Silence Therapeutics

Corporate Presentation

November 2021
Forward-Looking Statements

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Transform peoples’ lives around the world by silencing diseases through our precision engineered medicines and driving positive change for the communities around us.

Maximize our proprietary mRNAi GOLD™ platform through hybrid business model.
## Poised for Transformation

**Pioneers in RNAi**
- Two decades of know-how combined with robust and growing IP estate
- Global footprint – R&D in Berlin, headquarters in London and NYC office

**Rapidly Advance Clinical Programs**
- Positive topline healthy volunteer data in SLN124 program for iron-loading anemia conditions
- Advancing two proprietary phase 1 clinical programs
  - SLN360 targeting high and prevalent unmet need in cardiovascular disease due to high lipoprotein(a)
  - SLN124 targeting high unmet need in thalassemia and myelodysplastic syndrome

**Proprietary mRNAi GOLD™ Platform**
- Clinical data demonstrated safety, robust pharmacodynamic effect and long duration of action
- Anticipate 2-3 INDs per year from 2023 (proprietary and partnered programs)
- Significant opportunity to address disease causing targets in the liver

**Strong Financial Position**
- £76.5m at the end of September 2021
- AIM and Nasdaq listed (SLN) - market cap ~£500m /~$670m*

* Market Capitalization as of November 16, 2021
We believe the Path to Value Creation is Clear

Market capitalization of established RNAi companies

<table>
<thead>
<tr>
<th>Company</th>
<th>Highest phase</th>
<th>Program Count</th>
<th>Highest Phase Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Silence</td>
<td>1</td>
<td>8+ programs</td>
<td>2 clinical</td>
</tr>
<tr>
<td>Dicerna</td>
<td>3</td>
<td>15+ programs</td>
<td>6 clinical</td>
</tr>
<tr>
<td>Arrowhead</td>
<td>2</td>
<td>16+ programs</td>
<td>9 clinical</td>
</tr>
<tr>
<td>Alnylam</td>
<td>Commercial</td>
<td>11+ programs</td>
<td>11 clinical</td>
</tr>
</tbody>
</table>

Silence strategy: 50% balance owned/partnered

Maximizing mRNAi GOLD™ platform with a differentiated strategy

Market Capitalization as of November 16, 2021;
Programs defined as individually named programs from discovery phase through to marketed drugs on company website, October 2021.
Executive Leadership Team with Deep Sector Experience

Mark Rothera  
President and CEO  
• 30+ years of experience in the biopharmaceutical industry  
• Former President & CEO of Orchard Therapeutics and CCO of PTC Therapeutics  
• Drove the transition of multiple emerging biotech companies from R&D stage to commercialization

Giles Campion  
EVP, Head of R&D and CMO  
• 30+ years of experience in the biopharmaceutical industry  
• Former CMO and SVP R&D at Prosensa, playing a major role in their Nasdaq IPO and subsequent sale to Biogen for $680m  
• Most recently CMO at Albumedix and held senior R&D roles at GE Healthcare, Novartis and SmithKline Beecham prior  
• Medical degree and doctorate from Bristol University

Craig Tooman  
Chief Financial Officer  
• 30+ years of experience in the biopharmaceutical industry  
• Over a decade of experience as public company CFO  
• Proven track record raising capital and leading M&A deals

Dr. Barbara Ruskin  
SVP, General Counsel and CPO  
• 25+ years of global experience in life science IP and corporate law  
• Former Partner at Ropes and Gray, associate at Fish & Neave, and SVP GC / CPO at biopharma companies  
• Managed general legal and IP matters related to financing and regulatory, BD, licensing and patent portfolio management

Dr. Marie Wikström Lindholm  
SVP, Molecular Design  
• 13+ years’ experience with oligonucleotide therapeutics  
• Former Expert Scientist in Discovery Technology and Head of Targeted Delivery at Santaris Pharma / Roche  
• Authored 60+ patent applications and peer-reviewed scientific publications

Jorgen Wittendorff  
SVP, Head of Manufacturing  
• 25+ years experience in pharmaceutical development  
• Extensive experience in complex manufacturing and regulatory compliance (FDA, EMA, and PMDA)
siRNA Can Inhibit Expression of Disease-Associated Genes

**HEALTHY**

- Genes encode messages for all features in the body.
- The information in DNA is transcribed into messenger RNA (mRNA).
- mRNA is then made into proteins. Proteins are responsible for most functions in the body.

