Peptide Drugs and Oligonucleotide CRDMO Market Study

Independent Market Research Report

Confidential For

Medtide Inc.

Frost & Sullivan
June 2025

Date : June 20, 2025

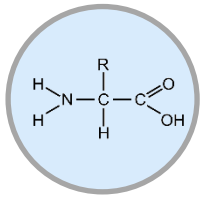
For and on behalf of
Frost & Sullivan (Beijing) Inc., Shanghai Branch Co.

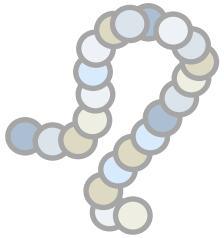
Name: Terry Tse
Title: Consulting Director

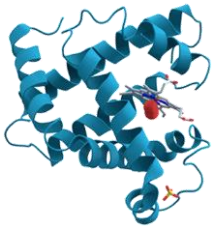
Table of Contents

Overview of Peptides

- **Peptides** are organic compounds composed of 2-99 natural amino acids (AA) in living organisms with a molecular weight (MW) of less than 10,000 Da. A compound composed of more than 99 amino acids will produce a protein.
- **Peptide drugs** are drugs that made up of peptides, which includes structure-modified peptides.
- **Synthetic conjugate drugs** include oligonucleotide conjugates, peptide-drug conjugates and etc.
- As intrinsic signaling molecules for many physiological functions, peptides present an opportunity for therapeutic intervention that closely mimics natural pathways. The utilization of peptides as therapeutics has evolved over time and continues to evolve with changes in drug development and treatment paradigms in recent years. Peptide therapeutics have played a notable role in medical practice since the advent of insulin therapy in the 1920s.





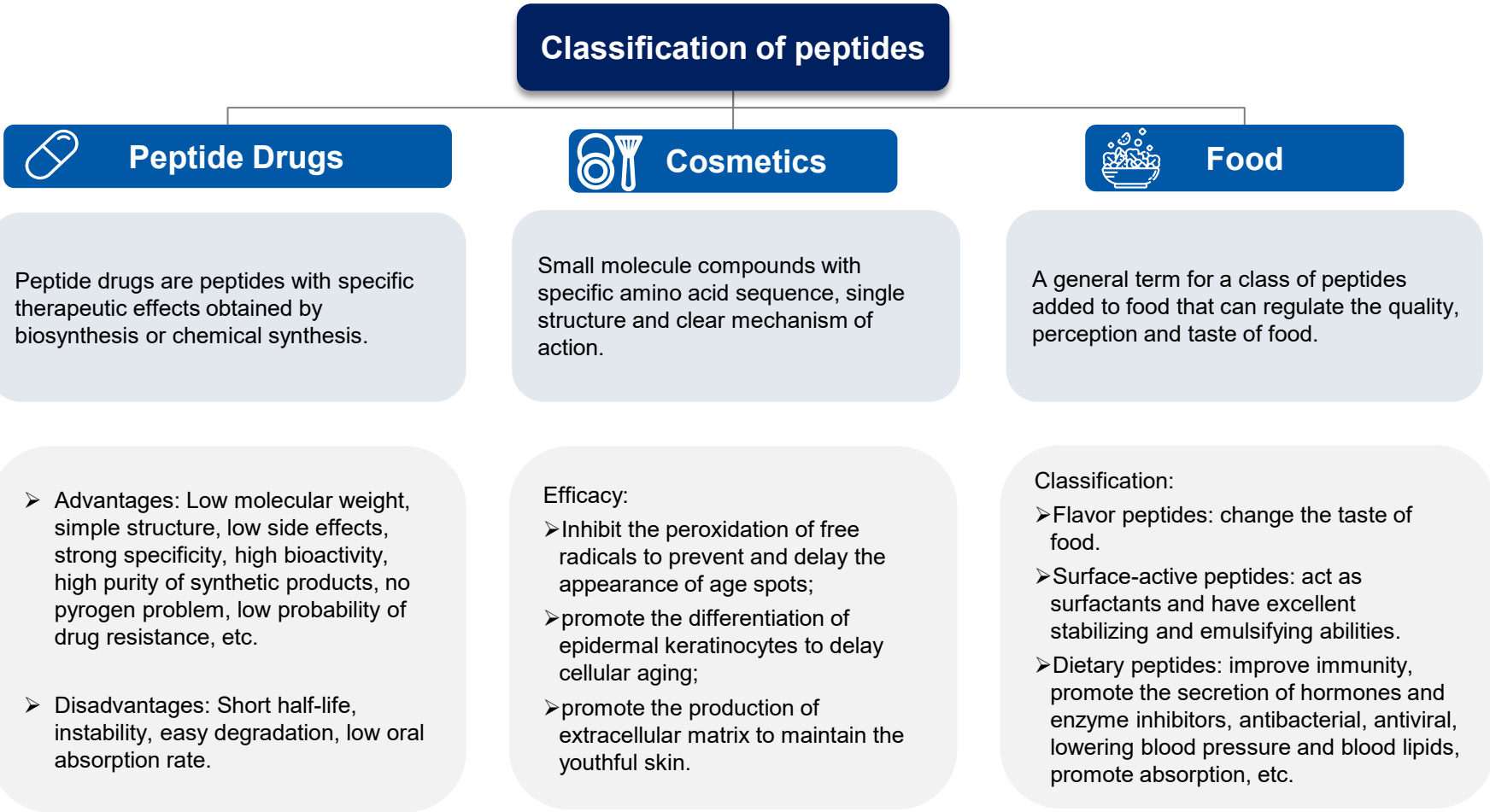


	Amino Acid	Peptide	Protein
AA #	1	2-99	>99
MW	~100 Da	<10,000 Da	>10,000 Da

Source: Frost & Sullivan Analysis, Literature researches

Application of Peptides

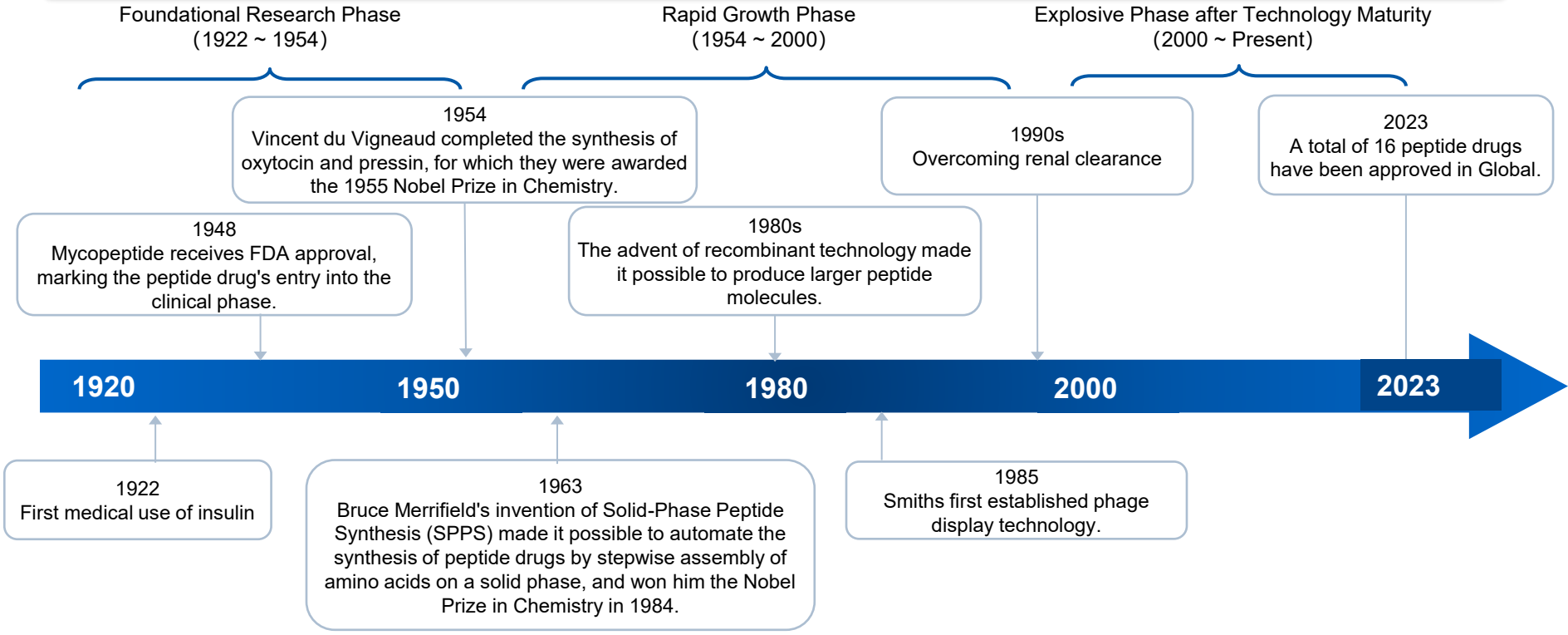
- According to their functions and application fields, peptides are mainly divided into peptide drugs, cosmetic peptides and food sensory peptides.



Source: Frost & Sullivan Analysis

Overview of Peptide Drug Development and Industry

- Exploration of peptide drugs can be traced back to the early 20th century. The invention of solid-phase peptide synthesis technology in the 1963 provided the possibility of industrialization of peptide synthesis. With the increasing maturity of synthesis and purification technologies, synthetic peptides began to be used in clinical applications after the 1970s.
- In recent years, however, the field has experienced significant growth and diversification. Researchers are now exploring peptide drugs for a wide array of medical conditions, including diabetes, cancer, heart failure, chronic kidney disease, and viral and bacterial infections. Notably, several peptide drugs, including Leuprorelin, Goserelin, Cetrorelix, Degarelix, and Octreotide, have proven effective in treating various types of cancer，highlighting their potential in offering targeted therapeutic options.
- In 2023 Global peptide drug market size reaches 89.5 billion USD. Novo Nordisk's Ozempic is approved in 2017 for the treatment of type 2 diabetes and is the top-selling peptide drug at $13.9 billion in 2023.



Source: Literature Review，Frost & Sullivan Analysis

Application of Peptides – Peptide Drugs

- Peptide drugs are mainly focusing on metabolic diseases and tumors.
- Peptide drugs have been expanded to multiple medical fields, including urinary system, respiratory system, orthopedic, digestive system, endocrine system, central nervous system, cardiovascular diseases, musculoskeletal system and connective tissue diseases, as well as the direction of antiviral and antibacterial, allergy and immunity, and acute critical care treatment.
- Peptides have been used in the production of vaccines and are seen as alternatives to conventional vaccines in an attempt to address the problem of possible side effects of vaccination with heterogeneous multicomponent preparations.
- Peptides are often excellent biomarkers and can therefore also be used for diagnostic purposes.

Metabolic diseases

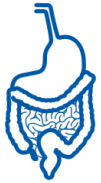
- Peptide drugs in the field of metabolic diseases are mainly for diabetes and obesity, mainly GLP-1 receptor agonists. There are also many new intestinal targeted peptide drugs in the research and development stage.
- Currently, GLP-1 receptor agonists such as exenatide (including microsphere preparations), Liraglutide, Beinaglutide, Dulaglutide, Albiglutide, Lixisenatide, Semaglutide (including oral preparations), polyethylene glycol Loexenatide and Ticalopatide, GIP/GLP-1 dual-target receptor agonist are available for sale worldwide.

Tumors

- The marketed peptide drugs in the field of oncology are mainly focused on gynecological tumors and prostate cancer, which have irreplaceable roles as hormone therapy and castration therapy. With the continuous deepening of research, there has been a significant breakthrough in the scope of indications of peptide drugs in the field of oncology.
- The marketed drugs include Leuprorelin, Goserelin, Cetrorelix, Degarelix, Octreotide, etc.

Source: Frost & Sullivan Analysis , Literature research

Application of Peptides – Peptide Drugs



Digestive system diseases

- Digestive system diseases mainly include somatostatin analogues and vasopressin analogues, with three main indications, including hemostasis in acute gastrointestinal bleeding, gastrointestinal neuroendocrine tumors and acromegaly.
- Main drugs include Somatostatin, Desmopressin, Octreotide, Terlipressin, Linaclotide, etc.

Cardiovascular diseases

- Mainly used in the rescue of cardiovascular diseases, including anticoagulants and acute heart failure drugs, the main products include Caperitide, Nesiritide, Eptifibatide, Bivalirudin, etc.

Rare diseases

- At present, the main varieties of peptide drugs in the treatment of rare diseases include Glatiramer for multiple sclerosis, Enfuvirtide for anti-AIDS treatment, Lanreotide for acromegaly and symptoms caused by neuroendocrine tumors (e.g., carcinoid syndrome), Icatibant for an hereditary angioedema (HAE), and Teduglutide for short bowel syndrome in adults.

Orthopedic Diseases

- Focusing on the treatment of osteoporosis and mainly facing postmenopausal women and elderly patients, the representative drugs include Salmon Calcitonin and Teriparatide.

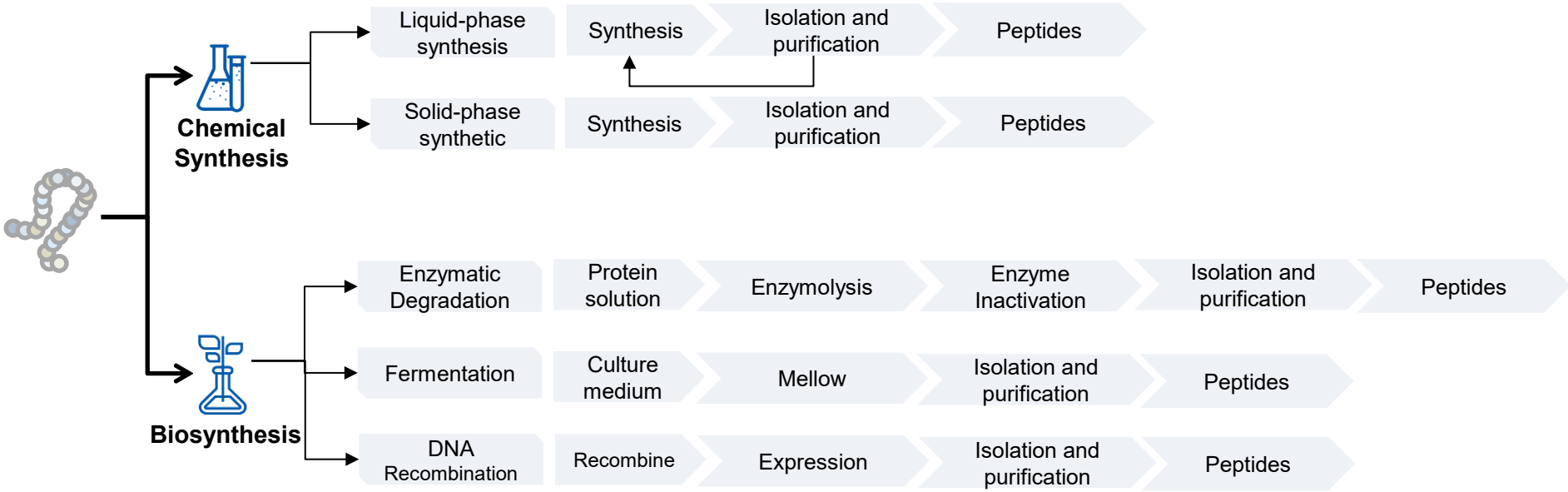
Immune Enhancement

- Peptide drugs in this field are commonly used to enhance immunity, which are common in China. The main varieties include thymopentin and Thymlfasin, which are used in the treatment or adjuvant treatment of tumors, infectious diseases, autoimmune diseases and other diseases.

Source: Frost & Sullivan Analysis , Literature research

Overview of Peptide Synthesis Techniques

- Peptide synthesis methods mainly include chemical synthesis and biosynthetic synthesis.
- Chemical synthesis refers to the targeted peptide obtained by the directed formation of amide bonds in accordance with a designed sequence of amino acids. Using chemical synthesis method, the structure of natural peptide can be modified, to increase the affinity and selectivity of the peptide to the receptor, enhance the resistance to enzymatic degradation or improve the pharmacokinetic properties, or even change from agonist to antagonist of the receptor.
- Biosynthesis is the hydrolysis of proteins in raw materials using enzymes or fermentation to produce biologically active peptides. Enzymatic digestion utilizes biological enzymes to degrade proteins into peptides and is the most common method to produce active peptides. Fermentation method is the use of microbial metabolic fermentation to produce peptides, which is low cost but difficult to isolate and purify.
- DNA recombination uses gene technology to transfer gene fragments into prokaryotic or eukaryotic cells for recombinant expression, and fermentation production to synthesize the required peptides.



Source: Frost & Sullivan Analysis, Literature research

Comparative Analysis of Oral and Injection Formulation

- Oral formulations require more APIs as compared to injection. In the future, more peptides are likely to be modified into oral formulations and hence there is a trend of gradual rise in the demand for APIs.

	Rybelsus	Ozempic
Product	Semaglutide	Semaglutide
Delivery mode	Oral	Injection
Indication	Type 2 diabetes mellitus	Type 2 diabetes mellitus / cardiovascular disease
Time	Once daily	Once weekly
Dosage	3mg/7mg/14mg	0.25mg/0.5mg/1mg/2mg

Source: Frost & Sullivan Analysis, FDA

Comparative Analysis of Main Peptide Synthesis Methods

- Chemical synthesis is preferred choice for the industrial preparation of peptides because versatile synthetic building blocks beyond the proteinogenic amino acids can be introduced and the process can be fully automated and easily scaled up. DNA recombination offers a flexible approach to producing long peptides. Enzymatic synthesis is suitable for short peptides. Fermentation has been well proven to be an environmentally friendly method for the production of bioactive peptides.

	Solid Phase Synthesis	Liquid Phase Synthesis	DNA Recombination	Enzymatic Degradation	Natural Extraction
Production Scale	Milligrams to kilograms	Grams to tons	Gram to kilogram	Gram to Ton	Gram to ton
Peptide length	Medium and long peptides	Short and medium peptides	Long peptides	Short Peptides	Long peptides
Reaction conditions	Mildness	Harsh	Mildness	Mildness	Mildness
Operating Difficulty	Easy	Difficult	Difficult	Simple	Simple
Non-natural amino acid modification	Easy	Easy	Difficult	Difficult	NA
Product purity	High	High	High	Medium	Low
Yield	High(Decreased yield of synthesized long peptides)	High	High	Low	Low
Time Consumption	Short(Long time consuming to synthesize long peptides)	Long	Long	Long	Low
Production cost	High	Medium	Low	Low	Low
R&D investment	Medium	Medium	High	Medium	Low

Source: Frost & Sullivan Analysis, Literature research

Comparative Analysis of Main Peptide Synthesis Methods

	Advantages	Challenges
Liquid-Phase Peptide Synthesis	• Low cost, multiple choices of protecting groups, easy scale-up of synthesis, purification of intermediates at each step, access to the physicochemical constants of intermediates, the possibility of non-amino-acid modifications, and the avoidance of amino acid deletions, which makes it suitable for the synthesis of short peptides.	• LPPS needs to be separated and purified after each step of the reaction, so when synthesizing long peptides, it has the disadvantages of low yield, cumbersome process, time-consuming and laborious
Solid-Phase Peptide Synthesis	• It simplifies the post-processing operation of each step of the reaction, avoids the loss due to manual operation and material transfer, and realizes higher yield and automation, etc.	• SPPS has the issues that the intermediate product of each step cannot be purified, a larger excess of amino acid must be used, the purity of the crude product is not as good as that of liquid-phase synthesized products, and it must be purified by reliable means of separation.
Enzymatic Degradation	• Controllability and reproducibility of the process and results; mild and safe conditions for enzymatic digestion of proteins; no side reactions and no reduction in the nutritional value of proteins; wide availability of raw materials and high yield of peptides.	• The introduction of inorganic salts in the process of adjusting the pH of hydrolysis, which increases the difficulty of separation and purification, and therefore is not suitable for obtaining pure peptides • Due to the strong specificity of the enzyme, the protease of the specific enzymatic site needs to carry out a variety of enzyme screening, which increases the difficulty of the application of this method, limiting the scope of its application.
Fermentation	• Eliminate the need for processes such as separation and purification, and the production of peptides by the fermentation method does not produce bitter peptides composed of a large number of hydrophobic amino acids.	• Fermentation method is difficult and requires a large investment of time and cost.
DNA Recombination	• With strong expression orientation and low production cost, peptide drugs with high quality, good efficacy and activity comparable to natural peptides can be obtained.	• DNA recombination method has a long and difficult development cycle, and the extraction and purification technology requires high requirements, usually 12 to 18 months.

Source: Frost & Sullivan Analysis, Literature research

Comparative Analysis of Chemical Drugs, Biologics and Peptide Drugs

- Peptide drugs represent a unique class of pharmaceutical compounds, molecularly poised between small molecules and proteins, yet biochemically and therapeutically distinct from both. Peptide drugs offer some benefits not typically found in their larger or smaller siblings (proteins and small molecules). For example, they are highly-specific, and offer improved toxicological profiles.
- Compare to small molecule drugs and antibodies, Peptide drugs demonstrate some unique benefits. It has higher activity and stronger selectivity than small molecule drugs, and better stability and lower immunogenicity than antibodies.

