UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): March 5, 2026

Silence Therapeutics plc
(Exact name of Registrant as Specified in Its Charter)

England and Wales	**001-39487**	**Not Applicable**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

12 Hammersmith Grove
London
United Kingdom
(Address of Principal Executive Offices)

W6 7AP
(Zip Code)

Registrant's Telephone Number, Including Area Code: +44 20 3457 6900

Not Applicable
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
American Depositary Shares, each representing 3 ordinary shares, nominal value £0.05 per share	SLN	The Nasdaq Stock Market LLC
Ordinary share, nominal value £0.05 per share*	*	The Nasdaq Stock Market LLC

* *Not for trading, but only in connection with the listing of the American Depositary Shares on The Nasdaq Stock Market LLC.*

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 2.02 Results of Operations and Financial Condition.

On March 5, 2026, Silence Therapeutics plc (the "Company") issued a press release announcing its financial results for the fourth quarter and full year ended December 31, 2025, as well as other recent corporate updates. A copy of the press release is furnished as Exhibit 99.1 to this report and incorporated by reference.

The information in this Item 2.02 of this Current Report on 8-K, including Exhibit 99.1 hereto, is being furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, and shall not be deemed incorporated by reference into any of the Company's filings under the Securities Act of 1933, as amended (the "Securities Act"), or the Exchange Act, whether made before or after the date hereof, regardless of any general incorporation language in such filing, except as shall be expressly set forth by specific references in such filing.

Item 7.01 Regulation FD Disclosure.

On March 5, 2026, the Company issued an updated corporate presentation to reflect certain business updates. The presentation is available in the "Investors" section of the Company's website at silence-therapeutics.com/investors, a copy of which is furnished as Exhibit 99.2 to this Current Report on Form 8-K and is incorporated by reference herein. The Company's website and any information contained on the Company's website are not incorporated by reference into this Current Report on Form 8-K.

The information contained in Item 7.01 of this Current Report on Form 8-K, including Exhibit 99.2 hereto, is being furnished and shall not be deemed "filed" for purposes of Section 18 of the Exchange Act or otherwise subject to the liabilities of that section, and shall not be deemed incorporated by reference into any of the Company's filings under the Securities Act or the Exchange Act, whether made before or after the date hereof, regardless of any general incorporation language in such filing, except as shall be expressly set forth by specific reference in such filing.

Item 9.01 Financial Statements and Exhibits.
(d) Exhibits.

Exhibit Number	Description
99.1	Press Release dated March 5, 2026
99.2	Silence Therapeutics plc corporate presentation dated March 2026
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Silence Therapeutics plc

Date: March 5, 2026

By: /s/ Iain Ross

Name: Iain Ross

Title: Interim Principal Executive Officer and Chairman of the Board of Directors

(Principal Executive Officer)

EXHIBIT 99.1

Silence Therapeutics Highlights Recent Business Achievements and Reports Fourth Quarter and Full Year 2025 Financial Results

Topline results for Phase 2 SANRECO trial of divesiran, a first-in-class siRNA for polycythemia vera (PV), on-track for third quarter of 2026

5 March 2026

LONDON, Silence Therapeutics plc, Nasdaq: SLN, a global clinical-stage company developing novel siRNA (short interfering RNA) therapies, today reported financial results for the fourth quarter and full year ended December 31, 2025, and provided an update on recent business achievements.

"The past year was focused on clinical execution, demonstrated by the expedited enrollment in the Phase 2 SANRECO trial of divesiran in PV which is on-track for topline results in third quarter of 2026," said Iain Ross, Chairman and Interim Principal Executive Officer at Silence. "Divesiran is a first-in-class siRNA product candidate in PV with broad potential in blood disorders and this program is our highest priority. We believe we are well positioned today with excellent optionality and multiple near-term value drivers ahead."

Business Highlights

Divesiran: First-in-class siRNA for PV

- Accelerated timing for topline results in the Phase 2 SANRECO trial of divesiran, a first-in-class siRNA for PV; now anticipated in 3Q'26 (formerly 2H'26) due to faster than expected enrollment.

Zerlasiran: Phase 3 ready program for cardiovascular disease due to high Lp(a)

- Completed core Phase 3 readiness activities; program is well positioned for a potential third-party partner to initiate Phase 3 development.

SLN312: Phase 1 siRNA with a competitive profile for dyslipidemia

- AstraZeneca shared results from an interim analysis of a Phase 1 randomized, single-blind, placebo-controlled trial of SLN312, an siRNA silencing ANGPTL3 discovered using Silence's mRNAi GOLD™ platform and developed by AstraZeneca, in 98 patients with dyslipidemia. Data highlights include:
    - SLN312 demonstrated durable dose-dependent reductions in ANGPTL3, triglycerides and atherogenic lipoproteins after single and multiple doses.
    - Strong durability profile observed supporting potential for infrequent dosing.
    - SLN312 was well tolerated with no safety concerns identified.
    - Phase 1 data presentations are planned for medical and research congresses in 2026.
- On March 4, 2026, AstraZeneca notified Silence that they will not pursue further development of SLN312 beyond Phase 1. Silence will re-gain exclusive rights globally to this clinical asset following Phase 1 and is evaluating plans for further development. AstraZeneca and Silence maintain a broader collaboration leveraging Silence's mRNAi GOLD™ platform for cardiovascular, cardiometabolic, renal and respiratory diseases.

Discovery Pipeline

- Generated promising preclinical data for two new mRNAi GOLD™ platform programs.
    - SLN365, a potential first-in-class siRNA silencing GPR146, a novel mechanism-of-action for cholesterol management independent of LDL-C receptor function.

- SLN098, an siRNA silencing INHBE, a novel target for obesity supported by human genetics and strong pre-clinical data.

- Advanced extra-hepatic cell targeting leveraging the Company's proprietary siRNA platform, generating promising preliminary results in several cell types.

Anticipated 2026 Milestones

- Topline results for Phase 2 SANRECO trial of divesiran in PV in third quarter of 2026.
- Additional preclinical data for SLN365 (GPR146) in second quarter of 2026.
- Additional preclinical data for SLN098 (INHBE) in second quarter of 2026.
- Phase 1 data presentations for SLN312 at medical and research congresses in 2026.

Corporate Updates

- On December 15, 2025, Iain Ross, Chairman of the Board of Directors, was announced as Interim Principal Executive Officer following the departure of the Company's former CEO; a search is underway for a new CEO.
- In December 2025, James Ede Golightly, a former Silence Non-Executive Director, was reappointed to the Board. Additionally, Rhonda Hellums, CFO of Silence, was appointed to the Board as an Executive Director.

Full Year 2025 Financial Results

- **Cash Position:** Cash, cash equivalents, and short-term investments were $85.1 million as of December 31, 2025. This includes cash and cash equivalents of $11.3 million and short-term investments of $73.8 million.
- **Collaboration Revenue:** Collaboration revenue was $0.6 million for the year ended December 31, 2025, compared to $43.3 million for the year ended December 31, 2024. The decrease for 2025 was primarily due to revenue associated with the Hansoh collaboration that concluded in 2024 and a $17.4 million decrease in revenue related to the AstraZeneca collaboration.
- **R&D Expenses:** Research and development (R&D) expenses were $67.8 million for the year ended December 31, 2025, compared to $67.9 million for the year ended December 31, 2024.
- **G&A Expenses:** General and administrative (G&A) expenses were $22.3 million for the year ended December 31, 2025, compared to $26.9 million for the year ended December 31, 2024. The decrease for 2025 was primarily a result of a decrease in SEC reporting requirements and other cost-savings initiatives.
- **Net Loss:** Net loss was $88.6 million, or $0.63 basic and diluted net loss per share for the year ended December 31, 2025, compared to a net loss of $45.3 million, or $0.33 basic and diluted net loss per share for the year ended December 31, 2024.
- Total outstanding shares were 141,701,848 ordinary shares (including shares in the form of American Depositary Shares) as of December 31, 2025.