**DISEASE**

- In certain diseases, the DNA is mutated or abnormally expressed.
- Abnormal DNA message is carried into resulting mRNA.
- In some cases, mutations instruct the cell to produce too much protein or the protein made does not work.
siRNA Can Precisely Target and Silence Disease-Associated Genes

- **Mutated DNA**
- **mRNA**
- **Target-specific short interfering RNA (siRNA)** binds to the mRNA
- **mRNA is degraded and gene is “silenced”**
- **Reduction in disease-causing protein**

**Natural**
Harnesses natural cellular mechanisms present in every cell in the human body

**Durable**
Long-lasting gene knockdown possible for > 2 months following a single injection

**Precise**
siRNA designed to bind only to target sequence
Our Toolbox Considers all Elements of siRNA and Ligand Design

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

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

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

Continuous Fine-Tuning to Further Improve Performance
Platform Approach: Precision-Engineered Therapies

GalNAc Oligonucleotide Discovery Platform

- Improves molecular design
- Maximizes efficacy
- Minimizes off-target effects
- Stabilizes molecules
- Optimizes manufacturing
- Robust and growing IP estate

High-quality discovery programs
We Believe the Opportunity for our Platform is Substantial

Only ~1% of genes expressed in the liver have been targeted by publicly known siRNAs.

Opportunity to identify new siRNAs targeting many of the remaining 99% (~14,000) of liver-expressed genes.

Assuming only 1-2% of remaining genes are targetable, that is still another 140-280 new programs.

Source: Human Protein Atlas, GlobalData
Early-stage GalNAc-conjugated RNAi Programs Have a Much Greater Likelihood of Approval vs. Industry Average

Phase success is defined as the movement of the program to the next phase, not an evaluation of whether endpoints were met. GalNAc-conjugated RNAi includes both GalNAc-conjugated siRNA and GalNAc-conjugated ASO.

Source: Pharmapremia, Informa Pharma Custom Intelligence analysis
Partnership Programs Further Expand Pipeline and Provide ~$7.5 Billion in Potential Milestones Plus Royalties

Signed major deal to discover, develop and commercialize siRNA therapeutics for cardiovascular, renal, metabolic and respiratory diseases in March 2020
- Upfront cash payment of $60 million and an equity investment of $20 million
- Up to $4 billion in potential milestones plus tiered royalties for a total of 10 targets
- AZN to cover preclinical, CMC, clinical development and commercialization costs

Expanded collaboration to develop siRNA therapeutics for complement-mediated diseases in July 2020
- Upfront cash payment of $20 million and an equity investment of $5 million
- Up to $2 billion in potential milestones plus royalties for 3 targets
- Exercised option to license 3 complement targets

New collaboration to develop siRNA therapeutics for three undisclosed targets announced in Oct. 2021
- Upfront cash payment of $16 million and up to $1.3 billion in potential milestones plus royalties
- Silence has exclusive rights to 2 targets in all territories except China region; Hansoh has China region rights to those 2 targets
- Hansoh has global rights to a third target
## Pipeline Balances Proprietary & Partnered Programs

<table>
<thead>
<tr>
<th>Indication</th>
<th>Target</th>
<th>Discovery</th>
<th>Preclinical</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
<th>Proprietary/Partnered</th>
</tr>
</thead>
<tbody>
<tr>
<td>SLN360</td>
<td>Cardiovascular disease due to high Lp(a)</td>
<td>Lp(a)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>SILENCE THERAPEUTICS</td>
</tr>
<tr>
<td>SLN124</td>
<td>Beta Thalassemia</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>SILENCE THERAPEUTICS</td>
</tr>
<tr>
<td></td>
<td>Myelodysplastic Syndrome</td>
<td>TMPRSS6</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>SILENCE THERAPEUTICS</td>
</tr>
<tr>
<td></td>
<td>Polycythemia Vera (PV)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>SILENCE THERAPEUTICS</td>
</tr>
<tr>
<td>Multiple Programs</td>
<td>Undisclosed</td>
<td>Undisclosed</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>SILENCE THERAPEUTICS</td>
</tr>
<tr>
<td>SLN-HAN-1</td>
<td>Undisclosed</td>
<td>Undisclosed</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>SILENCE THERAPEUTICS</td>
</tr>
<tr>
<td>SLN501</td>
<td>Complement-mediated diseases</td>
<td>C3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>SILENCE THERAPEUTICS</td>
</tr>
<tr>
<td>SLN-MNK-2</td>
<td>2nd complement target</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>MALLINCKRODT</td>
</tr>
<tr>
<td>SLN-MNK-3</td>
<td>3rd complement target</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>MALLINCKRODT</td>
</tr>
<tr>
<td>SLN-AZ-1</td>
<td>cardiovascular, renal, metabolic and respiratory diseases</td>
<td>Undisclosed</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>AstraZeneca</td>
</tr>
<tr>
<td>SLN-AZ-2</td>
<td>Undisclosed</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>AstraZeneca</td>
</tr>
</tbody>
</table>