Comparative Analysis of Chemical Drugs, Biologics and Peptide Drugs

Influence Level: High Mid Low

	Stability	Side Effects	Half-life	Tolerance	Immuno -genicity	Specificity	Bioactivity	R&D Costs
Chemical Drugs	High	High	High	Low	Low	Low	Low	Low
Peptides	Mid	Low	Low	High	Mid	High	High	Mid
Biologics	Low	Low	Low	High	High	High	High	High

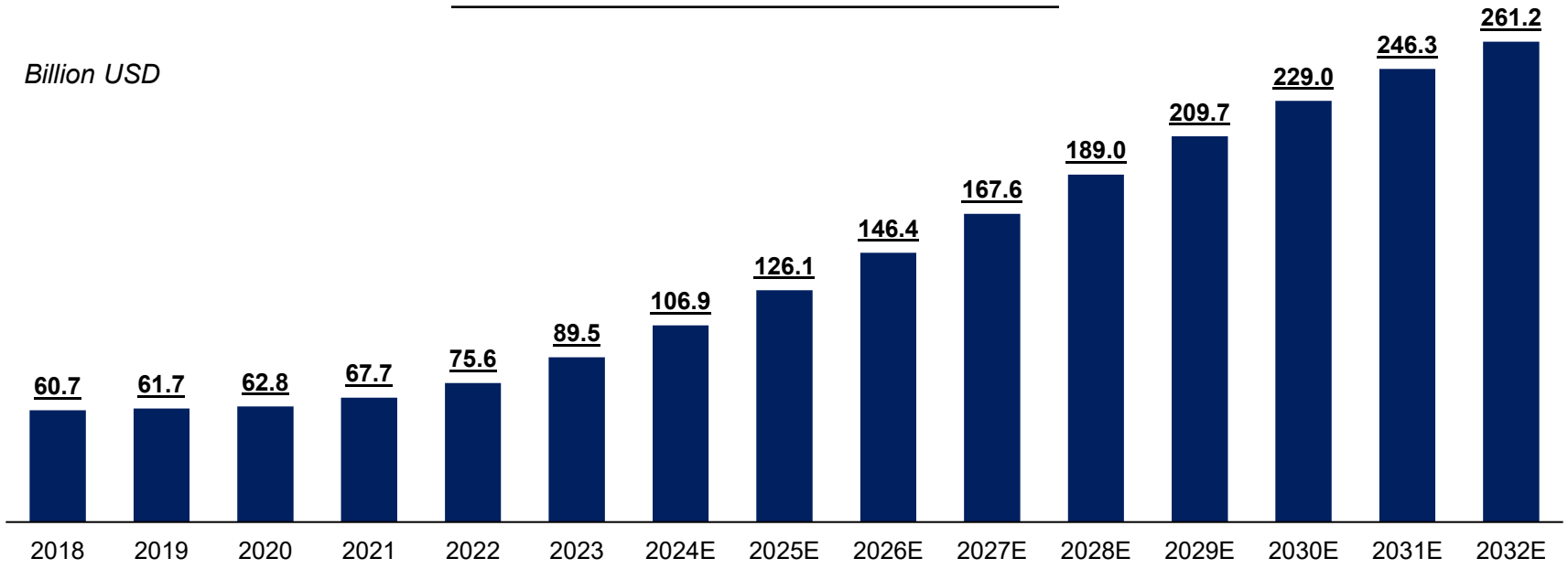
Source: Frost & Sullivan Analysis, Literature research

Global Peptide Drug Market Size, 2018-2032E

- Global peptide drug market size continues to grow, rising from 60.7 billion USD in 2018 to 89.5 billion USD in 2023.The global peptide drug market size is expected to grow at a CAGR of 12.6% between 2023 and 2032, increasing to 261.2 billion USD in 2032.

Global Peptide Drug Market Size, 2018-2032E

	CAGR
2018-2023	8.1%
2023-2032E	12.6%



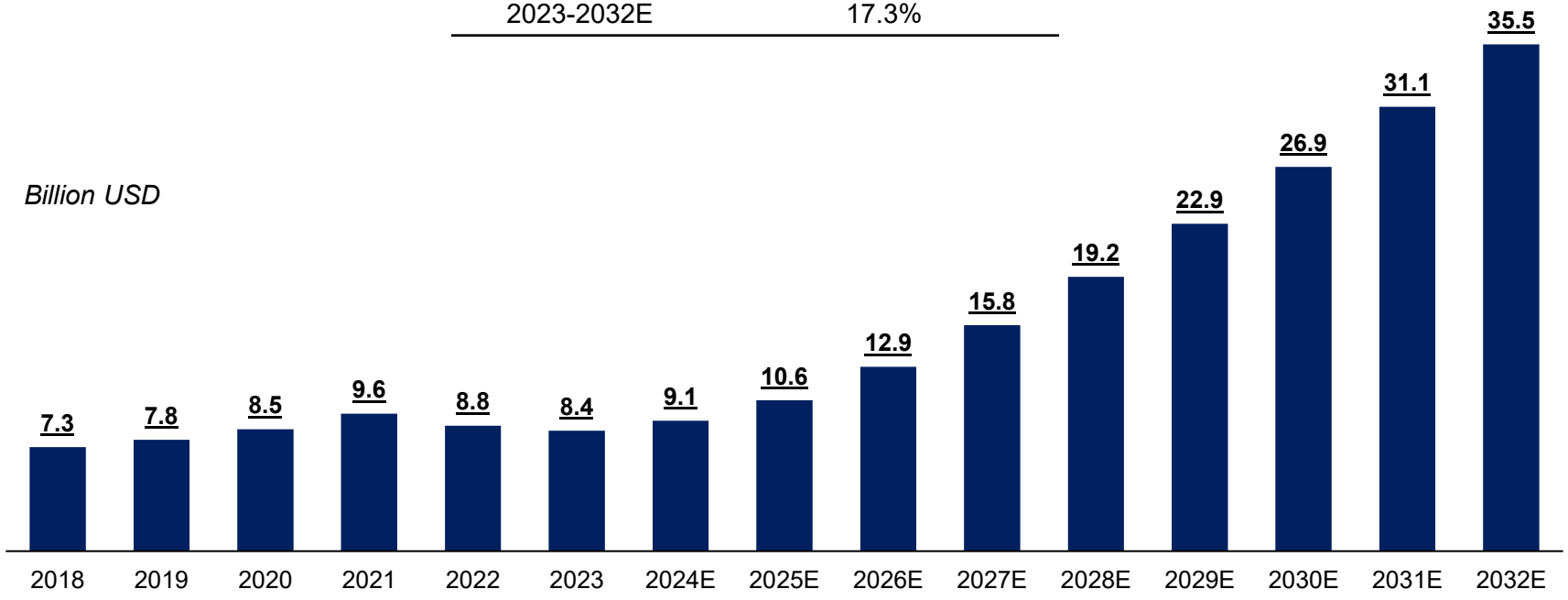
Source: NMPA, FDA, Annual Report, Frost & Sullivan Analysis

China Peptide Drug Market Size, 2018-2032E

- China peptide drug market size grew from 7.3 billion USD in 2018 to 8.4 billion USD in 2023, and it is expected to grow at a CAGR of 17.3% between 2023 and 2032, reaching 35.5 billion USD in 2032.

China Peptide Drug Market Size, 2018-2032E

	CAGR
2018-2023	3.0%
2023-2032E	17.3%



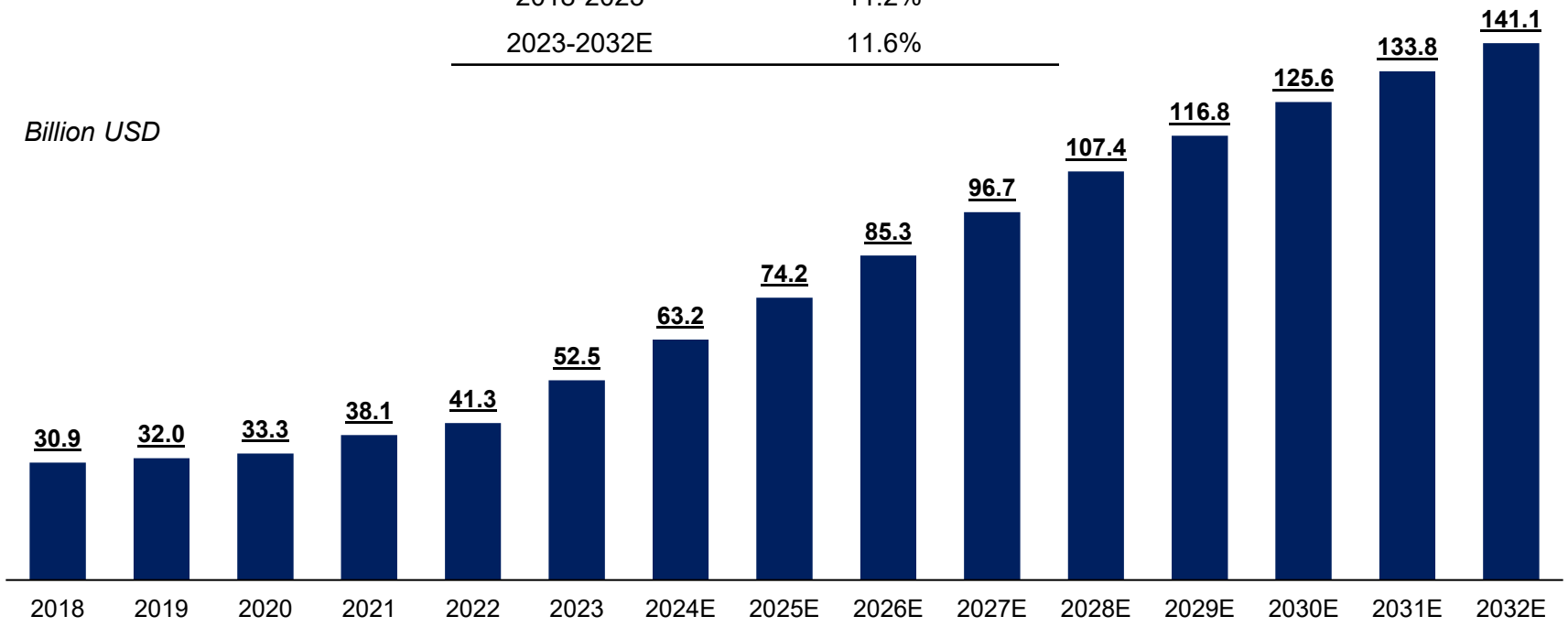
Source: NMPA, Annual Report, Frost & Sullivan Analysis

US Peptide Drug Market Size, 2018-2032E

- The U.S. peptide drug market size continues to grow, rising from 30.9 billion USD in 2018 to 52.5 billion USD in 2023.The U.S. peptide drug market size is expected to grow at a CAGR of 11.6% between 2023 and 2032, increasing to 141.1 billion USD in 2032.

The U.S. Peptide Drug Market Size, 2018-2032E

	CAGR
2018-2023	11.2%
2023-2032E	11.6%



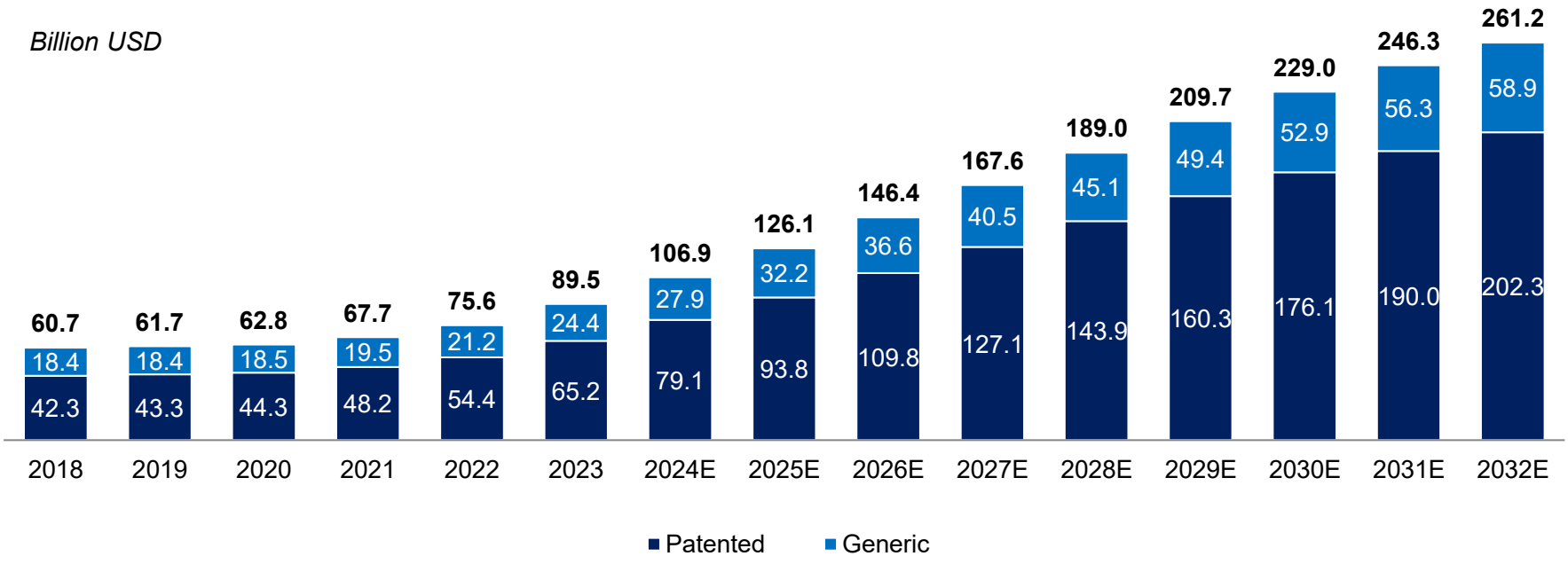
Source: FDA, Annual Report, Frost & Sullivan Analysis

Breakdown of Global Peptide Drug Market by Patented Drugs and Generic Drugs, 2018-2032E

- Global patented drug market grew from 42.3 billion USD in 2018 to 65.2 billion USD in 2023, and size is expected to grow at a CAGR of 13.4% between 2023 and 2032, reaching 202.3 billion USD in 2032.
- Global generic drug market increased from 18.4 billion USD in 2018 to 24.4 billion USD in 2023. Global generic drug market size is projected to show an increasing trend and reach 58.9 Billion USD in 2032.

Breakdown of Global Peptide Drug Market by Patented Drugs and Generic Drugs, 2018-2032E

CAGR	Patented Drug	Generic Drug	Total
2018-2023	9.0%	5.8%	8.1%
2023-2032E	13.4%	10.3%	12.6%



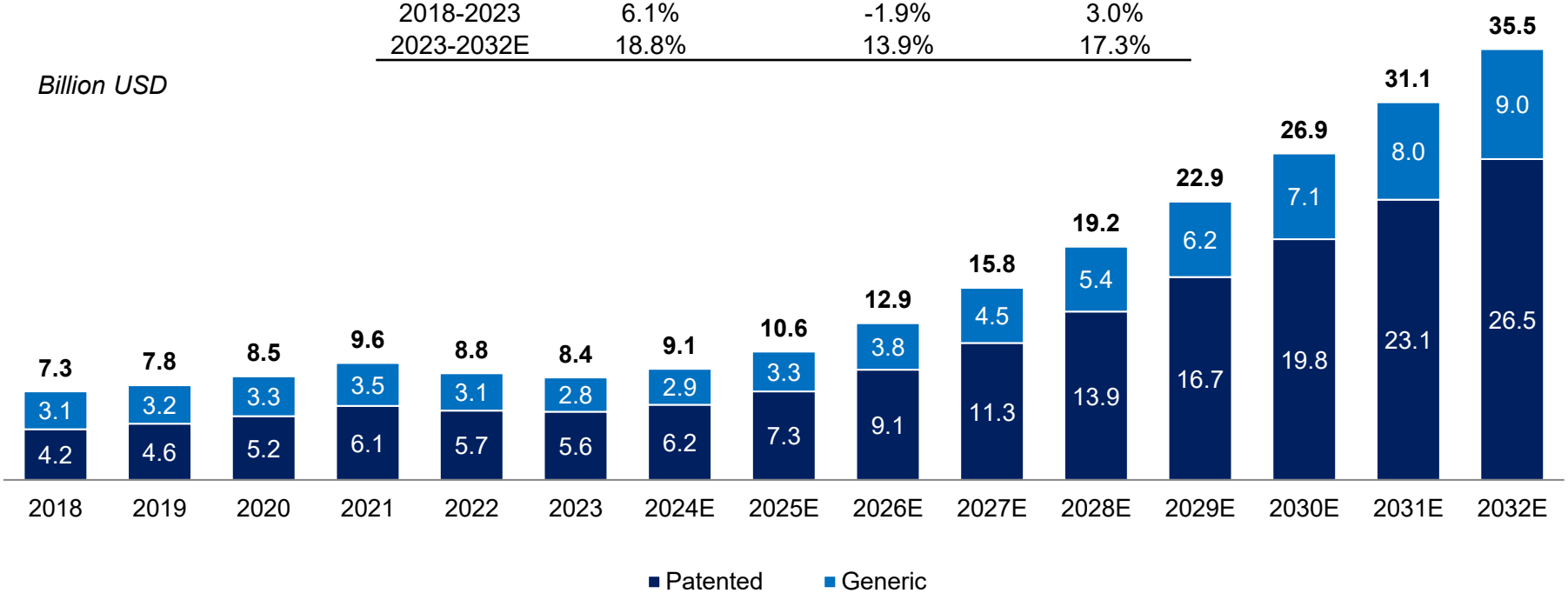
Source: NMPA, FDA, Annual Report, Frost & Sullivan Analysis

Breakdown of China Peptide Drug Market by Patented Drugs and Generic Drugs, 2018-2032E

- China patented drug market grew from 4.2 billion USD in 2018 to 5.6 billion USD in 2023, and size is expected to grow at a CAGR of 18.8% between 2023 and 2032, reaching 26.5 billion USD in 2032.
- China generic drug market decreased from 3.1 billion USD in 2018 to 2.8 billion USD in 2023. China generic drug market size is expected to grow at a CAGR of 13.9% between 2023 and 2032, reaching 9.0 billion USD in 2032.

Breakdown of China Peptide Drug Market by Patented Drugs and Generic Drugs, 2018-2032E

CAGR	Patented Drug	Generic Drug	Total
2018-2023	6.1%	-1.9%	3.0%
2023-2032E	18.8%	13.9%	17.3%



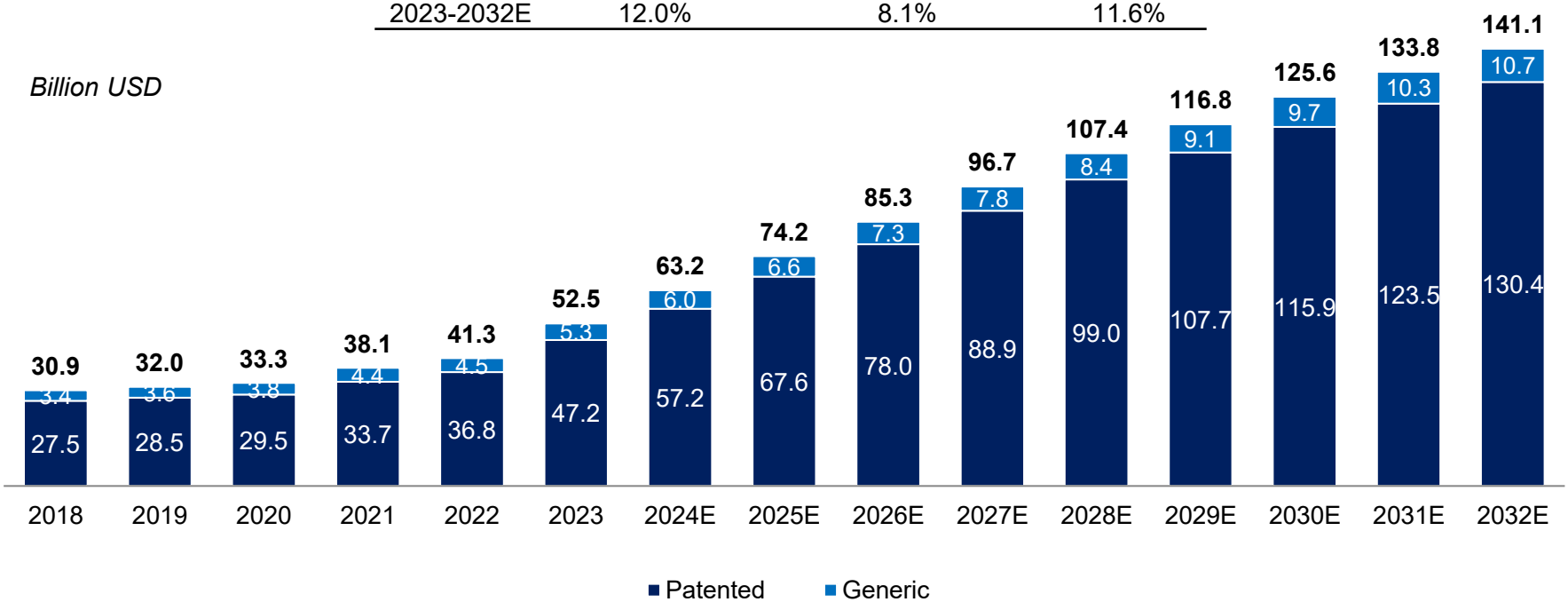
Source: NMPA, Annual Report, Frost & Sullivan Analysis

Breakdown of US Peptide Drug Market by Patented Drugs and Generic Drugs, 2018-2032E

- The U.S. patented drug market grew from 27.5 billion USD in 2018 to 47.2 billion USD in 2023, and size is expected to grow at a CAGR of 12.0% between 2023 and 2032, reaching 130.4 billion USD in 2032.
- The U.S. generic drug market increased from 3.4 billion USD in 2018 to 5.3 billion USD in 2023 and is projected to show an increasing trend, reaching 10.7 Billion USD in 2032.

