SILENCE THERAPEUTICS

Silence Therapeutics

RBC Capital Markets Global Healthcare Conference

May 19, 2021

Forward-Looking Statements

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Today Announced First Clinical Data from mRNAi GOLD™ Platform

- Positive data in healthy volunteer study of SLN124 confirmed strong preclinical profile of our siRNA targeting *TMPRSS6* in humans - excellent safety, robust gene knockdown and long duration of action
- Data support ongoing phase 1 study of SLN124 in patients with thalassemia and myelodysplastic syndrome (MDS)
- Represents first clinical data from our **mRNAi GOLD™** platform and underscore the promising potential for our technology to deliver precision medicines

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

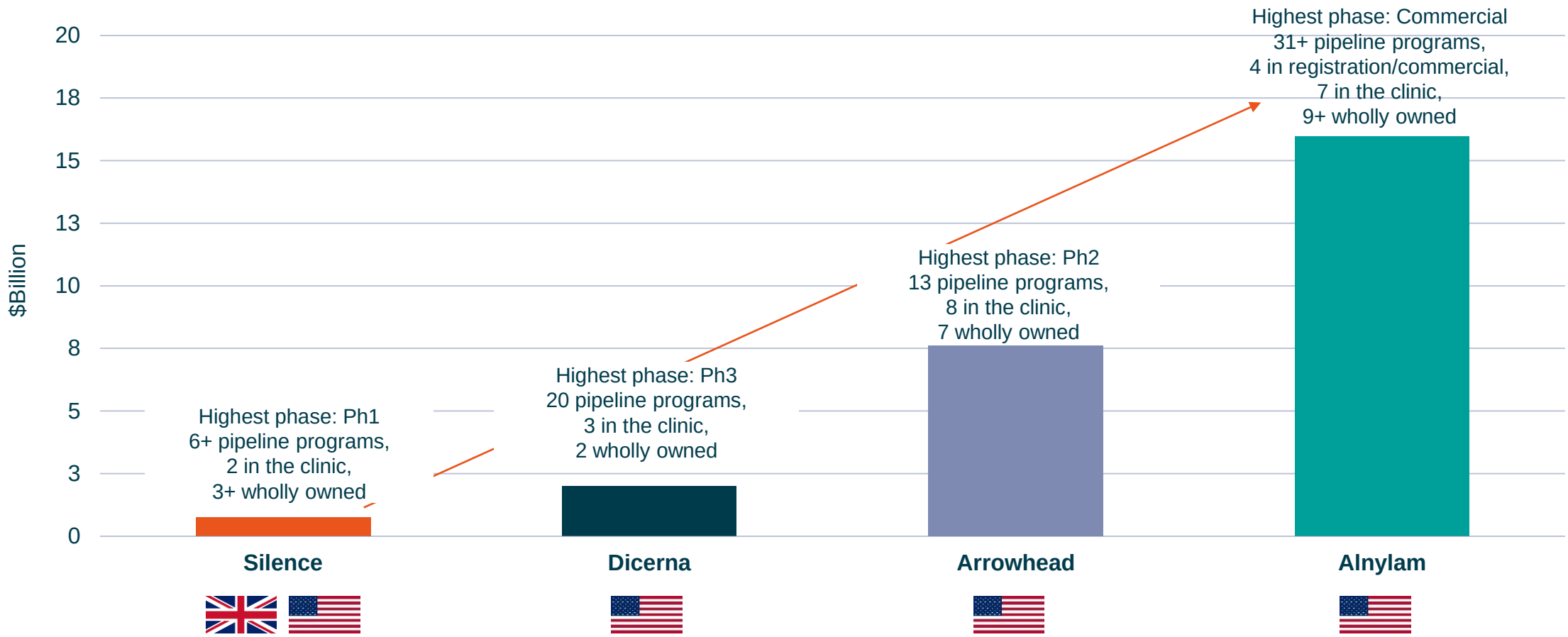
Rapidly Advance Clinical Programs	• Positive topline healthy volunteer data in SLN124 program for iron-loading anemia conditions
	• On-track to deliver patient data in two wholly owned programs this year
	  • SLN360 targeting high and prevalent unmet need in cardiovascular disease due to high lipoprotein(a)
	  • SLN124 targeting high unmet need in thalassemia and myelodysplastic syndrome