About Silence Therapeutics

Silence Therapeutics is a global clinical-stage biotechnology company committed to transforming people's lives by silencing diseases through precision engineered medicines created with proprietary siRNA (short interfering RNA) technology. Silence leverages its mRNAi GOLD™ platform to create innovative siRNA therapies designed to precisely target and silence genes that cause disease. The Company is advancing a growing pipeline of siRNA product candidates targeting areas of high unmet need across rare and common diseases where treatments are limited or inadequate. For more information, please visit https://www.silence-therapeutics.com/.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. In some cases, you can identify forward-looking statements by terminology such as “aim,” “anticipate,” “assume,” “believe,” “contemplate,” “continue,” “could,” “design,” “due,” “estimate,” “expect,” “goal,” “intend,” “may,” “objective,” “plan,” “positioned,” “potential,” “predict,” “seek,” “should,” “target,” “will,” “would” and other similar expressions that are predictions of or indicate future events and future trends, or the negative of these terms or other comparable terminology. All statements other than statements of historical facts contained in this press release are forward-looking statements. These forward-looking statements include, but are not limited to, statements about: the Company’s business strategy and plans, including the Company’s clinical development activities and timelines; the potential therapeutic benefits of the Company’s product candidates; the anticipated timing of initial topline and future results from the SANRECO Phase 2 trial; the Company’s ability to deliver near- or long-term value; the Company’s ability to advance additional candidates from its mRNAi GOLD™ platform; the Company’s ability to advance extra-hepatic cell targeting or identify extra-hepatic product candidates; and the Company’s ability to identify and engage potential third-party partners for one or more of its product candidates, including the Company’s preclinical and Phase 3 ready assets. Forward-looking statements are not guarantees of future performance and are subject to risks and uncertainties that could cause actual results and events to differ materially from those anticipated, including, but not limited to, risks and uncertainties related to: the company’s history of net operating losses; the company’s ability to obtain necessary capital to fund its clinical programs; the early stages of clinical development of the company’s product candidates; the company’s ability to obtain regulatory approval of and successfully commercialize its product candidates either on its own or with potential partners; any undesirable side effects or other properties of the company’s product candidates; the company’s reliance on third-party suppliers and manufacturers; the outcomes of any future collaboration agreements; and the company’s ability to adequately maintain intellectual property rights for its product candidates. These and other risks are described in greater detail under the section titled “Risk Factors” contained in the company’s Annual Report on Form 10-K and Quarterly Reports on Form 10-Q and the company’s other filings with the SEC. Any forward-looking statements that the Company makes in this press release are made pursuant to the Private Securities Litigation Reform Act of 1995, as amended, and speak only as of the date of this press release. Except as required by law, the company undertakes no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise.

Inquiries:

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Tel: +1 (646) 637-3208

SILENCE THERAPEUTICS plc
Consolidated Statements of income (loss)
(in thousands, except for loss per share and share data)

	Note	Year ended December 31, 2025	2024
Revenue	3	$ 559	$ 43,258
Cost of sales		(215)	(11,810)
Gross profit		**344**	**31,448**
Research and development costs		(67,753)	(67,883)
General and administrative expenses		(22,344)	(26,884)
Restructuring charges	6	(1,324)	-
Operating loss		**(91,077)**	**(63,319)**
Foreign currency (loss)/gain, net		(8,467)	646
Other income, net	7	3,480	4,472
Benefit from R&D credit		7,463	13,737
Loss before income tax expense		**(88,601)**	**(44,464)**
Income tax expense	18	(11)	(845)
Net Loss		**$ (88,612)**	**$ (45,309)**
Loss per share (basic and diluted)	8	$ (0.63)	$ (0.33)
Weighted average shares outstanding (basic and diluted)		141,694,702	138,752,224

The accompanying notes form an integral part of these consolidated financial statements.

SILENCE THERAPEUTICS plc
Consolidated balance sheets
(in thousands, except share data)

	Note	Year ended December 31, 2025	2024
Current assets			
Cash and cash equivalents	12	$ 11,277	$ 121,330
Short-term investments	12	73,837	26,004
R&D benefit receivable		22,007	24,396
Other current assets	13	11,537	14,664
Trade receivables	14	-	972
Total current assets		**118,658**	**187,366**
Property, plant and equipment, net	9	1,581	1,818
Operating lease right-of-use assets	16	167	157
Goodwill	10	10,621	9,392
Intangible assets	11	288	312
Other long-term assets	13	127	3,590
Total assets		**$ 131,442**	**$ 202,635**
Current liabilities			
Contract liabilities	17	$ (168)	$ (306)
Trade and other payables	15	(13,356)	(16,399)
Operating lease liabilities, current	16	(89)	(117)
Total current liabilities		**(13,613)**	**(16,822)**
Contract liabilities	17	(55,454)	(51,790)
Operating lease liabilities, long-term	16	(71)	-
Total liabilities		**$ (69,138)**	**$ (68,612)**
Commitments and contingencies (Note 21)			
Shareholders' equity			
Ordinary shares - par value £0.05 per share; 141,701,848 shares issued at December 31, 2025 (2024: 141,674,074)	19	(10,290)	(10,288)
Additional paid-in capital		(617,562)	(609,560)
Accumulated deficit		562,572	474,044
Accumulated other comprehensive loss		2,976	11,781
Total shareholders' equity		**(62,304)**	**(134,023)**
Total liabilities and shareholders' equity		**$ (131,442)**	**$ (202,635)**

The accompanying notes form an integral part of these consolidated financial statements.

Exhibit 99.2

SILENCE THERAPEUTICS

Corporate Presentation

March 2026

Forward-Looking Statements

The information contained in this presentation is being supplied and communicated to you solely for your information and may not be reproduced, further distributed to any other person or published, in whole or in part, for any purpose.

The distribution of this presentation in certain jurisdictions may be restricted by law, and persons into whose possession this presentation comes should inform themselves about, and observe, any such restrictions. Although reasonable care has been taken to ensure that the facts stated in this presentation are accurate and that the opinions expressed are fair and reasonable, the contents of this presentation have not been verified by Silence Therapeutics plc (the "Company") or any other person. Accordingly no representation or warranty, express or implied, is made as to the fairness, accuracy, completeness or correctness of the information and opinions contained in this presentation and no reliance should be placed on such information or opinions. None of the Company, or any of its respective members, directors, officers or employees nor any other person accepts any liability whatsoever for any loss howsoever arising from any use of such information or opinions or otherwise arising in connection with this presentation. No part of this presentation, or the fact of its distribution, should form the basis of or be relied upon in connection with any contract or commitment or investment decision whatsoever. This presentation does not form part of any offer of securities, or constitute a solicitation of any offer to purchase or subscribe for securities or an inducement to enter into any investment activity. Recipients of this presentation are not to construe its contents, or any prior or subsequent communications from or with the Company or its representatives as investment, legal or tax advice. In addition, this presentation does not purport to be all-inclusive or to contain all of the information that may be required to make a full analysis of any transaction. Further, the information in this presentation is not complete and may be changed. Recipients of this presentation should each make their own independent evaluation of the information and of the relevance and adequacy of the information in this document and should make such other investigations as they deem necessary.

This presentation may contain forward-looking statements that reflect the Company's current views and expectations regarding future events. In particular certain statements with regard to management's strategic vision, aims and objectives, the conduct of clinical trials, the filing dates for product license applications and the anticipated launch of specified products in various markets, the Company's ability to find partners for the development and commercialization of its products as well as the terms for such partnerships, anticipated levels of demand for the Company's products (including in development), the effect of competition, anticipated efficiencies, trends in results of operations, margins, the market and exchange rates, are all forward-looking in nature.

