



Scribe Therapeutics Projected to Enter the Clinic in Mid-2026 with STX-1150, a PCSK9-targeting CRISPR Epigenetic Silencing Therapy for Durable LDL-C Reduction

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- *Scribe expects to initiate a first-in-human hypercholesterolemia study in mid-2026 with STX-1150, its lead cardiometabolic asset*
- *STX-1150 is designed to deliver durable therapeutic LDL-C lowering with reduced dosing burden, enabled by epigenetic silencing that does not permanently modify the DNA*
- *Preclinical studies highlight durability, with >50% LDL-C reduction in non-human primates maintained for ~18 months after a single administration at a dose <1.0 mg/kg*
- *These data underscore potential of Scribe's CRISPR-CasX-based epigenetic silencing platform, with a new preprint detailing the engineering behind the technology that offers an additional allosteric control layer designed to enhance precision and potency*

ALAMEDA, Calif., January 20, 2026 – Scribe Therapeutics, Inc. (Scribe), a biotechnology company pioneering highly engineered CRISPR technologies designed to reshape the treatment of disease by enabling earlier intervention, improved outcomes, and longer, healthier lives, announced plans to enter the clinic in mid-2026 with STX-1150, its lead product candidate for the treatment of hypercholesterolemia, a major driver of atherosclerotic cardiovascular disease (ASCVD). STX-1150 is a novel liver-targeted therapy designed to epigenetically silence *PCSK9* and durably reduce low-density lipoprotein cholesterol (LDL-C) without permanent DNA changes.

The announcement was revealed at the 44th Annual J.P. Morgan Healthcare Conference, underscoring Scribe's mission to shift cardiovascular care from late, symptom-driven intervention to earlier, durable risk reduction grounded in human genetics.

"Entering the clinic with STX-1150 represents a defining moment for Scribe and the wider genetic medicine field," said Benjamin Oakes, Ph.D., co-founder and Chief Executive Officer of Scribe Therapeutics. "Scribe has been engineering CRISPR-based medicines with the potency, specificity, and durability profile that can elevate the current standard of care, particularly for large cardiometabolic populations. We designed STX-1150 to overcome many of the limitations of today's lipid-lowering therapies through powerful epigenetic silencing, and to meaningfully change how cardiovascular risk is managed for millions of patients."

"Scribe is focused on delivering the cardioprotective effects of naturally occurring genetics as durable CRISPR medicines," continued Dr. Oakes. "Our preclinical data for the STX-1150 program demonstrate our commitment to advancing nature's blueprint for better cardiovascular health by developing scalable treatments designed to sustain lipid control and reduce cumulative risk."

STX-1150: a transformative approach to PCSK9 inhibition for durable, scalable LDL-C lowering

STX-1150, Scribe's lead cardiometabolic asset, is an epigenetic silencing therapy leveraging the company's proprietary Epigenetic Long-Term X-Repressor (ELXR) technology and is designed to durably lower LDL-C by repressing expression of *PCSK9*, a genetically and clinically validated target. Inhibition of *PCSK9* is among the most effective known mechanisms to reduce LDL-C.

Unlike CRISPR gene editing, base editing, or prime editing approaches, STX-1150 is designed to achieve long-lasting therapeutic benefit without permanently altering the underlying DNA sequence. By combining durable pharmacology with a non-permanent mechanism, STX-1150 is intended to help address the persistent gap between efficacy observed in controlled settings and real-world outcomes for chronic lipid-lowering therapies, where long-term persistence, repeat dosing, and cumulative polypharmacy burden over years can limit adherence and treatment effectiveness.

In preclinical studies, a single administration of a STX-1150 prototype delivered via lipid nanoparticles has demonstrated >50% LDL-C reduction in non-human primates, with effects sustained for nearly 18 months and ongoing, and was generally well tolerated with no significant liver enzyme elevations compared to control. Scribe believes STX-1150's designed efficacy and safety profile has the potential to support earlier, longer-lasting LDL-C control and reduce cumulative exposure over time, an important consideration in a disease that progresses over decades.

Scribe plans to initiate the first-in-human Phase 1 study of STX-1150 in mid-2026. The planned study is intended to evaluate safety and tolerability of STX-1150 in individuals with hypercholesterolemia at elevated cardiovascular risk.†

New preprint details engineering behind ELXR, Scribe's proprietary CRISPR epigenetic silencing technology

Scribe also announced the release of a [new manuscript](#) describing the engineering behind its ELXR technology that underlies STX-1150. The manuscript reports the strategic design of ELXR molecules incorporating an allosteric regulatory domain to synthetically reconstruct a cell's native autoinhibitory control to constrain DNA methyltransferase activity, adding a built-in

specificity control designed to reduce off-target effects and improve safety while maintaining or enhancing on-target activity.

In the study, allosteric ELXR reduced off-target transcriptome-wide perturbations while maintaining or enhancing on-target repression across genomic loci (average ≥ 4 -fold increased activity), and demonstrated durable target silencing *in vivo* following lipid nanoparticle delivery with minimal off-target transcriptional effects. Together, the findings introduce an additional regulatory layer designed to improve the fidelity and specificity of CRISPR-based epigenetic silencing for therapeutic applications, differentiating ELXR from the current generation of epigenetic editors used in the field and in the clinic.†

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

ELXR is Scribe's epigenetic silencing technology designed to durably and reversibly repress gene expression without altering the underlying DNA sequence. ELXR uses a nuclease-inactivated, CasX-derived CRISPR protein fused to epigenetic effector domains to install histone modifications and DNA methylation marks at specified genomic loci, mimicking natural epigenetic processes to provide long-term, tunable silencing of disease-causing genes while maintaining genomic integrity. Uniquely, ELXR incorporates an allosteric regulatory domain, adding a built-in specificity control that is designed to reduce off-target effects and improve safety, as well as maintain or enhance on-target activity, differentiating ELXR from other epigenetic editors used in the field or in the clinic. Furthermore, ELXR's intrinsic reversibility and inherent specificity may make it particularly well suited for applications where permanent genome modification is less desirable, such as in preventive or chronic disease settings. Scribe believes that ELXR offers a durable alternative to established gene silencing methods, including ASOs, and siRNAs targeting the same mechanism of mRNA reduction, providing the potential to enable sustained, clinical trial-level suppression of disease drivers in real-world use.‡

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 and the Need for an Improved Treatment Paradigm

Cardiovascular disease is 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, and each year heart disease costs the nation more than \$400 billion.

Elevated levels of low-density lipoprotein cholesterol (LDL-C), lipoprotein(a), and triglycerides are well-established causal 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 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 biotechnology company developing optimized *in vivo* CRISPR-based technologies and 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 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.