Breakdown of US Peptide Drug Market by Patented Drugs and Generic Drugs, 2018-2032E

CAGR	Patented Drug	Generic Drug	Total
2018-2023	11.4%	9.5%	11.2%
2023-2032E	12.0%	8.1%	11.6%



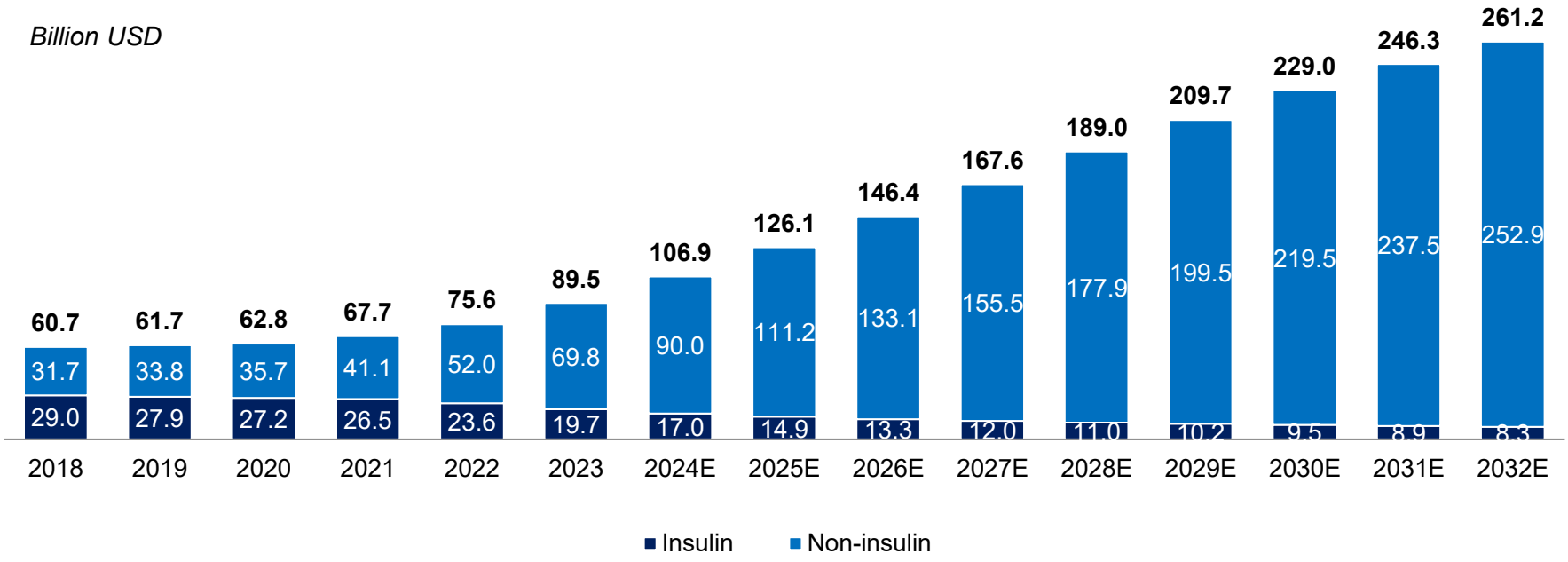
Source: FDA, Annual Report, Frost & Sullivan Analysis

Breakdown of Global Peptide Drug Market by Insulin Drugs and Non-insulin Drugs, 2018-2032E

- The global insulin drug market size is on a declining trend from 29.0 billion USD in 2018 to 19.7 billion USD in 2023.
- Global non-insulin drug market size continues to grow, rising from 31.7 billion USD in 2018 to 69.8 billion USD in 2023.The global non-insulin drug market size is expected to grow at a CAGR of 15.4% between 2023 and 2032, reaching 252.9 billion USD in 2032.

Breakdown of Global Peptide Drug Market by Insulin and Non-insulin, 2018-2032E

CAGR	Insulin Drug	Non-insulin Drug	Total
2018-2023	-7.4%	17.1%	8.1%
2023-2032E	-9.2%	15.4%	12.6%



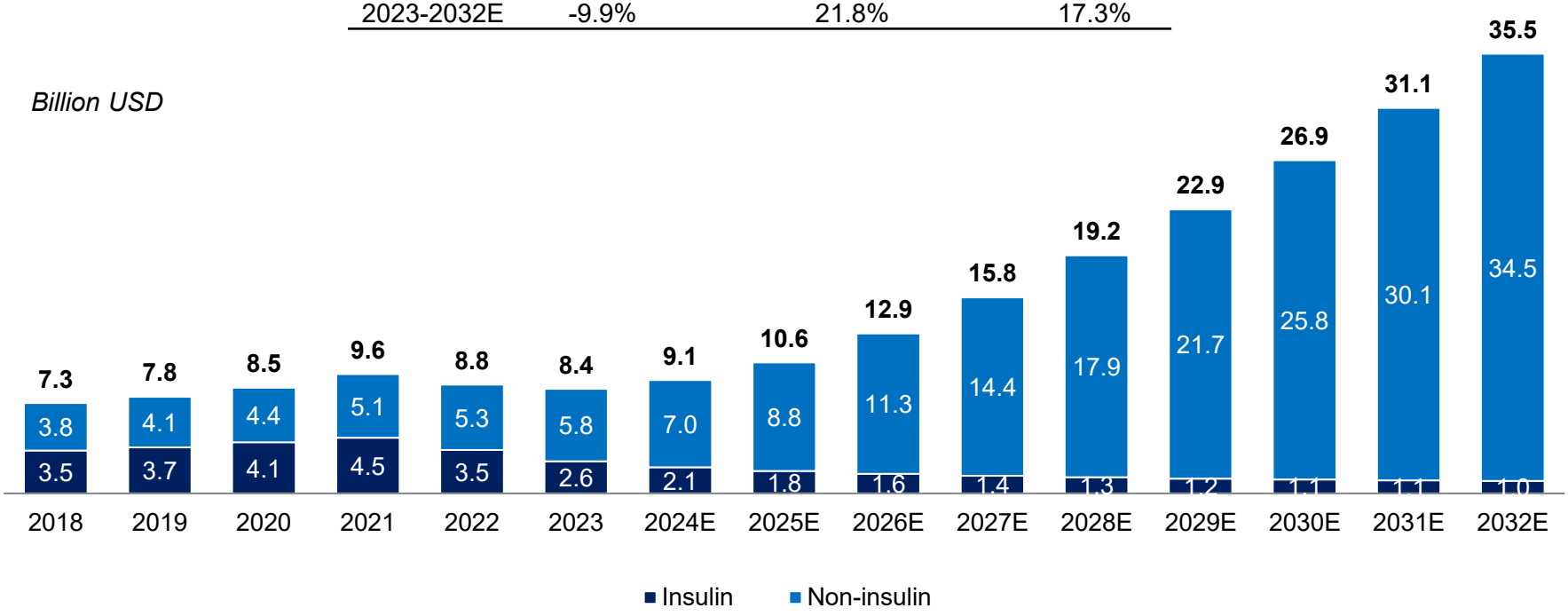
Source: NMPA, FDA, Annual Report, Frost & Sullivan Analysis

Breakdown of China Peptide Drug Market by Insulin Drugs and Non-insulin Drugs, 2018-2032E

- China insulin drug market size is on a declining trend from 3.5 billion USD in 2018 to 2.6 billion USD in 2023.
- China non-insulin drug market size continues to grow, rising from 3.8 billion USD in 2018 to 5.8 billion USD in 2023. China non-insulin drug market size is expected to grow at a CAGR of 21.8% between 2023 and 2032, reaching 34.5 billion USD in 2032.

Breakdown of China Peptide Drug Market by Insulin Drugs and Non-insulin Drugs, 2018-2032E

CAGR	Insulin Drug	Non-insulin Drug	Total
2018-2023	-5.7%	8.9%	3.0%
2023-2032E	-9.9%	21.8%	17.3%



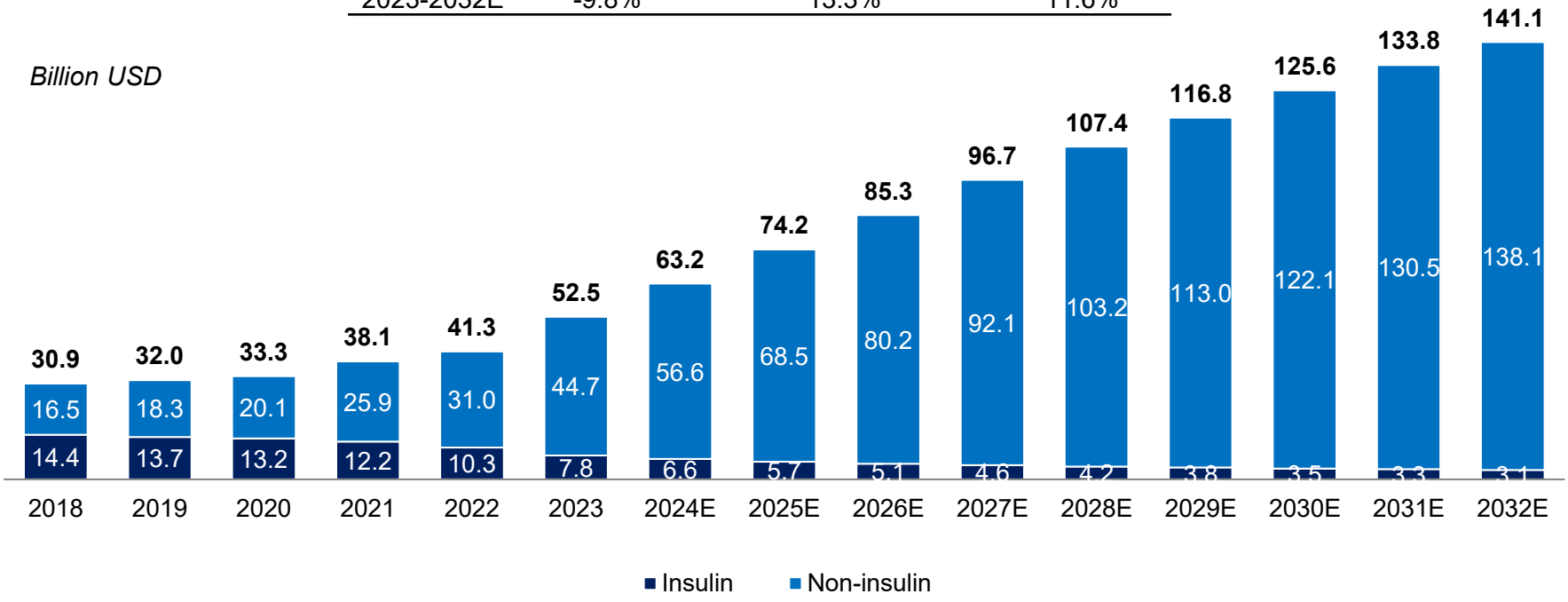
Source: NMPA, Annual Report, Frost & Sullivan Analysis

Breakdown of US Peptide Drug Market by Insulin Drugs and Non-insulin Drugs, 2018-2032E

- The U.S. insulin drug market size is on a declining trend from 14.4 billion USD in 2018 to 7.8 billion USD in 2023.
- The U.S. non-insulin drug market size continues to grow, rising from 16.5 billion USD in 2018 to 44.7 billion USD in 2023.The U.S. non-insulin drug market size is expected to grow at a CAGR of 13.3% between 2023 and 2032, reaching 138.1 billion USD in 2032.

Breakdown of US Peptide Drug Market by Insulin and Non-insulin, 2018-2032E

CAGR	Insulin Drug	Non-insulin Drug	Total
2018-2023	-11.7%	22.1%	11.2%
2023-2032E	-9.8%	13.3%	11.6%



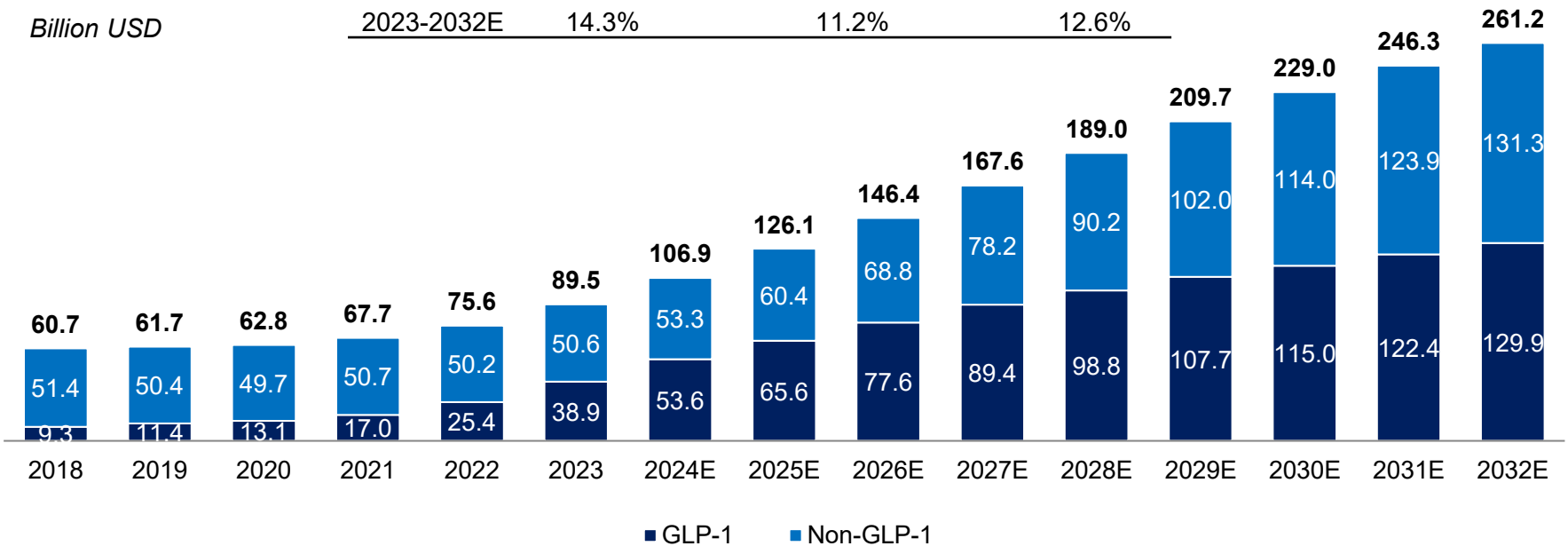
Source: FDA, Annual Report, Frost & Sullivan Analysis

Breakdown of Global Peptide Drug Market by GLP-1 and Non-GLP-1, 2018-2032E

- One particular type of peptide drug product, namely the GLP-1 agonist, has become the major driver for the rapid growth of the global peptide drug market. The number of GLP-1 drugs that had obtained regulatory approvals reached 12 between January 1, 2015 and the Latest Practicable Date.
- Global GLP-1 drug market grew at a CAGR of 33.2% from 9.3 billion USD in 2018 to 38.9 billion USD in 2023, and is expected to increase to 129.9 billion USD in 2032. GLP-1 drug products accounted for a market share of 43.5% in 2023 within the global peptide drug market in terms of sales revenue, which is expected to further grow to 49.7% in 2032
- Global Non-GLP-1 drug market size slightly decreased from 2018 to 2023 and was 50.6 Billion USD in 2023. Global non-GLP-1 drug market size is projected to show an increasing trend and reach 131.3 Billion USD in 2032.

Breakdown of Global Peptide Drug Market by GLP-1 and Non-GLP-1, 2018-2032E

CAGR	GLP-1 Drug	Non-GLP-1 Drug	Total
2018-2023	33.2%	-0.3%	8.1%
2023-2032E	14.3%	11.2%	12.6%



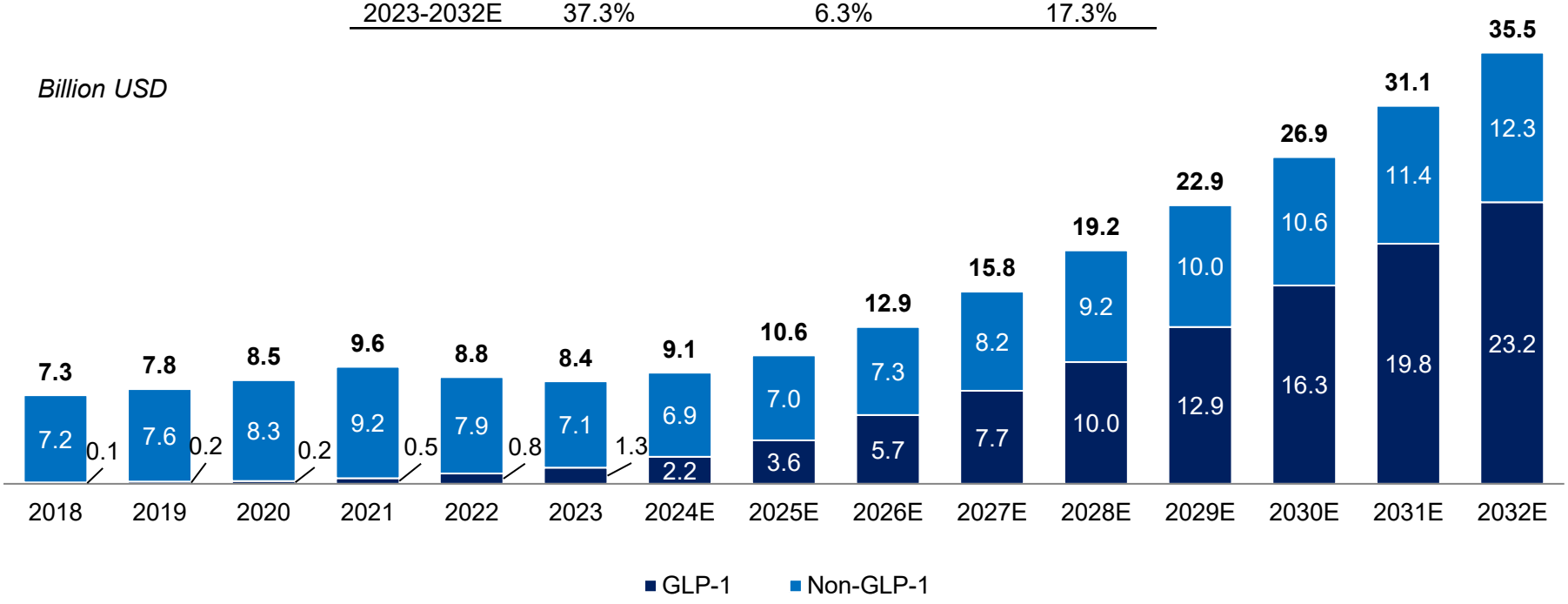
Source: NMPA, FDA, Annual Report, Frost & Sullivan Analysis

Breakdown of China Peptide Drug Market by GLP-1 and non GLP-1, 2018-2032E

- China GLP-1 drug market size continues to grow, rising from 0.1 billion USD in 2018 to 1.3 billion USD in 2023. China GLP-1 drug market size is expected to grow at a CAGR of 37.3% between 2023 and 2032, reaching 23.2 billion USD in 2032.
- China Non-GLP-1 drug market size decreased from 7.2 billion USD in 2018 to 7.1 billion USD in 2023. China non-GLP-1 drug market size will increase to 12.3 billion USD in 2032.

