



Scribe Therapeutics Presents Late-Breaking Preclinical Data Supporting STX-1150, a Clinical-Stage Epigenetic Silencing Therapy Designed to Achieve Years of LDL-C Lowering After a Single Dose

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- Late-breaking oral presentation at EAS Congress 2026 reports up to 90% PCSK9 reduction and up to 68% LDL-C lowering, with the lowest dose achieving >50% LDL-C reduction for >22 months and ongoing, in non-human primates with a clean tolerability profile
- These data support STX-1150's recent advancement as a clinical-stage epigenetic silencing therapy designed to attain ultra-long LDL-C lowering without permanent DNA alterations

ALAMEDA, Calif., May 28, 2026 – Scribe Therapeutics, Inc. (Scribe), a clinical-stage biotechnology company engineering purpose-built *in vivo* CRISPR technologies designed to extend healthy lifespan through disease prevention and durable therapeutic intervention, announced latest preclinical data from its lead cardiometabolic program STX-1150, supporting the possibility of this novel investigational therapy as an ultra-long-acting approach to LDL-C lowering that could redefine the standard of care for patients with atherosclerotic cardiovascular disease (ASCVD).

The data were featured in a late-breaking oral presentation at the 94th European Atherosclerosis Society (EAS) Congress by Scribe co-founder and CEO Benjamin Oakes, Ph.D. STX-1150 is an investigational, liver-targeted CRISPR-based epigenetic silencing therapy designed to durably reduce LDL-C by silencing transcription of *PCSK9*, a genetically and clinically validated regulator of cholesterol. The therapy is now being evaluated in a [first-in-human Phase 1 study](#) in adults with elevated LDL-C and increased cardiovascular risk.

A significant challenge in ASCVD management today is the mismatch between disease progression and treatment durability. Existing lipid-lowering options can be effective but require chronic administration, and many patients remain above recommended LDL-C levels in real-world settings due to onerous polypharmacy treatment burden and limited long-term persistence. At the same time, permanent gene editing approaches that could induce irreversible off-target toxicities may be less desirable for broad preventive settings where specificity, durability, and scalability are critical. STX-1150 is engineered to address this gap by enabling ultra-long PCSK9 silencing and LDL-C lowering after a single dose, without permanently altering the underlying DNA.

"Recent advances in the field have made it clear that the future of ASCVD management will be defined by genetic medicine," said Dr. Oakes. "With STX-1150, we are pursuing a fundamentally distinct approach designed to deliver potent and highly durable LDL-C lowering while fully preserving the underlying DNA sequence. Our goal is to broaden access to the protective biology observed in *PCSK9* loss-of-function genetics through what we believe is the next evolution of genetic medicine: an epigenetic silencing therapy designed to combine the precision and durability of CRISPR with the reversibility and safety of RNAi, making long-term cardiovascular prevention practical for millions of patients."

A Durable PCSK9 Epigenetic Silencing Therapy Designed to Fill the Gap between Current Chronic LDL-C Lowering Therapies and Permanent Gene Editing

Scribe recently secured regulatory clearance from the Australian Therapeutic Goods Administration (TGA) to initiate a clinical study of STX-1150 in adults with elevated LDL-C at increased cardiovascular risk, with enrollment underway in Australia and additional sites planned in New Zealand. The open-label, single ascending dose study will evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of the therapy.

STX-1150 consists of a messenger RNA (mRNA) encoding Scribe's proprietary CRISPR-CasX-based epigenetic silencer, termed ELXR, and a single guide RNA targeting *PCSK9* encapsulated in lipid nanoparticles (LNPs). ELXR is built on a nuclease-inactivated, highly engineered CRISPR-CasX protein fused to epigenetic effector domains and incorporates allosteric regulation designed to enhance both specificity and on-target activity. Scribe engineered ELXR to enable the potency, specificity, and durability required to support broad patient use. Unlike traditional gene-editing approaches that cut DNA, STX-1150 is designed to silence *PCSK9* transcription through targeted epigenetic mechanisms, enabling long-term gene silencing while preserving the underlying DNA.

In the preclinical studies presented at EAS, a single dose of a STX-1150 prototype achieved LDL-C reductions up to 68% and the lowest dose reduced LDL-C by >50% for more than 22 months and ongoing in non-human primates (NHPs). The STX-1150 prototype also durably reduced circulating PCSK9 in NHPs by up to ~90%. Additional preclinical data showed that CMC-scaled STX-1150 exhibited at least five-fold greater potency in primary human hepatocytes compared with primary cynomolgus hepatocytes, supporting positive human dose translation.

Furthermore, *in vitro* assessments of the prototype showed no off-target gene expression changes at 3X EC90, while *in vivo* liver enzyme profiles at 0.75 mg/kg were comparable to saline control. A GLP toxicology study of STX-1150 revealed no test-article-

related adverse findings across evaluated dose levels.

