SILENCE THERAPEUTICS

Silence Therapeutics

# Half Year Results Call

August 12, 2021

# Forward-Looking Statements

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# Our Strategy to Build a Leading Global RNAi Business




Clinical Programs SLN360 / SLN124

Proprietary Pipeline

Partnered Pipeline

Achieve Clinical Milestones

Deliver 2-3 INDs/yr from 2023

# H1 2021 Marked by Strong Execution

## Advanced Proprietary Pipeline

- ✓ Achieved first clinical data from **mRNAi GOLD™** platform – SLN124 healthy volunteer study successfully translated pre-clinical models into humans
- ✓ Started dosing in the SLN360 phase 1 study for cardiovascular disease due to high lipoprotein(a)
- ✓ Started dosing in the SLN124 phase 1 studies for thalassemia and myelodysplastic syndrome

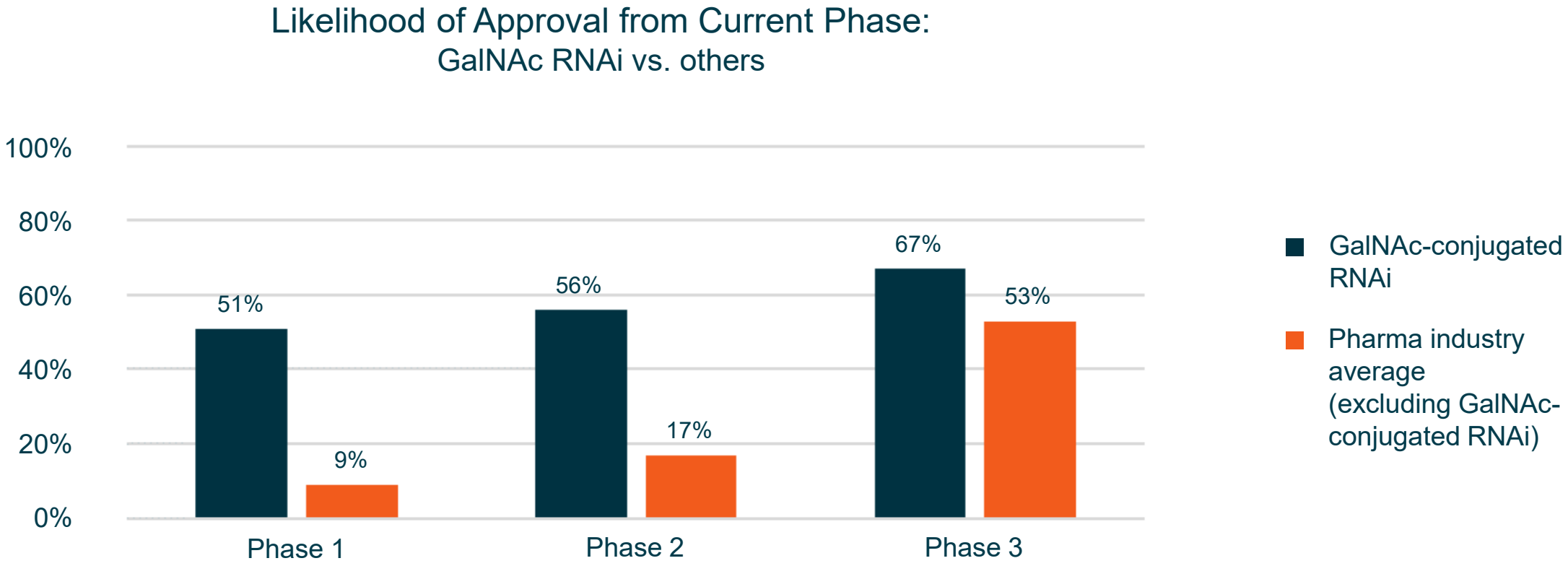
## Advanced Partnered Pipeline

- ✓ Started work on a second target with AstraZeneca
- ✓ Started work with Mallinckrodt on third target for complement mediated diseases and initiated IND-enabling studies for SLN501