Forward-looking statements involve risks and uncertainties that could cause actual results to differ materially from those expressed or implied by the forward looking statements. Although not exhaustive, the following factors could cause actual results to differ materially from those the Company expects: difficulties inherent in the discovery and development of new products and the design and implementation of pre-clinical and clinical studies, trials and investigations, delays in and results from such studies, trials and investigations that are inconsistent with previous results and the Company's expectations, the failure to obtain and maintain required regulatory approvals, product and pricing initiatives by the Company's competitors, inability of the Company to market existing products effectively and the failure of the Company to agree beneficial terms with potential partners for any of its products or the failure of the Company's existing partners to perform their obligations, the ability of the Company to obtain additional financing for its operations and the market conditions affecting the availability and terms of such financing, the successful integration of completed mergers and acquisitions and achievement of expected synergies from such transactions, and the ability of the Company to identify and consummate suitable strategic and business combination transactions and the risks described in our most recent Admission Document.

By participating in this presentation and/or accepting any copies hereof you agree to be bound by the foregoing restrictions and the other terms of this disclaimer.


Silencing diseases through
precision engineered medicines
created with proprietary
siRNA technology

2025 Key Milestones Achieved

- ✓ Achieved rapid enrollment in SANRECO Phase 2 PV study - topline results anticipated in 3Q 2026
- ✓ Completed core Phase 3 readiness activities for zerlasiran in high Lp(a)
- ✓ Generated promising pre-clinical results for two new GOLD platform programs
- ✓ Advanced extra-hepatic cell targeting of siRNA with promising initial data

Our Global Footprint

NEW JERSEY
US OFFICE

LONDON
COMPANY HQ

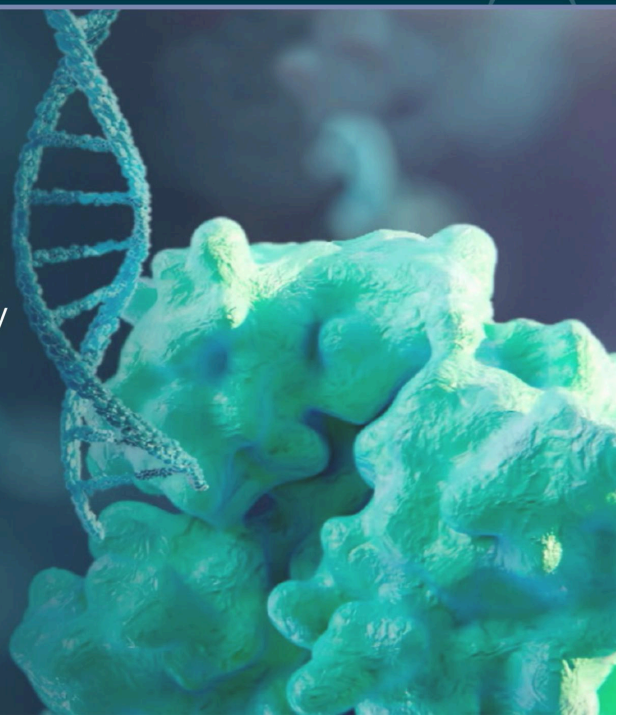
BERLIN
R&D OPERATIONS

siRNA expertise spanning drug discovery, design and clinical development

We are Silencing Genes to Treat Disease

The siRNA Approach

- **Natural:** RNAi is a natural biological process that regulates gene expression
- **Precise:** each siRNA is intentionally designed to bind only to the target gene transcript
- **Durable, yet Reversible:** siRNA therapies can be administered infrequently and do not produce permanent changes to DNA
- **Broad Utility:** siRNA therapies can be designed to target essentially any gene



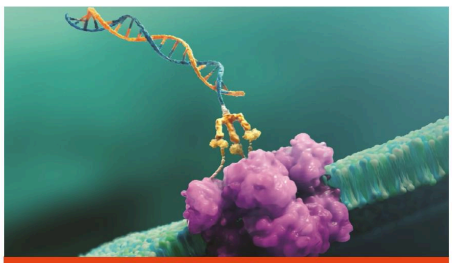
Our Toolbox Considers all Elements of siRNA and Ligand Design

siRNA molecule

- siRNA matched to target gene
- Silence has developed chemical modification patterns that enhance stability and improve activity

Linker

- Silence has developed proprietary linkers, enabling the attachment of targeting ligands to the siRNA molecule

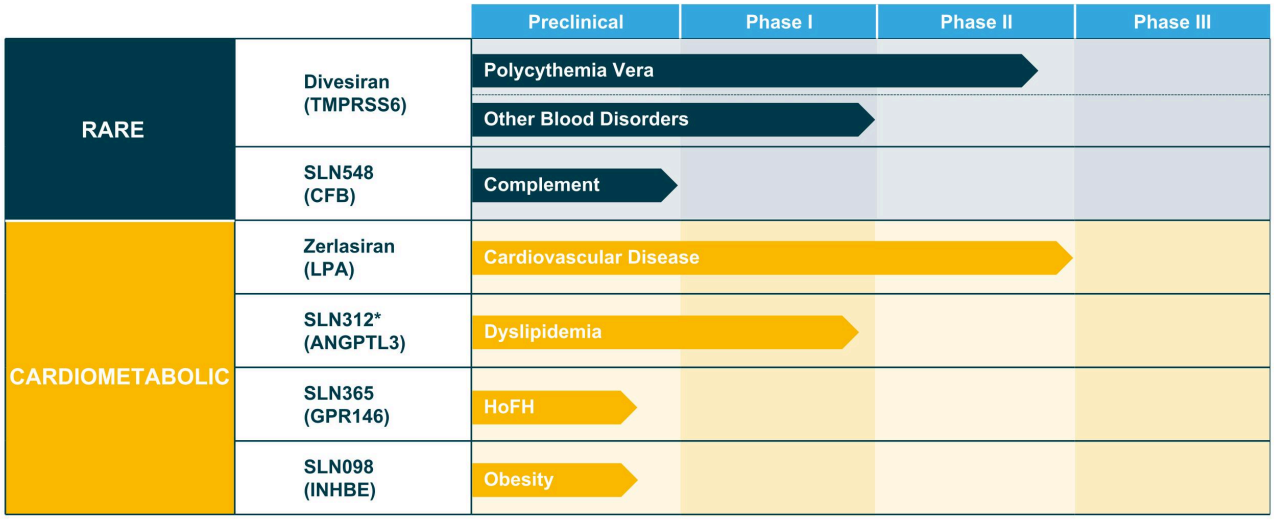


GalNAc Ligand (delivery tool)

- GalNAc ligand delivers molecule to specific liver tissues/cells
- Highly targeted to liver

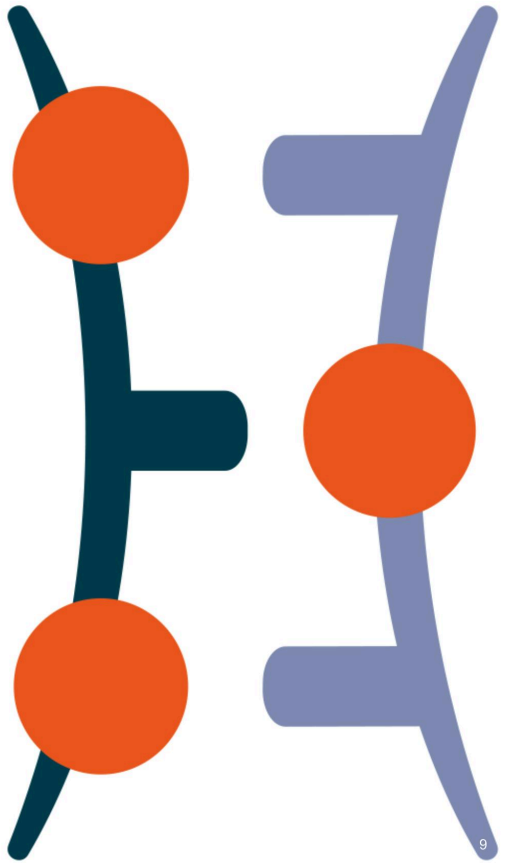
Continuous Fine-Tuning to Further Improve Performance

mRNAi GOLD™ Development Pipeline of siRNA Therapies



*SLN312 is currently licensed to AstraZeneca. As announced in a Company Press Release dated March 5, 2026, Silence will re-gain exclusive rights globally to SLN312 following Phase 1.
HoFH=Homozygous familial hypercholesterolemia

