Silence Therapeutics Announces JAMA Publication of Additional Phase 1 Data for Zerlasiran in Subjects with Elevated Lipoprotein(a)

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Published findings demonstrate zerlasiran was well-tolerated and significantly reduced Lp(a) after single and multiple dosing

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 additional results from the APOLLO phase 1 study of zerlasiran (SLN360) in subjects with baseline lipoprotein(a), or Lp(a), levels at or over 150 nmol/L were published in the Journal of the American Medical Association (JAMA), **linked here.**

Zerlasiran is a siRNA (short interfering RNA) designed to lower the body's production of Lp(a), a key genetic risk factor for cardiovascular disease affecting up to 20% of the world's population.

"Positive phase 1 data published in JAMA demonstrate treatment with zerlasiran produced sustained reductions in Lp(a) concentrations with a well-tolerated profile using varying dosing regimens," said Curtis Rambaran, MD, Chief Medical Officer at Silence and senior author of the publication. "The promising findings from this study are particularly encouraging as we complete the phase 2 study for zerlasiran and underscore our commitment to address this major unmet need in cardiovascular disease."

The single ascending and multiple dose trial enrolled 32 healthy participants and 36 patients with atherosclerotic cardiovascular disease (ASCVD) and Lp(a) concentrations ≥150 nmol/L. Results from the single ascending dose portion of the trial in healthy participants were previously published in the April 2022 issue of JAMA, **linked here**. Today's JAMA publication reviews findings from the extended 365 day follow up of healthy participants who

received the two highest zerlasiran doses (300 or 600 mg) and 201 days of follow up for ASCVD patients administered 2 doses.

Healthy participants were randomized and received a single subcutaneous dose of placebo, 300 mg or 600 mg; ASCVD patients received two doses of placebo, 200 mg at a 4-week interval or 300 mg or 450 mg at an 8-week interval. The primary outcome was safety and tolerability. Secondary outcomes included the serum levels of zerlasiran and effects on Lp(a) serum concentrations.

Zerlasiran was safe and well tolerated. The median change from baseline in serum Lp(a) concentrations 365 days after single doses for placebo, 300 mg, and 600 mg were +14%, −30%, and −29% respectively. The maximal median change from baseline after two doses of placebo, 200 mg, 300 mg and 450 mg were +7%, -97%, -98% and -99%, attenuating to 0.3%, -60%, 90% and 89% respectively, after 201 days.

Zerlasiran is currently being evaluated in the ALPACAR-360 phase 2 study in subjects with baseline Lp(a) levels at or over 125 nmol/L at high risk of ASCVD events.

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 designed to address the high and prevalent unmet medical need in reducing cardiovascular risk in people born with high levels of lipoprotein(a) and divesiran designed to address hematological diseases, including polycythemia vera. Silence also maintains ongoing research and development collaborations with AstraZeneca 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 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 13, 2024. 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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