Breakdown of China Peptide Drug Market by GLP-1 and Non-GLP-1, 2018-2032E

CAGR	GLP-1 Drug	Non-GLP-1 Drug	Total
2018-2023	65.3%	-0.2%	3.0%
2023-2032E	37.3%	6.3%	17.3%



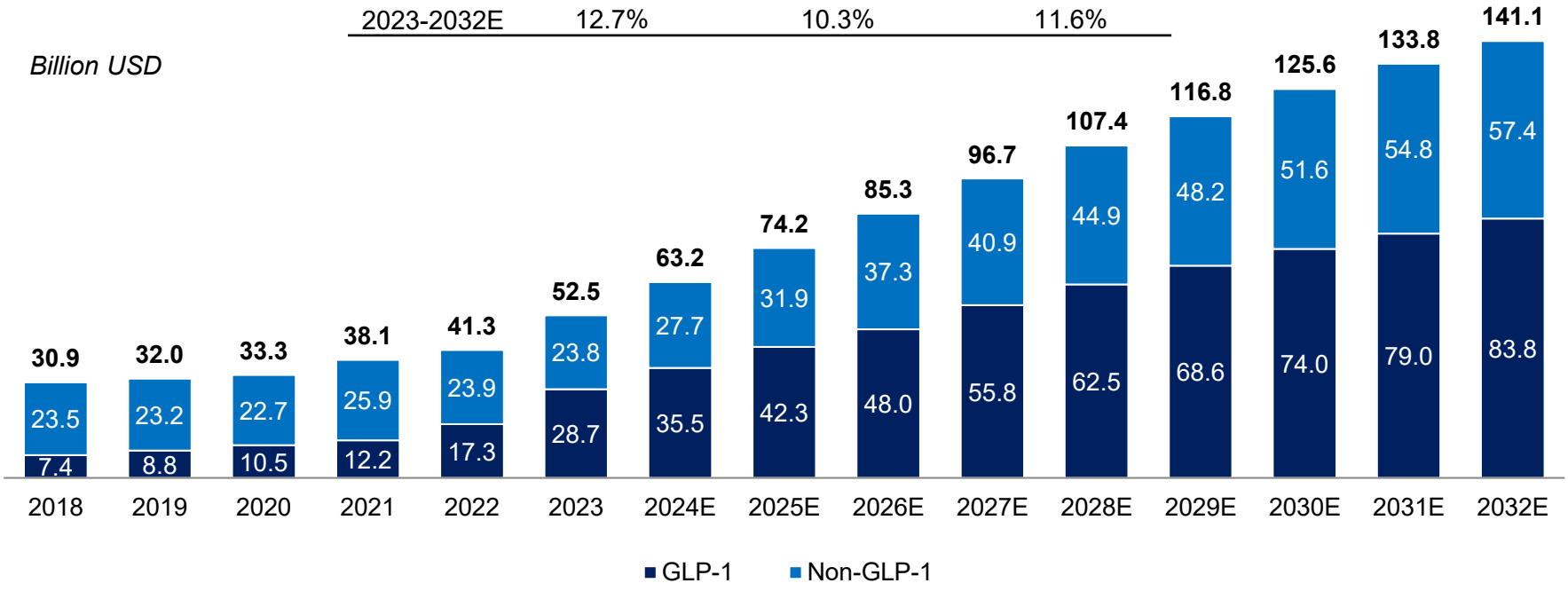
Source: NMPA, Annual Report, Frost & Sullivan Analysis

Breakdown of US Peptide Drug Market by GLP-1 and Non-GLP-1, 2018-2032E

- The U.S. GLP-1 drug market grew at a CAGR of 31.2% from 7.4 billion USD in 2018 to 28.7 billion USD in 2023, and is expected to increase to 83.9 billion USD in 2032.
- The U.S. Non-GLP-1 drug market size remained stable from 2018 to 2023 and was 23.8 Billion USD in 2023. The U.S. non-GLP-1 drug market size is projected to show an increasing trend and reach 57.4 Billion USD in 2032.

Breakdown of US Peptide Drug Market by GLP-1 and Non-GLP-1, 2018-2032E

CAGR	GLP-1 Drug	Non-GLP-1 Drug	Total
2018-2023	31.2%	0.3%	11.2%
2023-2032E	12.7%	10.3%	11.6%

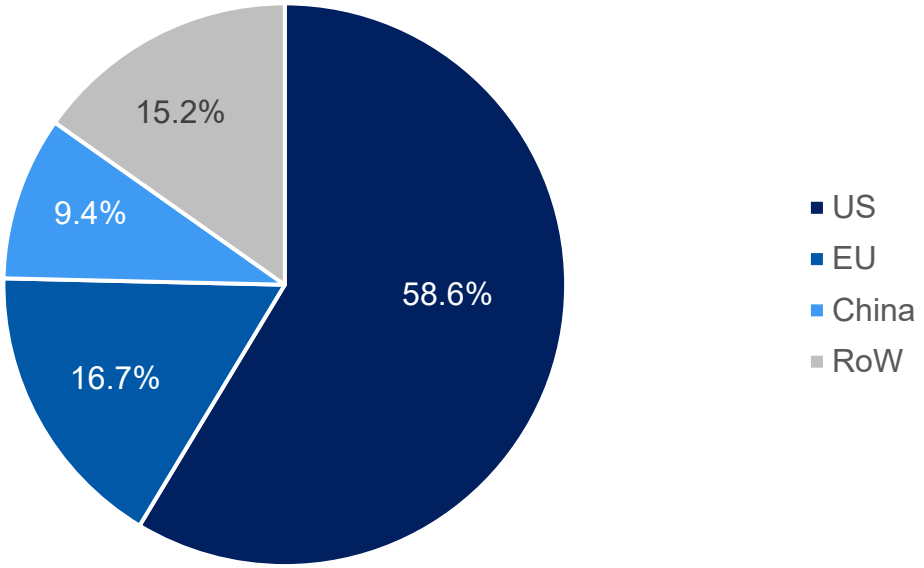


Source: FDA, Annual Report, Frost & Sullivan Analysis

Breakdown of Global Peptide Drug Market by Region, 2023

- In 2023, the global peptide drug market size reaches 89.5 billion USD, of which the U.S. peptide drugs market reaches 52.5 billion USD, accounting for 58.6%. China peptide drug market size is 8.4 billion USD, accounting for 9.4% of the global market.

Breakdown of Global Peptide Drugs Market US, EU, China, and Row, 2023



Source: NMPA, FDA, EMA, Annual Report, Frost & Sullivan Analysis

Global Top 10 Non-insulin Peptide Drugs in Terms of Sales Revenue, 2023

INN Name	Total Sales Revenue (Million USD)	Brand Name (FDA Approval)	Company	Sales Revenue (*Million USD*)	Major Indication	Therapeutic Area
Semaglutide	21,162.1	Ozempic (2017)	Novo Nordisk	13891.9	Type 2 Diabetes Mellitus	Metabolism
		Wegovy (2021)	Novo Nordisk	4548.9	Obesity/Overweight	Metabolism
		Rybelsus (2019)	Novo Nordisk	2721.3	Type 2 Diabetes Mellitus	Metabolism
Dulaglutide	7132.6	Trulicity (2014)	Eli Lilly	7132.6	Type 2 Diabetes Mellitus	Metabolism
Tirzepatide	5,338.9	Mounjaro (2022)	Eli Lilly	5163.1	Type 2 Diabetes Mellitus	Metabolism
		Zepbound (2023)	Eli Lilly	175.8	Obesity/Overweight	Metabolism
Liraglutide	2,750.7	Saxenda (2014)	Novo Nordisk	1493.3	Obesity/Overweight	Metabolism
		Victoza (2010)	Novo Nordisk	1257.4	Type 2 Diabetes Mellitus	Metabolism
Carfilzomib	1403.0	Kyprolis (2012)	Amgen	1403.0	Multiple Myeloma	Oncology
Octreotide	1314.0	Sandostatin (1988)	Novartis	1314.0	Carcinoid Tumors and Acromegaly	Oncology

Note: 1. Calculate at the exchange rate of 1 USD=6.8902 DKK, 1 USD=0.9242EURO, and 1 USD=140.5107 JPY.

Source: Frost & Sullivan Analysis, Annual Report

Global Top 10 Non-insulin Peptide Drugs in Terms of Sales Revenue, 2023

INN Name	Total Sales Revenue (Million USD)	Brand Name (FDA Approval)	Company	Sales Revenue (*Million USD*)	Major Indication	Therapeutic Area
Linaclotide	1,154.3	Linzess/Constella (2012)	Abbvie	1108.0	Constipation	Digestive system
		Linzess (2012)	Astellas	46.3	Constipation	Digestive system
Lanreotide	1153.0	Somatuline (2007)	Ipsen	1153.0	GEP-NETs; Carcinoid Syndrome	Oncology
Goserelin	952.0	Zoladex (1989)	AstraZeneca	952.0	Prostate Cancer; Breast Cancer; Endometriosis	Oncology; Reproductive System
Leuprorelin	753.0	Leuplin/Enantone (1989)	Takeda	753.0	Prostate Cancer, Breast Cancer, Central Precocious Puberty	Oncology; Endocrine

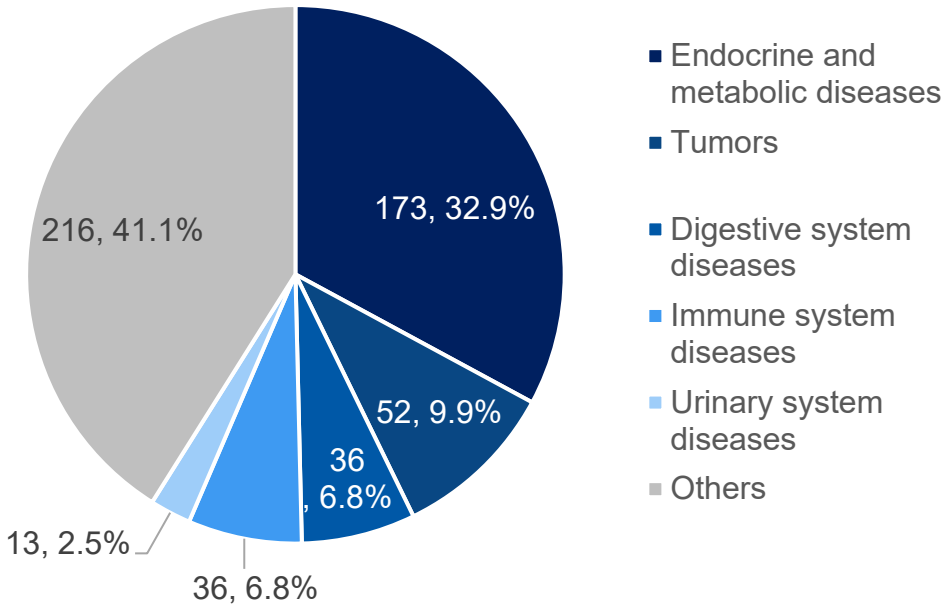
Note: 1. Calculate at the exchange rate of 1 USD=6.8902 DKK, 1 USD=0.9242EURO, and 1 USD=140.5107 JPY.

Source: Frost & Sullivan Analysis, Annual Report

Distribution of Phase 2 and beyond Clinical Trials by Disease Area, 2015-2024

- From January 1, 2015 and up to the Latest Practicable Date, the total number of company-initiated, phase II and III, ongoing clinical trials for peptide drugs reached 360. Splitting based on therapeutic area, the endocrine and metabolic system disease area has 173 trials, accounting for the highest share of 32.9%. The indications targeted by a trial may involve multiple therapeutic areas.

Distribution of Phase 2 and beyond Clinical Trials by Disease Area



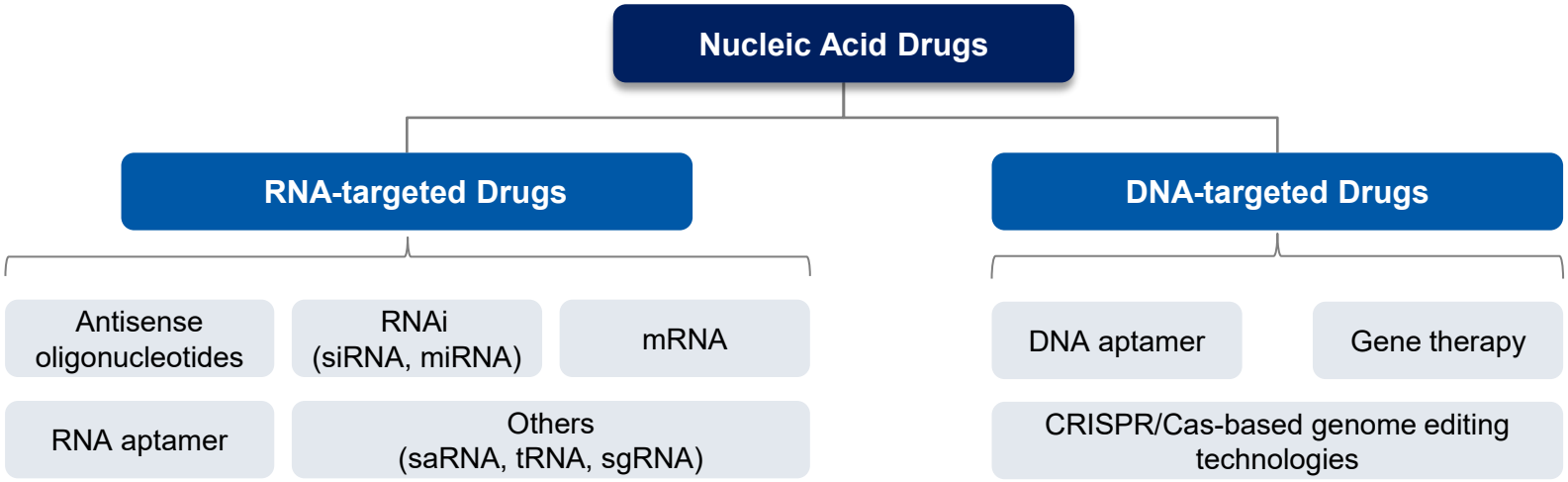
Note: 1. Numbers of clinical trials each year are calculated according to the first posted date.
2. Trials include ongoing clinical trials initiated by the corporate side.
3. The number of clinical trials in 2024 is counted up to the Latest Practicable Date.

Source: Frost & Sullivan Analysis, Clinical Trials

Table of Contents

Overview of Nucleic Acid Drugs

- Nucleic acid therapeutics are a versatile class of sequence-programmable drugs that offer a robust and clinically viable strategy to modulate expression or correct genetic defects contributing to disease.
- Nucleic acid drugs provide novel therapeutic modalities with characteristics that differ from those of small molecules and antibodies.



Advantages of nucleic acid therapeutics

- **Mechanism:** Nucleic acid drugs control the biological functions of cells, based on nucleotide sequence information. The functioning of these drugs is either based on their expression in cells or is mediated through the regulation of genes, specifically those having complementary sequences. These mechanisms provide a major advantage in that nucleic acid drugs can be designed regardless of the localization or structure of the target molecule, enabling approaches to target molecules that have not been possible with small molecules or antibodies.
- **Efficiency:** Once a platform is established, it is possible to create a drug simply by changing the nucleotide sequence of the target gene; thus, rapid and efficient drug development can be expected.

Source: Frost & Sullivan Analysis, Literature research

Overview of Oligonucleotides Drugs

- Oligonucleotides are a class of single- or double-stranded small synthetic nucleic acid polymers (≈20-mer) that can be used to modulate gene expression, including antisense oligonucleotides (ASO), RNA interference (RNAi), and aptamer. Oligonucleotide drugs have become one of the top development priorities in the global pharmaceutical industry.

The main types of oligonucleotides

RNA interference (RNAi)

- RNA interference (RNAi) is a naturally occurring posttranscriptional pathway of gene silencing mediated by short fragments of double-stranded RNA, which combine with homologous sequences in mRNAs and induce their breakdown.

Antisense oligonucleotides (ASO)

- An antisense oligonucleotide (ASO) is a single-stranded deoxyribonucleotide, which is complementary to the mRNA target.
- The goal of the antisense approach is the downregulation of a molecular target, usually achieved by induction of RNase H endonuclease activity that cleaves the RNA-DNA heteroduplex with a significant reduction of the target gene translation.

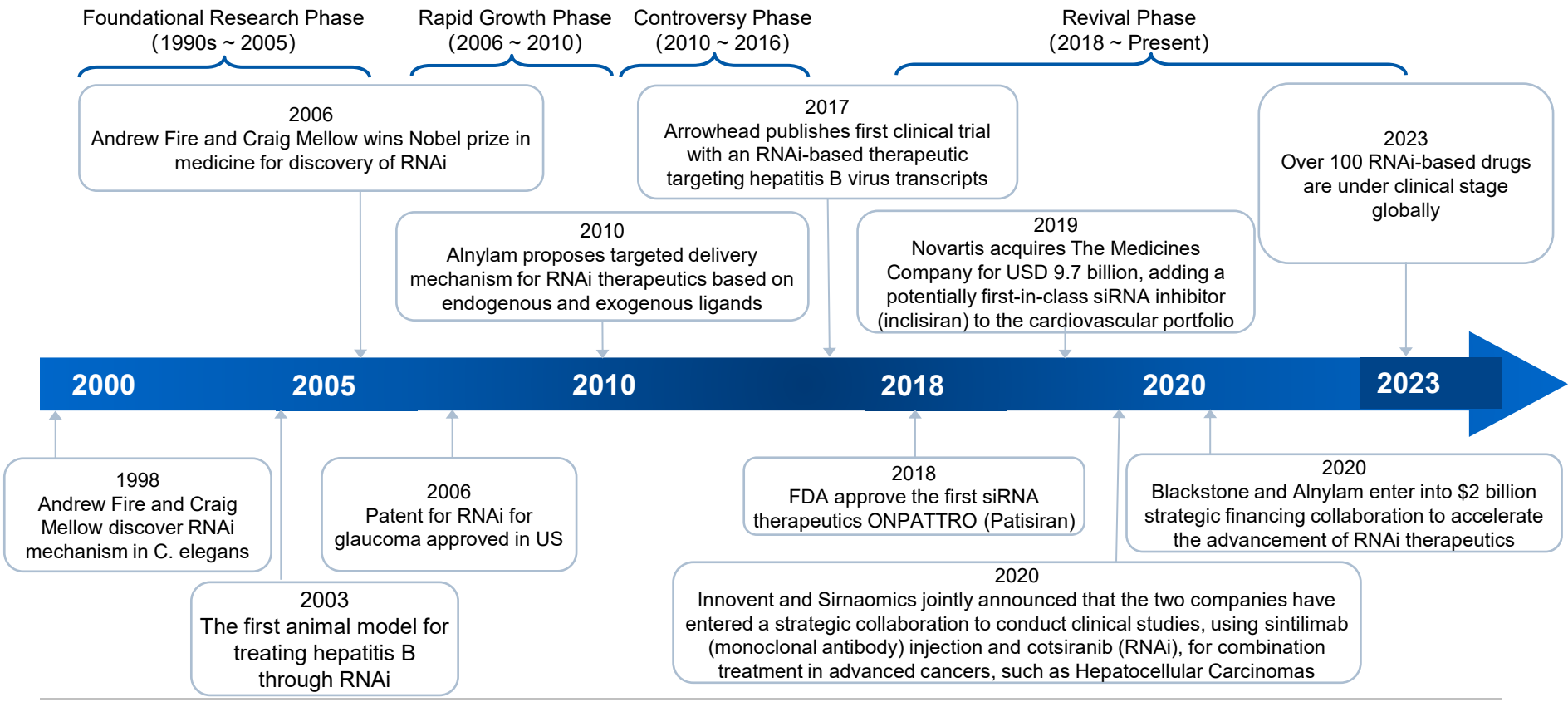
Comparison of the major oligonucleotides

	siRNA	ASO
Mechanism of action	• The first step of RNAi involves processing and cleavage of longer double-stranded RNA into siRNAs, generally bearing a 2 nucleotide overhang on the 3′ end of each strand. The enzyme responsible for this processing is an RNase III-like enzyme termed Dicer. When formed, siRNAs are bound by a multiprotein component complex referred to as RISC (RNA induced silencing complex) . • Within the RISC complex, siRNA strands are separated and the strand with the more stable 5′-end is typically integrated to the active RISC complex. • The antisense single-stranded siRNA component then guides and aligns the RISC complex on the target mRNA and through the action of catalytic RISC protein, a member of the argonaute family (Ago2), mRNA is cleaved.	• By induction of endogenous RNase H activity (ASO-RNase H) that cleaves the mRNA-ASO hetero-duplex which leads to degradation of the target toxic mRNA and leaves the ASO intact; or • Binding to the RNA and causing translational inhibition by steric hindrance, exon skipping, exon inclusion, destabilization of pre-mRNA in the nucleus, or targeting the destruction of microsomal RNAs that control the expression of other genes.
Structure and length	• 20–25 nucleotides, double-stranded	• Usually 15 to 30 nucleotides，single-stranded
Features	• Relatively easier to obtain a potent siRNA since unmodified RNA works with high potency as opposed to ASOs • Double-stranded confers on siRNAs a greater stability, making it more appealing for in vitro studies as compared with ASOs • The presence of two strands of RNA may bring a higher off-target effect in siRNA-based drugs since both the sense and antisense strands could be active	• Since ASOs are single stranded, as opposed to siRNA, they have lower cost of production • Easier to deliver ASOs in vivo, since they do not a vector and a simple chemical modification can increase their resistance to nucleases