Divesiran
(TMPRSS6)



Divesiran: Potential First-in-Class, First-Line siRNA Treatment for Polycythemia Vera (PV)

Compelling Profile

Robust, rapid and durable efficacy in Ph1

Favorable and potentially differentiated safety profile

Broad potential in iron-related disorders

Convenient Dosing

Less frequent dosing (every 6 or 12 weeks)

Fixed dosing, no titration needed

Consistent Control

Potential for rapid and continuous symptom improvement

Opportunities for improved quality of life

Targeting First-Line Treatment in All Phlebotomy-Dependent PV Patients

Polycythemia Vera (PV) is a Rare Blood Cancer with Significant Unmet Needs

- **Myeloproliferative neoplasm characterized by the excessive production of red blood cells (RBCs)**
  - Elevated hematocrit (HCT) is a hallmark of the disease, indicating overproduction of RBCs
  - Associated with JAK2 gain-of-function driver mutation in hematopoietic stem cells in over 90% of patients
- **Serious, chronic disease associated with increased thrombotic and cardiovascular risks[1-3]**
- **Rare disease with ~150,000 in the US and ~3.5m worldwide[4]**
  - Diagnosed typically in individuals 50-70 years of age
  - Median survival ~20 years

Treatment goal is to control HCT <45% to reduce CV and major thrombotic events

1. NORD Rare Disease Database, Polycythemia Vera. https://rarediseases.org/rare-diseases/polycythemia-vera/ 2. Spivak JL. Ann Hematol 2018; 19(2):1-14. 3. Marchioli R, et al. N Engl J Med 2013; 368:22-33 4.Using 44/100,000 global population: 7,800m, Kattamis, A. et al. Eur J Haematol (2020);

People Living with PV Have Significant Unmet Needs

Inconsistent HCT Control

- Patients with HCT between 45-50% are ~4x more likely to die from CV causes or have major thrombotic events than those <45%[1]
- Most patients have uncontrolled HCT with tests ≥45%[2]

Iron Deficiency

- Most patients with PV are iron deficient due to depleted bone marrow iron levels[3]
- Some treatments exacerbate disease-related symptoms by inducing iron deficiency[3,4]

Disease Burden

- Patients with elevated HCT often require frequent phlebotomies to manage condition
- 30-40% of PV patients who receive cytoreductive therapy have a suboptimal response and toxicity issues[5]
- Patients have burdensome symptoms, including fatigue and concentration problems[5]

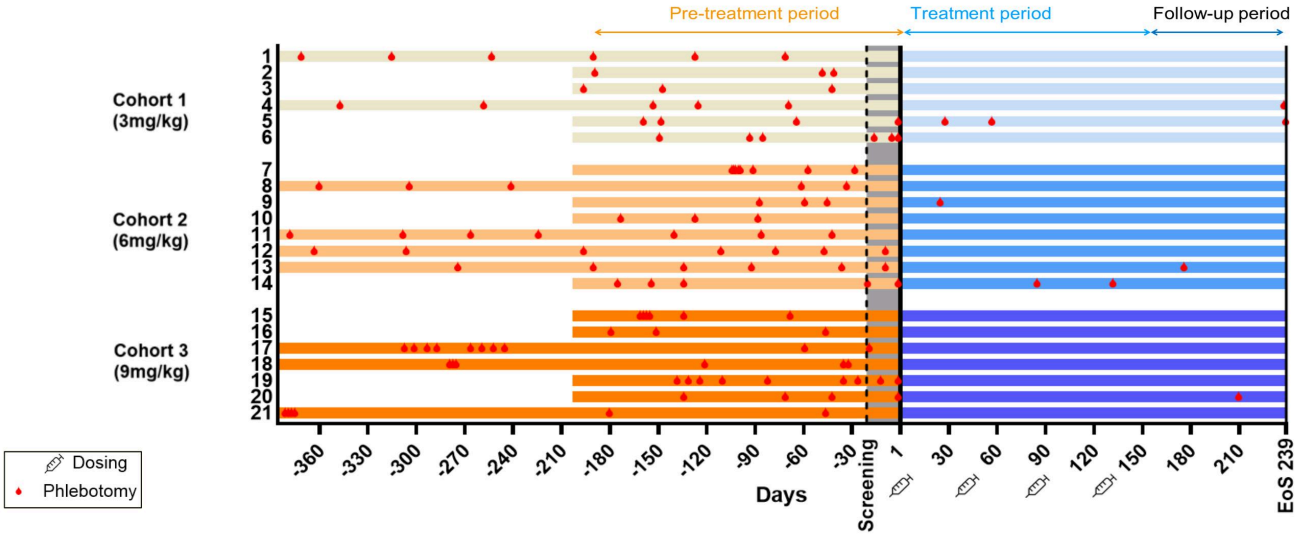
"The PV aspect means that you have to have phlebotomies regularly and I think the most crippling thing about that is the fatigue."
– Nona Baker

1. Marchioli et al. 2013 NEJM paper; 2. Verstovsek S, et al. Ann Hematol. 2023 Mar;102(3):571-581; 3. Verstovsek S, et al. Leuk Res. 2017;56:52-59. doi:10.1016/j.leukres.2017.01.032.4. McMullin MF, et. al. Br J Haematol. 2019 Jan; 184(2): 176-191.; 5. Mesa, R. Clin Adv Hematol Oncol (2017)

SANRECO Phase 1 Study Overview
Completed in February 2025

Design	• 34-week, open-label, dose-finding study of divesiran in 21 phlebotomy-dependent PV patients • Study included 16-week follow-up period following last administered dose
Key Inclusion Criteria	• PV diagnosis • At least 3 phlebotomies in the last 6 months or 5 in the last year prior to screening • Stable dose of cytoreductive agents allowed • No hematocrit threshold
Dosing & Administration	• 6 patients at 3 mg/kg, 8 patients at 6 mg/kg and 7 patients at 9 mg/kg • Administered subcutaneously (s.c.) every six weeks (Q6W) for four doses
Key Objectives	• Safety and tolerability • Assessment of the number of phlebotomies at 3 intervals (pre-treatment, treatment and follow-up)

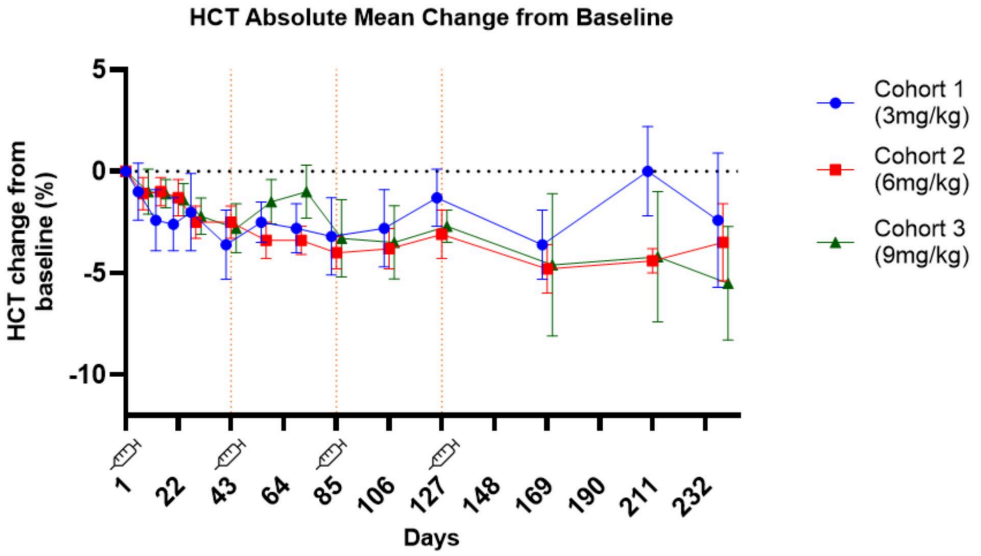
Divesiran Reduced Phlebotomy Frequency in All PV Patients



79 Phlebotomies Prior to Dosing; No Well-Controlled Patients Required a Phlebotomy through the 6-month Treatment Period

1. Data Presented at the European Hematology Association. June 12, 2025. SANRECO, an On-going Phase 1/2 Study Evaluating Divesiran, Novel GalNAc-conjugated SiRNA, in Patients with Polycythemia Vera. Abstract Code: SS24;
2. Pre-dose from D-201 to D-1, Treatment period D1 to D169 and FU D169 to D239; EoS = End of Study visit; 3. Data cut-off 24th April 2025.