## Secured Strong Cash Position

- ✓ Completed £30.8m private placement led by top U.S. healthcare funds
- ✓ Received £33.7m in non-dilutive capital from collaborations
- ✓ £81.2m in cash, cash equivalents, and term deposits at end of June

# 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

# Upcoming Events & Anticipated Milestones

| | H2 2021 | H1 2022 | H2 2022 |
|---|---|---|---|
| **SLN360** | ✓ Fully enrolled 4 cohorts of APOLLO single-ascending dose study in healthy subjects with high Lp(a) | ★ Topline data from APOLLO single-ascending dose study (4 cohorts) | |
| **SLN124** | ★ Present more data from GEMINI healthy volunteer study | | ★ Topline data from GEMINI II single-ascending dose studies in thalassemia and MDS |

**R&D Day in NYC on October 21st**

✓ = milestone achieved

★ = data milestone

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

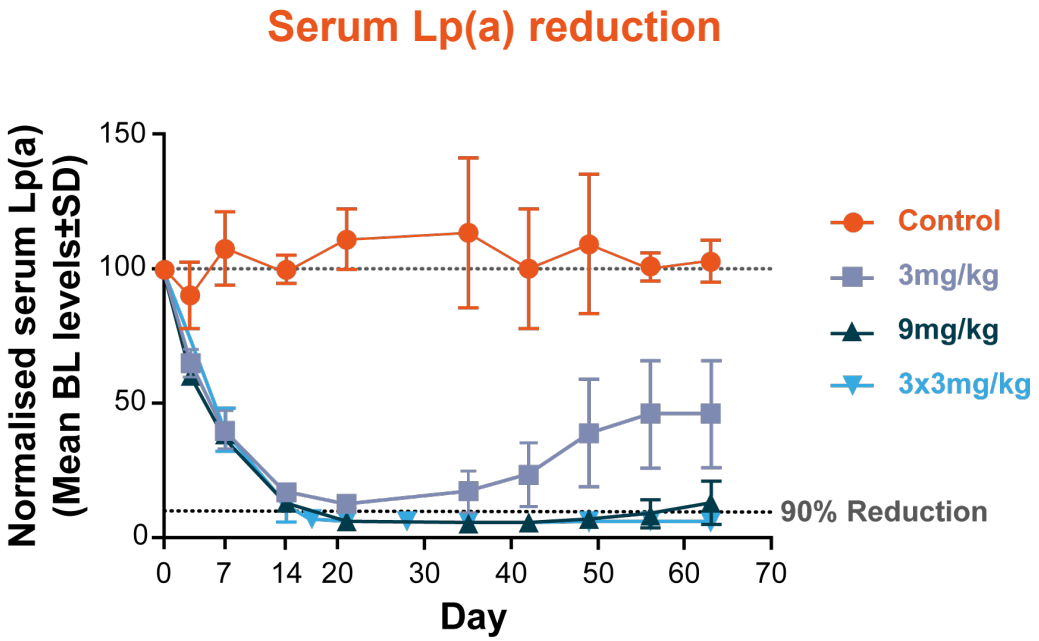
# SLN360 Phase 1 Program Overview

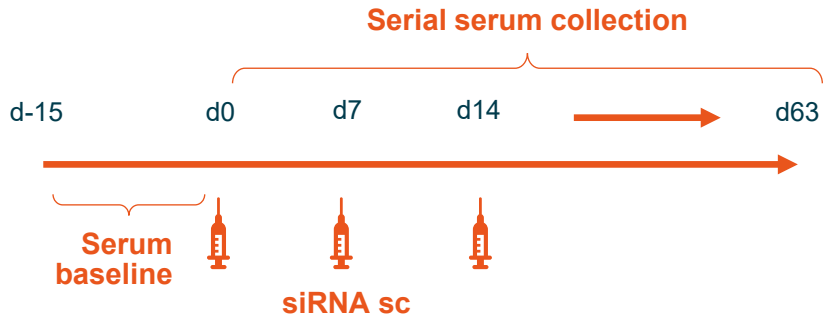
| | |
|---|---|
| **Design** | Global randomized, double-blind, placebo controlled single-ascending dose and multiple dose study |
| **Aim** | Investigate the safety, tolerability, PK and PD response of SLN360 in subjects with high Lp(a) |
| **Single-Ascending Dose Cohorts** | 8 subjects per cohort (6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