Source: Frost & Sullivan Analysis, Literature research

Overview of RNAi Drug Development and Industry

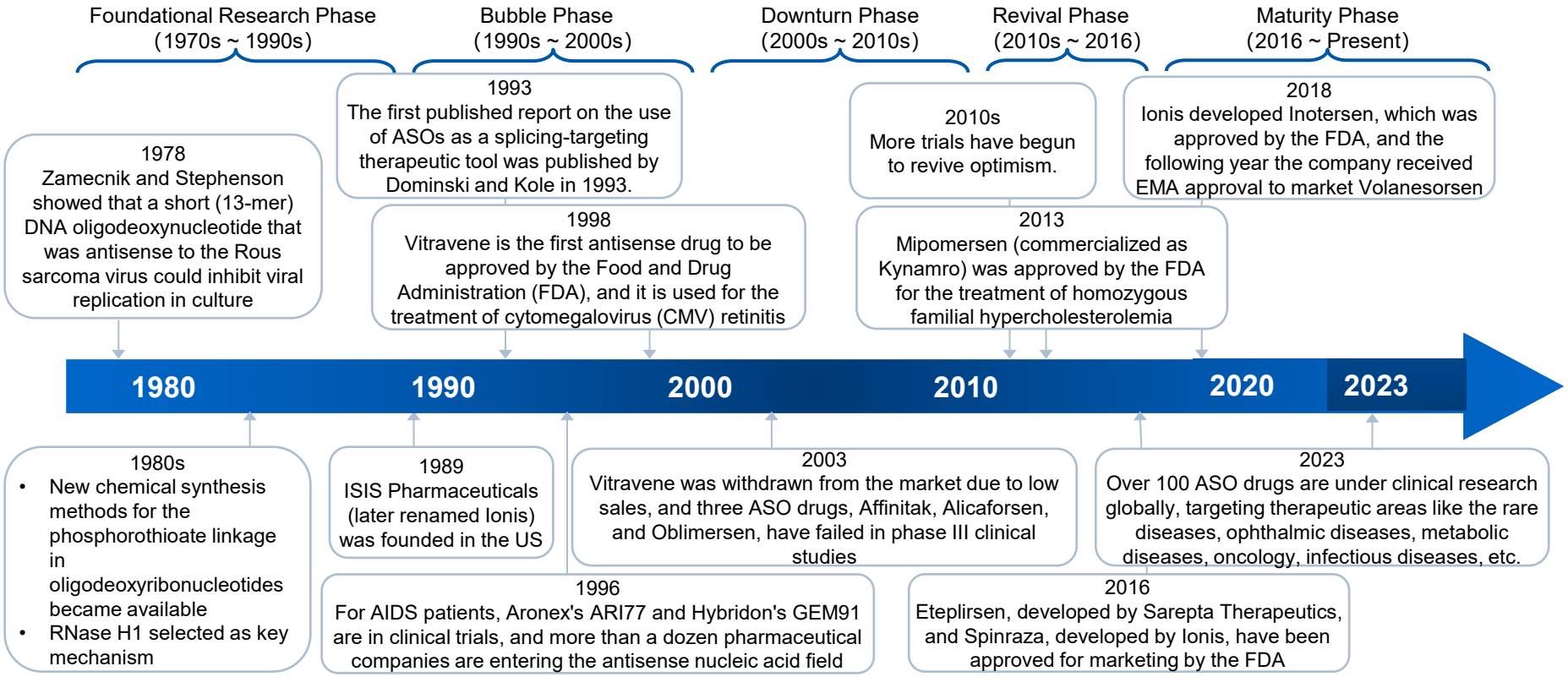
- Since the FDA approved the first RNAi drug in 2018, RNAi has gained momentum, driving collaboration and mergers among companies. Notably, Novartis' $9.7 billion acquisition of The Medicines Company and Blackstone's $2 billion investment in Alnylam have underscored this trend. Clinical trials for RNAi are currently exploring diverse indications, including cardiovascular diseases, endocrine and metabolic diseases, infectious diseases and etc.



Source: Frost & Sullivan Analysis, Literature research

Overview of ASO Drug Development and Industry

- In the 1970s, the emergence of antisense nucleic acid (AN) technology attracted great attention from the academic community, and a large number of researchers and pharmaceutical companies devoted themselves to this field, which led to the rapid development of AN technology.
- The introduction of bridged nucleic acid (BNA) modifications, including locked nucleic acid (LNA), enhanced the stability and pharmacokinetic properties of antisense nucleotides, revitalizing the industry.



Source: Frost & Sullivan Analysis, Literature research

Comparison of Oligonucleotide Drugs, Small Molecule Drugs and Antibody Drugs

- Only one-third of the roughly 20,000 proteins in the human genome are druggable by small molecules and protein-based drugs (e.g., monoclonal antibodies.)
- In principle, oligonucleotides can be rationally designed against virtually any genetic target. Their unique mechanism of action differentiates this class of therapeutics from small molecules and antibodies.

	Small molecules	Antibody	Nucleic Acid	
			mRNA	Oligonucleotides
Molecular Weight	< 500Da	> 100KDa	> 100 KDa	7-14 KDa
Number of targets of action	Medium	Relatively little	Relatively high	Relatively high
Mechanism of action	Regulation of proteins	Regulation of proteins	Regulation of proteins	Regulation of genes
Specificity	Relatively low	high	Relatively high	Relatively high
Half-life	Short	Medium	Relatively Long	Long
Difficulty of development	Medium	High	High	High
Cell permeability	Usually good	Not good	Not good	Not good
Manufacturing	Chemical synthesis	Produced in living cells or organisms	Synthetic technologies	Synthetic technologies
Clinical trial success rate	Low	Relatively high	N/A	Relatively high

Source: Frost & Sullivan Analysis, Literature research

Manufacturing Process of Oligonucleotide Drugs

- Different challenges in the development of oligonucleotide therapeutics necessitate corresponding technological solutions. Following the sequence of oligonucleotide therapeutic development, core technologies encompass RNA synthesis and screening techniques, RNA chemical modification techniques, and RNA delivery techniques.
- The most critical core technology is the oligonucleotide therapeutic delivery technique. Drug delivery plays a pivotal role in preserving RNA structure, enhancing targeting efficacy, reducing dosages, and mitigating toxic side effects.

	Definition	Application purpose/Issue addressed	Technical classification
RNA synthesis and screening techniques	• The technique involves designing, synthesizing, and screening single-stranded or double-stranded RNA sequences that can complementarily pair with the target disease gene based on its genetic information.	• Enhance target binding specificity • Reduce off-target toxicity	• Oligonucleotide Synthesis: Chemical synthesis, in vitro transcription, in vitro enzymatic cleavage, plasmid vectors or viral vectors or in vivo expression mediated by siRNA expression cassettes. • Oligonucleotide Screening: Microplate screening techniques, cell chip screening techniques, software-assisted screening techniques.
RNA chemical modification techniques	• The technique involves utilizing chemical methods to modify the structure of oligonucleotide therapeutics, thereby altering and optimizing their in vivo characteristics.	• Improved serum stability • Reduced immune-mediated toxicity • Improve the binding specificity of RNA and RISC	• Phosphonate modification • Ribose modification • Base modification
RNA delivery techniques	• The technique involves employing carriers to enhance the biological activity of nucleic acid therapeutics, improve their distribution within the body, increase drug concentration in target tissues, and enhance their bioavailability.	• Preserve RNA structure • Enhance drug targeting • Improve tissue and cellular penetration • Reduce off-target toxicity • Lower drug dosage • Enabling flexible administration methods	• Naked RNA modification delivery system • Liposomal nanoparticle delivery system • Polymeric delivery system • Targeting molecule-conjugated delivery system • Peptide delivery system • Exosome delivery system and other delivery systems

Source: Frost & Sullivan Analysis, Literature research

Key Issues and Challenges in Oligonucleotides Drugs Production (1/3) Pharmacodynamics-Related Factors

Poor targeting specificity	• The main challenge of oligonucleotides is efficient drug delivery. It is hard to get them anywhere but the liver, so the goal is selectively targeting the oligo to desired tissues. Various kinds of oligos required different strategies to ensure efficient uptake at the cellular level and release within the cytosol.
Off-target related toxicities	• The off-target toxicities may arise with oligonucleotide therapeutics if the oligonucleotide sequence is strictly complementary to the target sequence, partial similarity with genes on other unintended target sequences may induce off-target effects that may lead to downstream changes in gene expression.
Immuno-stimulatory responses	• Several oligonucleotides are reported to attach to toll-like receptors (TLRs) that play a vital role in the innate immune system and subsequently induce immune responses identical to those stimulated by viral and bacterial nucleic acids. For example, using single-stranded phosphorothioate oligonucleotides has often been associated with injection site reactions, fever, chills, and rigors at high doses. Different sequence motifs have been identified as agonists of TLR family members; as such, avoiding these sequence motifs and using chemical modifications can minimize these immune-stimulatory effects. Similarly, lipid-nanoparticle formulations of siRNA are found to promote inflammatory responses as they induce complex antiviral-like innate immune responses. Adaptive immune responses have been more muted comparatively.
Persistent gene silencing	• RNA-induced silencing complex is used in the siRNA strategy, which results in persistent post-transcriptional gene knockdown for up to 2–4 weeks. This long-term gene silencing allows siRNA therapies to be administered less often. However, without the injection of an antidote, multiple mechanism-based harmful and off-target side effects can last for weeks.

Source: Frost & Sullivan Analysis, Literature research

Key Issues and Challenges in Oligonucleotides Drugs Production (2/3) Pharmacokinetics-Related Factors

Stability	• Oligonucleotides must overcome several extracellular and intracellular obstacles to interact with their biological RNA targets inside cells. These obstacles include degradation by extracellular nucleases, scavenging by the reticuloendothelial system, filtration by the kidney, traversing the capillary endothelium to access the tissue interstitium, cell-surface receptor-mediated endocytic uptake, and escape from endolysosomal compartments to access the nuclear and/or cytoplasmic compartments where their targets reside.
Poor cell penetration	• Oligonucleotides are typically large, hydrophilic polyanions (single-stranded ASOs are ~4–10 kDa, double-stranded siRNAs are ~14 kDa), properties that mean they do not readily pass through the plasma membrane.

Source: Frost & Sullivan Analysis, Literature research

Key Issues and Challenges in Oligonucleotides Drugs Production (3/3)CMC(Chemistry, Manufacturing, and Control)-Related

The control of impurities	• The characterization of product-related impurities is an important activity in the development of any new chemical entity. In this regard, to the extent practical, manufacturers are expected to make an effort to determine the structures of all impurities present or likely to be present in significant quantities. Such an undertaking typically requires a detailed appreciation of the synthetic route and its chemical transformations, knowledge of starting materials and the fate of starting material impurities, and an understanding of potential degradation pathways. The information is used to guide the empirical process of impurity characterization itself, which may consist of a variety of steps, including impurity isolation or enrichment, chemical and physicochemical evaluation, and structural confirmation through unambiguous synthesis. Often, complete structural elucidation of impurities is one of the most challenging aspects of drug development. For instance, one of the most common types of impurities is a "deletion" of one or two nucleotides, which leads to an n-1 or n-2 impurity.
Raw material	• DNA and RNA oligonucleotides are chemically synthesized using nucleic acid monomers known as phosphoramidites. However, the repetitive nature of the oligonucleotide synthesis will amplify the impact that phosphoramidite impurities may have, resulting in poor final oligonucleotide quality. So, the quality of the raw materials has a major impact on the quality of the drug since some of these impurities can be incorporated into the oligonucleotide final product and be difficult to purify out. Therefore, raw material impurities that arise need to be controlled and monitored by establishing limits based on the safety and process capability to ensure that the quality and performance of the drug are not compromised.
Quality and efficiency assurance	• As the therapeutic oligonucleotide pipeline continues to grow globally, manufacturers should learn how to overcome some of the analytical and process challenges that help ensure quality and efficiency. Current manufacturing practices lack the efficiency necessary to meet large-scale demand. Oligonucleotide therapeutics rely on short nucleic acid blocks to target specific sequences of mRNA and alter their capacity for gene expression. Although this makes them impressive therapeutic agents, companies could stand to benefit from an improved approach to manufacturing. Currently, each nucleotide base is added sequentially on a solid-phase resin to build desired products. Any waste is washed down the column with the reactants used, but after several reactions the overall efficiency and purity of the process is reduced, necessitating chromatographic purification to generate a viable medicine.

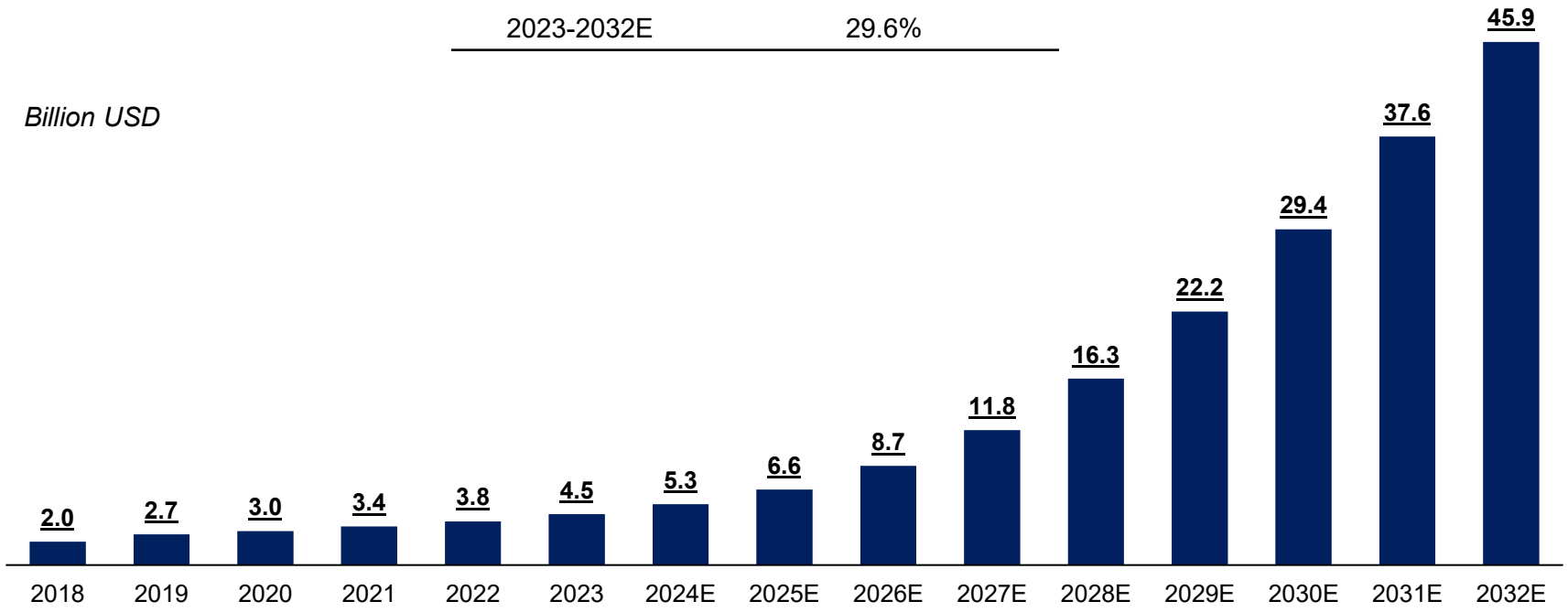
Source: Frost & Sullivan Analysis, Literature research

Global Oligonucleotide Drugs Market Size, 2018-2032E

- Global oligonucleotide drug market size continues to grow, rising from 2.0 billion USD in 2018 to 4.5 billion USD in 2023.The global oligonucleotide drug market size is expected to grow at a CAGR of 29.6% between 2023 and 2032, increasing to 45.9 billion USD in 2032.

Global Oligonucleotide Drugs Market Size, 2018-2032E

	CAGR
2018-2023	16.9%
2023-2032E	29.6%



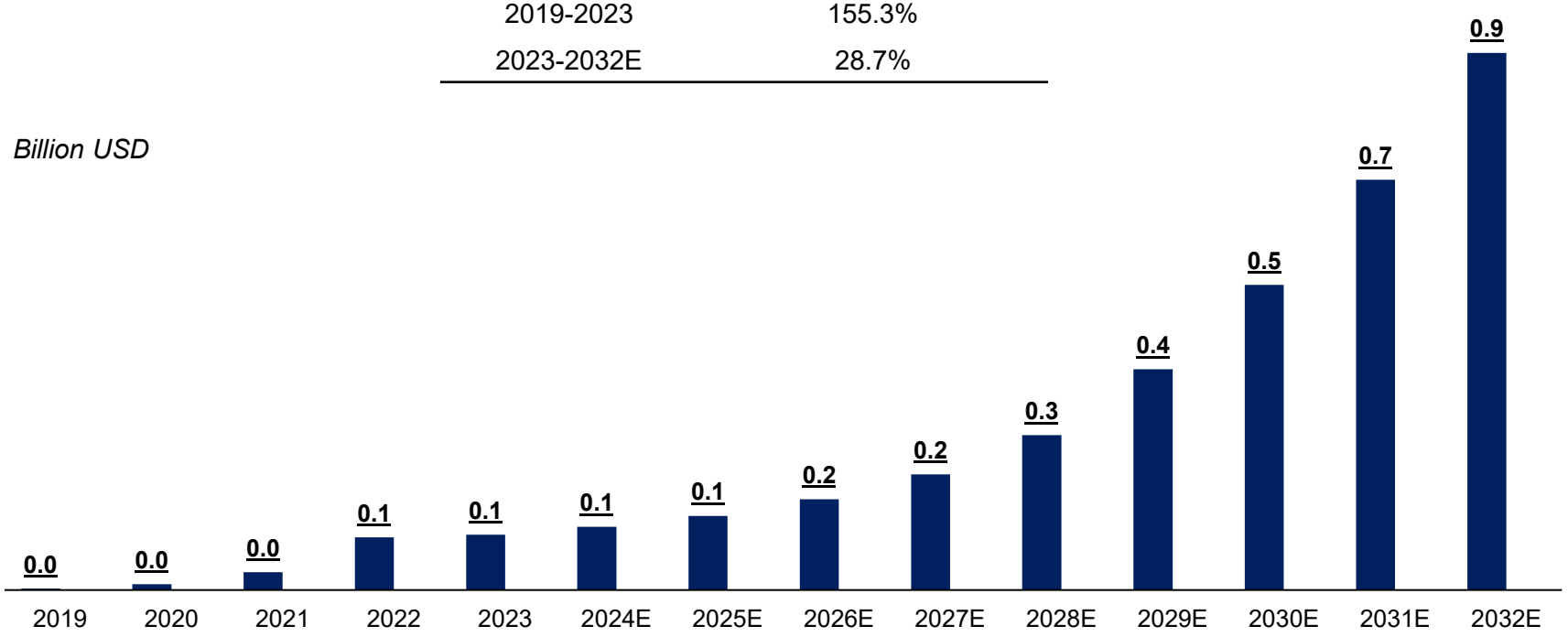
Source: NMPA, FDA, Annual Report, Frost & Sullivan Analysis

China Oligonucleotide Drugs Market Size, 2018-2032E

- SPINRAZA, first oligonucleotide drug approved by NMPA launched in 2019. China oligonucleotide drug market rises to 0.1 billion USD in 2023. The China oligonucleotide drug market size is expected to grow to 0.9 billion USD in 2032.