Clinically Validated mRNAi GOLD™ Platform	• Clinical data demonstrated safety, robust gene knockdown 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 ~£535m /~$755m*

* Market Capitalization as of May 18, 2021

We believe the Path to Value Creation is Clear

Market capitalization of established RNAi companies

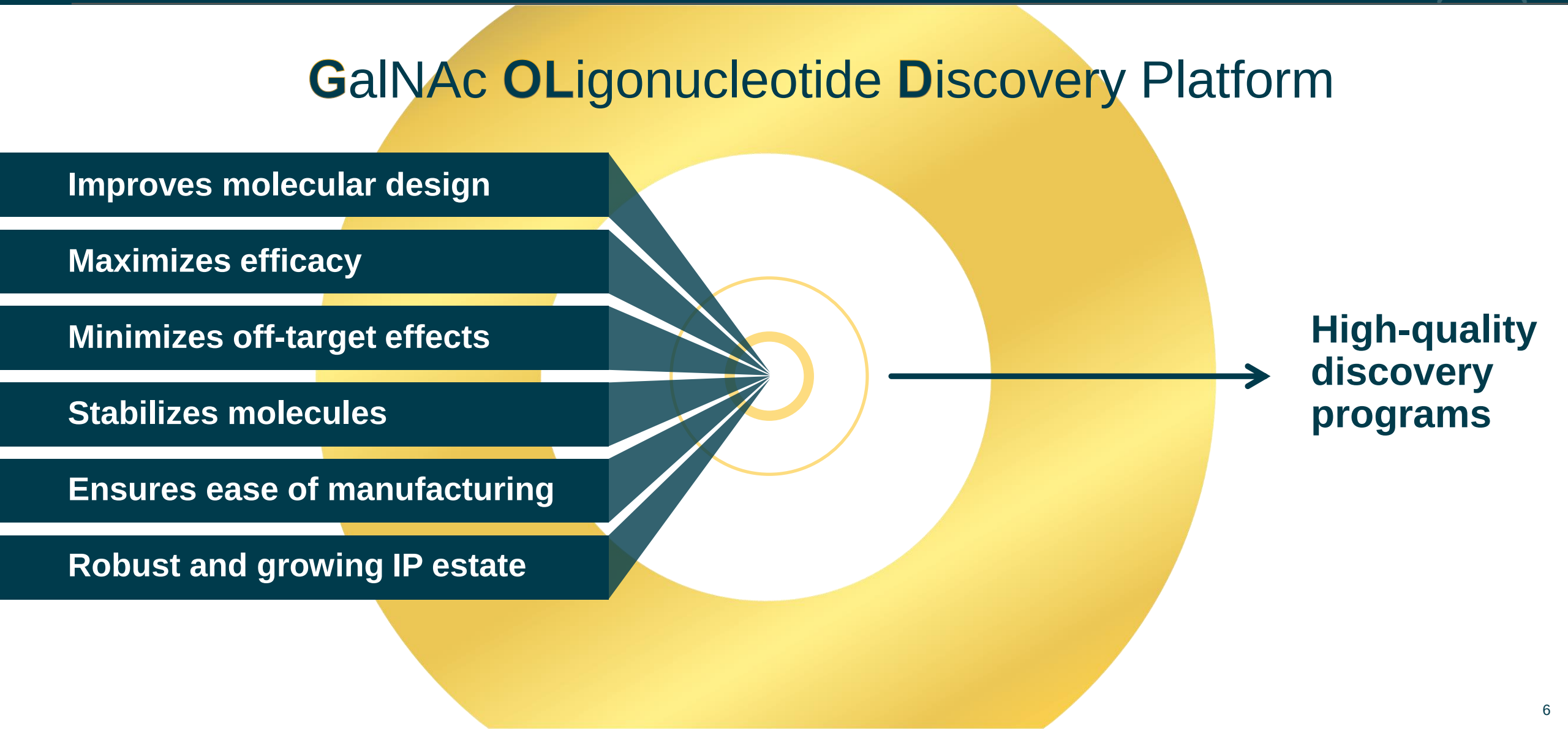


Market Capitalization as of May 18, 2021

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

mRNAi GOLD™ Platform Approach: Precision Engineered Therapies

GalNAc OLigonucleotide Discovery Platform



Our mRNAi GOLD™ Pipeline Targets

	Indication	Target	Discovery	Preclinical	Phase I	Phase II	Phase III	Proprietary/Partnered
SLN360	Cardiovascular disease with high Lp(a)	Lp(a)						SILENCE THERAPEUTICS
SLN124	Thalassemia	TMPRSS6						SILENCE THERAPEUTICS
SLN124	Myelodysplastic Syndrome	TMPRSS6						SILENCE THERAPEUTICS
Multiple programs	Undisclosed	Undisclosed						SILENCE THERAPEUTICS
SLN500	Complement-mediated diseases	C3						Mallinckrodt
SLN-MNK-2	Complement-mediated diseases	2nd complement target						
SLN-MNK-3	Complement-mediated diseases	3rd complement target						
SLN-AZ-1	Undisclosed	Undisclosed						AstraZeneca

Major Potential Value Creating Milestones in 2021

	H1 2021	H2 2021
SLN360		★ APOLLO Phase 1 Single-Ascending Dose Study
SLN124	✓ GEMINI Phase 1 Healthy Volunteer Study	★ GEMINI II Phase 1 Single-Ascending Dose Study

