Silence Therapeutics Announces Publication in Blood Demonstrating Role for Iron Regulation in Polycythemia Vera

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– Study provides therapeutic rationale for SLN124, Silence's clinical candidate for polycythemia vera and other hematological disorders

LONDON--(BUSINESS WIRE)-- Silence Therapeutics plc, Nasdaq: SLN ("Silence" or "the Company"), an experienced and innovative biotechnology company committed to transforming people's lives by silencing diseases through precision engineered medicines, today announced publication of human genomic and in vivo preclinical data linking iron regulation to polycythemia vera (PV) in the latest issue of Blood, the medical journal of the American Society of Hematology (ASH), linked **here**.

The paper is authored by senior medical and scientific experts from Silence and leading population health and hematology researchers from WEHI (Walter and Eliza Hall Institute) in Melbourne, Australia as well as Cambride UK. The research, led by WEHI's Dr Cavan Bennett and Professor Sant-Rayn Pasricha, identified links between PV and variants of the iron-regulating gene HFE in a genomewide association study (GWAS) of 440 PV cases and over 400,000 healthy controls. The study further demonstrated in a mouse model of PV that hepcidin, a master regulator of iron availability whose expression is influenced by HFE, governs the red blood cell (erythroid) phenotype in PV.

"The phenotype of PV involves the over-production of red blood cells, leading to a range of adverse symptoms and a high risk of life-threatening cardiovascular events," said Dr. Ute Schaeper, Drug Discovery Project Leader at Silence and a co-author on the paper. "The results we reported in Blood provide a genetic and biological rationale for treating PV with SLN124 by raising hepcidin to control systemic iron levels, thus reducing red blood cell count. This therapeutic approach could potentially prevent the need for patients to undergo periodic blood withdrawals to treat their disease and reduce their risk of cardiovascular events without the fluid shifts and severe iron deficiency

associated with phlebotomies."

SLN124, an siRNA (short interfering RNA) targeting TMPRSS6, is currently being studied in the SANRECO phase 1/2 study in adults with PV. SLN124 is also being studied in other hematological disorders such as beta thalassemia. SLN124 works by silencing TMPRSS6, a gene that negatively regulates hepcidin expression, to increase production of hepcidin in the liver.

About SLN124

SLN124 is a gene 'silencing' therapy – one that is designed to temporarily block a specific gene's message that would otherwise trigger an unwanted effect. In this case, SLN124 aims to temporarily 'silence' TMPRSS6, a gene that prevents the liver from producing a particular hormone that controls iron levels in the body – hepcidin. As hepcidin increases, iron levels in the blood are expected to decrease. which could in turn allow more healthy red blood cells to be produced, thereby improving anemia in conditions of anemia with ineffective erythropoiesis and iron overload, like β-thalassemia. In conditions of red cell overproduction, like polycythemia vera, it is expected that SLN124 will attenuate the red cell hyperproliferation by hepcidin mediated iron restriction. SLN124 has demonstrated proof of concept in healthy volunteers and is currently being evaluated in the GEMINI II phase 1 study in adults with thalassemia and the SANRECO phase 1/2 study in adults with PV. To learn more about the GEMINI II study, please **click here**. To learn more about the SANRECO study, please **click here**. SLN124 has rare pediatric disease and orphan drug designations for beta-thalassemia as well as orphan drug designation for PV. SLN124 also has FDA Fast Track Designation for PV.

About Silence Therapeutics

Silence Therapeutics is developing a new generation of medicines by harnessing the body's natural mechanism of RNA interference, or RNAi, to inhibit the expression of specific target genes thought to play a role in the pathology of diseases with significant unmet need. Silence's proprietary mRNAi GOLD™ platform can be used to create siRNAs (short interfering RNAs) that precisely target and silence disease-associated genes in the liver, which represents a substantial opportunity. Silence's wholly owned product candidates include zerlasiran (SLN360) designed to address the high and prevalent unmet medical need in reducing cardiovascular risk in people born with high levels of lipoprotein(a) and SLN124 designed to address hematological diseases. Silence also maintains ongoing research and development collaborations with AstraZeneca, Mallinckrodt Pharmaceuticals, and Hansoh Pharma, among others. For more information, please visit **https://www.silence-therapeutics.com/**.

About WEHI (Walter and Eliza Hall Institute of Medical Research)

WEHI is where the world's brightest minds collaborate and innovate to make life-changing scientific discoveries that help people live healthier for longer. Our medical researchers have been serving the community for more than 100 years, making transformative discoveries in cancers, infectious and immune diseases, developmental disorders,

and healthy ageing.

WEHI brings together diverse and creative people with different experience and expertise to solve some of the world's most complex health problems. With partners across science, health, government, industry, and philanthropy, we are committed to long-term discovery, collaboration, and translation. At WEHI, we are brighter together. Find out more at **www.wehi.edu.au**.

Forward-Looking Statements

Certain statements made in this announcement are forward-looking statements within the meaning of the U.S. Private Securities Litigation Reform Act of 1995 and other securities laws, including with respect to the Company's cash runway and forecast operating cash flow, the Company's clinical and commercial prospects, regulatory approvals of the Company's product candidates, potential partnerships or collaborations or payments under new and existing collaborations, the initiation or completion of the Company's clinical trials and the anticipated timing or outcomes of data reports from the Company's clinical trials. These forward-looking statements are not historical facts but rather are based on the Company's current assumptions, beliefs, expectations, estimates and projections about its industry. Words such as "anticipate," "expect," "intend," "plan," "believe," "seek," "estimate," and similar expressions are intended to identify forward-looking statements. These statements are not guarantees of future performance and are subject to known and unknown risks, uncertainties, and other factors, some of which are beyond the Company's control, are difficult to predict, and could cause actual results to differ materially from those expressed or forecasted in the forward-looking statements, including those risks identified in the Company's most recent Admission Document and its Annual Report on Form 20-F filed with the U.S. Securities and Exchange Commission on March 15, 2023. The Company cautions security holders and prospective security holders not to place undue reliance on these forward-looking statements, which reflect the view of the Company only as of the date of this announcement. The forward-looking statements made in this announcement relate only to events as of the date on which the statements are made. The Company will not undertake any obligation to release publicly any revisions or updates to these forward-looking statements to reflect events, circumstances, or unanticipated events occurring after the date of this announcement except as required by law or by any appropriate regulatory authority.

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