China Oligonucleotide Drugs Market Size, 2018-2032E

	CAGR
2019-2023	155.3%
2023-2032E	28.7%



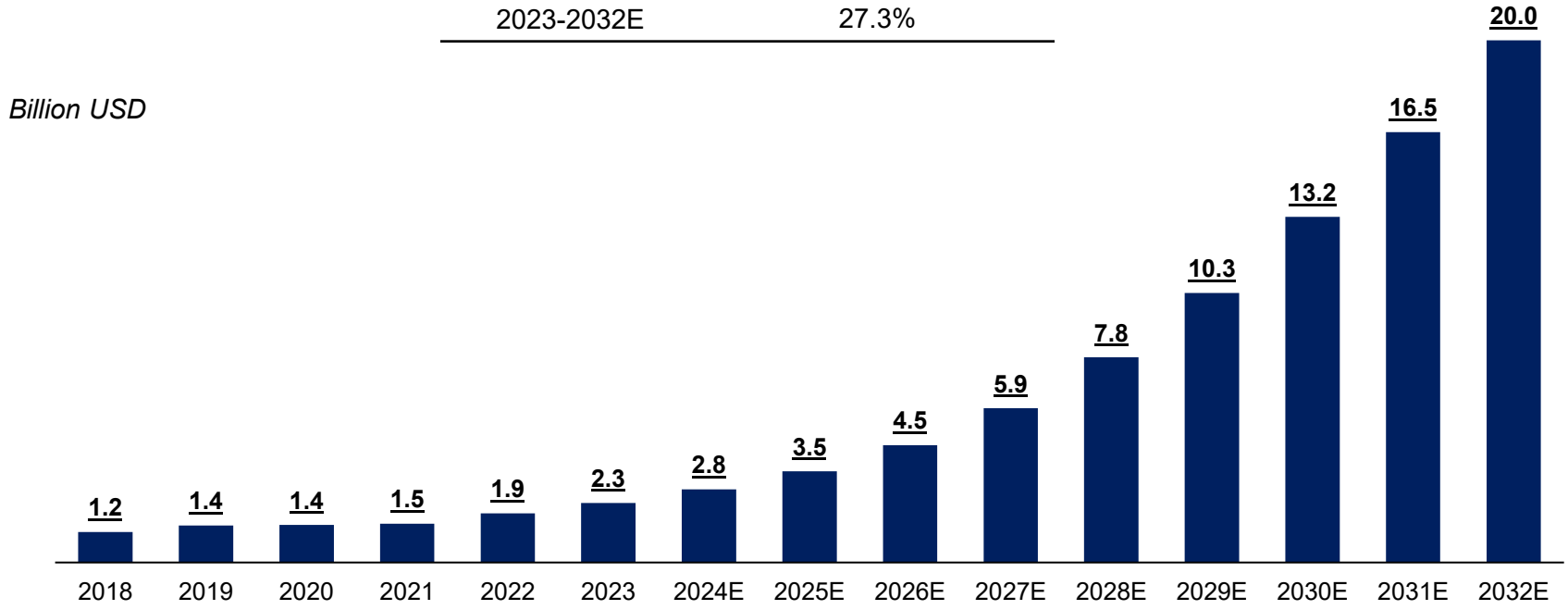
Source: NMPA, Annual Report, Frost & Sullivan Analysis

US Oligonucleotide Drugs Market Size, 2018-2032E

- The U.S. oligonucleotide drug market size increased from 1.2 billion USD in 2018 to 2.3 billion USD in 2023.The U.S. oligonucleotide drug market size is expected to grow at a CAGR of 27.3% between 2023 and 2032, increasing to 20.0 billion USD in 2032.

US Oligonucleotide Drugs Market Size, 2018-2032E

	CAGR
2018-2023	14.4%
2023-2032E	27.3%

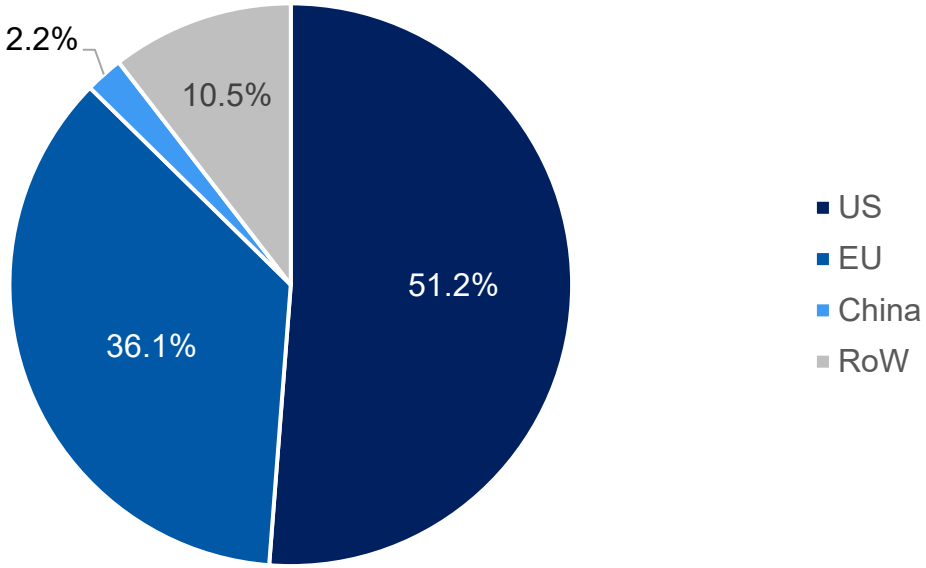


Source: FDA, Annual Report, Frost & Sullivan Analysis

Breakdown of Global Oligonucleotide Drugs Market by Regions, 2023

- In 2023, the global oligonucleotide drug market size reaches 4.5 billion USD, of which the U.S. oligonucleotides market reaches 2.3 billion USD, accounting for 51.2%. China oligonucleotides market size is 0.1 billion USD, accounting for 2.2% of the global market.

Breakdown of Global Oligonucleotide Drugs Market US, EU, China, and Row, 2023

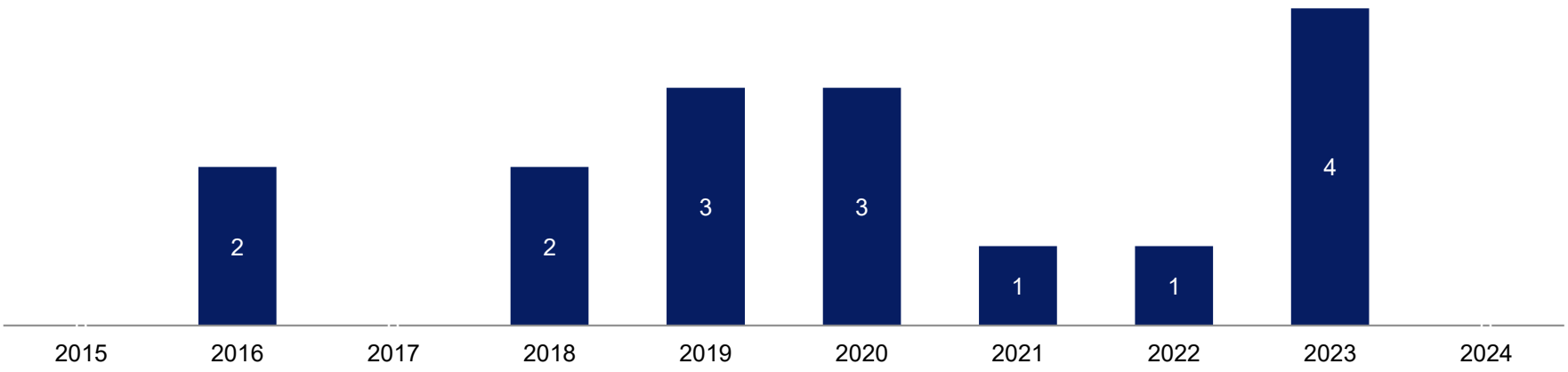


Source: NMPA, FDA, EMA, Annual Report, Frost & Sullivan Analysis

Number of Approved Oligonucleotide Drugs since 2015

- As of the latest practicable date, a total of 16 oligonucleotide drugs have been approved for marketing worldwide. These include 9 ASO drugs,6 siRNA drugs and one aptamers.

Number of Approved Oligonucleotide Drugs in Global, 2015-2024



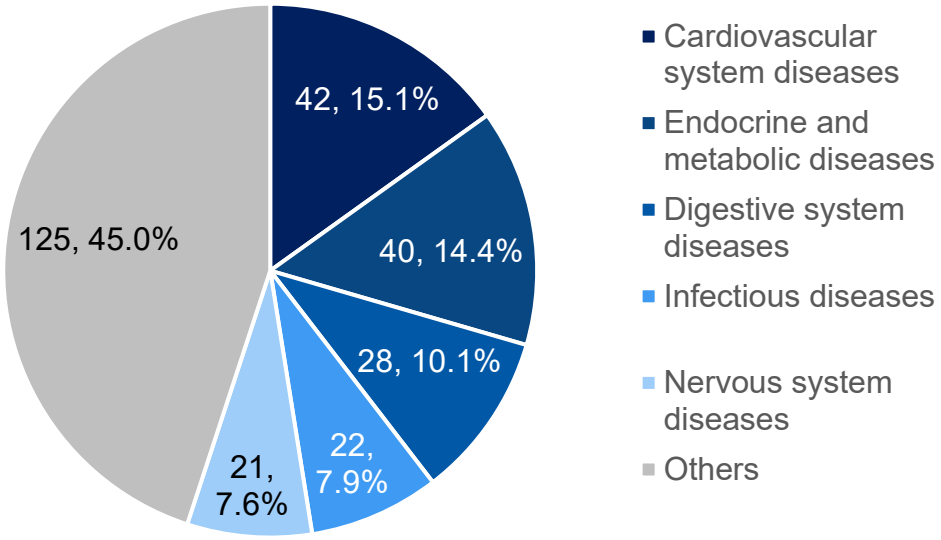
Note: 1. The number of oligonucleotide drug approvals in 2024 is counted up to April 25, 2024.

Source: Frost & Sullivan Analysis, Literature Research

Distribution of Phase 2 and beyond Clinical Trials by Disease Area, 2015-2024

- From January 1, 2015 and up to the Latest Practicable Date, the total number of company-initiated, phase II and III, ongoing clinical trials for oligonucleotide drugs reached 136. By therapeutic area, the number of trials targeting cardiovascular system diseases is highest, 42 trials, accounting for 15.1%. The indications targeted by a trial may involve multiple therapeutic areas.

Distribution of Phase 2 and beyond Clinical Trials by Disease Area



Note: 1. Numbers of clinical trials each year are calculated according to the first posted date.
2. Trials include ongoing clinical trials initiated by the corporate side.
3. The number of clinical trials in 2024 is counted up to the Latest Practicable Date.
4. Oligonucleotide drugs include ASO, siRNA, and Aptamers.

Source: Frost & Sullivan Analysis, ClinialTrials

Marketed Oligonucleotide Drugs in Global

- 18 oligonucleotide drugs had obtained regulatory approvals globally between January 1, 2015 and the Latest Practicable Date.

Category	Brand Name	Product	Target	Company	Indication	First Approval Date
siRNA	Qfitlia	Fitusiran	SERPINC1	Alnylam Pharmaceuticals	Hemophilia A or Hemophilia B	2025/03/28(FDA)
ASO	TRYNGOLZA	Olezarsen	APOC3	Ionis Pharmaceuticals	Familial chylomicronemia syndrome (FCS)	2024/12/19(FDA)
ASO	Wainua	Eplontersen	TTR	Ionis Pharmaceuticals，Akcea Therapeutics	Polyneuropathy of hereditary transthyretin-mediated amyloidosis	2023/12/21(FDA)
siRNA	Rivfloza	Nedosiran	LDHA	Dicerna Pharmaceuticals, Novo Nordisk Pharmaceuticals	Primary hyperoxaluria type 1 (PH1)	2023/9/29(FDA)
Aptamers	IZERVAY	Avacincaptad pegol	C5	Archemix	Geographic atrophy	2023/8/4 (FDA)
ASO	QALSODY	Tofersen	SOD1	Ionis Pharmaceuticals	Amyotrophic Lateral Sclerosis (ALS)	2023/4/25 (FDA) 2024/09/26 (NMPA)
siRNA	AMVUTTRA	Vutrisiran	TTR	Alnylam	Hereditary Transthyretin-mediated (hATTR) amyloidosis, polyneuropathy of hereditary transthyretin-mediated amyloidosis	2022/6/13 (FDA) 2022/9/15 (EMA) 2022/9/26 (Japan)
ASO	Amondys 45	Casimersen	DMD	Sarepta Therapeutics	Duchenne muscular dystrophy (DMD)	2021/2/25 (FDA)
siRNA	Leqvio	Inclisiran	PCSK9	Alnylam	Primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia	2020/12/9 (EMA) 2021/12/22 (FDA) 2023/08/22(NMPA)
siRNA	Oxlumo	Lumasiran	HAO1	Alnylam	Primary hyperoxaluria type 1 (PH1)	2020/11/19 (EMA) 2020/11/23 (FDA)
ASO	VILTEPSO	Viltolarsen	DMD	Nippon Shinyaku, NS Pharma	Duchenne muscular dystrophy (DMD)	2020/3/25 (Japan) 2020/8/12 (FDA)

Note: 1. Products that were withdrawn from the market are not included.

2. Filter conditions: (1) first approval date since 2020/1/1, up to the Latest Practicable Date.

Source: FDA, EMA, NMPA, PMDA, Frost & Sullivan Analysis

Marketed Oligonucleotide Drugs in China

- As of the latest practicable date, there are 3 oligonucleotide drugs have been approved for marketing in China.

Trade name	Product	Target	Company	Indication	NMPA Approval Date
QALSODY	Tofersen	SOD1	Ionis Pharmaceuticals	Amyotrophic Lateral Sclerosis (ALS)	2024/09/26
Leqvio®	Inclisiran	PCSK9	Alnylam	Primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia	2023/08/22
SPINRAZA	Nusinersen	SMN2	Ionis Pharma	Spinal muscular atrophy (SMA)	2019/2/22

Note: 1. Filter conditions: (1) first approval date since 2015/1/1, up to the Latest Practicable Date.

Source: Frost & Sullivan Analysis, NMPA

Key Barriers in the R&D, Production and Commercialization of TIDES Drugs

R&D Challenges

Synthesis and purification difficulty	• The synthesis processes of TIDES drugs are inherently complex, involving multiple intricate steps and delicate reaction conditions. In the realm of peptides, the identification and control of multi-ring peptide impurities resulting from disulfide bonds have long posed significant challenges in the industry. Moreover, synthesizing oligonucleotides demands high-precision automated instrumentation and intricate purification steps. In the case of peptides, limitations often stem from the synthesis process efficiency and the purity of the final products. The structural complexity and sensitivity of the molecules further exacerbate purification difficulties. Consequently, effectively monitoring impurities and efficiently purifying the target product emerge as critical hurdles in TIDE drug development.
Delivery System	• TIDES drugs face challenges in effectively crossing cell membranes and entering the cell interior. As such, the development of safe, effective and stable delivery systems has emerged as a significant technical hurdle. This requires consideration of several aspects such as drug stability, biocompatibility, and targeting.

Production challenges

Scale-up and efficiency	• Scaling up the production process of TIDES APIs from laboratory scale to commercial production scale presents significant challenges. It ivolves optimization of reaction conditions, equipment, and adjustment of production processes. Simultaneously, maintaining product quality while enhancing production efficiency is a critical problem to address. In addition, for peptide compounds, the complexity of side chain modifications (use of unusual amino acids and cyclic structures) adds further hurdles to efficient production. Another challenge lies in the inherent complexity of peptide structures, often characterized by intricate sequences and specific folding patterns critical to their biological activity. Striking a balance between optimal synthesis efficiency and high purity levels remains an ongoing challenge, particularly with longer or modified peptide sequences. Accordingly, the production cost of TIDES APIs is also usually high.

Sources: Frost & Sullivan Analysis

Key Barriers in the R&D, Production and Commercialization of TIDES Drugs

Commercialization Challenges

Regulations and policies	• In various countries and regions, drug regulatory policies exhibit variations, and these policies are in a constant state of flux. For example, The CDE on February 17, 2023 issued and implemented the "Chemical Synthesis Peptide Drug Pharmacy Research Technical Guidelines (for Trial Implementation)" (《化學合成多肽藥物藥學研究技術指導原則(試行)》), for the guidance of chemical synthesis peptide drug pharmacy, to provide reference to the technical standards. The FDA published two new general chapters: USP1503 addressing specific quality considerations for synthetic peptide drug substances and USP1504 (Official date: December 1, 2023) providing recommendations on the minimum quality attributes for starting materials used in the manufacture of synthetic peptides. On May 19, 2021, FDA published ANDAs for Certain Highly Purified Synthetic Peptide Drug Products That Refer to Listed Drugs of rDNA Origin Guidance for Industry Guidance. This guidance is intended to assist potential applicants in determining when an application for a synthetic peptide drug product (synthetic peptide) that refers to a previously approved peptide drug product of recombinant DNA origin (peptide of recombinant DNA origin) should be submitted as an ANDA under section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) rather than as an NDA under section 505(b) of the FD&C Act. On October 18, 2023, EMA published a guidance on the Development and Manufacture of Synthetic Peptides for public consultation to cover synthetic peptides with more than 4 amino acids. In addition, oligonucleotides, as an emerging therapeutic class, require robust regulation through a well-established system. The U.S. FDA has highlighted several challenges in regulating oligonucleotide drugs, including the absence of clear guidelines for quality studies and standard-setting. To address these challenges, regulatory agencies worldwide are taking proactive steps. For instance, Japan's Pharmaceuticals and Medical Devices Agency (PMDA) issued the "Guideline for Pre-clinical Safety Assessment of Oligonucleotide Therapeutics" in 2020. Similarly, the U.S. FDA released guidance on IND submissions for ASO drug products in 2021. In the future, regulatory policies will likely continue to evolve and become more stringent as the field of oligonucleotide drugs advances. Consequently, pharmaceutical and biotechnological companies must thoroughly understand and adhere to these evolving regulatory frameworks.
Patient acceptance	• As a cutting-edge therapeutic class, TIDES drugs require recognition by both patients and physicians. Currently, injection remains the predominant delivery method for approved peptide drugs. However, injections pose challenges due to the suboptimal patient experience and associated risks. In the future, advancements in peptide drug technology, particularly the development of GLP-1 agonist oral delivery systems, will enhance the drug delivery cycle and enable long-lasting effects. These innovations are poised to significantly improve patient willingness to adhere to long-term medication regimens, enhance overall medication experiences, and promote better medication adherence.

Sources: Frost & Sullivan Analysis

Table of Contents

Processes in New Drug Research and Development

1. Discovery → **2. Preclinical** → **3. Clinical and Registration** → **4. Manufacturing**

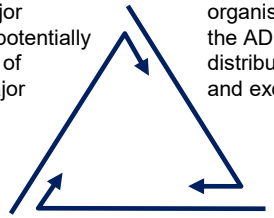
1. Discovery

- **Target Identification** — The process of identifying the direct molecular target of a small molecule.
- **Target Validation** — The process by which the predicted molecular target of a small molecule is verified.
- **Lead Generation** — The process by which the targeted small molecule is evaluated and undergo limited optimization to identify promising compounds.
- **Lead Optimization** — The process by which a drug candidate is designed after an initial lead compound is identified.

2. Preclinical

Safety Assessment:
- A comprehensive and systematic investigation and analysis of all aspects of risks to health and safety associated with major incidents that may potentially occur in the course of operation of the major hazard facility.

Pharmacokinetic and Pharmacology Research:
- The study of the disposition of a drug after its delivery to an organism, mainly refer to the ADME(absorption, distribution, metabolism, and excretion) research.



Pharmacodynamics Research:
- The quantitative study of the relationship between drug exposure (concentrations or dose) and pharmacologic or toxicologic responses.

3. Clinical and Registration

- **Phase I** — Clinical Pharmacology Research
- **Phase II** — Exploratory Clinical Trials
- **Phase III** — Confirmatory Clinical Trials
- **Phase IV** — Post-Marketing Study

4. Manufacturing

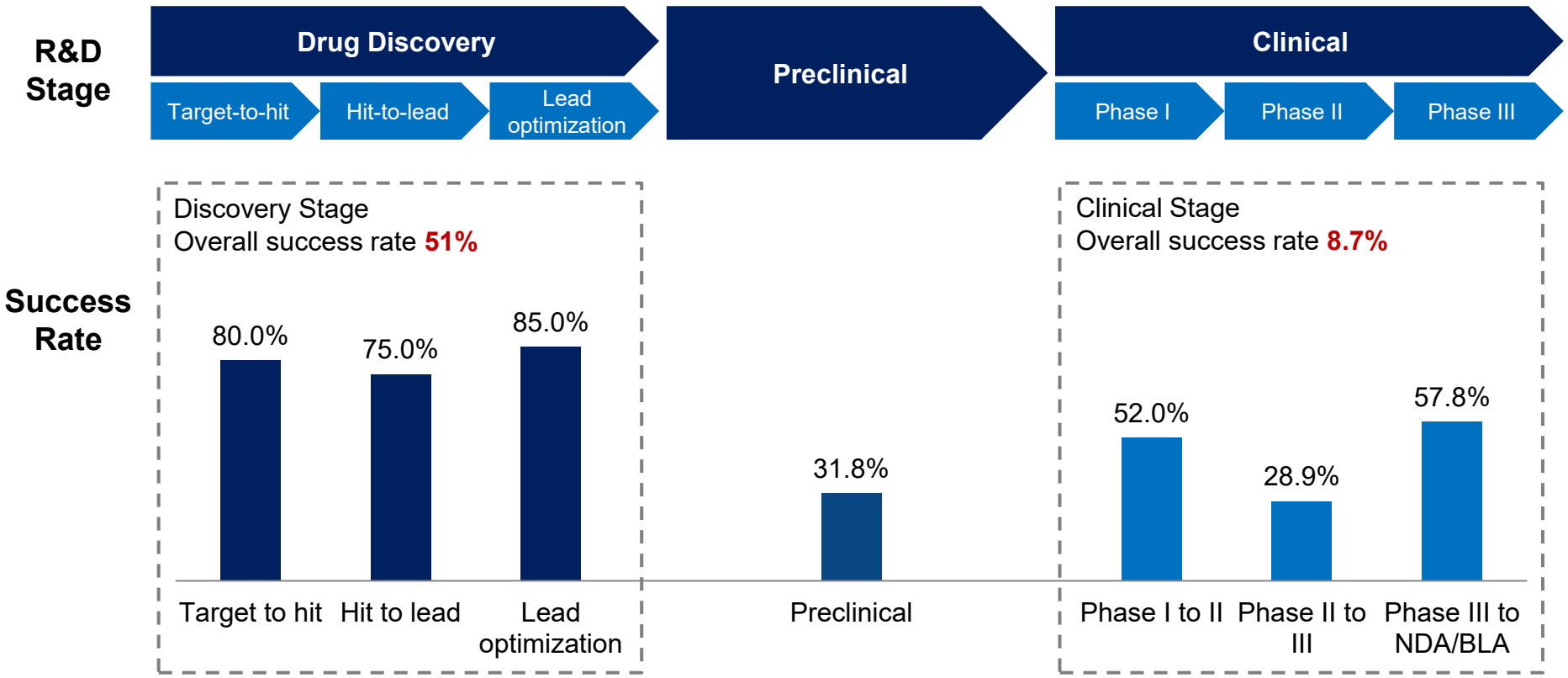
Early Stage Manufacturing (From Preclinical to Clinical)
- Including the CMC service, early stage CMO can provide the drug candidate synthesis and optimization such as process development, formulation design, clinical trial drugs, etc. to support the preclinical and clinical study.

