Silence Therapeutics Announces Positive Topline Data in SLN360 Phase 1 Single-Ascending Dose Study in Healthy Adults with High Lipoprotein(a)

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SLN360, an investigational siRNA to reduce risk of Lp(a)-mediated cardiovascular disease, was safe and well tolerated in the study

SLN360 significantly lowered Lp(a) in a dose-dependent manner up to 98% with reductions of up to 81% persisting at 150 days

Results to be presented in late breaker at the American College of Cardiology (ACC) Annual Scientific Session & Expo on April 3, 2022

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 announced positive topline results in its phase 1 single-ascending dose study of SLN360, an siRNA targeting lipoprotein(a) ("Lp(a)"), in healthy adults with high Lp(a).

High Lp(a), defined as ≥ 50 mg/dL (c.125nmol/L), affects approximately 20% of the world's population and is a genetic risk factor for cardiovascular disease. 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.

"These first-in-human data for SLN360, which align with our pre-clinical findings, reinforce our confidence in its potential to substantially lower Lp(a) levels with long-lasting action and address a major unmet need in cardiovascular disease," said Giles Campion, M.D., EVP, Head of R&D and Chief Medical Officer at Silence. "More broadly, siRNA is proving to be a powerful modality for treating genetic conditions, both common and rare, by

precisely engaging targets that have previously been considered ‘undruggable’.”

This phase 1 study evaluated the safety, tolerability, pharmacokinetics (PK) and pharmacodynamics of SLN360 at escalating doses in 32 adults with plasma concentrations at screening of Lp(a) ≥150 nmol/L (approximately ≥ 60 mg/dL) with no known cardiovascular disease. 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 for up to 150 days.

The primary safety objective was assessment of treatment-emergent adverse events. No clinically important safety concerns were identified. Low grade adverse events at the injection site were observed, most prominently at the highest dose. As expected, systemic exposures (PK) of SLN360 increased in a broadly dose-proportional manner.

The key efficacy assessment was percent change from baseline in Lp(a). SLN360 reduced Lp(a) in a dose dependent manner from 46% up to a maximum of 98% with up to an 81% reduction persisting at 150 days. The study follow-up period has been extended from 150 days to 365 days to further assess the duration of action. Silence anticipates data from the extended follow-up period in the third quarter of 2022.

“These very encouraging results for our wholly owned SLN360 program mark the second positive study from our proprietary mRNAi GOLD™ platform, further underscoring its potential to safely and substantially reduce levels of disease-related proteins in liver cells,” said Mark Rothera, President and Chief Executive Officer at Silence. “There is currently no specific treatment option approved for high Lp(a), a genetically determined cardiovascular risk factor affecting 20% of the world’s population. Today’s announcement brings us one step closer to addressing a major unmet need in cardiovascular disease. We are engaged in global partnership discussions to ensure we are well positioned to scale up SLN360 development and future commercialization.”

Detailed results from the SLN360 phase 1 single-ascending dose study will be presented by principal investigator and Professor of Cardiovascular Medicine at the Cleveland Clinic, Steven E. Nissen, MD, at the American College of Cardiology (ACC) Annual Scientific Session & Expo on April 3, 2022.

Patient enrollment continues in the multiple-ascending dose portion of the SLN360 phase 1 study in patients with high Lp(a) that have a confirmed history of stable atherosclerotic cardiovascular disease (“ASCVD”). Silence remains on-track to initiate the SLN360 phase 2 ASCVD study in the second half of 2022, pending regulatory discussions.

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, potential partnerships or 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 '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, its amended Annual Report on Form 20-F filed with the U.S. Securities and Exchange Commission (the "SEC") on April 29, 2021 and its Current Report on Form 6-K filed with the SEC on November 16, 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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