Divesiran Reduced Hematocrit in All PV Patients Regardless of Baseline Levels



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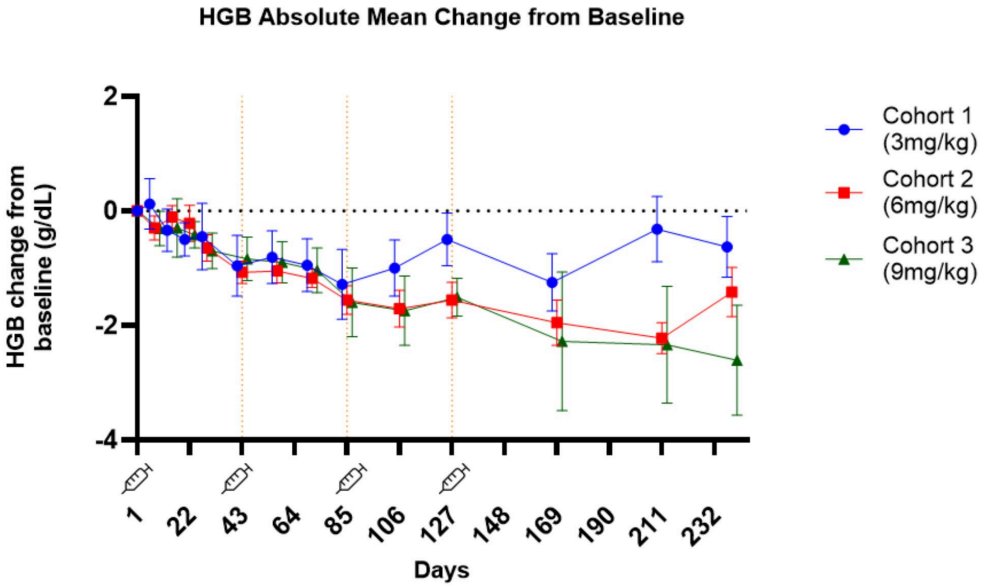
Divesiran Reduced Hemoglobin in All Cohorts



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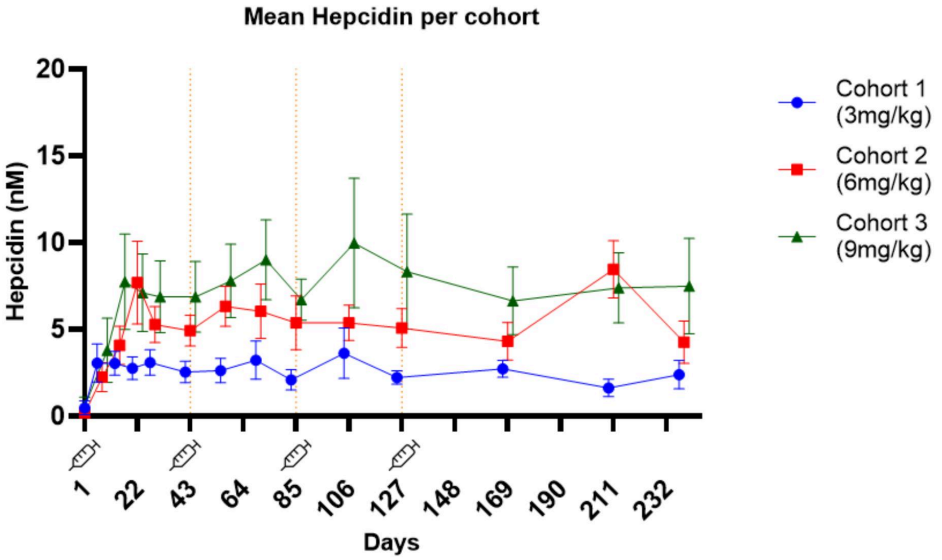
Divesiran Treatment Produced Sustained Increases in Hepcidin



1. Data Presented at the European Hematology Association. June 12, 2025. SANRECO, an On-going Phase 1/2 Study Evaluating Divesiran, Novel GalNAc-conjugated SiRNA, in Patients with Polycythemia Vera. Abstract Code: SS24; 2. Orange dotted line represent dosing dates. Error bars represent ± SEM; All data available for each time point is reported; 3. Data cut-off 24th April 2025.

Divesiran Demonstrated a Favorable Safety and Tolerability Profile

- Divesiran was well tolerated with no dose-limiting toxicities
- No treatment-related serious adverse events or TEAEs leading to discontinuation

SANRECO Phase 1 Results Highlight Potential for First-in-Class siRNA Treatment for PV

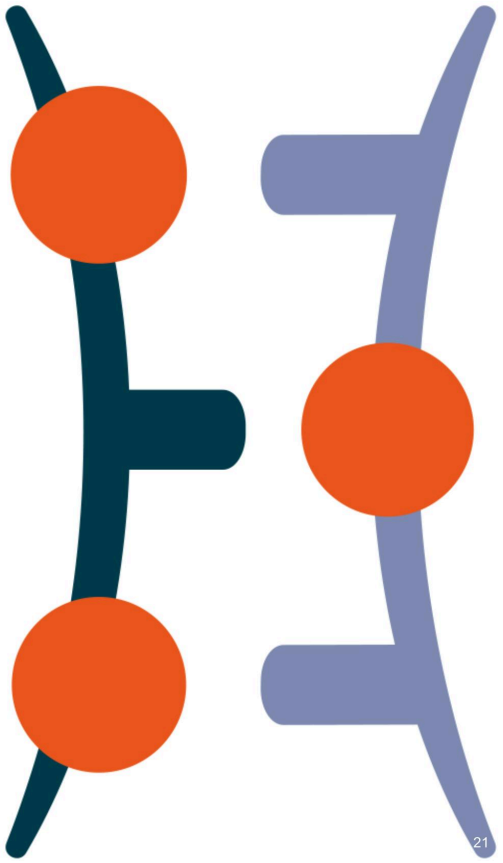
EFFICACY	Controlled HCT levels and eliminated the need for phlebotomy in target population
SAFETY	Well tolerated with no dose-limiting toxicities
DURABILITY	Effects sustained during the treatment and follow-up period with Q6W dosing

SANRECO Phase 2 Study Overview

Design	• 36-week, placebo-controlled, double-blind period followed by a 3-year, double-blind and open-label extension period evaluating divesiran in 48 phlebotomy-dependent PV patients
Key Inclusion Criteria	• PV diagnosis • At least 3 phlebotomies in the last 6 months or 5 in the last year prior to screening • Stable dose of cytoreductive agents allowed • HCT level <45% prior to dosing
Dosing & Administration	• Divesiran 6 mg vs. placebo • Administered s.c. at Q6W and Q12W intervals
Key Objectives	• Primary endpoint: proportion of patients who maintain HCT levels below 45% without phlebotomies between weeks 18 and 36 • Secondary endpoints include safety and tolerability, pharmacokinetics, and quality of life changes

Study Fully Enrolled - Topline Results Expected in 3Q 2026

Zerlasiran
(LPA)



