Forward-Looking Statements

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## Poised for Transformation in 2021

### Major Clinical Data Readouts in Wholly Owned Programs Combined with Rapid Discovery Pipeline Growth

<table>
<thead>
<tr>
<th>Pioneers in RNAi</th>
<th>Rapidly Advance Clinical Programs</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Two decades of know-how combined with robust and growing IP estate</td>
<td>• Positive topline healthy volunteer data in SLN124 program for iron-loading anemia conditions</td>
</tr>
<tr>
<td>• Global footprint – R&amp;D in Berlin, headquarters in London and NYC office</td>
<td>• On-track to deliver patient data in two wholly owned programs this year</td>
</tr>
<tr>
<td></td>
<td>• SLN360 targeting high and prevalent unmet need in cardiovascular disease due to high lipoprotein(a)</td>
</tr>
<tr>
<td></td>
<td>• SLN124 targeting high unmet need in thalassemia and myelodysplastic syndrome</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Clinically Validated</strong></td>
<td></td>
</tr>
<tr>
<td>• Clinical data demonstrated safety, robust pharmacodynamic effect and long duration of action</td>
<td></td>
</tr>
<tr>
<td>• Anticipate 2-3 INDs per year starting in 2023 (wholly owned and partnered programs)</td>
<td></td>
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<tr>
<td>• Significant opportunity to address disease causing targets in the liver</td>
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<td></td>
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<tr>
<td><strong>Platform</strong></td>
<td></td>
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<td></td>
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</tr>
<tr>
<td><strong>Strong Financial Position</strong></td>
<td></td>
</tr>
<tr>
<td>• Cash runway beyond key data milestones for both SLN360 and SLN124 clinical programs</td>
<td></td>
</tr>
<tr>
<td>• AIM and Nasdaq listed (SLN) - market cap <del>£572m /</del>$811m*</td>
<td></td>
</tr>
</tbody>
</table>

* Market Capitalization as of June 1, 2021
We believe the Path to Value Creation is Clear

Market capitalization of established RNAi companies

Market Capitalization as of June 1, 2021

<table>
<thead>
<tr>
<th>Company</th>
<th>Pipeline Programs</th>
<th>Phase</th>
<th>clinics</th>
<th>wholly owned</th>
</tr>
</thead>
<tbody>
<tr>
<td>Silence</td>
<td>6+</td>
<td>Ph1</td>
<td>2</td>
<td>3+</td>
</tr>
<tr>
<td>Dicerna</td>
<td>20</td>
<td>Ph3</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Arrowhead</td>
<td>20</td>
<td>Ph2</td>
<td>8</td>
<td>7</td>
</tr>
<tr>
<td>Alnylam</td>
<td>31+</td>
<td>Ph1</td>
<td>9+</td>
<td></td>
</tr>
</tbody>
</table>

Pipeline programs = company disclosed partnered and wholly owned programs
discovery phase – marketed

Highest phase: Commercial
31+ pipeline programs,
4 in registration/commercial,
7 in the clinic,
9+ wholly owned

Highest phase: Ph2
13 pipeline programs,
8 in the clinic,
7 wholly owned

Highest phase: Ph3
20 pipeline programs,
3 in the clinic,
2 wholly owned

Highest phase: Ph1
6+ pipeline programs,
2 in the clinic,
3+ wholly owned
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 Biomarin 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

- **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 modifications 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
- Ensures ease of manufacturing
- Robust and growing IP estate

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

Existing RNAi programs have only scratched the surface of the liver target space

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

Source: Human Protein Atlas, GlobalData
<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 Cardiovascular</td>
<td>Lp(a)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Silence Therapeutics</td>
</tr>
<tr>
<td>disease with high Lp(a)</td>
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<tr>
<td>SLN124</td>
<td>Thalassemia</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Silence Therapeutics</td>
</tr>
<tr>
<td>SLN124</td>
<td>Myelodysplastic Syndrome</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Silence Therapeutics</td>
</tr>
<tr>
<td>SLN500 Complement-</td>
<td>C3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Silence Therapeutics</td>
</tr>
<tr>
<td>mediated diseases</td>
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<td></td>
<td></td>
<td></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></td>
</tr>
<tr>
<td>SLN-AZ-1</td>
<td>Undisclosed</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>AstraZeneca</td>
</tr>
<tr>
<td>SLN-AZ-2</td>
<td>Undisclosed</td>
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</tr>
</tbody>
</table>
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
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.

