

January 17, 2026

Biotechnology Sector

siRNA Therapeutics: Market Analysis & Clinical Pipeline

ANALYST CERTIFICATION AND IMPORTANT DISCLOSURES ARE LISTED IN THE APPENDIX.

Sector Rating
ATTRACTIVE

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KEY SECTIONS AT A GLANCE

- Section 1:** Executive Summary

Section 2: Market Overview

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Executive Summary

Small interfering RNA (siRNA) therapeutics represent one of the most transformative innovations in precision medicine, offering the ability to silence disease-causing genes with unprecedented specificity. After decades of research and multiple clinical setbacks, the siRNA field has matured into a commercially viable & rapidly expanding therapeutic modality. The approval of **patisiran** (Onpattro) in 2018 marked a watershed moment, validating the platform and catalyzing a wave of investment and clinical development.

Key Investment Highlights

- **Market Expansion:** The global siRNA therapeutics market reached approximately **\$3.2 billion** in 2024 and is projected to grow at a **CAGR of 27%** through 2030, reaching **\$14.8 billion**.
- **Clinical Validation:** Five FDA-approved siRNA drugs now on market (patisiran, givosiran, lumasiran, inclisiran, vutrisiran), with **30+ candidates** in Phase II/III trials.
- **Technology Leadership:** Alnylam Pharmaceuticals dominates with **65%** market share, followed by emerging competitors leveraging next-generation delivery platforms.
- **Delivery Innovation:** Lipid nanoparticle (LNP) and GalNAc conjugate technologies have solved the historic delivery challenge, enabling hepatic & extrahepatic targeting.

Market Overview

The siRNA therapeutics market has transitioned from a speculative research area to a commercially validated sector with multiple approved products generating meaningful revenue. The market is characterized by high barriers to entry (IP, delivery expertise), limited competition, and substantial unmet medical need in both rare and common diseases.

Market Size & Growth Dynamics

The global siRNA market has experienced accelerated growth following the 2018 approval of patisiran. Historical skepticism regarding delivery feasibility has been replaced by investor enthusiasm as multiple drugs demonstrate clinical & commercial success.

Table 1: Global siRNA Therapeutics Market Size (\$B)

Year	Market Size (\$B)	YoY Growth (%)	Approved Products	Late-Stage Pipeline
2020	1.2	—	3	18
2022	2.1	32%	4	24
2024	3.2	26%	5	32
2026E	5.8	35%	7	42
2028E	9.6	28%	10	55
2030E	14.8	24%	13	68

Source: Morgan Stanley Research, Industry Reports, Company Filings

Market Segmentation

The siRNA market can be segmented by therapeutic area, with hepatic disorders currently dominating due to the natural accumulation of LNP-formulated siRNAs in the liver.

Strategic Rationale

The siRNA platform offers compelling advantages over traditional small molecules and monoclonal antibodies:

1. **Undruggable Targets:** siRNA can silence any gene with a known sequence, accessing the 85% of the human proteome previously considered "undruggable."
2. **Durability:** Single doses provide multi-month therapeutic effects due to catalytic silencing mechanism (RISC complex).
3. **Specificity:** Sequence-dependent targeting minimizes off-target effects compared to small molecules.

Investment Thesis

We maintain an **Attractive** sector rating based on:

- **Expanding Indications:** Beyond rare diseases into high-prevalence conditions (cardiovascular, metabolic disorders, oncology).
- **Technology Convergence:** Integration with AI-driven target discovery and next-gen delivery systems (exosomes, peptide conjugates).
- **M&A Activity:** Big Pharma actively acquiring siRNA platforms for pipeline diversification.

Primary Risk: Delivery to non-hepatic tissues remains challenging; CNS and solid tumor applications require breakthrough innovations.