Commercialization Manufacturing
- It is mainly engaged in commercialization to provide manufacturing services such as APIs, intermediates, preparation production and packaging, etc. in a large scale, as entrusted by pharmaceutical companies under contracts.

Source: Frost & Sullivan Analysis

Overview of Success Rate of New Drug R&D

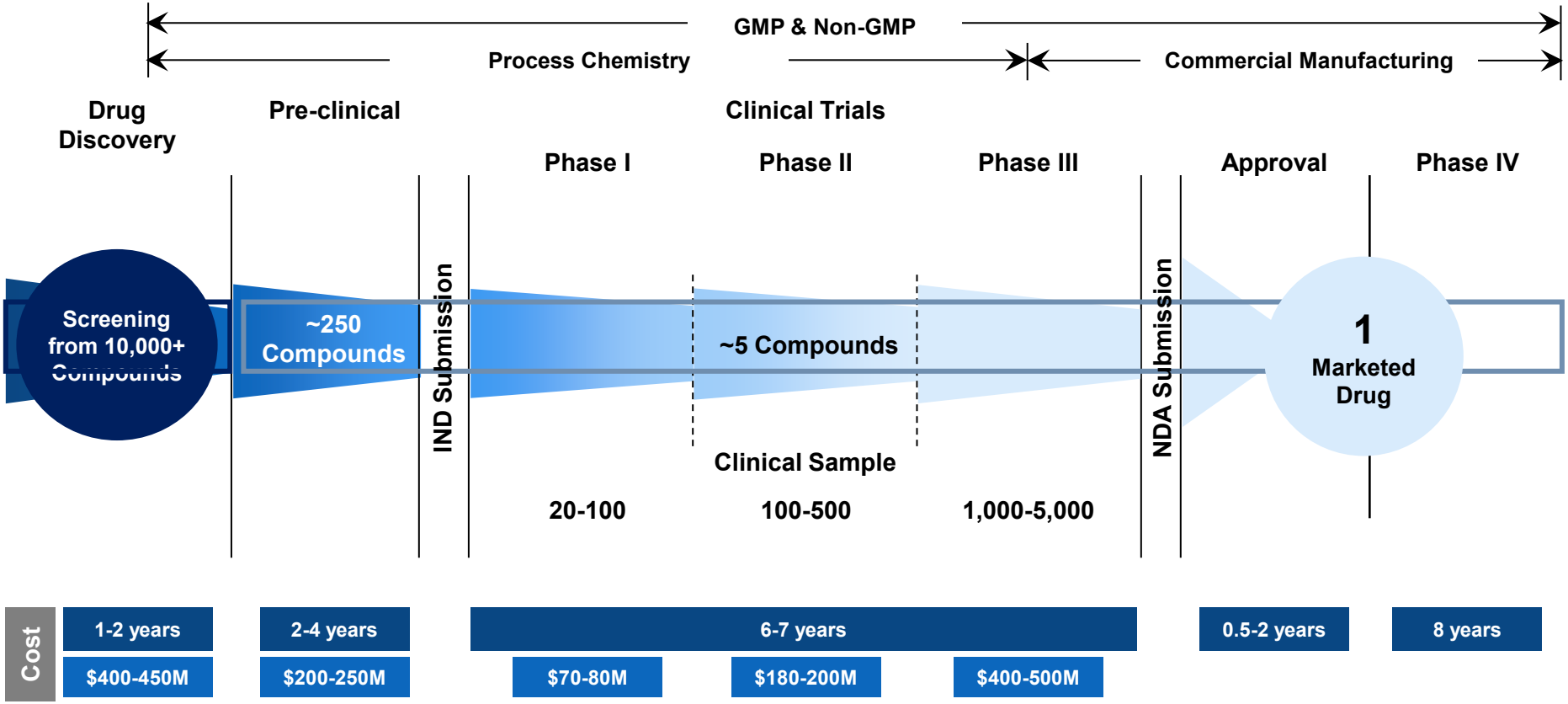
- Generally, the whole process of new drug R&D related with experiment and data management includes discovery, preclinical and clinical stage. The overall success rate in the clinical stage is only 8.7%.



Source: Literature Research, Frost & Sullivan Analysis

Time and Financial Cost of in Each Stage of New Drug R&D

- The main process of drug discovery and development includes drug discovery, pre-clinical, clinical trials, and authority review at last. The process is costly and time-consuming, which takes at least 10 years and over USD1 billion investment. Generally one launched drug comes from more than thousands of compounds at drug discovery stage.
- When the costs of compounds abandoned during testing were linked to the costs of compounds that obtained marketing approval and capitalizing costs to the point of marketing approval (discount rate 10.5%), the total cost for new drug can reach USD 2.6 billion.

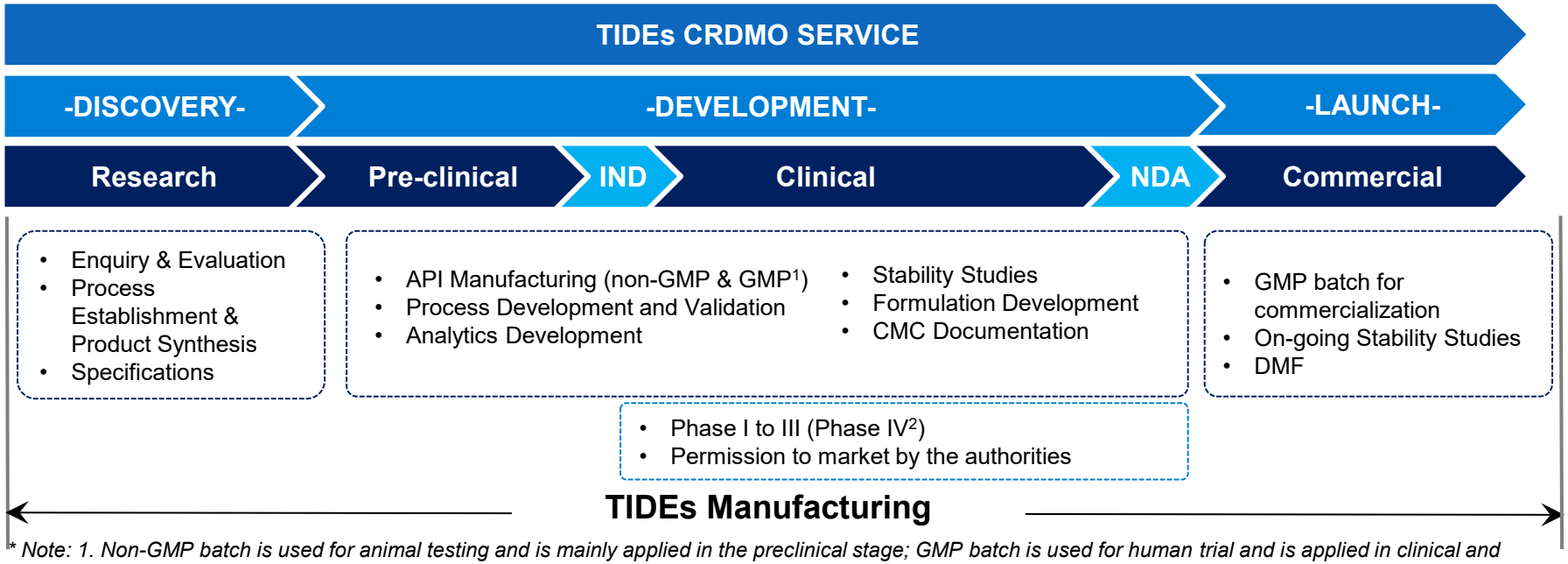


** The cost is based on out-of-pocket cost rather than capitalized cost.*

Source: Frost & Sullivan Analysis

Overview of TIDES CRDMO

- According to Al Shaer et al. (2024), **TIDES drugs** refer to peptide and oligonucleotide drugs. TIDES CRDMO is a company that specializes in providing CRDMO services to peptide and oligonucleotide drugs.
- TIDES CRDMO service providers offer comprehensive coverage for the production of drugs at various scales or batches, spanning from preclinical stages to post-market approval. Their services encompass the production of both non-GMP and GMP peptide raw materials, intermediates, and peptide preparations. When pharmaceutical companies identify TIDES with promising potential for drug development, they often require customized TIDES in larger quantities and higher purity for further research and development. As these projects progress towards clinical development, the provision of GMP-level raw materials becomes crucial for dosage form research, production, and subsequent animal or human testing. Simultaneously, TIDES CRDMO enterprises excel in providing comprehensive CMC services. These services include preparatory work for raw material process development, scale-up production, development and validation of analysis methods, stability research, and the maintenance of related batch records.



** Note: 1. Non-GMP batch is used for animal testing and is mainly applied in the preclinical stage; GMP batch is used for human trial and is applied in clinical and commercial stages; 2. A Phase IV trial is also known as a postmarketing surveillance trial or drug monitoring trial. It may be required by regulatory authorities or may be undertaken by the sponsoring company voluntarily*

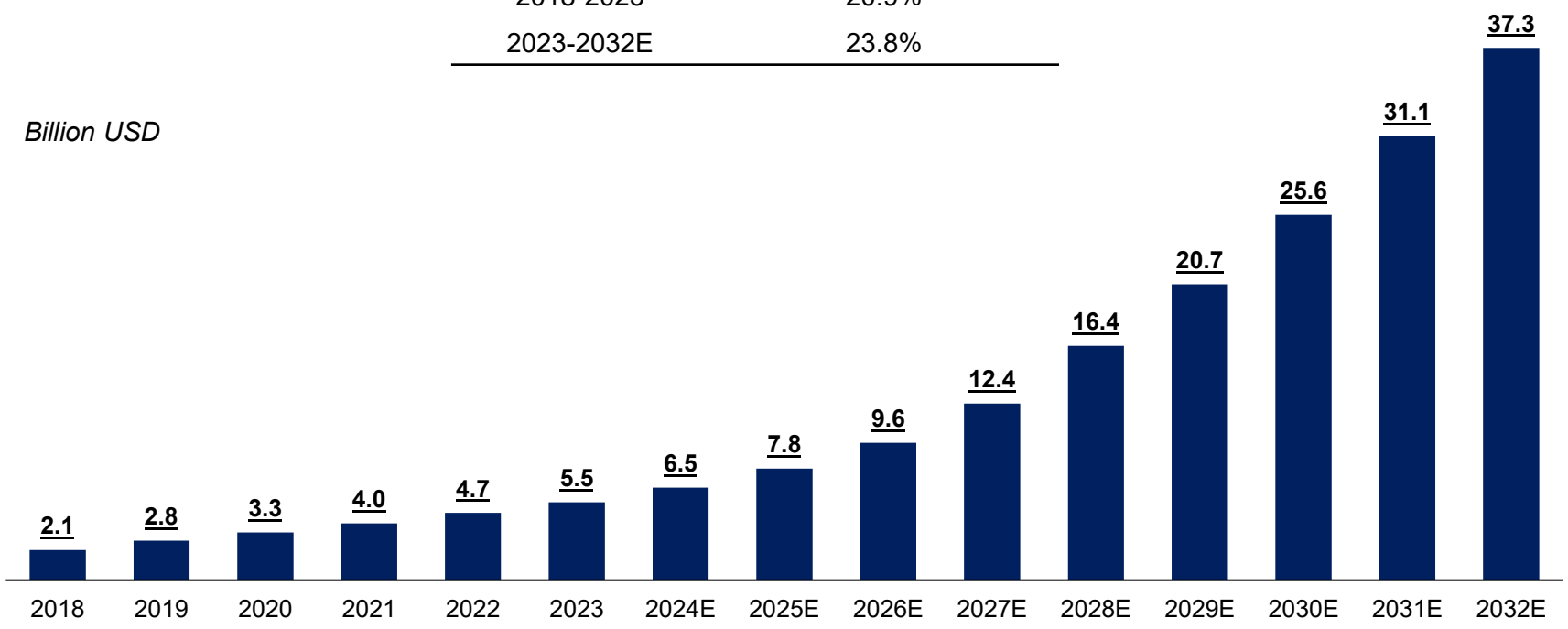
Source: Frost & Sullivan Analysis

Global TIDES CRDMO Market Size, 2018-2032E

- Global TIDES CRDMO market size continues to grow, rising from 2.1 billion USD in 2018 to 5.5 billion USD in 2023. Global TIDES CRDMO market size is expected to grow at a CAGR of 23.8% between 2023 and 2032, reaching 37.3 billion USD in 2032.

Global TIDES CRDMO Market Size, 2018-2032E

	CAGR
2018-2023	20.9%
2023-2032E	23.8%



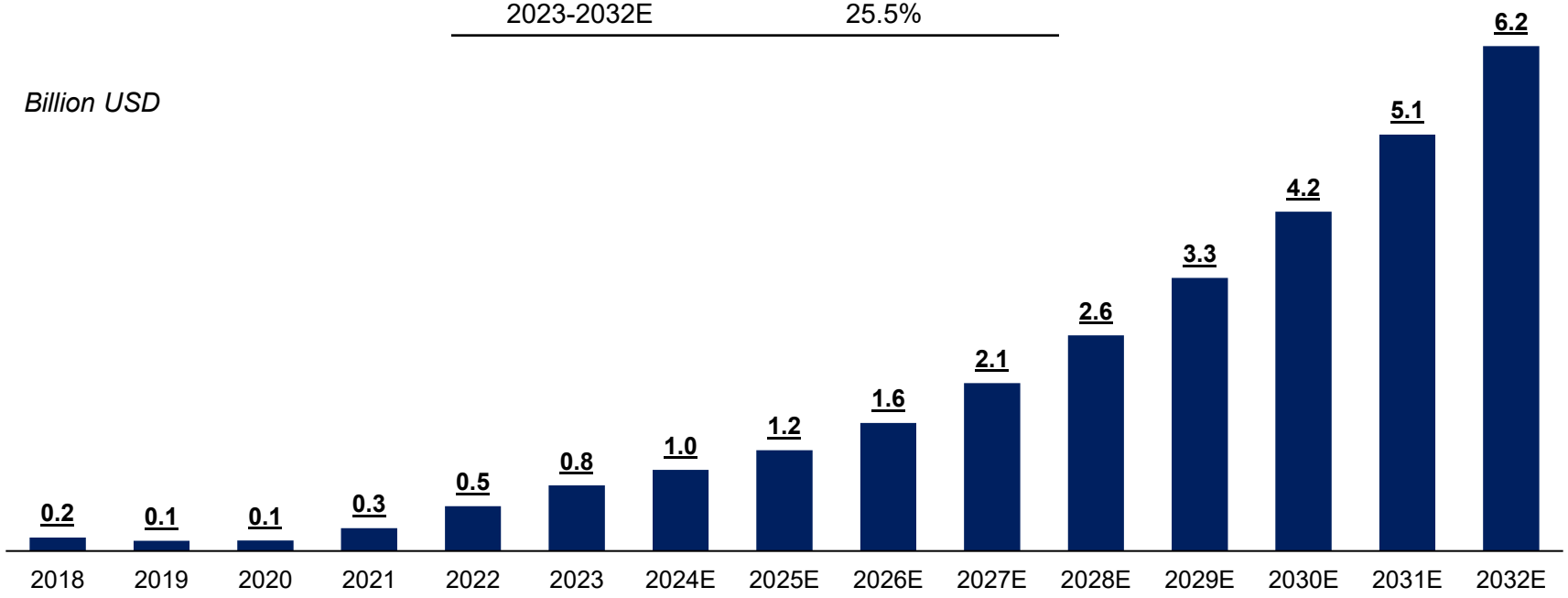
Source: Annual Report, Expert Interview, Public Information, Frost & Sullivan Analysis

China TIDES CRDMO Market Size, 2018-2032E

- China TIDES CRDMO market size grew from 0.2 billion USD in 2018 to 0.8 billion USD in 2023. China TIDES CRDMO market size is expected to increase at a CAGR of 25.5% between 2023 and 2032, reaching 6.2 billion USD in 2032.

China TIDES CRDMO Market Size, 2018-2032E

	CAGR
2018-2023	37.1%
2023-2032E	25.5%



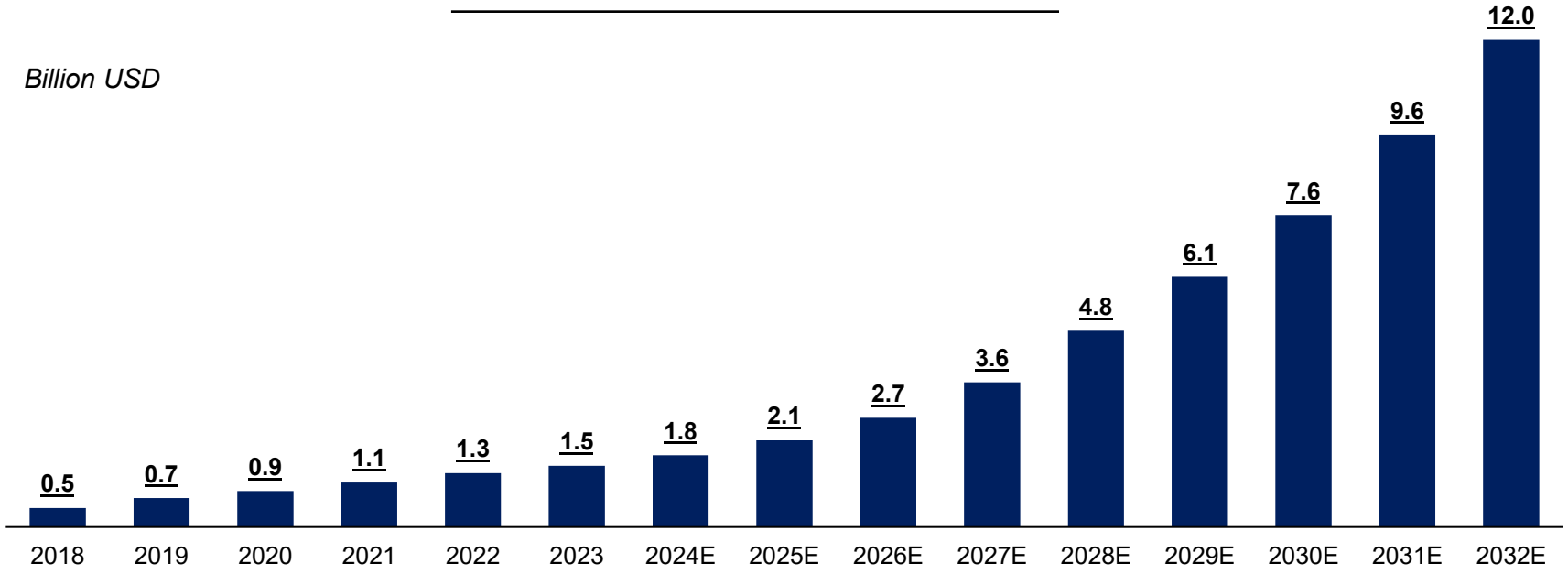
Source: Annual Report, Expert Interview, Public Information, Frost & Sullivan Analysis

US TIDES CRDMO Market Size, 2018-2032E

- The U.S. TIDES CRDMO market size grew from 0.5 billion USD in 2018 to 1.5 billion USD in 2023. The U.S. TIDES CRDMO market size is expected to increase at a CAGR of 25.9% between 2023 and 2032, reaching 12.0 billion USD in 2032.

