

INDUSTRY OVERVIEW

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OLIGONUCLEOTIDE DRUG MARKET

Overview of siRNA Therapeutics

siRNA (small interfering RNA) therapeutics are a class of RNA interference (RNAi) therapies that silence disease-related genes by degrading target mRNA and reducing the production of pathogenic proteins. Since the first RNAi drug was approved by the FDA in 2018, the field has expanded rapidly, driven by growing commercial adoption and a robust clinical pipeline. Major transactions, such as Novartis’ US\$9.7 billion acquisition of The Medicines Company and Novo Nordisk’s US\$3.3 billion acquisition of Dicerna Pharmaceuticals, highlight strong industry confidence in RNAi technology

Comparison of siRNA, Small Molecules and Antibodies

Small molecules and antibodies are limited by off-target effects or restriction to extracellular targets, leaving many intracellular disease-causing proteins undruggable. In contrast, siRNA therapeutics selectively silence target genes, reducing pathogenic protein expression in genetic, viral, oncology, and metabolic diseases. Additionally, compared with small molecules and antibodies, siRNA therapies have lower DDI risk (degraded by nucleases), minimal renal impact (not cleared by kidneys), infrequent dosing (sustained protein knockdown), and reusable sequence-based design.

Commercialized and Approved siRNA Therapies Globally

Trade name	Product ⁽¹⁾	Target	Company	Indication	First Posted Date	2024 sales (US\$ million)	Price in the US (US\$)	Price in China
ONPATRO	Patisiran	TTR	Alnylam	Polyneuropathy of hereditary transthyretin-mediated amyloidosis	2018-08 (FDA) 2018-08 (EMA)	~253.0	\$9,565.89/5mL	/ ⁽³⁾
GIVLAARI	Givosiran	ALAS1	Alnylam	Acute hepatic porphyria (AHP)	2019-11 (FDA) 2020-03 (EMA)	~256.0	\$42,883.56/mL	/ ⁽³⁾
OXLUMO	Lumasiran	HAO1	Alnylam	Primary hyperoxaluria type 1 (PH1)	2020-11 (EMA) 2020-11 (FDA)	~167.0	\$58,712.60/0.5mL	/ ⁽³⁾
LEQVIO	Inclisiran	PCSK9	Novartis	Primary hypercholesterolemia (heterozygous familial and non-familial) or mixed dyslipidemia	2020-12 (EMA) 2021-12 (FDA) 2023-08 (NMPA)	~754.0	\$3,512.40/1.5mL	¥9,988/1.5m
AMVUTTRA	Vutrisiran	TTR	Alnylam, Sanofi	Hereditary Transthyretin-mediated (hATTR) amyloidosis, polyneuropathy of hereditary transthyretin-mediated amyloidosis	2022-06 (FDA) 2022-09 (EMA)	~970.0	\$119,351.00/0.5mL	/ ⁽³⁾
RIVFLOZA	Nedosiran	LDHA	Novo Nordisk, Dicerna	Primary hyperoxaluria type 1 (PH1)	2023-09 (FDA)	N/A ⁽²⁾	\$31,639.81/0.5mL	/ ⁽³⁾
QFITLIA	Fitusiran	SERPINC1	Alnylam	Hemophilia A, Hemophilia A with Inhibitors, Hemophilia B, Hemophilia B with Inhibitors	2025-03 (FDA) 2025-12 (NMPA)	/ ⁽³⁾	\$63,070.11/0.2mL	N/A ⁽³⁾
REDEMPLO	Plozasiran	ApoC3	Arrowhead	An adjunct to diet to reduce triglycerides in adults with familial chylomicronemia syndrome (FCS)	2025-11 (FDA) 2026-01 (NMPA)	/ ⁽³⁾	\$14,659.90/0.5mL ⁽²⁾	N/A ⁽³⁾

Source: Literature Review, Frost & Sullivan Analysis

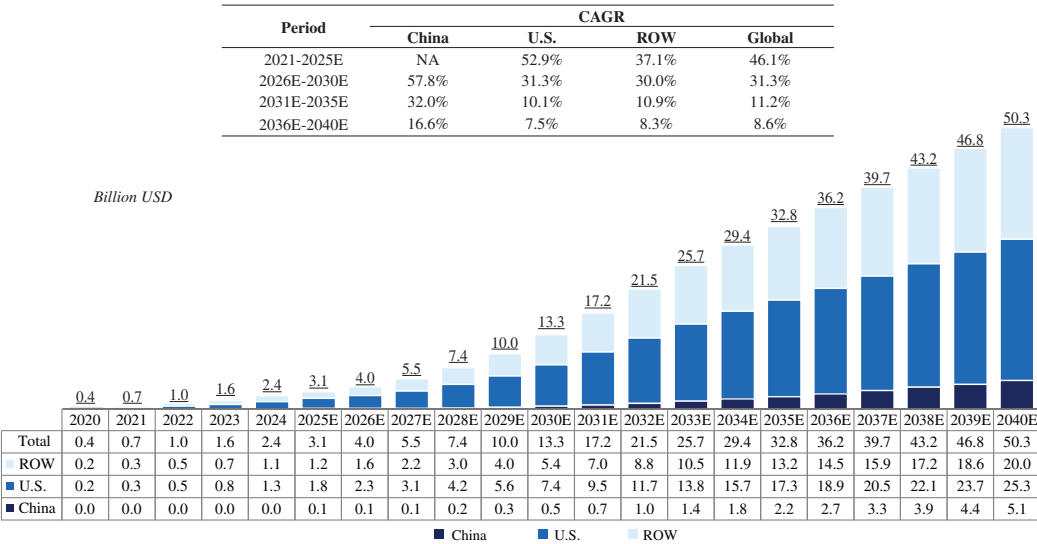
Note: (1) Products that were withdrawn from the market were not included. (2) “N/A” means the information is not disclosed. (3) “/” means the product is not listed.

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Global Market Size of siRNA Drug

As a specialized subclass of oligonucleotide drug, the global siRNA drug market increased from US\$0.4 billion in 2020 to US\$2.4 billion in 2024, with a CAGR of 60.9%. It is projected to reach US\$21.5 billion and 50.3 billion by 2032 and 2040, growing at a CAGR of 31.3% and 11.2%, respectively. In the U.S., the market reached US\$1.3 billion in 2024. By 2032, the U.S. siRNA market is expected to grow to US\$11.7 billion, with a CAGR of 31.3 %, and will further increase to US\$25.3 billion by 2040 with a CAGR of 10.1%. By 2032, the Chinese market is expected to grow to US\$1.0 billion and will further increase to US\$5.1 billion by 2040 with a CAGR of 22.1% from 2032 to 2040.