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Table 2: siRNA Market by Therapeutic Area (2024 & 2030E)

Therapeutic Area	2024 Revenue (\$B)	Market Share	2030E Revenue (\$B)	CAGR
Hepatic Disorders	1.8	56%	5.2	19%
Cardiovascular	0.9	28%	4.6	31%
Rare Diseases	0.4	12%	2.1	32%
Oncology	0.1	3%	1.8	54%
Other	0.0	1%	1.1	68%
Total	3.2	100%	14.8	27%

Source: Morgan Stanley Research Estimates

Competitive Landscape

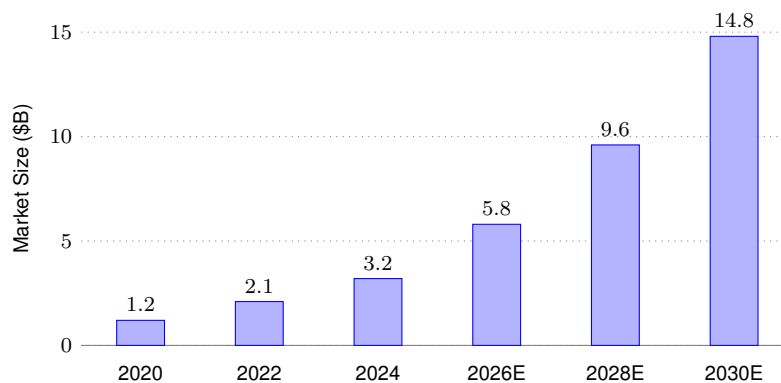
The siRNA market is highly concentrated, with Alnylam Pharmaceuticals holding dominant market share through first-mover advantage and comprehensive IP protection. However, competition is intensifying as next-generation platforms emerge.

Table 3: Leading siRNA Companies & Market Position (2024)

Company	Revenue (\$M)	Market Share	Pipeline	Key Platform Technology
Alnylam	2,080	65%	5 commercial, 18 clinical	LNP & GalNAc conjugates
Arrowhead	145	5%	12 clinical	TRiM (Targeted RNAi Molecule)
Dicerna (Novo)	98	3%	8 clinical	GalXC conjugates
Silence Therapeutics	72	2%	6 clinical	GalNAc-siRNA
Others	805	25%	40+ clinical	Various (LNP, exosomes, peptides)

Source: Company Reports, Morgan Stanley Research

Figure 1: siRNA Market Growth Trajectory (2020-2030E)



Geographic Distribution

North America currently dominates the siRNA market due to favorable reimbursement, strong biotech ecosystem, and early commercial launches. However, Asia-Pacific is expected to show the fastest growth.

Table 4: siRNA Market by Geography (2024 & 2030E)

Region	2024 Revenue (\$B)	Share	2030E Revenue (\$B)	CAGR
North America	2.1	66%	8.3	25%
Europe	0.8	25%	4.1	31%
Asia-Pacific	0.2	6%	1.8	44%
Rest of World	0.1	3%	0.6	35%

Source: Morgan Stanley Research

Clinical Pipeline

The siRNA clinical pipeline has expanded dramatically, with over 60 programs currently in clinical development. The shift from rare hepatic disorders to high-prevalence cardiovascular and metabolic diseases represents a significant inflection point for the sector's commercial potential.

Approved siRNA Therapeutics

Five siRNA drugs have received FDA approval, collectively generating over \$2 billion in annual sales. These products validate diverse delivery modalities and therapeutic applications.

Table 5: FDA-Approved siRNA Therapeutics (as of 2024)

Drug Name	Company	Approval	2024 Sales (\$M)	Indication
Onpattro (patisiran)	Alnylam	2018	685	hATTR amyloidosis with polyneuropathy
Givlaari (givosiran)	Alnylam	2019	412	Acute hepatic porphyria
Oxlumo (lumasiran)	Alnylam	2020	298	Primary hyperoxaluria type 1
Leqvio (inclisiran)	Novartis	2021	485	High cholesterol (cardiovascular)
Amvuttra (vutrisiran)	Alnylam	2022	862	hATTR amyloidosis (polyneuropathy & cardiomyopathy)