✓ = positive data reported

★ = data milestone

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

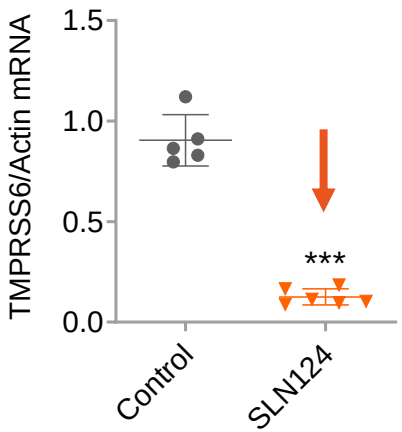
SLN124

for Iron-Loading Anemia Conditions

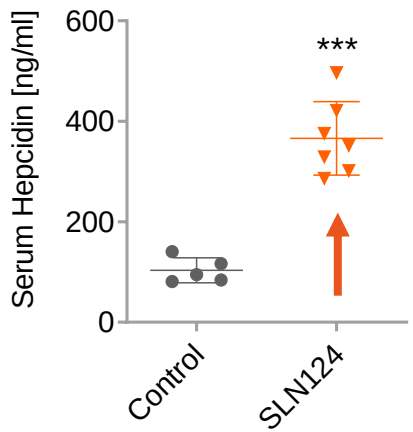


SLN124 is Designed to Restore Endogenous Hepcidin and Normalize Iron Levels

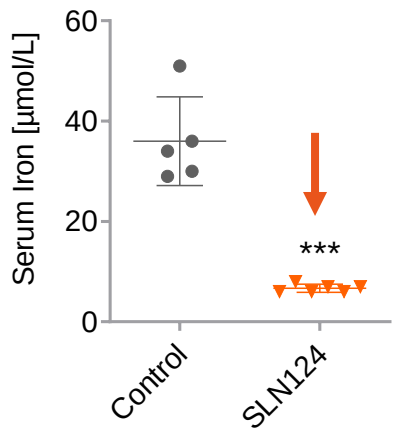
1 **Reduces TMPRSS6 in the liver**



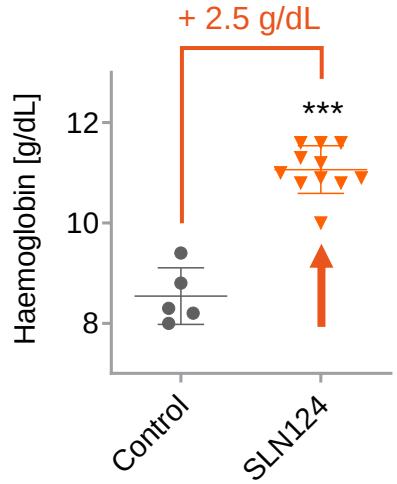
2 **Raises endogenous hepcidin**