*Silence retains exclusive rights to this program outside of the China region, including Hong Kong, Macau and Taiwan.
Maximizing Output through the Silence Platform

• **High-quality target identification** using translational genomics

• **Lower attrition rates** in discovery enabled by machine learning

• **GalNAc strategic partnerships** to enhance pipeline opportunities (e.g. target selection)

Targeting **2-3 INDs/yr** from 2023 through our proprietary and partnered GalNAc programs
SLN360 Targets Lp(a): an Independent Risk Factor for Cardiovascular Disease

- Lp(a) levels are genetically determined
- Recognized as a major untreated risk factor in cardiovascular disease
- Lp(a) levels are not significantly modifiable through lifestyle changes or approved medicines
- Large population worldwide with up to 10% with >90 mg/dL\(^1\) (2-3x increased heart attack risk)\(^2\)

Targeting Lp(a) with SLN360 Has the Potential to Address Major Unmet Needs in Cardiovascular Disease

Cardiovascular Event Risk Significantly Increases with High Lp(a)

### Substantial Risk of CV Event at Lp(a) ~90 mg/dL

<table>
<thead>
<tr>
<th>Event</th>
<th>Increased Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart Attack</td>
<td>2 - 3x</td>
</tr>
<tr>
<td>Aortic Stenosis</td>
<td>2 - 3x</td>
</tr>
<tr>
<td>Heart Failure</td>
<td>1.6 - 1.8x</td>
</tr>
<tr>
<td>Ischemic Stroke</td>
<td>1.2 - 1.6x</td>
</tr>
<tr>
<td>Mortality (all cause/CV)</td>
<td>1.2 - 1.7x</td>
</tr>
</tbody>
</table>

### 780 Million Worldwide with >90 mg/dL Lp(a)

<table>
<thead>
<tr>
<th>Lp(a) level:</th>
<th>&gt;50 mg/dL</th>
<th>&gt;90 mg/dL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevalence</td>
<td>~20%</td>
<td>~10%</td>
</tr>
<tr>
<td>USA</td>
<td>66m</td>
<td>33m</td>
</tr>
<tr>
<td>EU</td>
<td>103m</td>
<td>51m</td>
</tr>
<tr>
<td>Globally</td>
<td>1,560m</td>
<td>780m</td>
</tr>
</tbody>
</table>

*Populations: USA 328.2 million, EU 513.5 million (incl. UK), Global 7,800 million*

Lp(a)-lowering Drugs Present a Similar Opportunity to Cholesterol-lowering Drugs, Which Had Sales of >$30B at Peak

High Cholesterol vs High Lp(a) in Cardiovascular Disease

High Cholesterol is a **Modifiable Risk Factor**

High Lp(a) is a **Genetic Risk Factor**

- Some patients require cholesterol lowering treatment: Lifestyle changes can have a positive impact
- Most patients will require Lp(a) lowering treatment: Lifestyle changes have no effect on Lp(a) levels

Similar Medically Treated Population

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

<table>
<thead>
<tr>
<th>High Total Cholesterol</th>
<th>High Lp(a)</th>
<th>Estimated medically treated</th>
<th>Lifestyle changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>US ≥ 200 mg/dL</td>
<td>≥ 50 mg/dL</td>
<td>136M</td>
<td>132M</td>
</tr>
<tr>
<td>EU5 ≥ 190 mg/dL</td>
<td></td>
<td>103M</td>
<td></td>
</tr>
</tbody>
</table>