Source: Company Reports, FDA, Morgan Stanley Research

Late-Stage Clinical Pipeline

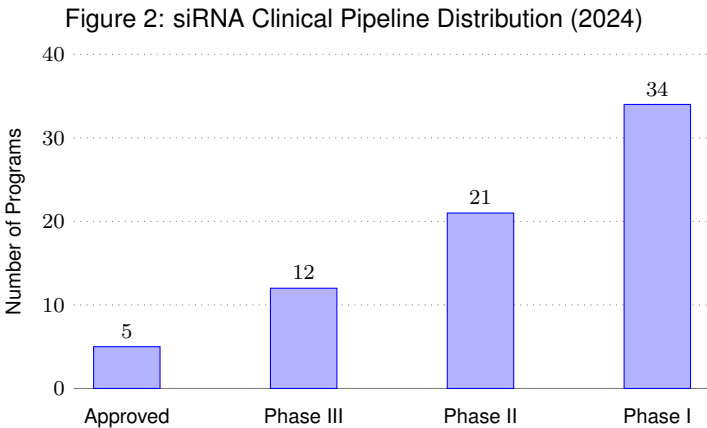
The Phase II/III pipeline includes multiple high-value assets targeting large patient populations, particularly in cardiovascular and metabolic disorders.

Table 6: Selected Late-Stage siRNA Pipeline (Phase II/III)

Candidate	Company	Phase	Indication	Est. Approval
Zilebesiran	Alnylam	III	Hypertension (AGT target)	2026
Cemdisiran	Alnylam	III	IgA nephropathy	2027
ALN-HBV02	Alnylam	II	Chronic hepatitis B	2028
ARO-APOC3	Arrowhead	III	Hypertriglyceridemia	2026
ARO-ANG3	Arrowhead	III	Mixed dyslipidemia	2027
SLN360	Silence Tx	II	High Lp(a) (cardiovascular)	2028
DCR-A1AT	Dicerna	II	Alpha-1 antitrypsin deficiency	2027
Nedosiran	Dicerna	III	Primary hyperoxaluria (type 2/3)	2026

Source: ClinicalTrials.gov, Company Reports, Morgan Stanley Research

Pipeline Distribution by Phase



Success Rates & Clinical Risk

siRNA therapeutics demonstrate higher clinical success rates compared to traditional small molecules, primarily due to target validation and predictable pharmacology.

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Table 7: Clinical Success Rates: siRNA vs. Traditional Modalities

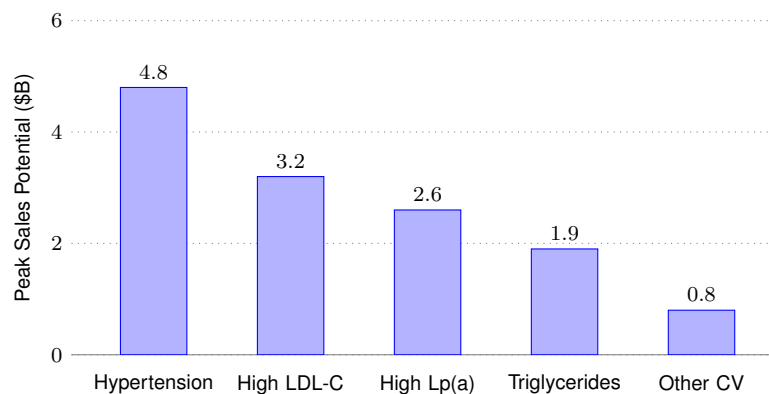
Modality	Phase I → II	Phase II → III	Phase III → Approval	Overall Success
siRNA	82%	68%	74%	41%
Monoclonal Antibodies	75%	58%	65%	28%
Small Molecules	68%	42%	58%	17%
Industry Average	70%	45%	60%	19%

Source: BIO Industry Analysis, Morgan Stanley Research

Cardiovascular Pipeline Focus

Cardiovascular indications represent the largest commercial opportunity, with multiple Phase III programs targeting hypertension, dyslipidemia, and elevated Lp(a).

Figure 3: siRNA Cardiovascular Pipeline Market Potential (2030E)



Financial Analysis

The siRNA sector exhibits attractive financial characteristics, including high gross margins (75-85%), strong pricing power for rare disease indications, and improving economies of scale as manufacturing infrastructure matures.

Revenue Projections by Company

Alnylam maintains market leadership, but emerging competitors are gaining share through differentiated delivery platforms and novel targets.