Zerlasiran Silences Lp(a): an Independent Risk Factor for Cardiovascular Disease

- At least 20% of the global population has high Lp(a) defined as ≥125 nmol/L (~50 mg/dL)[1]
- Lp(a) levels are genetically determined
- Recognized as a major untreated risk factor in cardiovascular disease
- Lp(a) levels are not significantly modifiable by approved medicines or lifestyle changes

Zerlasiran Has the Potential to Address Major Unmet Needs in Cardiovascular Disease

1. Lau, F. D., & Giugliano, R. P. (2022). Lipoprotein (a) and its significance in cardiovascular disease: a review. Jama Cardiology, 7(7), 760-769.
mg/dL: milligrams per deciliter, nmol/L: nanomoles per liter (approximate conversion factor of 2.5)

Zerlasiran Has Substantial Market Potential

High Cholesterol vs High Lp(a) in Cardiovascular Disease

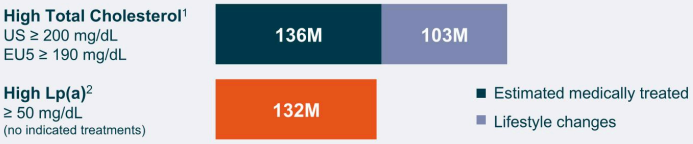
High Cholesterol is a **Modifiable Risk Factor** → Lifestyle changes **can** have a positive impact

High Lp(a) is a **Genetic Risk Factor** → Lifestyle changes **have no effect** on Lp(a) levels

Similar Medically Treated Population

Patients with High Total Cholesterol vs. High Lp(a)

US + EU5 Markets



Blockbuster Potential

Sales of Cholesterol-Lowering Drugs Peaked at >$30B[3,4]

Lipitor® (atorvastatin)	Crestor® (rosuvastatin)	Zocor® (simvastatin)
$12.9B peak sales	**$7.0B** peak sales	**$5.2B** peak sales

[1] Datamonitor Healthcare | Informa 2018,[2] Varvel et al Arterioscler Thromb Vasc Biol. 2016;36:2239, Tsimikas et al. Atherosclerosis 2020;300:1, Nordestgaard et al. Eur Heart J. 2010;31:2844,
[3] Biomedtracker, Internal Analysis; [4] Kidd, J., Nat Rev Drug Discov. 2006;5(10):813

Zerlasiran Phase 2 Results Support Competitive Profile with Opportunities to Further Differentiate in Phase 3

EFFICACY	Maximum Lp(a) reductions over 90%
SAFETY	Well tolerated with no major safety issues
DURABILITY	Lp(a) reductions persisted 60 weeks following first dose (Q16W and Q24W dosing)

1. Journal of the American Medical Association (JAMA). November 18, 2024. Zerlasiran – A Small Interfering RNA-Targeting Lipoprotein(a) A Phase 2 Randomized Clinical Trial | Clinical Pharmacy and Pharmacology | JAMA | JAMA Network.

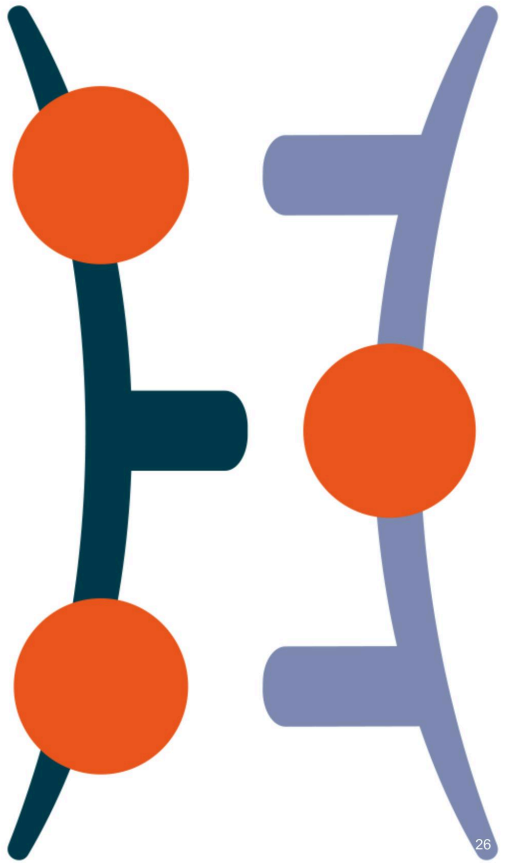
Zerlasiran Program Status

- ✓ Core Phase 3 readiness activities complete
- ✓ Alignment with global regulatory agencies on Phase 3 design and endpoints

Next Steps:

- Seeking potential third-party partners for Phase 3 development
- First industry CVOT evaluating Lp(a) lowering therapy impact on cardiovascular events scheduled to readout in 2026

SLN312
(ANGPTL3)



SLN312: Phase 1 siRNA with a Competitive Profile for Dyslipidemia

SLN312 is a Phase 1 siRNA silencing ANGPTL3

- ANGPTL3 inhibitors are **novel class** of therapeutic agents with **LDL receptor-independent** mechanism of action that may benefit patients that do not respond to **statins or PCSK9 inhibitors**
- Discovered as part of an ongoing **collaboration with AstraZeneca** to discover, develop and commercialize siRNA therapeutics for cardiovascular, renal, metabolic and respiratory diseases using **Silence's mRNAi GOLD™**
- **AZ completed an interim analysis of a Phase 1** trial in patients with dyslipidemia demonstrating a competitive profile; Silence will re-gain exclusive rights globally to SLN312 at the end of Phase 1

SLN312 Demonstrates Competitive Profile in Patients with Dyslipidemia

- **Safe and well-tolerated** with no serious adverse events
- Robust reductions in ANGPTL3 protein after single and multiple doses of SLN312 supporting **infrequent dosing**
- **Lipid reductions** on par with other ANGPTL3i in development

Program Outlook

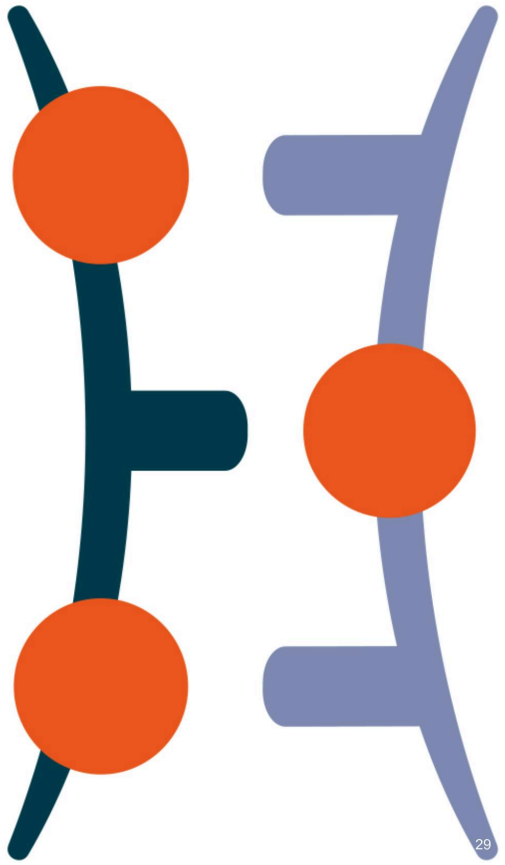
- Potential for **GPR146 and ANGPTL3 combination therapy** (differentiated approach)
- Several therapeutic options available including **mixed dyslipidemia, HoFH** and **HeFH**

SLN312 Phase 1 Results Demonstrate Robust ANGPTL3 Reductions Supporting Potential for Infrequent Dosing

EFFICACY	Substantial and dose-dependent reductions in ANGPTL3, triglycerides and atherogenic lipoproteins
SAFETY	Well tolerated with no major safety issues
DURABILITY	Sustained effects after single and multiple doses supporting potential for infrequent dosing

Phase 1 Data Presentations Planned for Research Congresses in 2026

SLN365
(GPR146)