PD: Pharmacodynamics; PK: Pharmacokinetics

# SLN360 Demonstrated Sustained and Deep Lp(a) Knockdown in Non-Human Primate Model




| Group | mg/kg | Days |
|---|---|---|
| 1 | 0 | 0 |
| 2 | 3 | 1 |
| 3 | 9 | 1 |
| 4 | 3 | 1, 7, 14 |

## SLN360 demonstrated ideal profile in NHP model

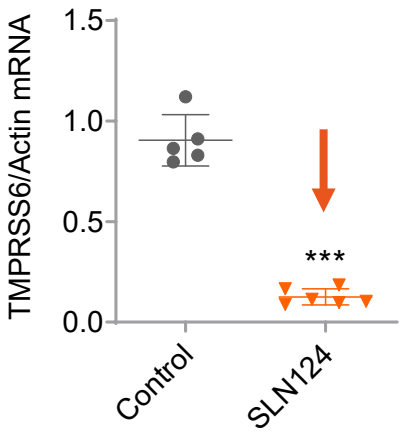
**Efficacy:** Robust Lp(a) knockdown observed after first dose (>90%)

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

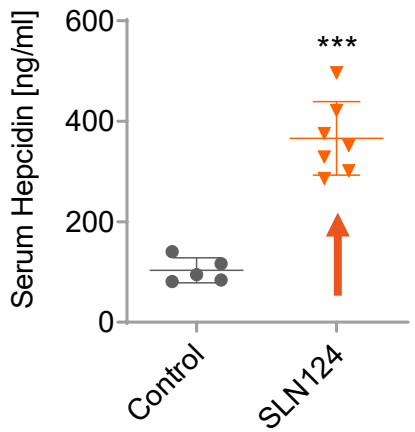
**Safety:** <1% exposure outside liver with no detected off target effects