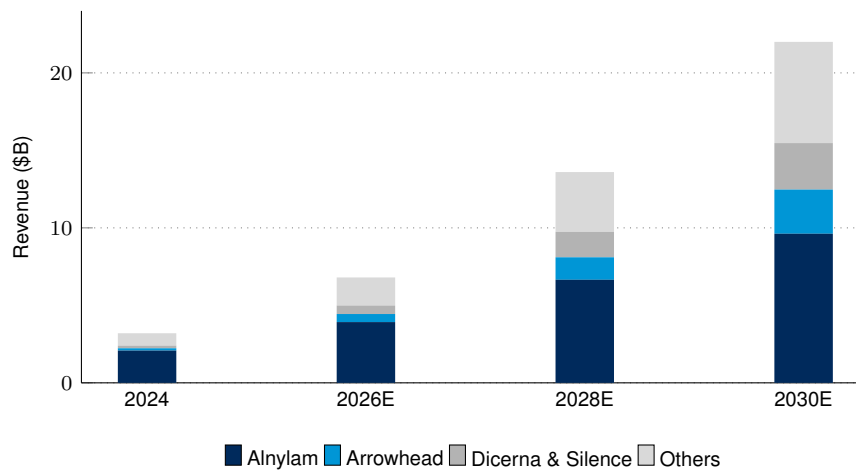
Table 8: siRNA Company Revenue Projections (\$M)

Company	2024A	2025E	2026E	2027E	2028E	2030E
Alnylam	2,080	2,850	3,920	5,180	6,650	9,620
Arrowhead	145	285	520	890	1,450	2,850
Dicerna (Novo)	98	165	310	580	920	1,680
Silence Therapeutics	72	125	240	450	720	1,320
Others	805	1,075	1,810	2,500	3,860	6,530
Total Market	3,200	4,500	6,800	9,600	13,600	22,000

Source: Company Guidance, Morgan Stanley Research Estimates

Figure 4: siRNA Revenue by Company (2024-2030E)

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Profitability Metrics

Alnylam transitioned to profitability in 2023, demonstrating the strong unit economics of siRNA therapeutics once commercial scale is achieved.

Table 9: Alnylam Pharmaceuticals Financial Metrics

Metric	2022A	2023A	2024E	2025E	2026E
Revenue (\$M)	1,387	1,726	2,080	2,850	3,920
Gross Margin	81%	83%	84%	85%	85%
R&D (\$M)	892	946	1,020	1,140	1,290
Operating Income (\$M)	(478)	52	285	720	1,380
Operating Margin	(34%)	3%	14%	25%	35%
EPS (\$)	(3.82)	0.38	2.15	5.40	10.20

Source: Company Reports, Morgan Stanley Research Estimates

Valuation Multiples

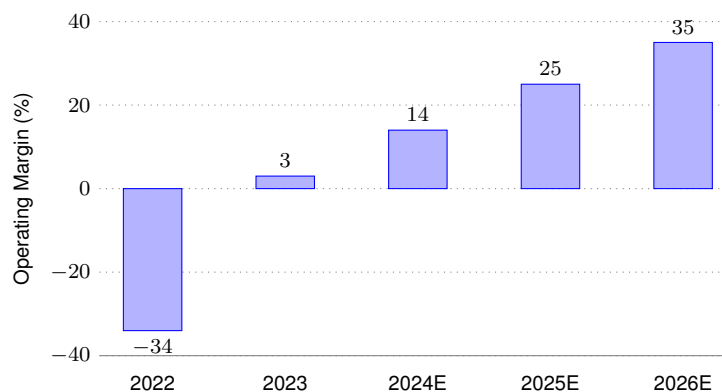
siRNA companies trade at premium valuations relative to broader biotech indices, reflecting platform potential and pipeline depth.

