



## Scribe Therapeutics Reports Preclinical Data at ASGCT 2026 Demonstrating Enhanced Potency and Specificity of Engineered CRISPR Technologies for Epigenetic Silencing and Gene Editing

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- Oral presentation on novel allosteric ELXR epigenetic silencer showcases Scribe's development in achieving highly precise, potent, and durable target repression
- XE gene editor oral presentation demonstrates how mechanistic insight underlying guide potency and AI-based predictive modeling supports the engineering of CRISPR-CasX systems for specific therapeutic targets
- Invited talk highlights how a full-stack of iterative, closed-loop CRISPR engineering, from XE foundation to ELXR silencing machinery, together enabled Scribe's lead cardiometabolic therapeutic program for LDL-C lowering

ALAMEDA, Calif., May 18, 2026 – Scribe Therapeutics, Inc. (Scribe), a biotechnology company engineering purpose-built CRISPR technologies to reshape the treatment of disease by enabling earlier intervention, improved outcomes, and longer, healthier lives, presented preclinical data on the latest advances across the company's engineered CRISPR technologies at the 29th American Society of Gene & Cell Therapy (ASGCT) Annual Meeting.

The oral presentations showcased Scribe's CRISPR by Design™ approach in engineering naturally occurring CRISPR systems into highly potent and highly specific platforms for genetic medicine, namely Epigenetic Long-Term X-Repressor (ELXR) and X-Editor (XE). ELXR underpins STX-1150, the company's lead LDL-C lowering program, while XE underpins additional cardiometabolic programs STX-1200, designed for Lp(a) lowering, and STX-1400 for triglyceride lowering.

"These data continue to demonstrate Scribe's engineering capabilities for improving potency, precision, and targetability of CRISPR-based medicines," said Benjamin Oakes, Ph.D., co-founder and CEO of Scribe Therapeutics. "Engineering epigenetic silencers and genome editors for therapeutic application has resulted in technologies that aim to improve dosing, specificity, and scalability, facilitating durable CRISPR medicines for broad cardiometabolic patient populations. These findings provide important preclinical support as we continue to advance our lead assets, including STX-1150, into the clinic."

### **Allosteric CRISPR-Based Epigenetic Silencer for Potent, Precise, and Durable Gene Silencing**

In an oral presentation, Scribe reported preclinical data featuring its ELXR technology, a next-generation CRISPR-based epigenetic silencing approach designed to deliver potent, durable gene repression with improved specificity. ELXRs are engineered to enable long-term target gene silencing through epigenetic mechanisms without introducing permanent DNA alterations.

The presentation highlighted an ELXR design that incorporates an allosteric regulatory domain intended to recapitulate DNMT3A's native autoinhibitory mechanism, providing an additional specificity control to help restrain DNA methyltransferase activity while preserving or improving on-target silencing. The result is a highly specific epigenetic editor that remains "locked", i.e., preventing unwanted off-target activity, until the molecule encounters a "key" also written at the on-target site, creating a mechanism akin to two-factor authentication. In preclinical studies, allosteric ELXRs demonstrated enhanced potency and specificity across multiple targets, including sustained *in vivo* knockdown of PCSK9 with an improved transcriptional specificity profile. These data support the development of Scribe's ELXR technology and its application in STX-1150, the company's lead pipeline program advancing towards clinical development.

Additional highlights from the presentation include:

- Engineering increased on-target repression across multiple targets, averaging at least 4-fold improvement in activity across spacers *in vitro*. Allosteric ELXRs also improved performance of lower-activity guide RNAs, suggesting potential utility in expanding guide options for target gene silencing
- Allosteric ELXRs showed improved specificity readouts, reducing off-target transcriptional effects by approximately 10-to-100-fold compared to non-allosteric molecules

### **Engineering X-Editor Technology for Therapeutic-Grade *In Vivo* Genome Editing**

In a second oral presentation, Scribe reported on its XE technology and featured DeepXE, an AI-enabled predictive model designed to accelerate identification of potent guide RNAs for XE-based therapeutics.

The presentation demonstrated how Scribe has engineered XE with substantially improved activity and specificity from naturally occurring CRISPR-CasX through large-scale protein and guide RNA engineering. Furthermore, Scribe emphasized its ability to engineer XE for effective editing of specific, high-priority genomic sites with a desired therapeutic mechanism of action. By applying mechanistic insight into how sequence and genomic context impact editing activity, Scribe fine-tunes its screening

platforms to enable the development of novel enzymes with potent and precise targeting of disease-relevant sites. DeepXE further supports and accelerates this engineering strategy by enabling prediction of guide RNA potency and reducing the need for empirical screening, helping to identify guide RNAs with high on-target activity for therapeutic targets more rapidly. Together, these findings show how Scribe integrates protein and guide engineering with predictive modeling to support the development of XE-based therapeutic programs.

Additional highlights from the presentation include:

- Preclinical *in vivo* data showed potent, saturating liver editing across multiple target loci in non-human primates, and specificity studies in primary human hepatocytes showed no significant detectable off-target editing for multiple therapeutic guides at a super-saturating dose of 10X EC90
- DeepXE is designed to accelerate guide selection by reducing screening burden by 50% with less than a 10% false-negative rate, and enable faster optimization of XE-based therapeutics

### **Translating CRISPR by Design™ into Scribe's Lead LDL-C Lowering Program**

In a third invited oral presentation, Scribe described how its CRISPR by Design™ engineering approach integrates engineering of both the CRISPR foundational molecule, XE, and the key epigenetic silencing components, including novel repressor and allosteric regulatory domains, to create the ELXR technology underlying STX-1150. The presentation emphasized how engineering advances used to transform naturally occurring CRISPR-CasX into XE also underpin ELXR performance, including improved guide RNA binding, RNP formation, target search kinetics, genomic targetability, potency, and specificity. By combining this engineered CasX-derived foundation with optimized epigenetic silencing components, Scribe developed ELXR molecules designed to achieve potent and durable silencing of target genes without permanent DNA alterations. These learnings were applied to STX-1150, with preclinical prototype data showing durable PCSK9 repression following single-dose LNP delivery and specific target repression in transcriptome-wide specificity studies, with sustained epigenetic silencing activity that translated into durable LDL-C lowering observed in non-human primates for nearly 18 months and ongoing. †

### **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](http://www.scribetx.com).