Global siRNA Drug Market Size, 2020–2040E



Source: Frost & Sullivan Analysis

Challenges and Entry Barriers of siRNA Design and Development

Despite the clinical and commercial success of approved siRNA therapeutics, the field remains challenging due to significant scientific and intellectual property barriers. New entrants to the field face a steep learning curve and substantial investment requirements.

- **Improvement in Potency and Durability:** Advances in chemical modifications have improved siRNA stability, reduced immunogenicity, and extended circulation time. These innovations are leading to less frequent dosing and enhanced gene silencing effectiveness.
- **Off-Target Effects & Toxicity:** siRNA may inadvertently bind to non-target mRNA, causing unintended gene silencing and potential toxicity. Advanced bioinformatics tools are needed to minimize off-target effects.
- **Extrahepatic Delivery Challenges:** Delivering siRNA to extrahepatic tissues is difficult due to instability in circulation, enzymatic degradation, and challenges in cellular uptake. Specialized delivery technologies are required to protect siRNA and ensure efficient targeting of non-hepatic tissues.

Key Market Drivers

The sustained growth of the siRNA therapeutics market is strongly supported by the following key drivers:

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- **Expansion to Chronic Diseases:** siRNA is moving beyond rare diseases to treat chronic conditions like cardiovascular diseases, expanding patient pools and increasing commercial opportunities. Successful treatments, such as inclisiran, are attracting investment and accelerating R&D.
- **Chemical Modifications:** Advances in siRNA technology, including chemical modifications, extend its duration of action, improve stability, and reduce immunogenicity, enabling less frequent dosing and better patient adherence.
- **Extrahepatic Delivery:** New delivery systems, including ligand-conjugated siRNA and engineered nanoparticles, overcome biological barriers, enabling precise targeting of previously “undruggable” tissues and expanding the therapeutic potential of siRNA.
- **Diagnostic-Treatment Integration:** The integration of advanced diagnostics with siRNA therapeutics enhances treatment precision and personalization, enabling real-time monitoring and optimized dosing, which drives market growth.

siRNA IN CHRONIC DISEASE MANAGEMENT

Overview of Chronic Disease

Chronic diseases are long-lasting conditions that cannot be prevented by vaccines or cured by traditional medications but can be managed with treatment and lifestyle changes. They contribute significantly to global health challenges, including high mortality and reduced quality of life. Management is shifting from reactive treatment to proactive prevention, emphasizing early intervention. This approach is crucial for conditions like AF, CAT, CKD, ASCVD, obesity, and hypertension, which together contribute to a significant health burden.

The global chronic disease drug market increased from US\$707.9 billion in 2020 to US\$831.4 billion in 2024, with a CAGR of 4.1%. It is projected to reach US\$1,167.5 billion and US\$1,575.4 billion by 2032 and 2040, growing at a CAGR of 4.3% and 3.8%. The following table demonstrates a few examples of drugs that have shifted from reactive treatment to prevention.

	Drug	Brand	Company	Therapeutic Indications	Approved Date	Prevention Indications	Approved Date	Price in US	Price in China
Diabetes	Empagliflozin	Jardiance	Boehringer Ingelheim	T2DM	2014	to reduce the risk of cardiovascular death in adult patients with type 2 diabetes mellitus and established cardiovascular disease	2016	10mg: 20.58-20.76 per Tablet	10mg: 4.24RMB per Tablet
	Dulaglutide	Tralicity	Eli Lilly	Type 2 diabetes mellitus (T2DM)	2014	Primary/Secondary prevention of cardiovascular events in patients with diabetes	2020	\$972.19/2 ml	0.5ml: 123.4 RMB
	Semaglutide	Ozempic	Novo Nordisk	Type 2 diabetes mellitus (T2DM)	2017	Secondary prevention of cardiovascular events in patients with diabetes	2020	\$982.34/3ml	3ml: 716.3 RMB
Hypertension	Lisinopril	Zestril	Merck	Hypertension	1987	for the treatment of hemodynamically stable patients within 24 hours of acute myocardial infarction, to improve survival	2003	2.5mg: \$0.02-\$0.24 per tablet	10mg: 0.22RMB per tablet (generic drug)
	Losartan	Cozaar	Merck	Hypertension	1995	Reduction of the risk of stroke in patients with hypertension and left ventricular hypertrophy	2003	25mg: \$0.12-\$0.56 per tablet	50mg: 5.61 RMB per tablet
	Valsartan	Diovan	Novartis	Hypertension	1996	Reduction of cardiovascular mortality in clinically stable patients with left ventricular failure or left ventricular dysfunction following myocardial infarction	2003	40mg: \$0.42-\$0.60 per tablet	80mg: 4.16 RMB per capsule
Lipid management	Atorvastatin	Lipitor	Pfizer	Hypercholesterolemia	1996	Primary/secondary prevention of cardiovascular events	1996	10mg: \$0.05-0.30 per tablet	40mg: 10.39 RMB per tablet
	Rosuvastatin	Crestor	AZ	Hyperlipidemia	2003	Primary prevention of cardiovascular events	2009	5mg: \$0.03-0.40 per tablet	10mg: 4.99 per tablet
	Bempedoic Acid+ Ezetimibe	Nexlizet	Esperion	Hyperlipidemia	2020	To reduce the risk of myocardial infarction and coronary revascularization in adults who are unable to take recommended statin therapy	2024	180mg+10mg: 13.94 per tablet	/

Source: FDA, Frost & Sullivan Analysis

Advantages of siRNA in Chronic Disease Management

Current chronic disease management faces challenges such as medication adherence, side effects, access to care, and treatment efficiency. Patients with chronic diseases often skip doses, leading to suboptimal outcomes and severe health risks. Long-term medication use can amplify side effects, such as muscle toxicity with statins, especially in those with renal or hepatic impairment.

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Polypharmacy complicates treatment due to potential drug-drug interactions. Additionally, renal impairment affects 30% of AF patients, 39% of CAD patients, and 24% of CAT patients, necessitating dose adjustments to ensure efficacy and minimize adverse effects. Existing treatments may be ineffective, particularly for those with statin intolerance or high-risk patients who fail to meet target metrics.

siRNA technology offers transformative advantages in chronic disease management by addressing key limitations of traditional therapies:

siRNA technology offers significant advantages in chronic disease management by addressing key limitations of traditional therapies. It provides long-lasting therapeutic effects with a single injection, maintaining efficacy for six months to a year, which improves patient adherence compared to daily oral medications. This reduces hospital visits and treatment gaps, enhancing long-term management. siRNA drugs also have a favorable safety profile, targeting specific genes to minimize off-target effects and reduce the risk of renal impairment and drug-drug interactions. By directly targeting the genetic drivers of disease, siRNA therapies block pathogenic protein synthesis, leading to sustained reductions in key clinical indicators.

