Act of 1995. These statements include, among others, those regarding the Company's plans to advance into additional clinical studies in PD, its expectations to disclose additional developments and data, the safety and efficacy of SLS-004 and its ability to downregulate or reduce SNCA mRNA and SNCA protein expression and its potential for a disease-modifying gene therapy in PD. These statements are based on Seelos' current expectations and beliefs and are subject to a number of risks and uncertainties that could cause actual results to differ materially from those described in the forward-looking statements. Risks associated with Seelos' business include, but are not limited to, the risk of not successfully executing its preclinical and clinical studies and not gaining marketing approvals for its product candidates, the risk that prior clinical results may not be replicated in future studies and trials (including the risk that the results from the preclinical study of SLS-004 are not replicated or are materially different from the results of future studies and trials), the risks that clinical study results may not meet any or all endpoints of a clinical study and that any data generated from such studies may not support a regulatory submission or approval, the risks associated with the implementation of Seelos' business strategy, the risks related to raising capital to fund its development plans and ongoing operations, risks related to Seelos' current stock price, risks related to the global impact of COVID-19, as well as other factors expressed in Seelos' periodic filings with the U.S. Securities and Exchange Commission, including its most recent Annual Report on Form 10-K and Quarterly Reports on Form 10-Q. Although we believe that the expectations reflected in our forward-looking statements are reasonable, we do not know whether our expectations will prove correct. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof, even if subsequently made available by us on our website or otherwise. We do not undertake any obligation to update, amend or clarify these forward-looking statements, whether as a result of new information, future events or otherwise, except as may be required under applicable securities laws.

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