Together, these findings support the continued development of STX-1150 as a differentiated approach to durable LDL-C reduction, addressing a critical gap in lipid management: enabling long-term preventive therapy that is practical for broad patient populations. By potentially addressing long-term treatment persistence challenges with currently available PCSK9-directed therapies, while avoiding the risks associated with permanently altering DNA, STX-1150 may offer a meaningful advance for early and persistent ASCVD risk reduction in patients with elevated LDL-C and increased cardiovascular risk.†

About STX-1150

STX-1150 is a novel, investigational, epigenetic silencing therapy designed to durably reduce LDL-C by silencing transcription of *PCSK9*, a genetically and clinically validated regulator of cholesterol. The therapy leverages Scribe's proprietary ELXR technology to enable long-lasting gene silencing in the liver without permanently altering DNA. STX-1150 consists of a messenger RNA encoding a highly engineered ELXR and a single guide RNA that targets the *PCSK9* gene encapsulated by a liver-tropic lipid nanoparticle licensed from Acuitas Therapeutics.‡

About Scribe's Epigenetic Long-Term X-Repressor (ELXR)

ELXR is an epigenetic silencing technology designed to durably yet reversibly silence gene expression without altering the underlying DNA sequence. Built on a nuclease-inactivated, highly engineered CasX-derived CRISPR protein fused to epigenetic effector domains, ELXR installs targeted histone and DNA methylation marks to enable long-term silencing while maintaining genomic integrity. ELXR also incorporates allosteric regulation designed to enhance both specificity and on-target activity, differentiating it from other epigenetic editors used in the field or in the clinic.

Epigenetic silencing technologies such as ELXR may represent the next evolution of mRNA-reducing therapies, potentially overcoming the durability and adherence limitations of existing modalities such as siRNAs and ASOs. Unlike therapies that require chronic dosing every few weeks to months, ELXR is designed to enable sustained, clinically meaningful mRNA reduction for years following a single administration, without permanently altering the underlying DNA. The durability, reversibility, and specificity inherent to epigenetic silencing may make ELXRs particularly well-suited for applications where permanent genome modification is less desirable, and long-term adherence and consistent target suppression are critical determinants of outcomes.‡

About PCSK9 and its Role in Elevated LDL-C

Elevated low-density lipoprotein cholesterol (LDL-C), often referred to as “bad” cholesterol, is a primary contributor to ASCVD. Inhibition of PCSK9 is among the most effective known mechanisms to reduce LDL-C, complementing or outperforming existing therapies such as statins, bempedoic acid, ezetimibe, and emerging CETP inhibitors. Individuals born with loss-of-function variants in the *PCSK9* gene live with meaningfully lower baseline LDL-C and experience up to 88% lower risk for coronary heart disease without any distinguishable adverse effects from lifetime lower LDL-C levels.‡

About ASCVD

Despite a wide variety of approved therapeutics, cardiovascular disease remains the leading cause of death worldwide and impacts over 120 million individuals in the United States alone. Every 40 seconds, someone in the United States suffers a heart attack.

Elevated levels of low-density lipoprotein cholesterol (LDL-C), lipoprotein(a), and triglycerides are key lipid drivers of atherosclerosis and ASCVD. Hypercholesterolemia, an excess of LDL-C in the bloodstream, promotes plaque formation in the arterial walls, restricting blood flow and increasing the risk of heart attacks and strokes. Despite major advances in the development of new classes of lipid-lowering therapies, today's standard of care for ASCVD treatment and prevention is insufficient. Existing treatments struggle to demonstrate broad impact as they suffer from significant lack of durability, diminishing levels of adherence-adjusted efficacy, and onerous treatment burdens including well-documented side effects. All of this leads to poor uptake, low adherence, and limited real-world effectiveness. Moreover, treatment is often initiated only after decades of substantial silent cumulative arterial injury or an acute cardiovascular event. These limitations underscore the importance of developing durable therapies that can be administered safely earlier in the course of disease. Scribe's goal is to develop CRISPR-based therapeutics that are safe, effective, durable, and scalable enough to preemptively reduce lifetime cardiovascular risk with the aim to reduce the global burden of ASCVD.‡

About Scribe Therapeutics

Scribe Therapeutics is a clinical-stage biotechnology company engineering CRISPR-based technologies into purpose-built *in vivo* genetic medicines designed to become standard of care treatments for patients suffering from highly prevalent diseases, starting with cardiometabolic disease. Leveraging its CRISPR by Design™ approach and nature's blueprint for improved cardiovascular health, Scribe's initial programs focus on addressing the key lipid drivers of ASCVD such as elevated LDL-C, lipoprotein(a), and triglycerides. The company's lead candidate, STX-1150, is a novel liver-targeted therapy designed to epigenetically silence the *PCSK9* gene and reduce LDL-C levels without inducing permanent DNA changes. To broaden and accelerate the impact of its engineered CRISPR technologies for patients, Scribe has formed strategic collaborations with world-leading pharmaceutical companies including Sanofi and Eli Lilly. Co-founded by Nobel Prize winner Jennifer Doudna and backed by leading life sciences investors, Scribe is advancing scalable, transformative, and preventative genetic medicines with the goal of improving outcomes

and democratizing access to the protective effects of beneficial human genetics. To learn more, visit www.scribetx.com.