Blockbuster Potential

Sales of Cholesterol-Lowering Drugs Peaked at >$30B

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

SLN360 demonstrated ideal profile in NHP model

**Efficacy:** Robust Lp(a) knockdown observed after first dose (>90%)

**Durability:** Sustained reduction of Lp(a) serum levels (>90%) for duration of study

**Safety:** <1% exposure outside liver and kidney with no detected off target effects
# SLN360 Phase 1 Program Overview

<table>
<thead>
<tr>
<th>Section</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Design</strong></td>
<td>Global randomized, double-blind, placebo controlled single-ascending dose and multiple dose study</td>
</tr>
<tr>
<td><strong>Aim</strong></td>
<td>Investigate the safety, tolerability, PK and PD response of SLN360 in subjects with elevated lipoprotein(a)</td>
</tr>
<tr>
<td><strong>Single-Ascending Dose Cohorts</strong></td>
<td>8 subjects per cohort (6 active, 2 placebo), up to 5 cohorts</td>
</tr>
<tr>
<td><strong>Multiple-Ascending Dose Cohorts</strong></td>
<td>12 subjects per cohort (9 active, 3 placebo), up to 4 cohorts</td>
</tr>
<tr>
<td><strong>Dosing</strong></td>
<td>30 mg, 100 mg, ≤ 300 mg, ≤ 600 mg</td>
</tr>
<tr>
<td><strong>Population</strong></td>
<td>Up to 88 subjects total with elevated Lp(a) approximately ≥ 60 mg/dL</td>
</tr>
</tbody>
</table>

PD = Pharmacodynamics; PK = Pharmacokinetics

Data from single-ascending dose portion expected in Q1 2022
Current Status of SLN360 Phase 1 Program

Milestones

- Single-ascending dose Cohorts 1-4 enrolment complete; Results expected Q1 2022
- Independent safety review committee recommendations:
  - Established dose range and can proceed to multiple-ascending dose portion (no need for Cohort 5)
  - Extend follow-up of single-ascending dose cohorts from 150 to 365 days

Strategy

- Single-ascending dose data drives ASCVD phase 2 start in 2H 2022, subject to regulatory discussions
- Dose and interval can be predicted from single-ascending dose data
- Multiple-ascending dose provides early safety assessment in our phase 2 ASCVD population

ASCVD = Atherosclerotic Cardiovascular Disease
SLN124

Hepcidin Regulation Program
We see SLN124 as a Hematology Franchise Opportunity

With the potential to reach several patient groups in indications with high unmet need

Launch Indication

Indication 2

Indication 3

Indication 4

Additional Indications…

Initial SLN124 Indications

- **Thal**: Beta Thalassemia
- **MDS**: Myelodysplastic Syndrome
- **PV**: Polycythemia Vera

Sequence of Indication Launches Anticipated
## PV Represents a Substantial New Opportunity

### Polycythemia Vera
- **Prevalence**: 44-57/100,000<sup>1</sup>
- **Incidence**: The annual incidence of PV is between 1-3/100,000.<sup>2</sup>
- **US Population**: 333m, global population: 7,800m
- *Using 44/100,000

### Myelodysplastic Syndrome
- **Prevalence**: 20/100,000<sup>3,4</sup>
- **Incidence**: The annual reported incidence of MDS is ~5/100,000 (age adjusted).<sup>3</sup>

### Beta Thalassemia
- **Prevalence**: 1/100,000<sup>5,6,7</sup>
- **Incidence**: Over 40,000 infants are born with Beta Thalassemia each year.<sup>7</sup>

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### SLN124 Key Facts

<table>
<thead>
<tr>
<th>Feature</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>SLN124 modulates hepcidin, the master regulator of plasma iron in the</td>
<td>By silencing TMPRSS6, SLN124 enables the body to increase endogenous hepcidin and modulate iron distribution</td>
</tr>
<tr>
<td>body</td>
<td></td>
</tr>
<tr>
<td>Strong preclinical data in animal disease models, demonstrating</td>
<td>Therapeutic potential in different pathologies (i.e., amelioration of anemia, reduction of iron overload or hematocrit control)</td>
</tr>
<tr>
<td>therapeutic potential in different pathologies (i.e., amelioration of</td>
<td></td>
</tr>
<tr>
<td>anemia, reduction of iron overload or hematocrit control)</td>
<td></td>
</tr>
<tr>
<td>Long duration of action of SLN124 combined with favorable safety profile</td>
<td></td>
</tr>
<tr>
<td>in healthy volunteers</td>
<td></td>
</tr>
<tr>
<td>Potential for broad mechanistic mode-of-action approach</td>
<td></td>
</tr>
<tr>
<td>US rare pediatric disease designation for beta thalassemia</td>
<td></td>
</tr>
<tr>
<td>Orphan Drug Designation for MDS (US) and beta thalassemia (EU; US)</td>
<td></td>
</tr>
</tbody>
</table>
SLN124 Aims to Reduce Anemia and the Need for Blood Transfusions and Iron Chelation Therapies

