Scribe Therapeutics Highlights Data Underpinning its Comprehensive Strategy Targeting Key Lipid Drivers of ASCVD at American Heart Association (AHA) Scientific Sessions 2025

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- *Four AHA presentations showcase Scribe's comprehensive cardiometabolic pipeline targeting ASCVD's main lipid drivers: LDL-C, Lp(a), and triglycerides*
- *Targeted epigenetic silencing therapy, STX-1150, achieved a ≥50% reduction in LDL-C for over 515 days in primates after a single, therapeutically relevant dose, establishing translational proof-of-concept for a novel therapeutic approach that does not alter the underlying genetic code*
- *Genome editing therapy STX-1200 potently lowered Lp(a) by >95% in vivo, with no detectable off-target editing in preclinical models, expanding the therapeutic window and supporting the safety margin needed for broad, large-population use*
- *STX-1400 achieves saturated hepatocyte APOC3 editing (>75%) in primate liver at therapeutically relevant doses and >95% triglyceride reduction in preclinical models with no detectable off-target editing in primary human hepatocytes*

ALAMEDA, Calif., November 17, 2025 – Scribe Therapeutics Inc. ("Scribe"), a genetic medicines company pioneering next-generation in vivo CRISPR-based medicines designed to be safe, durable, and effective enough to become standard-of-care treatments for prevalent diseases, presented breakthrough preclinical data across its cardiometabolic pipeline (STX-1150 for LDL-C lowering, STX-1200 for Lp(a) lowering, and STX-1400 for triglyceride lowering) at the American Heart Association (AHA) Scientific Sessions 2025.

"In cardiovascular care, the gap between efficacy in a controlled clinical trial setting and adherence-adjusted outcomes from real world evidence keeps patients from reaching treatment goals and avoiding preventable cardiovascular events," said Aarif Khakoo, M.D., M.B.A., Chief Scientific Officer and Head of Research & Development of Scribe. "With durable potency at a low dose and an exceptional specificity profile across multiple targets, our suite of genetic medicines aims to eliminate the need for dependence on chronic therapies that patients continue to struggle with today, and enable the level of cardiovascular risk reduction that today's standard-of-care has not been able to achieve; that is, shifting cardiovascular care towards long-term prevention."

"These results demonstrate that comprehensive engineering of CRISPR technologies can produce medicines with markedly improved safety and performance, surpassing the limitations of early Cas9-based systems," said Benjamin L. Oakes, Ph.D., co-founder and CEO of Scribe. "We are approaching a pivotal moment in creating therapies that can mirror the durable protection conferred by beneficial human genetics found only in the lucky few. Our mission to democratize these insights into standard-of-care medicines that shift the paradigm of cardiovascular care for all is on the cusp of becoming a reality."

STX-1150: A CRISPR-based epigenetic silencer with first-in-class durability (>515 days) of LDL-C lowering at therapeutically relevant dose, without permanent genome modification

At AHA 2025, Scribe reported non-human primate (NHP) data demonstrating durable LDL-C lowering with an LNP-delivered, CRISPR-CasX-based epigenetic silencer that represses *PCSK9* mRNA without permanent genomic modification. Lowering mRNA is an established and validated approach with multiple siRNA products indicated for diseases with genetic underpinnings. Like RNAi approaches, STX-1150 is designed to achieve a comparable level of safe and scalable mRNA lowering, but engineered for more durable therapeutic benefit. By reducing circulating PCSK9 and increasing LDL receptor availability, STX-1150 supports sustained LDL-C control while intending to remove chronic adherence barriers with existing antibody and RNAi-based lipid-lowering therapies. Human *PCSK9* loss-of-function variants confer lifelong low LDL-C and markedly lower ASCVD risk; STX-1150 is intended to pharmacologically recapitulate this protective biology as an ultra long-acting treatment option.