SLN365: Potential First-in-Class siRNA with Novel MOA in High Unmet Need Space

Potential First-in-Class siRNA Silencing GPR146

- Novel mechanism-of-action for managing cholesterol levels independent of LDL-C receptor (LDLR) function
- Hypercholesterolemia is a highly prevalent indication: around 1 in 300 individuals worldwide have the familial form HeFH (heterozygous) and around 1 in 300,000 worldwide have HoFH (homozygous)[1,2]

Demonstrated Preclinical Proof-of-Concept

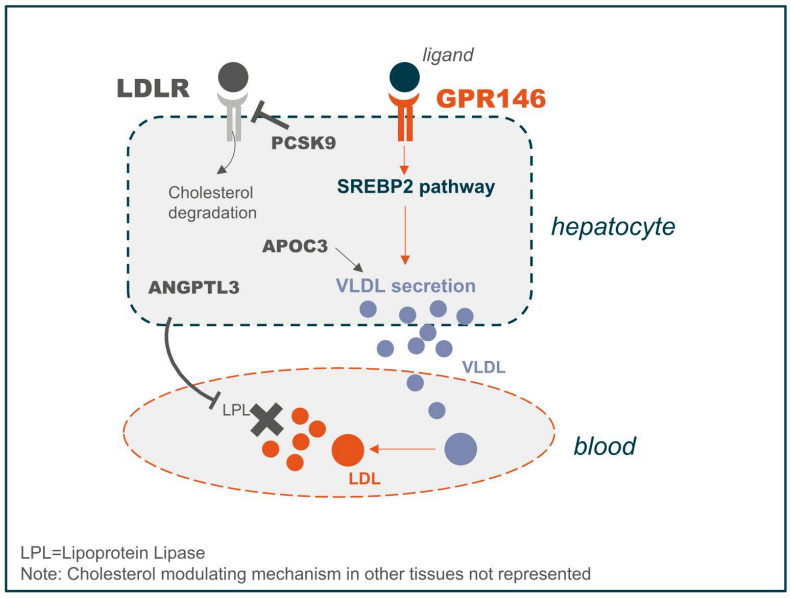
- Achieved > 80% mRNA knockdown after a single injection (non-human primates)
- Sustained effects throughout study with ~50% or greater mRNA knockdown observed 3 months after dosing (NHP)
- Significant reductions in total cholesterol, LDL and triglycerides in murine disease model (LDLR KO)

Program Outlook

- Potential IND filing in 1H 2027
- First potential indication planned for the treatment of HoFH which is the area of highest unmet need where 47% of patients don't reach the LDL-C goal despite being treated with multiple lipid lowering therapies

1. Heterozygous familial hypercholesterolemia: prevalence and control rates I 2021; 2. Homozygous Familial Hypercholesterolaemia – Worldwide Experience I 2023

GPR146: Novel Target for the Management of Cholesterol Independent of LDL-C Receptor Function



LPL=Lipoprotein Lipase
Note: Cholesterol modulating mechanism in other tissues not represented

- GPR146 is a receptor present on hepatocyte membranes and **responsible for VLDL production**
- **VLDL converts into LDL-C and triglycerides** in the blood stream
- GPR146's function is **independent from LDLR**
- **Differentiated MOA:** Inhibition of GPR146 expression blocks VLDL synthesis and thus TG and LDL levels and may be synergistic with ANGPTL3 and LDLR- dependent drugs

REF: Angiopoietin-Like Protein 3 (ANGPTL3) Modulates Lipoprotein Metabolism and Dyslipidemia

Genetic Evidence: GPR146 Deficiency Protects Against Hypercholesterolemia and Atherosclerosis

TRANSLATIONAL SCIENCES

Variants in the *GPR146* Gene Are Associated With a Favorable Cardiometabolic Risk Profile

https://doi.org/10.1161/ATVBAHA.122.317514

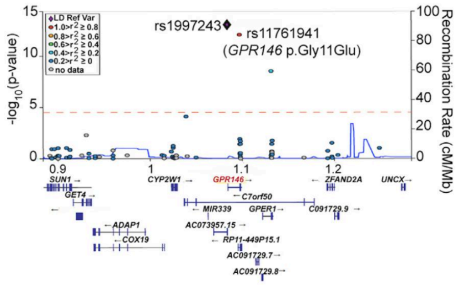
Cell Research

Hypercholesterolemia risk associated GPR146 is an orphan G-protein coupled receptor that regulates blood cholesterol level in human and mouse

https://doi.org/10.1038/s41422-020-0303-z

Cell

GPR146 Deficiency Protects against Hypercholesterolemia and Atherosclerosis

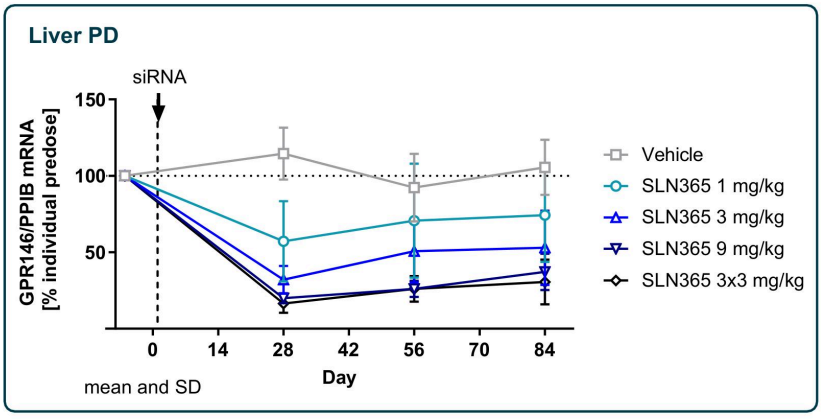


https://doi.org/10.1016/j.cell.2019.10.034

Human Genetic Studies Support GPR146 as a Susceptible Gene Regulating Cholesterol Levels

Common rs2362529-C allele →lower GPR146 expression →lower LDL-C, ApoB, HDL, apoAI, and CRP
Common rs1997243-G allele → higher GPR146 expression → exact opposite phenotype

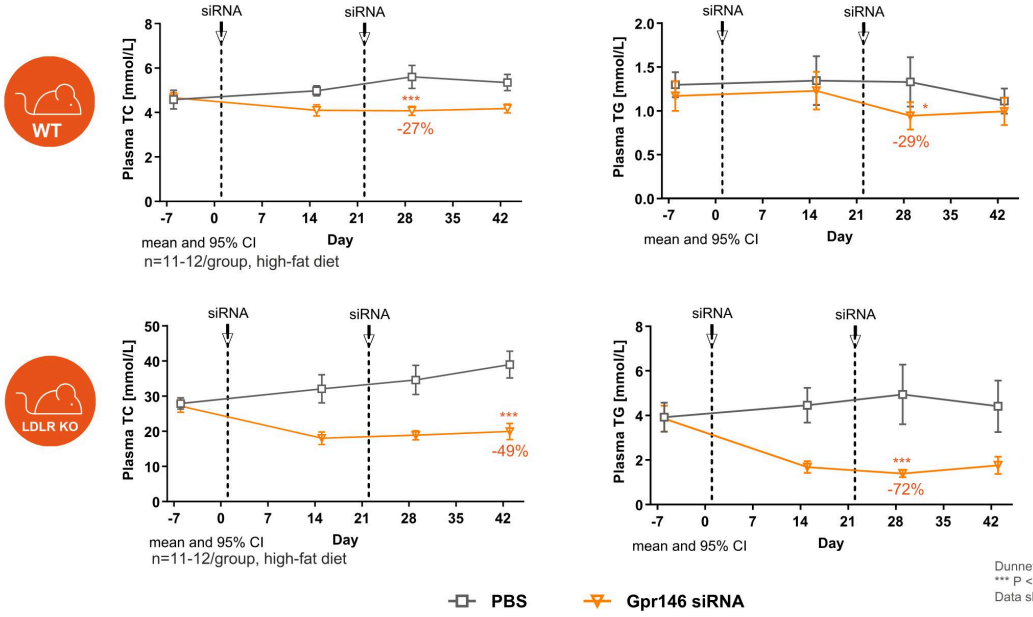
Dose-Dependent GPR146 mRNA Knockdown Observed with SLN365 Treatment in Non-Human Primates