COAGULANT DRUG MARKET

Overview of Coagulation Pathways

Blood clotting occurs through the intrinsic and extrinsic pathways, both of which activate factor X and generate thrombin to form a fibrin clot. The body normally maintains a balance between clot formation and anticoagulation. Current anticoagulants prevent thrombosis by blocking this process but often increase bleeding risk, highlighting the need for safer therapies.

Overview of Anticoagulant Drugs

Anticoagulants prevent thromboembolic disorders by inhibiting the coagulation cascade but carry bleeding risks. Vitamin K antagonists have largely been replaced by FXa inhibitors. As the current standard for long-term anticoagulation, FXa inhibitors account for about 90% of anticoagulant sales. In 2024, the DOAC market reached US\$29.2 billion, including US\$20.7 billion from Eliquis.

Global Market Size of Anticoagulant Drugs

The global anticoagulant drug market has experienced steady growth, expanding from US\$28.0 billion in 2020 to US\$33.0 billion in 2024, representing a CAGR of 4.2%. Looking ahead, the market is projected to continue its upward trajectory, reaching approximately US\$55.1 billion by 2032 and further growing to US\$72.2 billion by 2040, with CAGR being 6.6% and 3.4%, respectively.

In China, the anticoagulant market has grown rapidly and is estimated to reach US\$0.9 billion in 2024. The market is expected to sustain strong growth, climbing to US\$1.5 billion by 2032, with CAGR being 6.5%, and is forecasted to reach US\$2.6 billion by 2040 with CAGR being 6.8%, reflecting increasing demand driven by aging demographics, rising prevalence of cardiovascular diseases, and expanding access to advanced anticoagulant therapies.

The global anticoagulant drug market in 2024, broken down by major treatment types and expressed in billion USD, is as follows: direct oral anticoagulants (DOACs) account for USD 19.5 billion, or 59.3% of the total market; heparin-based drugs represent USD 10.7 billion, or 32.6%; warfarin contributes USD 1.5 billion, or 4.7%; and other therapies make up USD 1.1 billion, or 3.4%.

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Unmet Medical Needs and Market Expansion Potential

Among oral anticoagulants, apixaban stands as the market leader, commanding approximately US\$20.0 billion in annual revenue within the US\$29.2 billion global oral anticoagulation segments. As a direct Factor Xa inhibitor, apixaban offers advantages over traditional agents like warfarin, including reduced dietary restrictions and less frequent laboratory monitoring. Nevertheless, it shares common limitations with other drugs in its class, including:

- **Bleeding Risk.** Elevated risk of clinically relevant (including major) bleeding, particularly in high-risk populations, such as elder, patients with comorbidities, limiting safety for vulnerable groups.
- **Adherence Challenges.** Daily dosing or a higher dosing frequency burden reduces patient compliance, increasing the risk of thromboembolic events due to missed doses.
- **Renal Impairment.** Dependence on renal clearance restricts use in patients with severe CKD (defined below), excluding a significant portion of population.
- **Drug-Drug Interactions.** Potential interactions with concomitant medications complicate treatment in polypharmacy settings.
- **Intellectual Property Expiry.** All approved DOACs face patent cliffs. For example, apixaban’s US patent will expire in 2026.

Global Competitive Landscape of Drugs Targeting FXI Inhibitors

The below table shows the current landscape of FXI-targeted drug candidates excluding siRNA candidates.

Candidate	Modality	Company	Phase	Indication	First Post Date	Location
Abelacimab	Antibody	Novartis	Phase III	High-risk Patients With AF Who Have Been Deemed Unsuitable for Oral anti Coagulation	2023 -02	Global
Asundexian	Small molecule	Bayer	Phase III	Prevention of Ischemic Stroke	2023 -01	Global
Milvexian	Small molecule	BMS	Phase III	AF	2023 -03	Global
			Phase III	Stroke Prevention After AIS or High-Risk TIA	2023 -01	Global
REGN7508	Antibody	Regeneron	Phase III	VTE prevention after TKA	2025 -06	US
			Phase III	AF	2026-02	NA
			Phase II	Prevention of VTE in Patients with a PICC	2024 -03	Global
			Phase III	PAD	2026-01	NA
			Phase III	CAT	2026-02	US, Georgia
SHR-2004	Antibody	Hengrui	Phase III	Prevention of arteriovenous thrombosis	2025 -02	China
Frunexian-HSK36273	Small molecule	Haisco	Phase II	Systemic anticoagulation in HD and surgery patients	2022-10	China
			Phase II	VTE prevention after TKA	2022-11	Global
Amrecibart	Antibody	Regeneron	Phase III	AF	2026-02	NA
			Phase II	Prevention of VTE in Patients with a PICC	2024-03	Global
			Phase III	PAD	2026-01	NA
Ir-CPI	Protein	Bioxodes	Phase II	Intracerebral Hemorrhage	2023-08	Belgium
KN060	Antibody	Alphamab Oncology	Phase II	Prevention of thromboembolic disease	2023-11	China
SBK013	Small molecule	Shibeikang	Phase I	Prevention of VTE and ATE	2025-12	China

SBK013; Small molecule; Shibeikang; Phase I; Prevention of VTE and ATE; 2025-12; China

Source: Clinical Trials, CDE, Frost & Sullivan Analysis

Note: 1. last updated on 2026-03-25; 2. VTE after TKA refers to Venous Thromboembolism after Total Knee Arthroplasty; PICC refers to Peripherally Inserted Central Catheter; AIS and TIA refers to Acute Ischemic Stroke and Transient Ischemic Attack; CAD refers to Coronary Artery Disease; ESRD-HD refers to End-Stage Renal Disease Requiring Hemodialysis; HD refers to hemodialysis 3. Only IST Phase 2 and 3 trials with first posted date after 2020 are listed.

