NEWS RELEASE

Silence Therapeutics - Phase 1 Study in Healthy Volunteers Positive Data

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Silence Therapeutics Announces Positive Data from GEMINI Phase 1 Study of SLN124 in Healthy Volunteers

- ***Data showed SLN124, an siRNA which targets TMPRSS6, was safe and effective in reducing plasma iron levels and had a long duration of action***
- ***Data support ongoing phase 1 study of SLN124 in patients with thalassemia and myelodysplastic syndrome (MDS)***
- ***First clinical data from Silence's proprietary mRNAi GOLD™ platform - two more clinical data readouts anticipated this year***

19 May 2021

LONDON, Silence Therapeutics plc, AIM:SLN and Nasdaq: SLN ("Silence" or "the Company"), a leader in the discovery, development and delivery of novel short interfering ribonucleic acid (siRNA) therapeutics for the treatment of diseases with significant unmet medical need, today announced positive topline data from the GEMINI phase 1 study of its wholly owned product candidate, SLN124, in healthy volunteers. SLN124, an siRNA which targets *TMPRSS6*, is in development for the treatment of iron-loading anemia conditions, thalassemia and myelodysplastic syndrome (MDS).

The GEMINI phase 1, randomized, double-blind, placebo-controlled, single-ascending dose study evaluated the safety and tolerability of SLN124 (1.0, 3.0 and 4.5 mg/kg doses) in 24 healthy volunteers (18 active and 6 placebo). Pharmacokinetic parameters and pharmacodynamic biomarkers of iron metabolism were also measured to assess reduction in iron.

Initial data from the study showed all doses of SLN124 were generally well-tolerated with no serious or severe treatment emergent adverse events (TEAEs) or TEAEs leading to withdrawal. TEAEs did not appear to be dose dependent and the majority were mild, including transient injection site reactions which resolved without intervention.

Notably, up to an approximate four-fold increase in average hepcidin and 50% reduction in plasma iron levels were also observed after a single dose of SLN124. Effects on hepcidin and iron appear to be dose dependent and were still observed at the end of the 8-week study at all dose levels, indicating a sustained and long duration of action.

These clinical data support preclinical findings which demonstrated SLN124 effectively improved red blood cell production and reduced anemia by increasing levels of hepcidin - a key natural regulator of iron balance and distribution in the body. The Company expects to measure red blood cell production and effects on anemia in the ongoing GEMINI II phase 1 study of SLN124 in people with thalassemia and MDS, who unlike healthy volunteers have significantly elevated iron levels.

Mark Rothera, President and CEO of Silence Therapeutics, said: "*These data represent the first clinical data from our mRNAi GOLD™ platform and underscore the promising potential for our technology to deliver precision medicines. We look forward to further data in patients anticipated from both of our wholly owned clinical programs later this year - the GEMINI II study of SLN124 for iron-loading anemia conditions and the APOLLO study of SLN360 for cardiovascular disease due to high lipoprotein(a).*"

Giles Campion, M.D., EVP, Chief Medical Officer and Head of Research & Development of Silence Therapeutics, said: "*Today's results confirm the strong preclinical profile of SLN124 in humans - we observed excellent safety, robust gene knockdown expressed by up to an approximate four-fold increase in average hepcidin along with a 50% reduction in serum iron levels and a durable effect which lasted throughout the study. We are encouraged by these data in healthy volunteers and the opportunity for SLN124 to potentially address iron-loading anemia conditions such as thalassemia and MDS.*"

John Porter, M.D., Professor and Consultant Haematologist, Red Cell Disorders Unit, University College London and University of College London Hospitals, commented: "*Despite advances in our understanding of thalassemia and MDS, there are no existing treatments that specifically target the underlying mechanisms of these conditions as a way to improve the degree of anemia. There is a major unmet need for a therapy that can provide safe and continuous control of iron balance and distribution as a way to improve the efficiency of red cell production. I'm encouraged by data from the SLN124 study in healthy volunteers and look forward to further clinical testing.*"

Silence expects to present full data from the GEMINI phase 1 study of SLN124 in healthy volunteers at an appropriate scientific meeting later this year. In addition, the Company plans to report data from the single-ascending dose portion of the ongoing GEMINI II phase 1 study of SLN124 in people with thalassemia and MDS in the second half of this year. SLN124 has Orphan Drug Designation for both conditions and rare pediatric disease designation for beta thalassemia.

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About Thalassemia and Myelodysplastic Syndrome (MDS)

Thalassemia and MDS are both rare diseases that prevent a person from producing enough healthy red blood cells. Low levels of healthy red blood cells, known as anemia, result in less oxygen being delivered to different parts of the body. This can cause symptoms such as excessive tiredness and weakness. It can also lead to other serious health problems, such as heart disease. People living with thalassemia or MDS can also store too much iron in their bodies, leading to a phenomenon called 'iron overload', which damages organs such as the heart and liver.

Both conditions are typically treated with regular blood transfusions, which add to the problem of iron overload. Iron chelation therapy removes excess iron from the body using special medicines. While it helps reduce the amount of iron in the blood for people with thalassemia or MDS, it does not treat the underlying cause of the condition or stop it from progressing. There is, therefore, a need for therapies that directly address the biological drivers of disease.

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, it is hoped that iron levels in the blood will decrease, which could in turn allow more healthy red blood cells to be produced, thereby improving anemia. In preclinical studies, SLN124 has shown positive effects on improving levels of red blood cells and reducing harmful iron levels.

SLN124 is now being studied in the GEMINI clinical trial program. GEMINI II is a phase 1 study to investigate the effects of SLN124 in people with thalassemia or myelodysplastic syndrome (MDS), whose bodies produce fewer healthy red blood cells than normal and who can store too much iron in their bodies. For more information on the GEMINI II study, please **click here**.

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 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 iron-loading anemia conditions. Silence also maintains ongoing research and development collaborations with AstraZeneca, Mallinckrodt Pharmaceuticals, and Takeda, among others. For more information, please visit **https://www.silence-therapeutics.com/**.

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 clinical and commercial prospects and the anticipated timing 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 expectations, estimates, and projections about its industry; its beliefs; and assumptions. Words such as 'anticipates,' 'expects,' 'intends,' 'plans,' 'believes,' 'seeks,' 'estimates,' 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 amended Annual Report on Form 20-F filed with the U.S. Securities and Exchange Commission on April 29, 2021. 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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