# SLN124 Targets TMPRSS6 to Restore Endogenous Hepcidin and Normalize Iron Levels

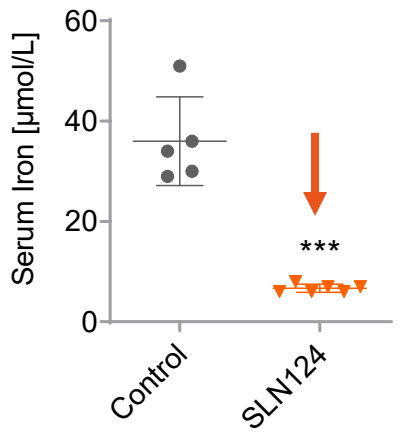
**1** **Reduces TMPRSS6 in the liver**



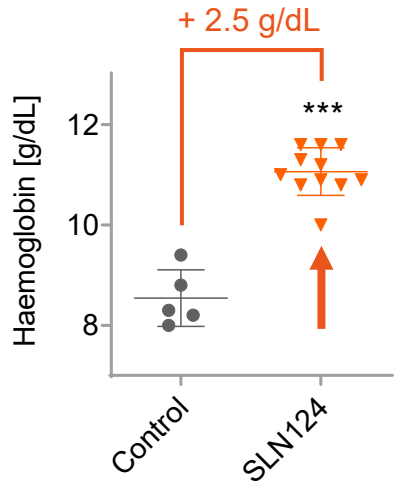

**2** **Raises endogenous hepcidin**




**3** **Lowers systemic iron levels and normalizes distribution**




**4** **Improves red blood cell production**



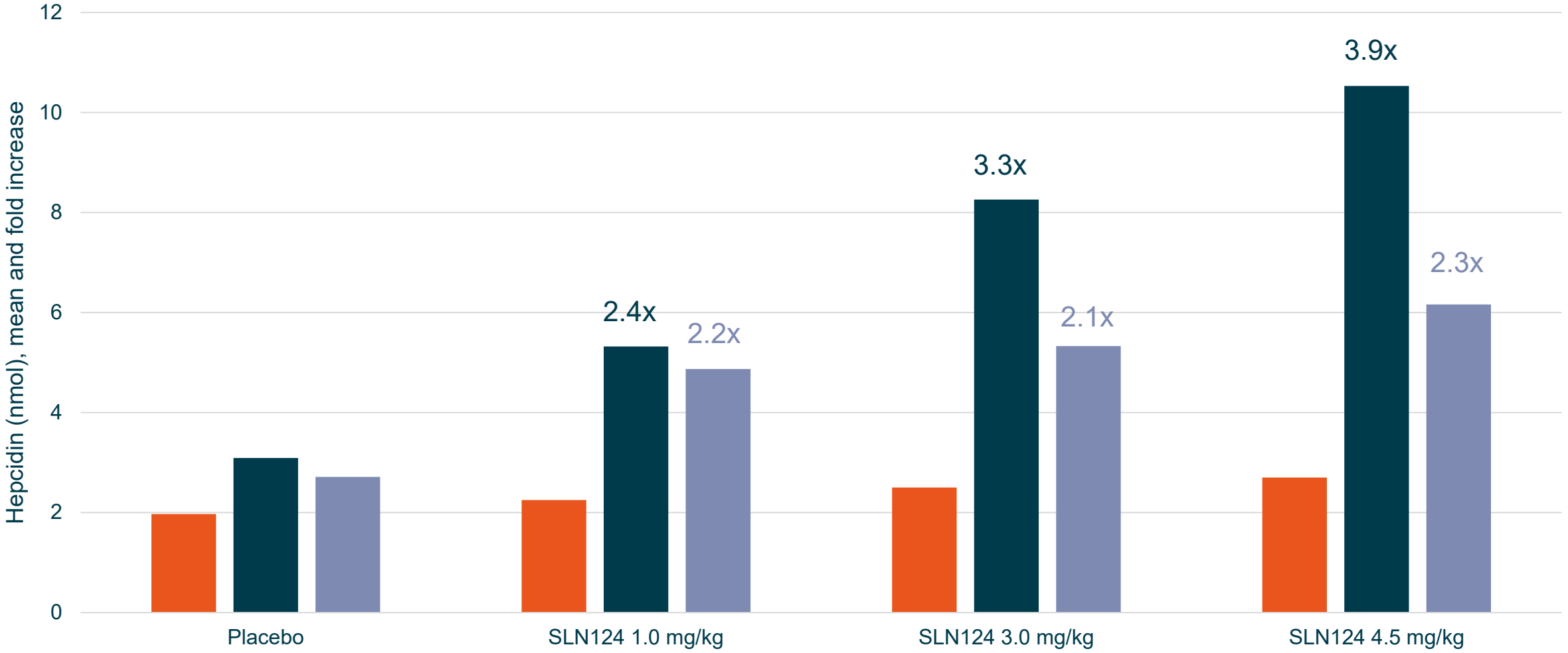

## SLN124 Aims to Reduce Anemia and the Need for Blood Transfusions and Iron Chelation Therapies

Study performed in a rodent model for beta thalassemia ($Hbb^{th3/+}$); *** p≤0.001