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FXI-targeting siRNA Drugs

Overview of FXI Inhibitors

FXI inhibitors are a novel class of anticoagulants that target factor XI in the intrinsic pathway to reduce thrombosis while preserving normal hemostasis. Compared with FXa inhibitors, they may offer lower bleeding risk. Genetic studies show that individuals with FXI levels below 30% have significantly lower cardiovascular event rates, and those below 50% have a reduced risk of VTE.

siRNA-Based Therapies Emerge as a Differentiated, Long-Acting, and Safe Approach Advancing FXI Inhibition Across Multiple Platforms

FXI inhibitors are being developed across multiple modalities, including small molecules, monoclonal antibodies, ASOs, and siRNA-based therapies, each offering distinct pharmacological and pharmacokinetic properties. Notably, siRNA-based FXI inhibitors are emerging as a highly differentiated approach with superior durability, safety, and patient convenience. The following table shows the key differences among small molecules, monoclonal antibodies, ASOs, and siRNA-based therapies in the aspects of mechanism of action, PK/PD profile and safety.

	Small Molecules	Monoclonal Antibodies	ASOs	siRNA
MoA	Reversible direct inhibition of FXIa catalytic site	Neutralize FXI/FXIa or lock FXI zymogen inactive	Degrade hepatic FXI mRNA, reduced protein synthesis	RISC-mediated silencing of hepatic FXI mRNA
Specificity	Medium (potential binding promiscuity and CYP/transporter DDIs)	High (minimal cross-reactivity)	Medium to high (theoretical sequence hybridization with unintended transcripts)	High (optimized design and hepatocyte targeting; rare innate immune triggers)
Dosing Frequency	Daily	Weekly to monthly	Weekly	Up to yearly
Immunogenicity	Low (Generally non-immunogenic)	Medium (Risk of anti-drug antibodies and infusion reactions)	Low	Low
Representative Drug	Milvexian (BMS/J&J)	Abelacimab (Anthos Therapeutics/Novartis)	IONIS-FXIRx (Ionis/Bayer)	SRSD107 (Sirius)

Source: Literature Review, Frost & Sullivan Analysis

Competitive Landscape of siRNA Therapy Targeting FXI Inhibitors

Candidate	Modality	Company	Phase	Indication	First Post Date	Location
RBD-4059	siRNA	Ribo	Phase II	Stable CAD	2024-12	Sweden
			Phase II	VTE	2025-08	EU
SRSD107	siRNA	Sirius	Phase II	CAD/PAD	2025-12	China
			Phase II	Thromboprophylaxis in Primary Unilateral TKA	2026-03	China
STP122G	siRNA	Sirnaomics	Phase I	NA	2023-05	US, Canada
ADX-626	siRNA	ADARx	Phase I	NA	2025-07	UK
CITY-FXI	siRNA	City	Phase I	Factor V Leiden (FVL) or prothrombin G20210A mutation	2026-02	UK

Source: Clinical Trials, CDE, Frost & Sullivan Analysis

Notes: 1. last updated on 2026-03-25; 2. VTE refers to Venous Thromboembolism ;CAD refers to Coronary Artery Disease
3. Only IST trials with first posted date after 2020 are listed.

As of the Latest Practicable Date, there are 13 FXI-targeted drug candidates across various modalities in clinical development globally: four are in Phase 1, four in Phase 2, five in Phase 3, and none are under NDA application.

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Market Opportunities of FXI-targeting siRNA Drugs

Despite apixaban’s prominence, its shortcomings as mentioned above contribute to a critical treatment gap, creating a compelling opportunity for innovation. The following table offers an overview of the addressable market for FXI inhibitors across various indications.

FXI Inhibitors Global Addressable Anticoagulation Patients

		TKA	CKD	CAT	Other VTE	AF	CAD	PVD	Stroke	Global Addressable Population 2024
	Global Addressable Population 2024	~4M	~300M	~2M	~50M	~40M				–
Primary Prevention	DOAC approval	✓			✓	✓				–
	DOAC for SOC or recommendation	Recommendation			Recommendation	SOC				~94M
	Global Addressable Population 2024		~3M	~3M	~4M		~200M	~300M	~100M	–
Secondary Prevention	DOAC approval				✓		✓	✓		–
	DOAC for SOC or recommendation		Recommendation	Recommendation	Recommendation		Recommendation	Recommendation		~510M

Source: Literature Review, FDA, Frost & Sullivan Analysis

Within the CVD spectrum, chronic anticoagulation is primarily indicated for selected conditions associated with a high risk of thromboembolic events, including AF, CAD, PVD, and CKD. In contrast, other CVD conditions, such as hypertension, cardiomyopathies, and stable atherosclerosis, generally do not require routine anticoagulation, as the risk of systemic thromboembolism in these populations is relatively lower. Accordingly, the CVD patient population presented in the table below includes only patients with AF, CKD, PVD, and CAD, which represent the primary cardiovascular indications requiring anticoagulation therapy. The following two diagrams illustrate the global and China prevalence of CVD by indication:

Global Prevalence of CVD by Indication, 2020-2040E

Million					Period		CAGR															
							AF		CKD		PVD		CAD		Total (CVD)							
					2021-2025E		1.6%		2.3%		3.6%		2.2%		2.5%							
					2026-2030E		1.9%		2.4%		2.1%		1.6%		2.2%							
					2031E-2035E		1.8%		2.5%		1.1%		1.2%		2.0%							
2036E-2040E		1.5%		1.9%		0.7%		0.9%		1.5%												
	2020	2021	2022	2023	2024	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E	2034E	2035E	2036E	2037E	2038E	2039E	2040E	
AF	61.3	62.8	63.7	64.7	65.7	67.0	68.3	69.6	71.0	72.3	73.7	75.0	76.4	77.8	79.2	80.6	82.1	83.4	84.7	85.9	87.0	
CKD	809.8	827.6	846.0	865.8	886.4	907.7	929.5	951.7	974.5	997.9	1,021.9	1,046.5	1,072.0	1,098.3	1,125.5	1,153.6	1,181.0	1,207.7	1,232.3	1,254.8	1,275.5	
PVD	271.6	280.2	288.8	301.8	312.0	322.3	330.4	338.2	345.4	352.2	358.5	364.6	370.1	375.4	378.1	380.8	383.4	386.0	388.6	391.1	393.6	
CAD	202.6	208.0	213.0	217.8	222.5	227.0	231.3	235.5	239.5	243.2	246.6	249.6	252.4	255.1	258.3	261.3	264.2	267.0	269.6	271.9	274.0	
Total (CVD)	1,345.3	1,378.6	1,411.5	1,450.1	1,486.6	1,524.0	1,559.5	1,595.0	1,630.4	1,665.6	1,700.7	1,735.7	1,770.9	1,806.6	1,841.1	1,876.4	1,910.8	1,944.1	1,975.1	2,003.7	2,030.1	