1. Reduces TMPRSS6 in the liver
2. Raises endogenous hepcidin
3. Lowers systemic iron levels and normalizes distribution
4. Improves red blood cell production

Study performed in a rodent model for beta thalassemia (Hbb\textsuperscript{β+/-}); *** ps0.001
### SLN124 Phase 1 Healthy Volunteer Study Design

<table>
<thead>
<tr>
<th><strong>Design</strong></th>
<th>Randomized, double-blind, placebo controlled, single-ascending dose study</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Aim</strong></td>
<td>Investigated the safety, tolerability, PK and PD response of SLN124 in healthy volunteers</td>
</tr>
<tr>
<td><strong>Single-Ascending Dose Cohort</strong></td>
<td>3 cohorts, 8 subjects per cohort (6 active, 2 placebo)</td>
</tr>
<tr>
<td><strong>Dosing</strong></td>
<td>1 mg/kg, 3 mg/kg and 4.5 mg/kg</td>
</tr>
<tr>
<td><strong>Population</strong></td>
<td>24 healthy adults</td>
</tr>
</tbody>
</table>

PD: Pharmacodynamics; PK: Pharmacokinetics
SLN124 Increased Average Hepcidin up to ~4-Fold After a Single Dose with Effect Sustained for ≥ 2 Months

n=6 healthy volunteers in each treatment group

Baseline  Day 29  Day 57
SLN124 Reduced Serum Iron by ~50% After a Single Dose with Effect Sustained for ≥ 2 Months

n=6 healthy volunteers in each treatment group
Positive Topline Results from SLN124 Healthy Volunteer Study

- First clinical data from mRNAi GOLD™ platform
- Demonstrated proof of mechanism for SLN124
- All 3 dose levels of SLN124 were safe and generally well-tolerated
- SLN124 increased average hepcidin up to ~4-fold after a single dose with effect sustained for at least 2 months
- SLN124 reduced serum iron by ~50% after a single dose with effect sustained for at least 2 months

Abstract Accepted for Presentation at ASH in December 2021
### SLN124 Phase 1 Program in Adult Thalassemia and MDS

<table>
<thead>
<tr>
<th><strong>Design</strong></th>
<th>Global, randomized, single-blind, placebo controlled single-ascending and multiple-ascending dose studies</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Aim</strong></td>
<td>Investigate the safety, tolerability, PK and PD response of SLN124 in adults with thalassemia and MDS</td>
</tr>
<tr>
<td><strong>Single-Ascending Dose Cohorts</strong></td>
<td>8 subjects per cohort (6 active, 2 placebo), up to 4 cohorts per study</td>
</tr>
<tr>
<td><strong>Multiple-Ascending Dose Cohorts</strong></td>
<td>8 subjects per cohort (6 active, 2 placebo), up to 3 cohorts per study</td>
</tr>
<tr>
<td><strong>Dosing</strong></td>
<td>1 mg/kg, 3 mg/kg and ≤ 10 mg/kg</td>
</tr>
<tr>
<td><strong>Population</strong></td>
<td>up to 112 adults with non-transfusion dependent thalassemia and VL/LR-MDS</td>
</tr>
</tbody>
</table>

MDS = myelodysplastic syndrome; PD = Pharmacodynamics; PK = Pharmacokinetics; VL/LR-MDS = very low- and low-risk MDS

Single-ascending dose data expected in Q3 2022
A Phase 1 study in PV is to be initiated in H2 2022

• SLN124 Phase 1 study to be initiated in H2 2022
  
  • Study Aim: Investigate the safety, tolerability, PK and PD response of SLN124 in patients with polycythemia vera

• Subsequent development:
  
  • Key clinical study endpoints focused on hematological measures
    – i.e. red packed cell volume, cell hemoglobin content, TSAT, hemoglobin
  
  • Early and late clinical studies use same end-points simplifying development path to approval

PD = Pharmacodynamics; PK = Pharmacokinetics
SLN124 Has The Potential For a Broad Mechanistic Mode-of-Action Approach

Silencing TMPRSS6 by SLN124 increases endogenous hepcidin, with potential beneficial effects in several hematological disorders.