Data highlights from the AHA presentation:

- A single administration of the STX-1150 prototype at a therapeutically relevant dose of 0.75 mg/kg achieved ≥50% LDL-C lowering for >515 days in NHPs
- Up to 90% reduction in circulating PCSK9 and up to 68% LDL-C lowering was observed in NHPs across dose levels
- Favorable tolerability demonstrated in treated NHPs with liver enzyme levels indistinguishable from controls, and no meaningful transcriptome-wide off-target expression changes in primary human hepatocytes (PHHs).

Collectively, these data demonstrate robust preclinical efficacy with favorable safety/tolerability, supporting continued advancement of the STX-1150 program toward clinical development and strengthening the case for a new class of durable epigenetic medicines for large patient populations.

STX-1200: first CRISPR-based therapy to achieve >95% Lp(a) lowering at doses less than 0.5 mg/kg *vivo*

STX-1200 utilizes Scribe's engineered CasXE gene editor to durably inactivate *LPA* in hepatocytes. Elevated Lp(a) affects roughly one in five people worldwide and is a highly prevalent, causal, independent driver of ASCVD with no approved therapies for direct and durable lowering. At AHA 2025, Scribe presented *in vivo* results demonstrating highly potent Lp(a) lowering at low doses, together with an exceptional specificity profile, supporting the goal of a one-time, genetic Lp(a)-lowering therapy suitable for large genetically defined patient populations.

Data highlights from the AHA presentation:

- First *in vivo* demonstration of a meaningful Lp(a) lowering (>95% reduction) from a single low dose (<0.5 mg/kg) in a pharmacologically relevant transgenic *LPA* mouse model
- No detectable off-target editing across >100 nominated sites in PHHs at 10X EC90, demonstrating high-fidelity editing at a supersaturating dose
- Findings support a one-time, durable, and safe CRISPR-based Lp(a) lowering therapy engineered to transform treatment for millions of patients

STX-1400 achieves first- and best-in-class primate hepatocyte saturated editing (>75% of whole liver) when delivered at pharmacologically relevant doses

STX-1400 is an LNP-delivered, CasXE-based gene editor that targets *APOC3* (encoding for apolipoprotein C-III protein) to reduce protein production and lower triglyceride-rich lipoproteins. *APOC3* loss-of-function is associated with reduced coronary risk and dramatically lower triglycerides, making *APOC3* a compelling target for addressing severe hypertriglyceridemia (SHTG) and familial chylomicronemia syndrome (FCS), with potential relevance to broader triglyceride-driven cardiovascular risk.

Data highlights from the AHA presentation:

- Potency testing of surrogate STX-1400 molecule in NHPs revealed >75% hepatic editing of the *APOC3* locus at the 1.0 mg/kg dose, making it the first CRISPR-based therapy to demonstrate saturated APOC3 editing in NHP liver at a therapeutically relevant dose
- Delivery in hypertriglyceridemic mice led to >95% reduction of APOC3 expression and triglycerides levels
- Off-target studies in PHHs found no detectable editing at more than 200 nominated sites at a 10X EC90 supersaturating dose, reinforcing an exquisite specificity profile

About Scribe Therapeutics

Scribe Therapeutics is revolutionizing medicine by developing optimized *in vivo* CRISPR-based genetic medicines designed to become standard of care treatments for patients suffering from highly prevalent diseases, starting with cardiometabolic disease. The company is on a mission to build the first CRISPR-based therapeutics that are effective and safe enough to transform everyone's lifetime risk for disease. Scribe's CRISPR by Design™ approach engineers bacterial immune systems into a premier suite of genome and epigenome editing tools built for unique molecular advantages in activity, specificity, and deliverability, enabling the creation of therapies with a broader therapeutic window and safe for use as a preventative treatment. The company's lead candidate, STX-1150, is a novel liver-targeted therapy designed to epigenetically silence the PCSK9 gene, resulting in significant and durable reduction of LDL-C levels. 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 engineering the future of genetic medicine. To learn more, visit www.scribetx.com.