Source: Frost & Sullivan Analysis

China Prevalence of CVD by Indication, 2020-2040E

Million	Period										CAGR					Total (CVD)					
											AF	CKD	PVD	CAD							
	2021-2025E										3.4%	3.7%	2.2%	2.5%							
	2026-2030E										2.7%	4.9%	2.1%	2.2%							
	2031E-2035E										2.3%	4.8%	1.8%	1.8%							
2036E-2040E										2.1%	3.6%	1.6%	1.3%								
	2020	2021	2022	2023	2024	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E	2034E	2035E	2036E	2037E	2038E	2039E	2040E
AF	19.8	20.3	20.7	21.6	22.5	23.2	23.9	24.5	25.2	25.9	26.5	27.2	27.8	28.5	29.1	29.8	29.9	30.5	31.2	31.8	32.5
CKD	126.5	131.1	136.5	140.8	145.8	151.4	157.7	164.7	172.6	181.2	190.6	200.4	210.5	220.8	231.4	242.1	252.8	263.4	273.3	282.5	291.2
PVD	50.7	51.9	53.1	54.2	55.4	56.6	57.9	59.1	60.3	61.6	62.8	64.0	65.2	66.4	67.6	68.8	70.0	71.2	72.4	73.5	74.7
CAD	25.3	26.0	26.6	27.3	28.0	28.7	29.4	30.1	30.8	31.5	32.1	32.8	33.4	34.0	34.6	35.2	35.8	36.4	36.9	37.3	37.8
Total (CVD)	222.3	229.3	236.9	243.9	251.7	259.9	268.9	278.4	288.9	300.2	312.0	324.4	336.9	349.7	362.8	375.9	388.5	401.4	413.7	425.2	436.1

Source: Frost & Sullivan Analysis

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The global prevalence of VTE increased from 22.1 million in 2021 to 26.1 million by 2025, with a CAGR of 4.3%. This figure is projected to reach 36.9 million by 2040, corresponding to a CAGR of 1.0% from 2036-2040. In China, the prevalence of VTE is projected to rise from 3.0 million in 2021 to 3.5 million by 2025, with a CAGR of 4.4%. By 2040, this figure is expected to reach 5.3 million, reflecting a CAGR of 1.8% from 2036 to 2040.

Atrial Fibrillation (AF)

Overview of Atrial Fibrillation

Atrial fibrillation (AF) is a common arrhythmia where fast, disorganized electrical activity in the atria reduces atrial contraction by 20-30%, impairing ventricular efficiency. This leads to blood stasis, endothelial dysfunction, and increased risk of clot formation. The stroke risk in AF patients ranges from 1% to 20% annually, depending on comorbidities. Clots can cause ischemic stroke and other systemic events, increasing cardiovascular risk. AF is classified into non-valvular, which makes up 90% of cases, and valvular, where surgery is the primary treatment

Potential Addressable Market of FXI Drugs in AF

SRSD107 is intended to be used as first line anticoagulant treatment in AF patients who are intolerant of FXa inhibitors. In AF patients, approximately 90% of AF patients are non-valvular AF, and more than 80% of these patients are at high risk of stroke requiring anticoagulation. Accordingly, the targeted population represents non-valvular AF patients with high stroke risk indicated for anticoagulant therapy. This population is estimated to be approximately 32.6 million in 2024, rising to around 39.7 million by 2040.

Modalities with longer dosing intervals and improved safety profiles often achieve strong adoption. For example, once-yearly zoledronate reached 66% market share by 2020, while escitalopram captured approximately 58% of the SSRI market due to improved selectivity and safety.

The following table provides an overview of the potential addressable market of FXI drugs in AF, focusing on AF prevalence, anticoagulant penetration, DOACs penetration, and modality share.

Atrial fibrillation (AF)	
Patient Population	
AF prevalence	~4.5% (US) / ~1% (CN)
Non-valvular AF population	Non-valvular AF accounts for ~90% of total AF population
High risk AF population	Over 80% of non-valvular patients have CHA2DS2-VA score above 2
Anticoagulant Penetration	
Penetration rate – anticoagulant prescription	Fewer than 33% of new AF patients are prescribed anticoagulation Prescription rate of anti-coagulants for non-valvular AF is 66%-70%
Penetration rate – common chronic diseases drugs	Drug penetration for common chronic diseases, such as hypertension, diabetes, and hyperlipidemia, is above 90% among diagnosed patients, driven by strong awareness and diverse medication options
DOAC penetration among anticoagulant	
DOAC penetration in AF patient under anticoagulant medication	DOACs counts for 74% of patients with anticoagulant prescription in non-valvular AF patients; Nearly 100% of new AF patients with anticoagulation prescription are prescribed to DOACs
DOAC dose adjustment	43.1% of non-valvular atrial fibrillation patients prescribed to DOACs was underdosed

Source: Literature Review, Frost & Sullivan Analysis

Treatment Paradigms for Non-valvular AF

Management of non-valvular AF focuses on symptom control and stroke prevention. DOACs are the first-line anticoagulants recommended by ACC/AHA/HRS and ESC guidelines, including edoxaban, rivaroxaban, and apixaban, while warfarin is used when DOACs are unsuitable. Although about 80% of patients are at high stroke risk, fewer than 70% receive anticoagulation. DOACs account for about 70% of prescriptions, yet around 40% are underdosed due to age, low body weight (<60 kg), or renal impairment.

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Cancer Associated Thrombosis (CAT)

Overview of CAT

Cancer-associated thrombosis (CAT) arises from tumor-driven activation of the coagulation system, inflammatory responses, and cancer treatments such as chemotherapy, surgery, and central venous catheters. Approximately 74.4% of CAT patients receive anticoagulant therapy. CAT mainly presents as VTE (DVT or PE), driven by blood stasis, hypercoagulability, and endothelial injury. Certain cancers carry particularly high VTE risk, including pancreatic cancer (15%–25%), as well as gastric, lung, ovarian, and hematologic malignancies.

Potential Addressable Market of FXI Drugs in CAT

In CAT patients, about 40% of cancer patients receive chemotherapy or immunotherapy, and among them, approximately 25% have a Khorana score ≥ 2 , representing the high-risk population eligible for anticoagulant therapy. This defines the targeted population of approximately 2.1 million in 2024 reaching 3.0 million by 2040.

The following table provides an overview of the addressable market of FXI drugs in CAT.