- **Silencing TMPRSS6 by SLN124**
  - **Reduce**
  - **Increase endogenous hepcidin**
  - **Decrease NTBI**
  - **Inhibit iron accumulation**
  - **Restrict iron to erythropoiesis**

**Iron loading anemias** (e.g. beta thalassemia, MDS)

- **Reduce anemia**

**Hereditary hemochromatosis**

- **Prevent iron overload**

**Polycythemia vera**

- **Reduce red packed cell volume**

---

NTBI = non-transferrin-bound iron; Studies performed in a rodent model for 1: beta thalassemia (Hbb\textsuperscript{βthas}), *** p≤0.001; 2: hemochromatosis (Hfe\textsuperscript{-/-}), * p≤0.05; 3: polycythemia vera, **** p≤0.0001

Vadolas et al. 2021 Br J Haematol. PMID: 33942901

Altamura et al., HemaSphere 2019 (PMID 31976476)

Presented at EHA 2021
Summary of Recent News

SLN124 Program (Hepcidin Regulation) Updates:
- FDA acceptance of the US IND in MDS
- On-track for topline data from single-ascending dose studies in Thalassemia/MDS in Q3 2022
- Significant opportunity to expand SLN124 in multiple indications - potential for hematology franchise
- Initiating phase 1 study in polycythemia vera (PV) in H2 2022
- SLN124 healthy volunteer data accepted for presentation at ASH in December

SLN360 Program (Lp(a) Lowering) Updates:
- On-track for topline data in single-ascending dose study in Q1 2022
- Key outcomes from independent safety review committee meeting:
  - Extending follow-up period in the single-ascending dose study from 150 days to 365 days to fully assess the duration of action
  - Established therapeutic dose range and can proceed to multiple-ascending dose study (no need for Cohort 5)

SLN501 (Complement C3 Lowering with Mallinckrodt) Phase 1 initiation in H1 2022
On-track for 2-3 INDs per year from 2023
## Anticipated Events Through 2022

<table>
<thead>
<tr>
<th></th>
<th>2021</th>
<th>2022</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>H1</td>
<td>H2</td>
</tr>
<tr>
<td><strong>Proprietary Programs</strong></td>
<td></td>
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<tr>
<td>SLN360 CVD due to high Lp(a)</td>
<td>Started dosing in single-ascending dose study</td>
<td>Fully enrolled single-ascending dose study</td>
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<tr>
<td>SLN124 Thalassemia and MDS</td>
<td>Started dosing in single-ascending dose studies</td>
<td>Reported positive topline data in healthy volunteer study</td>
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<tr>
<td>Polycythemia Vera (PV)</td>
<td>Presented POC data at EHA</td>
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<tr>
<td><strong>Undisclosed Programs</strong></td>
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<tr>
<td><strong>Partnered Programs</strong></td>
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<tr>
<td>Mallinckrodt 3 complement targets</td>
<td>Started work on third target</td>
<td>Started IND enabling studies for SLN501 C3 program</td>
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<tr>
<td>AstraZeneca up to 10 undisclosed targets</td>
<td>Started work on second target</td>
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<tr>
<td>Hansoh 2 proprietary targets, 1 partnered target</td>
<td>Initiated collaboration &amp; work on first proprietary target</td>
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</tbody>
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### mRNAi GOLD™ Platform Partnership Opportunities

Note: all programs are at potential risk of delay due to COVID-19; CVD = cardiovascular disease; MDS = Myelodysplastic syndrome

- = milestone achieved
- = data milestone
Developing a New Extra-Hepatic siRNA Delivery Platform

Present

Future

Tap into the huge opportunity to silence genes outside of the liver
## Financial Highlights

**[SLN: AIM] and [SLN: Nasdaq]**

<table>
<thead>
<tr>
<th>Category</th>
<th>Value</th>
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<tbody>
<tr>
<td>Stock Price (11/16/21)</td>
<td>542p / $22.44</td>
</tr>
<tr>
<td>Common Shares Outstanding (9/30/21)</td>
<td>89,777,000</td>
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<tr>
<td>Market Capitalization (11/16/21)</td>
<td><del>£500m /</del>$670m</td>
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<tr>
<td>Cash (9/30/21)</td>
<td>£76.5m</td>
</tr>
<tr>
<td>Debt</td>
<td>$0</td>
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