Silence Therapeutics Announces Detailed Results From SLN360 Phase 1 Study in High Lipoprotein(a) Presented in Late Breaker at the American College of Cardiology (ACC.22) Annual Meeting

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– SLN360 reduced Lp(a) – a key genetic risk factor for heart disease - by up to 98% with reductions of up to 81% persisting at 150 days

– Results were simultaneously published in The Journal of the American Medical Association (JAMA)

LONDON--(BUSINESS WIRE)-- Silence Therapeutics plc, 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 presented detailed results from its phase 1 APOLLO trial that showed SLN360, an investigational siRNA, reduced levels of lipoprotein(a) ("Lp(a)"), an important genetic risk factor for heart disease, by up to 98% in healthy adults with high Lp(a).

Findings from the "APOLLO Trial: Magnitude and Duration of Effects of a Short-interfering RNA Targeting Lipoprotein(a): A Placebo-controlled Double-blind Dose-ranging Trial" were presented today during a Late Breaking Science Session at the American College of Cardiology's 71st Annual Scientific Session (ACC.22) and simultaneously published online in the Journal of the American Medical Association, **linked here**.

"We thought it would work, but we were surprised by the magnitude and the duration of the effect," said Steven E. Nissen, M.D., Chief Academic Officer of the Heart, Vascular and Thoracic Institute at Cleveland Clinic and the study's lead author. "Lipoprotein(a) is the last frontier in lipids, and there has never been a treatment that's been shown to benefit these patients. These findings from the APOLLO study support further development of SLN360."

High Lp(a) affects around 20% of the world's population and is associated with a high risk of heart attack, stroke and aortic stenosis. There are no approved medicines that selectively lower Lp(a). SLN360 is a siRNA that is designed to lower Lp(a) production by targeting messenger RNA transcribed from the LPA gene.

The phase 1 APOLLO trial evaluated SLN360 in 32 adults at five medical centers in the U.S., UK and Netherlands. All participants had plasma concentrations at screening of Lp(a) ≥150 nmol/L with a median level of 224 nmol/L (75 nmol/L or less is considered normal). Individuals were randomly assigned to receive a single subcutaneous dose of SLN360 (30 mg, 100 mg, 300 mg or 600 mg) or placebo and were observed closely for the first 24 hours, then periodically assessed for 150 days.

There were no serious safety concerns reported and the most common side effect was temporary redness at the injection site.

Participants receiving 300 mg and 600 mg of SLN360 had up to 96% and 98% median reduction in Lp(a) levels, respectively, and median reductions of up to 71% and 81% from baseline persisted at 150 days. Those receiving a placebo saw no change in Lp(a) levels. The study follow-up period has been extended to 365 days to further assess the duration of action.

Other efficacy measures included the effects of SLN360 on low-density lipoprotein cholesterol (LDL cholesterol) and apolipoprotein B (ApoB), both of which are associated with an increased risk of cardiovascular events. The highest doses of SLN360 reduced LDL cholesterol and ApoB by about 25%.

"These first-in-human data for SLN360 demonstrate its potential to address a major unmet need in cardiovascular disease affecting 1 in 5 people worldwide," said Giles Campion, MD, EVP, Head of R&D and Chief Medical Officer at Silence. "The study showed SLN360 was well tolerated and substantially reduced Lp(a) levels with long lasting effects. We remain very encouraged by these data and look forward to further evaluating SLN360 in the clinic."

Silence is evaluating SLN360 in the multiple-ascending dose portion of the APOLLO phase 1 study in patients with high Lp(a) that have a confirmed history of stable atherosclerotic cardiovascular disease ("ASCVD"). Silence plans to initiate the SLN360 phase 2 ASCVD study in the second half of 2022, pending regulatory discussions.

About SLN360

Silence's wholly owned lead product candidate, SLN360, 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, it aims to 'silence' LPA, a gene that tells the body to make a specific protein that is only found in Lp(a). By silencing LPA, the levels of Lp(a) are lowered, which in turn is expected to lower the risk of heart diseases, heart attacks and strokes.

SLN360 is being studied in the APOLLO clinical trial program. For more information about the APOLLO study, please **click here**.

About Lipoprotein(a)

Lipoprotein(a), known as Lp(a) for short, is a particle made by the liver, which consists of cholesterol, fats and proteins. Most people have some Lp(a) in their body, but about 1 in 5 people have high levels of Lp(a), because of a specific gene variation in their DNA. Most people are unaware if they have elevated Lp(a).

People living with elevated Lp(a) have a higher risk of developing early heart disease, heart attacks and strokes. Most standard cholesterol tests do not currently include screening for Lp(a). Current medicines that are used to lower other lipid levels in the blood do not have a meaningful effect on Lp(a) and are less effective overall in people with high levels of Lp(a).

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 rare 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/**.

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, regulatory approvals of the Company's product candidates, 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 '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 Annual Report on Form 20-F filed with the U.S. Securities and Exchange Commission (the “SEC”) on March 17, 2022. 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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