# Positive Results from SLN124 Healthy Volunteer Study

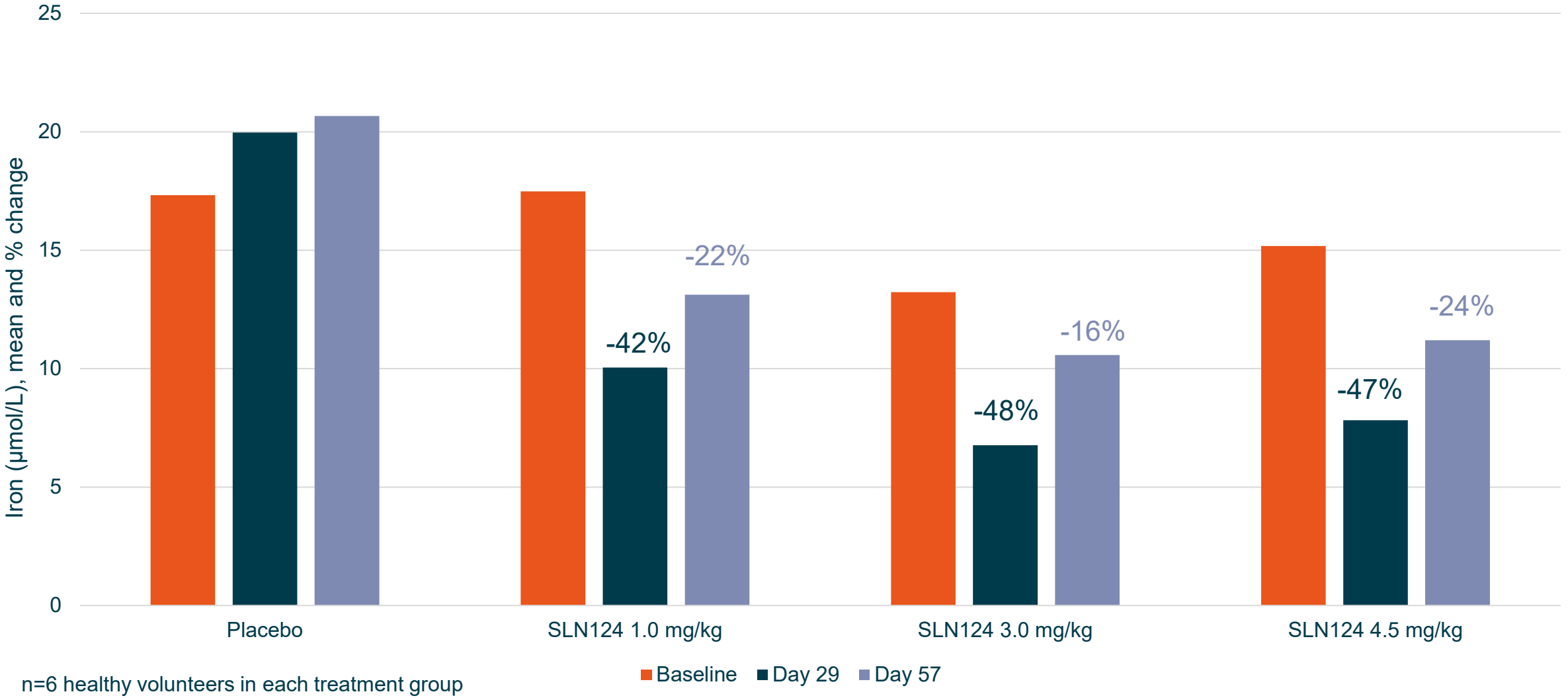
- First clinical data from **mRNAi GOLD™** platform
- Demonstrated proof of mechanism for SLN124
- All doses of SLN124 (1.0, 3.0 and 4.5 mg/kg) were safe and generally well-tolerated
  - No serious or severe treatment emergent adverse events (TEAEs) or TEAEs leading to withdrawal
  - Majority of TEAEs 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




n=6 healthy volunteers in each treatment group

# SLN124 Phase 1 Program in Adult Thalassemia and MDS

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

GEMINI II

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

# Financial Highlights

| Consolidated Income Statement (GBP '000) | Six months ended June 30, 2021 | June 30, 2020 |
|---|---|---|
| Revenue | £5.8m | £1.1m |
| Cost of sales | (£3.4m) | |
| Research and development costs | (£15.6m) | (£10.2m) |
| Administrative expenses | (£9.1m) | (£5.2m) |
| Operating loss | (£22.3m) | (£14.2m) |
| Tax | £2.5m | £2.3m |
| Loss for the period after taxation | (£20.0m) | (£11.0m) |

# Financial Highlights

| (SLN:AIM) and (SLN:Nasdaq) | |
|---|---|
| Stock Price (08/10/21) | 607p / $25.73 |
| Common Shares Outstanding (6/30/21) | 89,735,448 |
| Market Capitalization (08/10/21) | ~£544m /~$754m |
| Cash (6/30/21) | £81.2m |
| Debt | $0 |

# Q&A Session