Results

- SLN365 treatment resulted in 84% mRNA KD at 4 weeks in the multiple dose group (3 x 3 mg/kg)
- Sustained KD throughout the study duration – 70% mRNA KD at week 12 in the multiple dose group
- Single dose of 9 mg/kg resulted in 80% mRNA KD at 4 weeks and 63% KD at week 12
- No major treatment-related effect on body weight and no effect on clinical chemistry, hematology or clinical observation

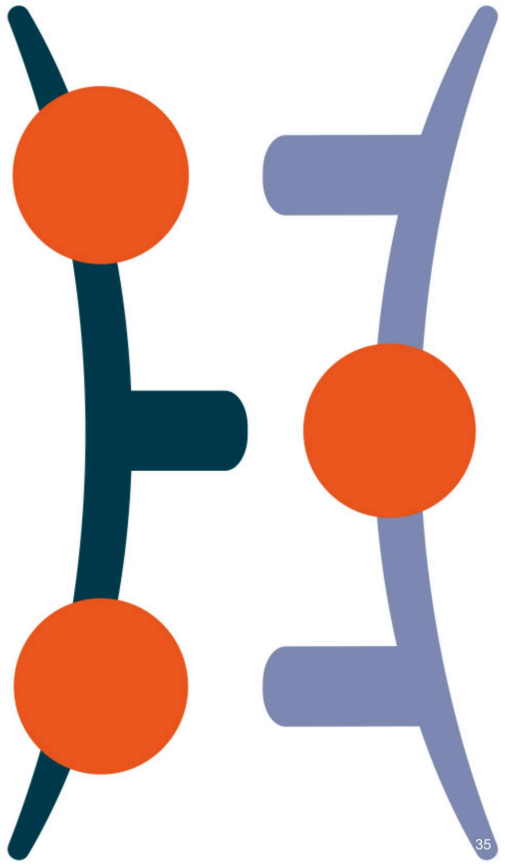
Reduction of Plasma Cholesterol and Triglycerides in Mice Following GPR146 siRNA Treatment



- Mouse surrogate siRNA reduced Gpr146 *mRNA* levels by >75%
- Significant reduction of total cholesterol and triglycerides following siRNA treatment observed in WT and LDLR KO mice on Western diet
- No accumulation of lipids in the liver following siRNA treatment

Dunnet's test on two-factor linear model with interaction
*** P < 0.001; * P<0.05 compared to PBS control
Data shown for one compound, similar data was obtained with two different siRNAs

SLN098
(INHBE)



Despite Recent Advances in Obesity Treatment, Limitations of Current SoC Leave Millions at Risk of Further Complications

- ~ 1 billion patients worldwide affected by obesity and associated comorbidities
- Current obesity treatments offer weight loss of ~15-25% which plateaus after 12-24 months and are associated with up to 40% lean muscle mass loss
- More than two-thirds weight loss is regained within first year after discontinuation of treatment
- Poor tolerability and compliance with up to 30% patients discontinuing GLP/GIP agonists treatment

Need for Improved Quality of Weight Loss with Differentiated Approach to Current Treatments

1. NCD-RisC, Lancet. 2024; 2. Melson et al Clinical Research 2024; 3. Kevin Hall, bioRxiv. 2023; Wilding et al, NEJM. 2021; Jastreboff et al, NEJM.2022; 4.Gomar et al, Curr Cardiol Rep. 2025; 5. West et al, BMJ.2026

SLN098 Silences INHBE: Novel Target for Obesity Supported by Human Genetics and Recent Clinical Validation

Potential to Transform Weight Loss

- Opportunity to address unmet needs including increasing fat loss, preventing muscle mass loss and slowing weight regain
- INHBE is a novel target supported by human genetics, strong preclinical data, and emerging third-party clinical data

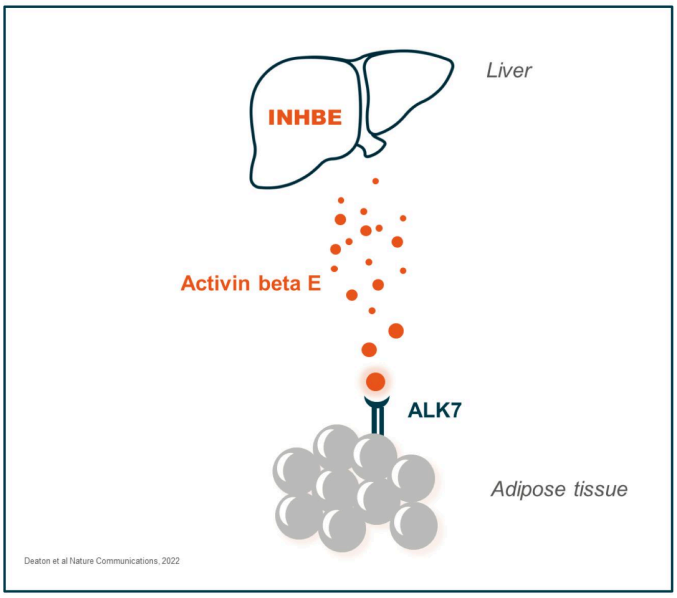
Demonstrated Deep and Durable Knockdown

- >70% knockdown of INHBE mRNA levels sustained for nearly 3 months in non-human primates
- Disease model data expected Q2 2026 to further validate mechanism of action

Program Outlook

- Potential for IND filing by 2027 year-end
- Opportunity to develop either as monotherapy or add-on to GLP/GIP agonists or as weight maintenance treatment

Targeting INHBE Synthesis Blocks Signalling via ALK7, Effectively Enabling Lipolysis in Adipose Tissue



- INHBE (Inhibin beta E) encodes **Activin beta E**, a **peptide hormone** & member of the Transforming Growth Factor Beta (TGF-b) super family
- **Expression is elevated** upon fasting, in **obesity** and in patients with **T2D**
- Activin beta E is a hepatokine that **activates ALK7 receptor** in adipose tissue, where it blocks lipolysis
- **Inhibition of INHBE expression enhances lipolysis and redistributes fat**
- In combination with GLP/GIP agonists, opportunity to **enhance weight loss** while **preserving muscle mass**

SLN098 Preclinical Data Demonstrating Impact on Weight Loss in Obesity Disease Model Anticipated in 2Q 2026

Study Objectives:

- SLN098 impact on weight gain
- SLN098 impact on weight loss in combination with GLP/GIP agonist
- SLN098 impact on quality of weight loss (lean mass/fat mass & impact on weight gain after phasing out GLP/GIP agonists)
- Safety data (i.e. impact on fatty liver and blood lipid levels, ALT/AST)

Anticipated 2026 Milestones

	1Q 2026	2Q 2026	3Q 2026	4Q 2026
Divesiran Polycythemia Vera			★ SANRECO Ph2 topline results	
Zerlasiran High Lp(a)		*Results from first industry CVOT in high Lp(a) anticipated in 2026*		
SLN312* Dyslipidemia		*Ph1 data presentations anticipated in 2026*		
SLN365 HoFH		★ Preclinical data IND enabling studies (potential filing in 1H 2027)		
SLN098 Obesity		★ Preclinical data IND enabling studies (potential filing in 2H 2027)		
Extra-hepatic		★ Preclinical data		★ Preclinical data

*SLN312 is currently licensed to AstraZeneca. As announced in a Company Press Release dated March 5, 2026, Silence will re-gain exclusive rights globally to SLN312 following Phase 1.
HoFH=Homozygous familial hypercholesterolemia


Silencing diseases through precision engineered medicines created with proprietary siRNA technology
Great Place To Work. Certified OKT 2024-OKT 2025 DE
Great Place To Work. Certified OCT 2024-OCT 2025 UK
Great Place To Work. Certified OCT 2024-OCT 2025 USA
SILENCE THERAPEUTICS