Likelihood of Approval from Current Phase:
GalNAc RNAi vs. others

Phase 1: 51% GalNAc RNAi vs. 9% others
Phase 2: 56% GalNAc RNAi vs. 17% others
Phase 3: 67% GalNAc RNAi vs. 53% others

Source: Pharmapremia, Informa Pharma Custom Intelligence analysis
SLN360
for Cardiovascular Disease
Due to High Lp(a)
Targeting Lp(a) with SLN360 has the potential to address major unmet needs in cardiovascular disease

**SLN360 Targets Lipoprotein(a) or 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 >90mg/dL \(^1\) (2-3x increased heart attack risk) \(^2\)**

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Cardiovascular Event Risk Significantly Increases with High Lp(a)

<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>

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

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

<table>
<thead>
<tr>
<th>High Total Cholesterol¹</th>
<th>High Lp(a)²</th>
</tr>
</thead>
<tbody>
<tr>
<td>US ≥ 200 mg/dL</td>
<td>≥ 50 mg/dL</td>
</tr>
<tr>
<td>EU5 ≥ 190 mg/dL</td>
<td>(no indicated treatments)</td>
</tr>
</tbody>
</table>

- Estimated medically treated
- Lifestyle changes

Blockbuster Potential

Sales of Cholesterol-Lowering Drugs Peaked at >$30B³,⁴

<table>
<thead>
<tr>
<th>Drug</th>
<th>Peak Sales</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lipitor® (atorvastatin)</td>
<td>$12.9B peak sales</td>
</tr>
<tr>
<td>Crestor® (rosuvastatin)</td>
<td>$7.0B peak sales</td>
</tr>
<tr>
<td>Zocor® (simvastatin)</td>
<td>$5.2B peak sales</td>
</tr>
</tbody>
</table>

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 with no detected off target effects
# SLN360 Phase 1 Program Overview

<table>
<thead>
<tr>
<th>Design</th>
<th>Global randomized, double-blind, placebo controlled single-ascending dose and multiple dose study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aim</td>
<td>Investigate the safety, tolerability, PK and PD response of SLN360 in subjects with high Lp(a)</td>
</tr>
<tr>
<td>Single-Ascending Dose Cohorts</td>
<td>8 subjects per cohort (6 active, 2 placebo), up to 5 cohorts</td>
</tr>
<tr>
<td>Multiple-Ascending Dose Cohorts</td>
<td>12 subjects per cohort (9 active, 3 placebo), up to 4 cohorts</td>
</tr>
<tr>
<td>Dosing</td>
<td>30 mg, 100 mg, ≤ 300 mg, ≤ 600 mg and ≤ 900 mg</td>
</tr>
<tr>
<td>Population</td>
<td>88 subjects total with high Lp(a) approximately ≥ 60 mg/dL</td>
</tr>
</tbody>
</table>

PD: Pharmacodynamics; PK: Pharmacokinetics

*Now enrolling – Data from single-ascending dose portion expected in H2 2021*
SLN124 for Iron-Loading Anemia Conditions
# SLN124: Addressing a Major Unmet Need in Thalassemia and Myelodysplastic Syndrome (MDS)

## MYELODYSPLASTIC SYNDROME (MDS)

<table>
<thead>
<tr>
<th>Prevalence$^1$: (US+EU5)</th>
<th>~160,000 pts</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Onset:</strong></td>
<td>Later in life (60+)</td>
</tr>
</tbody>
</table>

- Group of rare malignant blood disorders that impact older patients
- Low quality of life and poor response to current therapies
- Burdens include severe anemia, transfusion dependence, toxic iron overload
- Progression to acute myeloid leukemia (30% of MDS patients)

- Orphan Drug Designation

## THALASSEMA

<table>
<thead>
<tr>
<th>Prevalence$^2$: (US+EU5) TDT and NTDT</th>
<th>~35,000 pts</th>
</tr>
</thead>
</table>
| **Onset:**                            | TDT: early childhood  
                                          NTDT: teens or later |

- A rare genetic blood disorder that affects children and adults
- The majority are dependent on regular blood transfusions (TDT), while others are transfused less frequently (NTDT)
- Severe limitations and low quality of life with current treatments
- Opportunity to improve quality of life by reducing the frequency of blood transfusions
- Burdens include severe anemia, transfusion dependence, toxic iron overload