Cancer-associated thrombosis (CAT)	
Total cancer incidence	~2 million (US)/~5 million (CN)
Proportion of cancer patients receive chemotherapy or immunotherapy	~40%
High-risk population eligible for anticoagulant therapy	25% have a Khorana score ≥ 2

Source: Literature Review, Frost & Sullivan Analysis

Primary Prevention and Secondary Prevention of CAT

No medication is specifically approved for CAT. Primary prevention aims to prevent first VTE in high-risk cancer patients, with LMWH as the main prophylaxis, while DOACs are used in selected low-bleeding-risk patients in the U.S. and Europe but adopted more cautiously in Asia. Secondary prevention focuses on preventing recurrence. Treatment typically starts with LMWH for at least 5 days, followed by long-term anticoagulation such as warfarin or DOACs. Anticoagulation is usually continued for 3–6 months, or longer in high-risk patients. Close monitoring for bleeding, particularly gastrointestinal or genitourinary, is essential, and dose adjustments are needed for those with thrombocytopenia or renal impairment.

Peripheral Vascular Disease (PVD)

Overview of PVD

PVD encompasses all vascular disorders affecting peripheral vessels, excluding those of the heart and brain. In recent years, the incidence of PVD has been increasing steadily due to population aging and changes in dietary patterns. According to the literature review, the global prevalence of PVD is estimated to be approximately 10% among the adult population. PVD includes PAD and venous PVD, among which PAD accounts for approximately 60%. PVD affects nearly 200 million individuals globally, including an estimated 40–45 million in the U.S.

PAD is a chronic atherosclerotic disease that commonly affects the lower extremities, causing symptoms like pain, claudication, pale extremities, erectile dysfunction, and in severe cases, gangrene or limb loss. PAD patients share many of the same risk factors as those with CAD, including smoking, high cholesterol, diabetes, obesity, hypertension, and a family history of vascular disease. Moreover, individuals with PAD are at a significantly higher risk of experiencing

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stroke and myocardial infarction compared to the general population. This elevated risk underscores the systemic nature of atherosclerosis and the importance of managing PAD not only as a localized vascular condition, but also as a marker of broader cardiovascular vulnerability. In patients with PAD, the rate of revascularization is approximately 2.4%, and among them, about 90% receive anticoagulant therapy. Furthermore, one in six PAD patients aged 50 years who have undergone peripheral revascularization experienced a major atherothrombotic vascular event within one year. Following endovascular intervention for PAD, the incidence of VTE ranges from 4.4% to 7.1% at different follow-up times.

Venous PVD include DVT of the lower limbs and chronic venous insufficiency. PVD is often asymptomatic or presents with only mild symptoms in its early stages, however, if left unrecognized and untreated, it can progress and significantly impair patient health. Therefore, early detection and comprehensive management are of great importance.

Potential Addressable Market of FXI Drugs in PVD

SRSD107 is intended to be used as first line anticoagulant treatment in PVD patients undergoing peripheral revascularization procedures, which represents the primary addressable population estimated at approximately 1.2 million in 2024, growing to 7.2 million by 2040.

The following table presents a comprehensive analysis of the potential addressable market of FXI-targeted therapies in PVD.

Potential Addressable Market of FXI Drugs in PVD

Peripheral vascular disease (PVD)	
PAD proportion in PVD	~60%
PAD prevalence rate	~8% (US)/~4% (CN)
Chronic limb threatening ischaemia (CLTI) incidence rate	incidence of CLTI is estimated to be between 11%-20% among patients with known PAD. Revascularization procedures are generally offered to treat PAD with CLTI
Revascularization rate	2.4% of those diagnosed with PAD underwent a revascularization procedure

Source: Literature Review, Frost & Sullivan Analysis

Treatment Paradigms for PVD

PAD, the most common form of PVD, is treated with antiplatelet agents, statins, and revascularization. Revascularization procedures restore blood flow in patients with chronic limb-threatening ischemia. In the U.S., about 359 thousand revascularization procedures are performed annually. Venous PVD is treated with anticoagulants such as unfractionated heparin, LMWH, vitamin K antagonists, and DOACs.

Unmet Medical Needs in PVD

PVD presents a constellation of unmet medical needs that span the continuum of patient care.

First, long-term antithrombotic therapy in PVD is associated with significant bleeding risk. The COMPASS trial showed that rivaroxaban plus aspirin reduced major cardiovascular events by 24% and all-cause mortality by 18%, but increased major bleeding by 70%. Second, many PVD patients remain asymptomatic until advanced stages, often requiring invasive interventions such as surgical revascularization. Third, residual thrombotic risk remains high despite treatment. The VOYAGER-PAD study reported nearly 20% incidence of cardiovascular death, MI, ischemic stroke, ALI, or major amputation over 3 years, with ALI occurring in 7.8% of aspirin-treated patients, while DVT recurrence in venous PVD can reach 25%.

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Coronary Artery Disease (CAD)

Overview of CAD

CAD, also known as coronary atherosclerotic heart disease or ischemic heart disease, is a broad therapeutic area encompassing a group of disorders affecting the heart and blood vessels. It is the most common organ-specific disease caused by atherosclerosis, with high morbidity and mortality rates, posing a significant threat to human health. CAD accounts for the most common cause of death. The typical risk factors for CAD include age, hypertension, smoking, obesity, physical inactivity, family history, and diabetes. These factors contribute to the development of atherosclerosis and increase the likelihood of plaque formation and thrombosis.

In CAD, cholesterol buildup causes atheroma formation, narrowing arteries and leading to myocardial ischemia, while plaque rupture triggers thrombosis, myocardial infarction, and ongoing thrombin generation, with angina occurring when oxygen demand exceeds coronary supply.

Treatment Paradigms for CAD

CAD treatment aims to reduce cardiovascular events and improve outcomes, including pharmacological therapy, interventional procedures, and surgery. Statins are the first-line lipid-lowering therapy, with additional agents such as evolocumab, ezetimibe, or fibrates used when further lipid control is needed. Antiplatelet therapy (e.g., aspirin and P2Y₁₂ inhibitors) is the cornerstone of thrombosis prevention. The COMPASS study showed that low-dose rivaroxaban plus aspirin reduces major cardiovascular events compared with aspirin alone, though with increased bleeding risk. PCI is commonly used for revascularization, while CABG remains the standard for complex disease. SRSD107 is intended to be used as first-line anticoagulant therapy in patients with chronic CAD.