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



4 **Improves red blood cell production**



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

SLN124 Phase 1 Healthy Volunteer Study Design

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

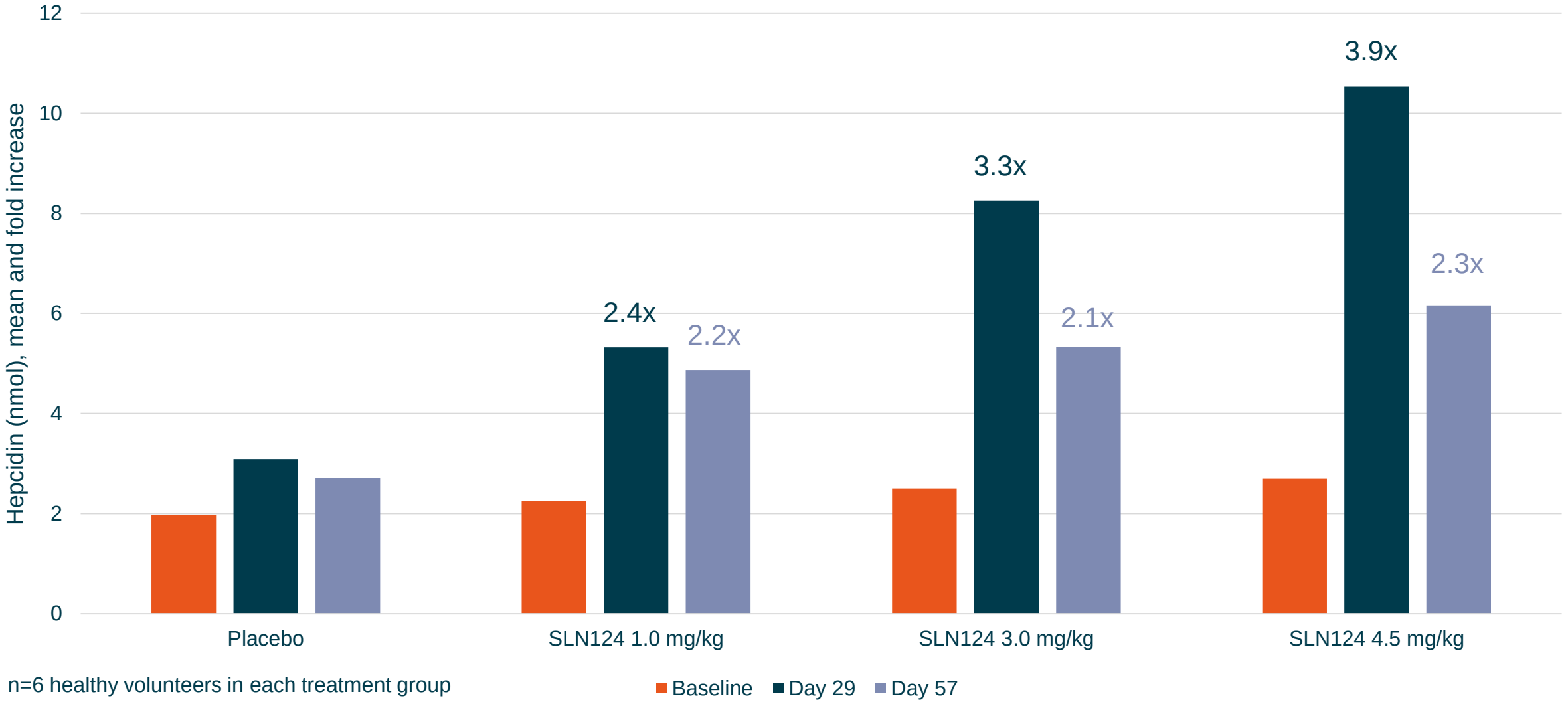


PD: Pharmacodynamics; PK: Pharmacokinetics

SLN124 Safe and Well-Tolerated in Healthy Volunteers

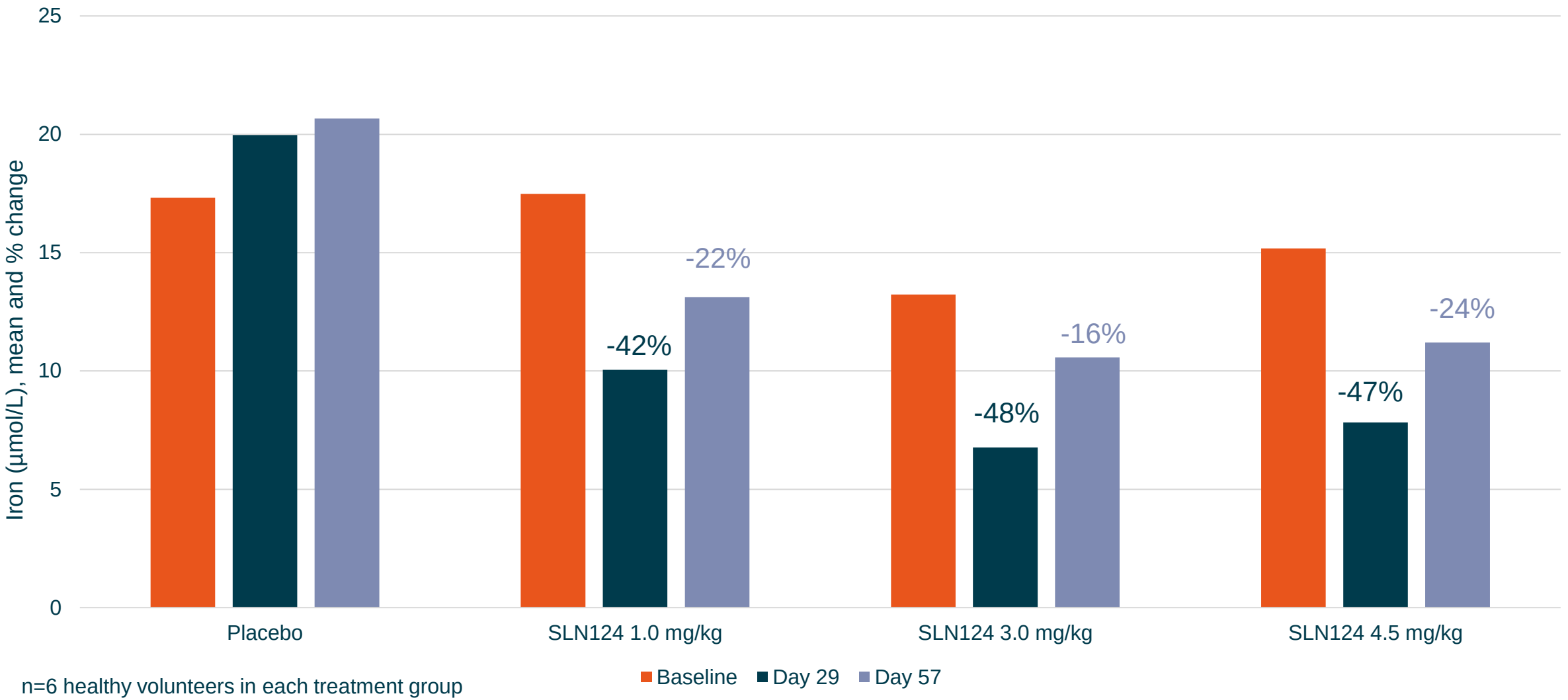
- First clinical data from **mRNAi GOLD™** platform
- Demonstrates proof of mechanism for SLN124
- Single subcutaneous doses of SLN124 (1.0, 3.0 & 4.5 mg/kg) were generally well-tolerated:
  - No serious or severe treatment emergent adverse events (TEAEs) or TEAEs leading to withdrawal
  - Majority of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

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
- 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

Major Potential Value Creating Milestones in 2021

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