- Orphan Drug Designation
- Rare Pediatric Disease Designation

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$^1$ Internal analysis;  
SLN124 is Designed to Restore Endogenous Hepcidin and Normalize Iron Levels

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^theta/theta); *** p<0.001
### 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
Strong Positive Results from SLN124 Healthy Volunteer Study

• First clinical data from mRNAi GOLD™ platform

• Demonstrates proof of mechanism for SLN124

• All 3 dose levels of SLN124 were safe and generally well-tolerated
  • No serious or severe treatment emergent adverse events (TEAEs) or TEAEs leading to withdrawal
  • Majority of TEAEs were mild, including transient injection site reactions which resolved without intervention

• 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
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
SLN124 Reduced Serum Iron by ~50% After a Single Dose with Effect Sustained for ≥ 2 Months

Iron (µmol/L), mean and % change

Baseline
Day 29
Day 57

Placebo
SLN124 1.0 mg/kg
SLN124 3.0 mg/kg
SLN124 4.5 mg/kg

n=6 healthy volunteers in each treatment group
### SLN124 Phase 1 Study 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 study</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</td>
</tr>
<tr>
<td><strong>Multiple-Ascending Dose Cohorts</strong></td>
<td>8 subjects per cohort (6 active, 2 placebo), up to 3 cohorts</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

Now enrolling - Data expected in H2 2021
## Major Potential Value Creating Milestones in 2021

<table>
<thead>
<tr>
<th></th>
<th>H1 2021</th>
<th>H2 2021</th>
</tr>
</thead>
<tbody>
<tr>
<td>SLN360</td>
<td></td>
<td>APOLLO Phase 1 Single-Ascending Dose Study</td>
</tr>
<tr>
<td>SLN124</td>
<td>GEMINI Phase 1 Healthy Volunteer Study</td>
<td>GEMINI II Phase 1 Single-Ascending Dose Study</td>
</tr>
</tbody>
</table>

Note: all programs are at potential risk of delay due to COVID-19

- ✓ = positive data reported
- ★ = data milestone
Partnership Programs Further Expand Pipeline and Provide Up to $6 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\(^1\)
- 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 complement pathway RNAi collaboration 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 ($2M per target)

Commenced technology evaluation to explore the potential of using our platform to generate siRNA molecules against a novel, undisclosed target in January 2020

\(^1\) Of the $60m, $20m was paid in May 2020 and a further $40m is unconditionally payable in H1 2021.
Developing a New Extra-Hepatic siRNA Delivery Platform

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

### (SLN:AIM) and (SLN:Nasdaq)

<table>
<thead>
<tr>
<th>Description</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stock Price (05/18/21)</strong></td>
<td>636p / $26.82</td>
</tr>
<tr>
<td><strong>Common Shares Outstanding (12/31/20)</strong></td>
<td>83,306,259</td>
</tr>
<tr>
<td><strong>Common Shares Outstanding (2/12/21)</strong></td>
<td>89,398,841</td>
</tr>
<tr>
<td><strong>Market Capitalization (06/01/21)</strong></td>
<td>~£572m / ~$811m</td>
</tr>
<tr>
<td><strong>Cash (12/31/20)</strong></td>
<td>£37.4m</td>
</tr>
<tr>
<td><strong>Proforma cash balance (12/31/20)</strong></td>
<td>£97.5m*</td>
</tr>
<tr>
<td><strong>Debt</strong></td>
<td>$0</td>
</tr>
</tbody>
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*Includes £37.4m at 12/31/20, plus £30.8m capital raise in Feb'21 and £29.3m due from AstraZeneca in H1'21
Poised for Transformation in 2021

Major Clinical Data Readouts in Wholly Owned Programs Combined with Rapid Discovery Pipeline Growth

**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
- On-track to deliver patient data in two wholly owned programs this year
  - 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

**Clinically Validated Platform**
- Clinical data demonstrated safety, robust pharmacodynamic effect and long duration of action
- Anticipate 2-3 INDs per year starting in 2023 (wholly owned and partnered programs)
- Significant opportunity to address disease causing targets in the liver

**Strong Financial Position**
- Cash runway beyond key data milestones for both SLN360 and SLN124 clinical programs
- AIM and Nasdaq listed (SLN) - market cap ~£572m /~$811m*

* Market Capitalization as of June 1, 2021