Chronic Kidney Disease (CKD)

Overview of CKD

Chronic kidney disease is a progressive condition marked by impaired kidney function, primarily caused by diabetes and hypertension. Other factors include heart disease, glomerulonephritis, interstitial nephritis, and polycystic kidney disease. Risk factors for CKD include diabetes, hypertension, hyperuricemia, a family history of kidney disease, and advanced age. CKD patients often experience chronic inflammation and toxin accumulation, increasing the risk of thrombosis.

CKD is divided into five stages based on eGFR. Stages 3 and 4 affect about 25% of people, while stage 5 (ESRD) affects around 2%. The highest risks, including a greater chance of VTE, are seen in stages 3 and 4, where the relative risk of VTE is 1.71 times higher compared to mild CKD. Patients with moderate to severe CKD who develop VTE face nearly double the mortality rate compared to those with mild CKD. In ESRD, kidney function is nearly lost, and patients require renal replacement therapy, such as dialysis or a transplant. Around 40% of ESRD patients are treated with anticoagulants. The main challenges in CKD management include preventing progression to advanced stages and addressing complications like VTE.

Vascular Embolism Events in CKD Patients

Vascular events in CKD patients consist of two major types of thrombus, VTE and CKD-related ATE, each with distinct causes, pathogenesis, and clinical characteristics. The proportion of CKD patients with VTE is about 10.8%. CKD-related ATE (such as myocardial infarction and ischemic stroke) are mainly driven by platelet activation and atherosclerotic plaque rupture, rather than by activation of the coagulation cascade. Therefore, they are primarily managed with antiplatelet therapy. Routine systemic anticoagulation is not recommended, as it offers limited

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benefit in preventing arterial events in CKD patients. CKD also causes endothelial dysfunction and blood stasis, promoting clot formation. The risk of VTE in ESRD patients is 3.68 times higher than in those with normal renal function, and DVT risk is 13.92 times higher in ESRD patients.

Potential Addressable Market of FXI Drugs in CKD

The table below provides an overview of the potential addressable market of FXI drugs in CKD, including CKD prevalence, ESRD proportion and anticoagulant penetration. This patient subgroup represents the potential addressable market estimated at approximately 95.7 million in 2024 rising to 137.8 million in 2040, and includes both dialysis and nondialysis patients.

Chronic kidney disease (CKD)	
CKD Prevalence rate	~14% (US) / ~10% (CN)
Proportion of CKD patients are in Stage 3-5 (severe CKD)	~27%
Anticoagulant penetration	~ 40% of severe CKD patients are prescribed with anticoagulants

Source: Literature Review, Frost & Sullivan Analysis

Treatment Paradigms for CKD in AF Patients

The treatment paradigms for anticoagulation in AF patients with CKD vary by CKD stage. For Stage 1-3 (eGFR ≥ 30 ml/min/1.73m²), both warfarin and DOACs can be used, with a preference for DOACs. In Stage 4 (eGFR 15-29 ml/min/1.73m²), DOACs are preferred over warfarin, but direct thrombin or Factor Xa inhibitors may be used with dose reduction. In Stage 5 (eGFR < 15 ml/min/1.73m²), low-dose apixaban or warfarin is considered for high thromboembolic-risk patients, with close monitoring for potential complications. For Stage 5D (dialysis), routine anticoagulation is not recommended, but apixaban or dose-reduced rivaroxaban may be considered if necessary.

Patients with CKD face both high thrombotic and bleeding risks, creating a narrow therapeutic window for anticoagulation. Treatment options are limited: DOACs often require dose adjustment or are contraindicated in advanced CKD/ESRD, LMWHs may accumulate and require anti-Xa monitoring, and unfractionated heparin requires frequent monitoring, reducing convenience.

ATHEROSCLEROTIC CARDIOVASCULAR DISEASE (ASCVD) DRUG MARKET

Overview of Lp(a)

Lipoprotein(a) (Lp(a)) is a genetically determined protein that influences cholesterol levels. It consists of an LDL-like particle and apolipoprotein(a) (Apo(a)), which contribute to the development of atherosclerosis by promoting plaque formation and inflammation in blood vessels. Lp(a) also plays a role in aortic valve disease by encouraging calcification. Additionally, it impairs clot breakdown and increases platelet aggregation, raising the risk of thrombosis.

Association between Lp(a) and Cardiovascular Disease

Lp(a) and its individual components are associated with cardiovascular disease through multiple overlapping mechanisms. Several studies support these associations.

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Study	Study Size	Study Follow-up Period	Key Findings
Prevalence of Elevated Lipoprotein(a) and its Association With Subclinical Atherosclerosis in 2.9 Million Chinese Adults	2.9 Million Chinese Adults	no follow-up years were reported.	Compared with Lp(a)≤30 mg/dL, individuals with Lp(a) >30 to ~50 mg/dL exhibited 11%, 15%, 9%, and 11% greater odds of increased carotid intima-media thickness, carotid plaque, subclinical brain infarcts, and coronary artery calcification, respectively.
Lipoprotein(a) Is Markedly More Atherogenic Than LDL	502,000 UK residents of mainly European ancestry	12 years	Each unit increase in Lp(a) conferred approximately six times the cardiovascular risk per unit increase in LDL-C.
Lipoprotein(a) and recurrent atherosclerotic cardiovascular events: the US Family Heart Database	273,770 had diagnosed ASCVD	5.4 years	Compared to individuals with Lp(a) levels of 15 nmol/L, those with Lp(a) levels > 300 nmol/L were associated with a 44% increased risk of recurrent ASCVD events.

Source: Literature Review, Frost & Sullivan Analysis

Current Limitations in Lp(a) Management and ASCVD Treatment and Emerging Promise of siRNA Therapies

According to Frost & Sullivan, approximately 18–35% of the global population has elevated Lp(a), defined as levels above 75 nmol/L (or 30 mg/dL), a common and under-recognized cardiovascular risk factor. Unlike traditional risk factors such as LDL-C, Lp(a) levels are genetically determined, remain stable throughout life, and are minimally responsive to diet, exercise, or existing lipid-lowering therapies. Existing lipid-lowering therapies such as statins have no impact, and in some cases may increase Lp(a), while PCSK9 inhibitors lower Lp(a) by only 23-29%, an effect insufficient to fully address Lp(a)-mediated residual cardiovascular risk. As a result, high-Lp(a) patients continue to face elevated rates of ASCVD, ischemic stroke, calcific aortic valve disease, and other major adverse cardiovascular events, despite optimized LDL-C management.