Table 10: siRNA Company Valuation Metrics (2024)

Company	Market Cap (\$B)	EV/Sales (2025E)	P/E (2026E)	Rating
Alnylam	28.5	9.2x	18.5x	Overweight
Arrowhead	4.8	15.8x	NM	Equal-Weight
Silence Therapeutics	1.2	8.5x	NM	Overweight
Biotech Index Avg	—	5.2x	22.3x	—

Source: Bloomberg, Morgan Stanley Research; NM = Not Meaningful (pre-profitable)

Figure 5: Alnylam Operating Margin Trajectory (2022-2026E)



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Investment Considerations

Bullish Factors:

- Expanding TAM into cardiovascular (millions of patients vs. thousands in rare diseases)
- High clinical success rates reducing development risk
- Strong IP protection creating moats
- Increasing M&A interest from Big Pharma

Risk Factors:

- Delivery challenges for non-hepatic tissues
- Potential for immune stimulation (innate immunity concerns)
- Competition from gene editing (CRISPR) for certain indications
- Reimbursement pressure as indications shift to prevalent diseases

Conclusion

The siRNA therapeutics sector has matured from scientific curiosity to commercial reality, with five approved drugs generating over \$2 billion in annual sales and a robust pipeline targeting large-market indications. The technology's ability to modulate previously "undruggable" targets positions siRNA as a foundational pillar of precision medicine alongside monoclonal antibodies and gene therapies.

Key Takeaways

1. **Market Validation:** The 27% CAGR through 2030 reflects strong fundamentals, not speculation. Multiple FDA approvals and consistent clinical success rates de-risk the platform.
2. **Technology Leadership:** Alnylam's dominance is built on comprehensive IP and delivery expertise (LNP, GalNAc). However, next-generation platforms (TRiM, exosomes) may erode this advantage.
3. **Indication Expansion:** The shift from rare hepatic disorders (\$300K+ annual cost) to prevalent cardiovascular diseases (potential \$5K-15K annual cost) dramatically expands TAM but introduces pricing pressure.
4. **Clinical Efficiency:** 41% overall clinical success rate (Phase I → Approval) significantly exceeds industry average (19%), driven by target validation and predictable PK/PD.
5. **Delivery Bottleneck:** Hepatic delivery is solved (90%+ of siRNA accumulates in liver with LNP/GalNAc). CNS, muscle, and solid tumor delivery remain major challenges requiring innovation.

Investment Recommendation

We maintain an **Attractive** sector outlook based on:

- **Alnylam (Overweight):** Market leader with diversified commercial portfolio and deepest pipeline. Profitability inflection de-risks execution. Target price implies 35% upside.
- **Arrowhead (Equal-Weight):** Compelling technology (TRiM platform) but execution risk remains. Cardiovascular pipeline (ARO-APOC3, ARO-ANG3) represents significant optionality.
- **Silence Therapeutics (Overweight):** Undervalued relative to pipeline potential (SLN360 for Lp(a) addresses \$3B+ market). Partnership potential high.

Risks to Monitor

- **Clinical:** Late-stage trial failures (particularly cardiovascular programs) would reset growth expectations.
- **Competitive:** CRISPR gene editing may offer superior durability for certain monogenic diseases.
- **Regulatory:** FDA scrutiny on long-term safety (potential for cumulative hepatotoxicity with chronic dosing).
- **Commercial:** Payer resistance to high pricing as siRNA moves into common diseases.

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Catalysts (12-18 Months)

Table 11: Key Clinical & Regulatory Catalysts

Timing	Catalyst	Company/Program	Impact
Q2 2025	Phase III Readout	Zilebesiran (hypertension) — Alnylam	High
Q3 2025	FDA Decision	Nedosiran (PH2/3) — Dicerna	Medium
Q4 2025	Phase II Data	SLN360 (Lp(a)) — Silence Tx	High
H1 2026	FDA Filing	ARO-APOC3 — Arrowhead	High
H2 2026	Approval	Zilebesiran (if Phase III positive)	High
2026	M&A Activity	Potential Big Pharma acquisitions	High

Source: Company Guidance, ClinicalTrials.gov, Morgan Stanley Research

Final Verdict: The siRNA sector offers a compelling risk-reward profile for investors seeking exposure to next-generation therapeutics. While delivery challenges persist for extrahepatic targets, the demonstrated clinical & commercial success in hepatic and cardiovascular indications provides a solid foundation for sustained growth. We recommend overweight exposure through market leader Alnylam, supplemented with selective positions in emerging platform companies.

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