Elevated Lp(a) has a relatively high prevalence in the general population. Approximately 18%-35% of the total population has elevated Lp(a) levels, defined as >30mg/dL (>75 nmol/L). A high-Lp(a) is a lifelong condition that cannot be modified by lifestyle changes such as exercise or diet.

There are no approved drugs for Lp(a) reduction. Current LDL-C therapies, such as statins, have minimal effect on Lp(a) levels and may even slightly increase them. PCSK9 inhibitors like evolocumab and alirocumab can reduce Lp(a) by 23%-29%, but this reduction is not enough to fully address Lp(a)-related cardiovascular risk, especially in patients with high baseline Lp(a). For example, the ODYSSEY OUTCOMES 2018 study (n=18,924) found a 23% reduction in Lp(a) with alirocumab, but only a 2.5% relative reduction in cardiovascular events. Early trials of RNA-based therapies have shown great promise, with siRNA therapies potentially reducing Lp(a) by over 90%. These treatments could become a more effective option for managing high Lp(a) levels, providing better efficacy, tolerability, and simpler regimens.

Competitive Landscape of siRNA Therapy Targeting Lp(a)

Drug	Company	Modality	Phase	First Post Date	Location
Olpasiran	Amgen/Arrowhead	siRNA	Phase III	2022-10	Global
Lepodisiran	Eli Lilly/Dicerna	siRNA	Phase III	2024-03	Global
SRSD216	Sirius Therapeutics	siRNA	Phase II	2025 Q4	China, US
Kylo-11	Kylonova	siRNA	Phase II	2025-10	China
SYH2068	CSPC	siRNA	Phase I	2025-06	China
YKYY032	Youcare	siRNA	Phase I	2025-12	China
BW-20829	Argo	siRNA	Phase II	2025-11	Global
RN5681	Rona	siRNA	Phase I	2026-01	Australia

Source: Clinical Trials, CDE, Frost & Sullivan Analysis

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OBESITY TREATMENT DRUG MARKET

Overview of Obesity

According to the World Health Organization, overweight is defined as $BMI \geq 25 \text{ kg/m}^2$ and obesity as $BMI \geq 30 \text{ kg/m}^2$. In China, the National Health Commission of the People’s Republic of China defines overweight as $24 \leq BMI < 28 \text{ kg/m}^2$ and obesity as $BMI \geq 28 \text{ kg/m}^2$.

Obesity treatment includes lifestyle intervention, pharmacotherapy, and surgery, with nutrition, exercise, and behavioral management forming the foundation for all patients.

Limitations of Clinical Obesity Drug Treatment

Obesity is a major unmet medical need. GLP-1 receptor agonists, proven effective for weight management, have quickly become top-selling drugs, with US\$8.4 billion in global sales since 2021. This success highlights the significant market potential for obesity treatments.

Current standard of care clinical obesity drug treatment, including GLP-1 treatment, has several drawbacks, such as high discontinuation rate and frequent side effects.

- **Adherence Challenges:** Obesity is a chronic metabolic disease requiring long-term management to prevent complications like diabetes and cardiovascular diseases. While GLP-1 medications are effective for weight loss, real-world studies show a 50.3% discontinuation rate in the first year, even at lower doses than in clinical trials. Patients often regain weight after stopping treatment, reducing long-term effectiveness.
- **GI Intolerance and Safety Considerations:** Common side effects of GLP-1 treatment include nausea (44.2%), diarrhea (31.5%), vomiting (24.8%), and constipation (23.4%).
- **Muscle Loss:** GLP-1-mediated weight loss reduces both fat and fat-free mass, including muscle. Up to 40% of the total weight loss can come from non-adipose tissues, highlighting the need for more selective therapies targeting fat tissue.

INHBE as A Promising Therapeutic Target

INHBE is a protein mainly produced in the liver that plays an important role in regulating metabolism. Higher INHBE levels can reduce fat utilization, while lower levels are associated with reduced fat mass and increased lean mass, suggesting a role in obesity-related metabolic disorders. Human genetic studies show that individuals with naturally lower INHBE activity have better lipid levels and lower risks of type 2 diabetes and cardiovascular disease, indicating that partially reducing INHBE may offer metabolic benefits.

Competitive Landscape of INHBE Targeted Oligonucleotide Drug

Candidate	Company	Indication	Phase	First Post Date	Location
ARO-INHBE	Arrowhead	Obesity	Phase I/IIa	2024-11	New Zealand
WVE-007	Wave	Overweight or Obesity	Phase I	2025-02	Moldova
BC006	BaseCure	Obesity	Phase II	2026-01	New Zealand
RN3161	Rona	Overweight or Obesity	Phase I/II	2025-11	Australia
SGB-7342	Sanogene	Obesity	Phase I	2025-12	China
LDR2515	Leaderna	Overweight or Obesity	Phase I	2026-02	China
CMS-D008	CMS	Obesity	Phase I	2026-03	China

Source: Clinical Trials, CDE, Frost & Sullivan Analysis

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SOURCE OF INFORMATION

We commissioned Frost & Sullivan to conduct an analysis of and to prepare a report on the major markets for which our drug candidates are positioned. We agreed to pay Frost & Sullivan a total fee of US\$86.7 thousand. Except as otherwise noted, all of the data and forecasts contained in this section are derived from the Frost & Sullivan Report. Frost & Sullivan’s services include industry consulting, commercial due diligence, strategic consulting, etc. Its consulting team has been tracking the latest market trends across various industries, where it has relevant and insightful market intelligence.

The Frost & Sullivan Report was compiled based on the following assumptions: (i) the overall social, economic and political environment globally and in China is expected to remain stable during the forecast period; (ii) the economic and industrial development globally and in China is likely to maintain a steady growth trend over the next decade; (iii) related key industry drivers are likely to continue driving the growth of the market during the forecast period; and (iv) there is no extreme force majeure or industry regulation in which the market may be affected dramatically or fundamentally.

In compiling and preparing the Frost & Sullivan Report, Frost & Sullivan used the following key methodologies to collect multiple sources, validate the data and information collected, and cross-check each respondent’s information and views against those of others: (i) secondary research, which involved reviewing published sources including national statistics, annual reports of listed companies, industry reports and data based on Frost & Sullivan’s own research database; and (ii) primary research, which involved in-depth interviews with the industry participants.

Frost & Sullivan’s projections are made based on various market determinants and their coefficients assigned to a market which indicate their relative importance. The market determinants represent both subjective assumptions and objective factors, therefore, the projected data may not be consistent with the real data.