China TIDES CRDMO Market Size, 2018-2032E

	CAGR
2018-2023	26.2%
2023-2032E	25.9%



Source: Annual Report, Expert Interview, Public Information, Frost & Sullivan Analysis

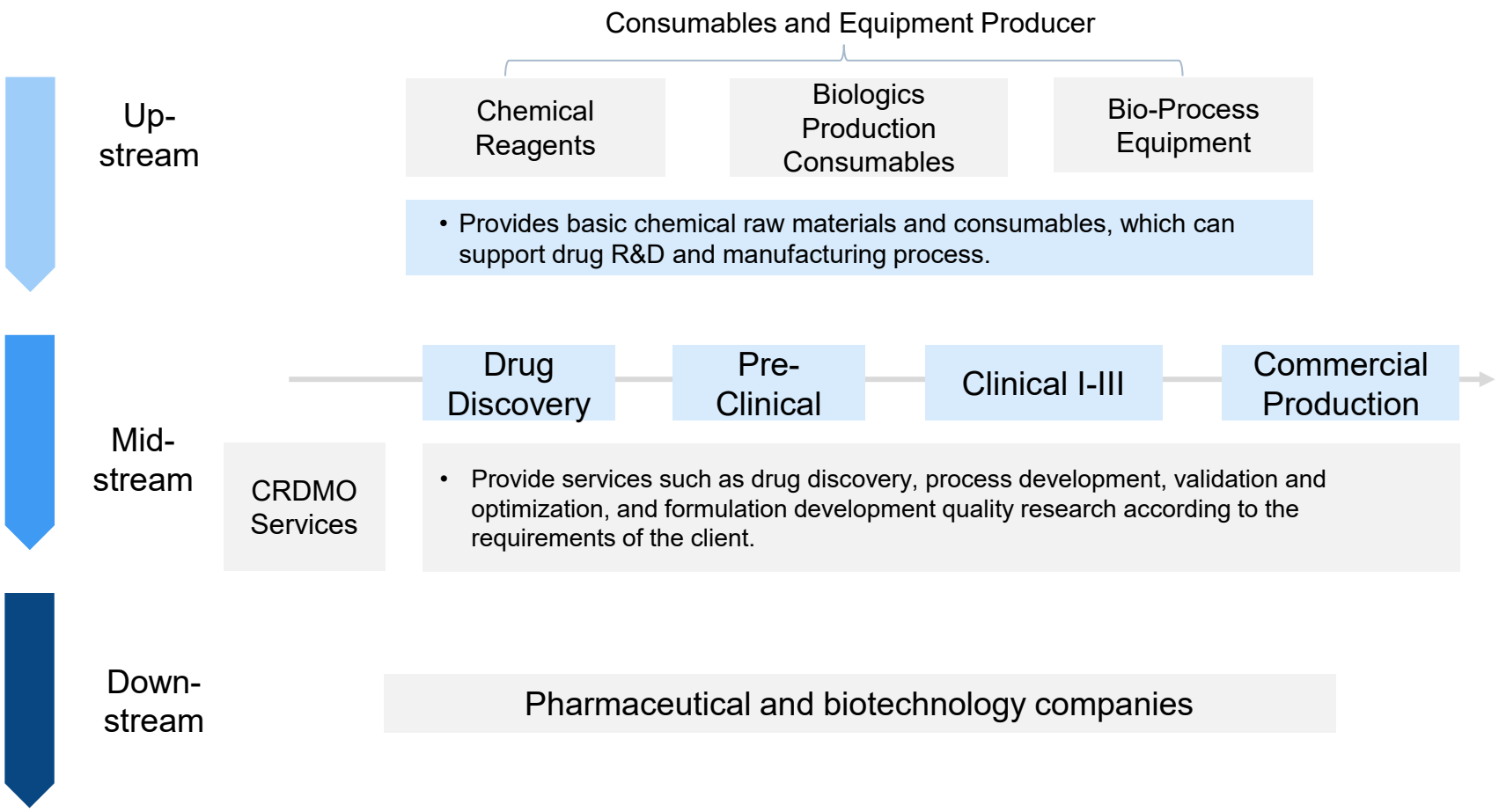
Advantages of CRDMO Services in the Industry Chain

Cost Saving	• CRDMO help pharmaceutical companies save costs on hiring personnel, establishing production capacity and developing processes flows by providing comprehensive services including early-stage drug synthesis, commercial production, and production processes design and optimization. • Pharmaceutical companies can effectively utilize external capabilities to support their in-house R&D and production activities without increasing fixed investment and production personnel cost, thus reducing upfront fixed investment.
Improving Efficiency	• The CRDMO model integrates the drug discovery, development and manufacturing processes to provide comprehensive services from early R&D to late-stage manufacturing. This integrated model reduces communication costs and time costs, thus improving overall efficiency. At the same time, CRDMO companies usually have rich experience and specialized knowledge, and are able to provide effective guidance and advice during the R&D process, accelerating the drug development process.
Promoting resource optimization and sharing	• Under the CRDMO model, pharmaceutical enterprises can share the R&D equipment, technical talents and other resources of CRDMO enterprises, avoiding duplication of investment and waste. • CRDMO enterprises can also reasonably deploy and optimize resources according to market demand and technology development trend, and improve the utilization efficiency of resources.
Innovation	• CRDMO enterprises have strong R&D strength and innovation ability, and can provide innovative drug development solutions for pharmaceutical companies. By cooperating with CRDMO, pharmaceutical companies can obtain more innovative resources and technical support, and enhance their innovation ability and market competitiveness.
Risk Reduction	• New drug R&D is characterized by high risk and high investment, while CRDMO can effectively reduce R&D risk through its strong R&D capability and rich experience.

Source: Frost & Sullivan analysis, Literature research

Analysis of CRDMO industry in Pharmaceutical Industry Chain

- As a contract research, process development and manufacturing organization, CRDMO provides fully integrated services to biopharmaceutical clients in the pharmaceutical industry chain, supporting drugs from discovery through development and manufacturing.



Regulatory Authorities in CRDMO Industry

Authorities	Main Responsibilities	Nature
National Medical Products Administration 国家药品监督管理局	Drafting laws and regulations on drug supervision and management, formulating policies and plans, formulating departmental regulations, promoting the establishment of a direct reporting system for major information on drugs, and organizing the implementation and supervision of inspection. Responsible for drug registration, organizing the formulation and publication of the national pharmacopoeia and other drug standards, classification and management system, and supervising its implementation. Responsible for the development of drug supervision and management of the inspection system and organize the implementation of the organization to investigate and deal with major violations. Responsible for the construction of emergency response system for drug safety affairs; guiding local drug supervision and management work.	The main national regulatory agency responsible for administering the registration of drugs, medical devices, and cosmetics.
National Health Commission of the People's Republic of China 国家卫生健康委员会	Promoting medical and health system reform. Formulating strategic objectives, plans and policies for health reform and development, drafting relevant laws and regulations, formulating rules and regulations on health, food safety, medicines and medical devices, and relevant standards and technical specifications in accordance with the law. Establishing the national essential drug system and organizing its implementation, as well as organizing the formulation of the drug code and the national essential drug catalog. Organizing the formulation of national drug policies. Formulating policies and measures for the procurement, distribution and use of national essential medicines, and putting forward proposals on national pricing policies for essential medicines.	The main national governing body responsible for public health and family planning.

Regulatory Authorities in CRDMO Industry

Authorities	Main Responsibilities	Nature
National Development and Reform Commission 国家发展与改革委员会	Responsible for setting national retail guide prices for essential medicines, and monitoring market purchase and sales prices and distribution costs, such as cost surveys, audits and bidding prices. Implementing the basic drug system, establishing and improvinvg the dynamic adjustment mechanism for the guide price of basic drugs, classify and manage the retail guide price of basic drugs, and exploring the implementation of unified national pricing for exclusive varieties of basic drugs and for varieties for which the price of multiple centralized purchases has been basically stabilized and which have been supplied in sufficient quantities.	The main national regulatory agency responsible for macro-guidance and management of economic performance.
Ministry of Ecology and Environment of the People's Republic of China 国家生态环境部	Formulating and organizing the implementation of ecological and environmental policies, planning and standards. Responsible for ecological and environmental monitoring and law enforcement, supervising and managing pollution prevention and control and nuclear and radiation safety, and organizing and carrying out central environmental protection inspections.	The main national management agency responsible for the overall coordination, supervision and management of ecological environmental protection.

Favorable Government Policy for CRDMO Industry

- The government issued many policy to support the development of pharmaceutical industry, such as clinical trial implied licensing system, optimized drug review and approval system etc. promoting the transformation of pharmaceutical industry from “generic drug” to “innovative drug”. In terms of the development of outsourcing services, the government published special plans, and favorable policies. The favorable policies for CRDMO including the introduction and implementation of Marketing Authorization Holder System, which allows separation the drug marketing license holder and the manufacturing license holder.

Pilot Plan for Drug Marketing Authorization Holder(MAH) System (药品上市持有人制度试点方案)

To encourage the R&D of new drugs, promote industrial upgrading, optimize resource allocation through adopting the mode of separating drug marketing license from production license, allowing the drug listing license holders to produce the drug by themselves or to other manufacturers to produce the drug.

Office of the State Council’s Certain Comments on the Policy Advancing the Refrom and Consummation of Pharmaceutical Production and Circulation of Usage (国务院办公厅关于进一步改革完善药品生产流通使用政策的若干意见)

To Require stricter examination for the drug marketing approval
To enhance consistency evaluation for post-market quality and curative effects of generic drugs.

The 14th Five-Year Plan for the Development of the Pharmaceutical Industry(“十四五”医药工业发展规划)

In the field of new drug research and development, support the development of high-level third-party institutions that can provide services such as drug discovery, pharmaceutical research, pharmacology and toxicology research, clinical research, and inspection and testing.

2016.5 2016.12 2017.1 2019.8 2022.2

13th Five-Year Plan for National Strategic Emerging industry Development (“十三五”国家战略性新兴产业发展规划)

To promote the innovation of chemical drugs and development of high-end preparations and conducting the development and mass production of patent expired drugs.

Provisions of Drug Registration (药品注册管理办法)

To implement the MAH system nationalwide.
A drug marketing authorization holder may produce drugs by itself, or entrust drug manufacturers to produce drugs.
The drug regulatory department of the State Council formulates the guidelines for drug entrusted production quality agreements to guide and supervise drug marketing authorization holders and entrusted manufacturers to fulfill their drug quality assurance obligations.

Source: Government Website, Frost & Sullivan Analysis

Primary Laws and Regulations in the CRDMO Industry

Drug Management

Laws and Regulations	Issuing Department	Issuing Date	Key Element
Drug Administration Law of the People's Republic of China (2019) 《中华人民共和国药品管理法》(2019 年)	Standing Committee of the National People's Congress	2019-08-26	China's Basic Law on drug management stipulates the research, production, use and supervision of drugs in China, improves the implementation of the drug marketing authorization holder system (MAH), and strengthens the management of the full life cycle of drugs.
Implementation Regulations of the Drug Administration Law of the People's Republic of China (Revised in 2019) 《中华人民共和国药品管理法》(2019 年)	The State Council	2019-03-02	In accordance with the Drug Administration Law, the administration and supervision of drug production and distribution enterprises and drugs shall be further clarified.
Pharmacopoeia of the People's Republic of China (2020 edition) 《中华人民共和国药典》（2020 年版)	National Medical Products Administration (NMPA)、National Health Commission	2020-07-02	Legal technical standards to be followed in drug development, production (import), distribution, use, supervision and administration.
Measures for the Management of Post-market Changes of Pharmaceuticals (Trial) 《药品上市后变更管理办法（试行）》	NMPA	2021-01-13	Change management of holder, change management of drug production site, change of other drug registration management matters.

Primary Laws and Regulations in the CRDMO Industry

Drug Registration

Laws and Regulations	Issuing Department	Issuing Date	Key Element
Measures for the Administration of Drug Registration 《药品注册管理办法》	State Administration for Market Regulation	2020-01-22	The important operational regulations of China's drug research and development and registration management mainly stipulate drug clinical trials, marketing authorization and marketing approval, drug verification and registration and inspection
Announcement of the State Food and Drug Administration on Matters related to Further Improving Drug Related Review, Approval and Supervision 《国家药监局关于进一步完善药品关联审评审批和监管工作有关事宜的公告》	NMPA(CFDA)	2019-7-15	The relevant matters related to the review, approval and supervision of raw materials, pharmaceutical excipients, packaging materials and containers in direct contact with drugs (referred to as original and auxiliary packages) and drug preparations are clarified
Announcement on Optimizing Matters Related to the Review and Approval of Drug Registration 《关于优化药品注册审评审批有关事宜的公告》	NMPA, National Health Commission	2018-05-17	The working mechanism for drug priority review and approval has been further implemented, and the approval procedures for clinical trials have been simplified and accelerated
Acceptance of adjustment of drug registration Announcement of Work 《关于调整药品注册受理工作的公告》	NMPA(CFDA)	2017-11-13	The drug registration applications that were previously accepted by the provincial food and drug administration and reviewed and approved by the State Food and Drug Administration are adjusted to the centralized acceptance by the State Food and Drug Administration (CFDA)

Primary Laws and Regulations in the CRDMO Industry

Drug Registration

Laws and Regulations	Issuing Department	Issuing Date	Key Element
Acceptance of Drug registration Notice of review guidelines (trial) 《关于发布药品注册受理审查指南（试行）的通告》	NMPA(CFDA)	2017-11-30	The guidelines for the examination of drug registration acceptance are formulated in accordance with the Announcement on Adjusting the Acceptance of Drug Registration (No. 134 of 2017)
Announcement of the State Administration of China on Adjusting the Review and Approval of Raw materials, Pharmaceutical excipients and Pharmaceutical Packaging Materials 《总局关于调整原料药、药用辅料和药包材审评审批事项的公告》	NMPA(CFDA)	2017-11-30	Drug supervision and administration departments at all levels will no longer accept applications for the registration of raw materials, pharmaceutical excipients and pharmaceutical packaging materials separately, and will be reviewed together after the application for registration of related drug preparations is submitted
Opinions on Deepening the Reform of the Review and Approval System to Encourage Innovation of Pharmaceutical Medical Devices 《关于深化审评审批制度改革鼓励药品医疗器械创新的意见》	General Office of the CPC Central Committee，The State Council	2017-10-08	Promote the structural adjustment and technological innovation of the pharmaceutical and medical device industry, and put forward guidance on reforming clinical trial management, accelerating listing review and approval, promoting drug innovation and generic drug development, strengthening the full life cycle management of pharmaceutical and medical devices, and improving technical support capabilities
Notice on Matters related to Promoting the Pilot Work of the Drug Marketing Authorization Holder System 《关于推进药品上市许可持有人制度试点工作有关事项的通知》	NMPA(CFDA)	2017-8-21	Further implement the legal responsibilities of drug marketing authorization holders, clarify the quality management system in entrusted production and the responsibility system of the whole chain of production and sales, and the regulatory cohesion, responsibility division and responsibility landing of cross-regional drug regulatory agencies

Primary Laws and Regulations in the CRDMO Industry

Drug Registration

Laws and Regulations	Issuing Department	Issuing Date	Key Element
Quality Management Practice for Non-Clinical Drug Studies 《药物非临床研究质量管理规范》	NMPA(CFDA)	2017-07-27	It provides for non-clinical safety evaluation studies of drugs for application for drug registration, including activities related to non-clinical safety evaluation studies of drugs and other pre-clinical related research activities of drugs for registration purposes
Notice of The General Office of the State Council on Issuing and Distributing the Pilot Program of the Holder System of Drug Marketing Authorization ((2016) No. 41) 《国务院办公厅关于印发药品上市许可持有人制度试点方案的通知》(国办发〔2016]41 号)	The State Council	2016-05-26	Further clarify the application conditions, legal obligations and responsibilities, application procedures and scope of pilot drugs for drug registration applicants and drug marketing authorization holders
Announcement of the General Administration on the Release of the Work Plan for the Reform of the Registration Classification of Chemical Drugs (No. 51 of 2016) 《总局关于发布化学药品注册分类改革工作方案的公告（2016 年第 51 号）》	NMPA(CFDA)	2016-03-09	In order to encourage the creation of new drugs, strictly review and approval, improve drug quality, and promote industrial upgrading, the classification of chemical drugs registration is adjusted

Primary Laws and Regulations in the CRDMO Industry

Drug Manufacturing

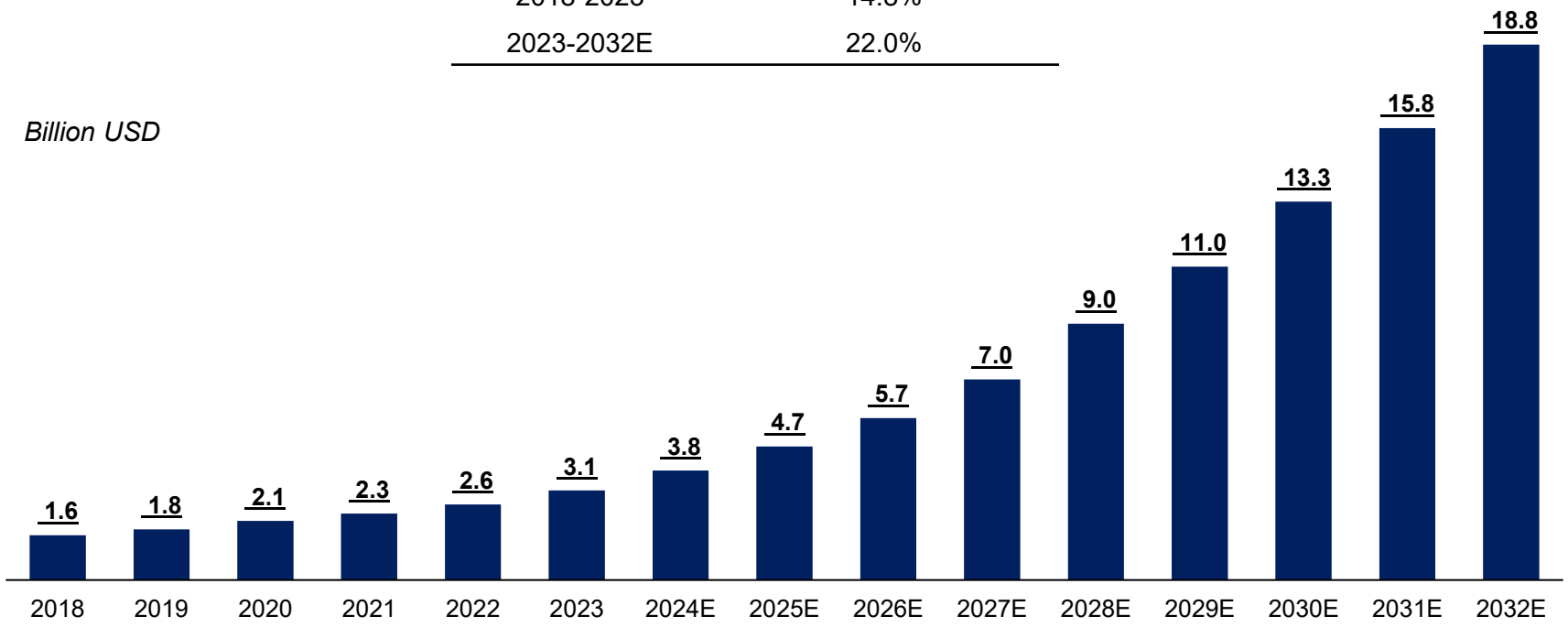
Laws and Regulations	Issuing Department	Issuing Date	Key Element
Announcement of the State Food and Drug Administration on the Implementation of the Newly revised "Measures for the Supervision and Administration of Drug Production" 《国家药监局关于实施新修订<药品生产监督管理办法>有关事项的公告》	NMPA	2020-03-31	Implement the production license of drug manufacturers and the quality supervision and inspection of the production process
Measures for the Supervision and Administration of Drug Production 《药品生产监督管理办法》	State Administration for Market Regulation	2020-01-22	Comprehensively standardize the production license of drug manufacturers and the quality supervision and inspection of the production process
Implementation Regulations of the Drug Administration Law of the People's Republic of China (Revised in 2019) 《中华人民共和国药品管理法实施条例（2019 年修订）》	The State Council	2019-03-02	The establishment of a drug manufacturing enterprise shall be subject to the approval of the drug regulatory department of the province, autonomous region or municipality directly under the Central Government where the enterprise is located and shall be issued a Drug Manufacturing License. To be responsible for the safety, effectiveness and quality control of drugs during the whole process of drug development, production, distribution and use in accordance with law
Good Practice for Quality Control of Pharmaceutical Manufacturing (revised in 2010) 《药品生产质量管理规范》（2010 年修订）	Former Ministry of Health	2011-01-17	Standardize the basic requirements of drug production management and quality control, and systematically standardize the quality requirements of drug production from the aspects of drug production personnel arrangement, plant and facilities, and production equipment

Global Peptide CRDMO Market Size, 2018-2032E

- Global peptide CRDMO market size continues to grow, rising from 1.6 billion USD in 2018 to 3.1 billion USD in 2023.The global peptide CRDMO market size is expected to grow at a CAGR of 22.0% between 2023 and 2032, reaching 18.8 billion USD in 2032.

Global Peptide CRDMO Market Size, 2018-2032E

	CAGR
2018-2023	14.8%
2023-2032E	22.0%



Note: Cosmetic peptides are not included.

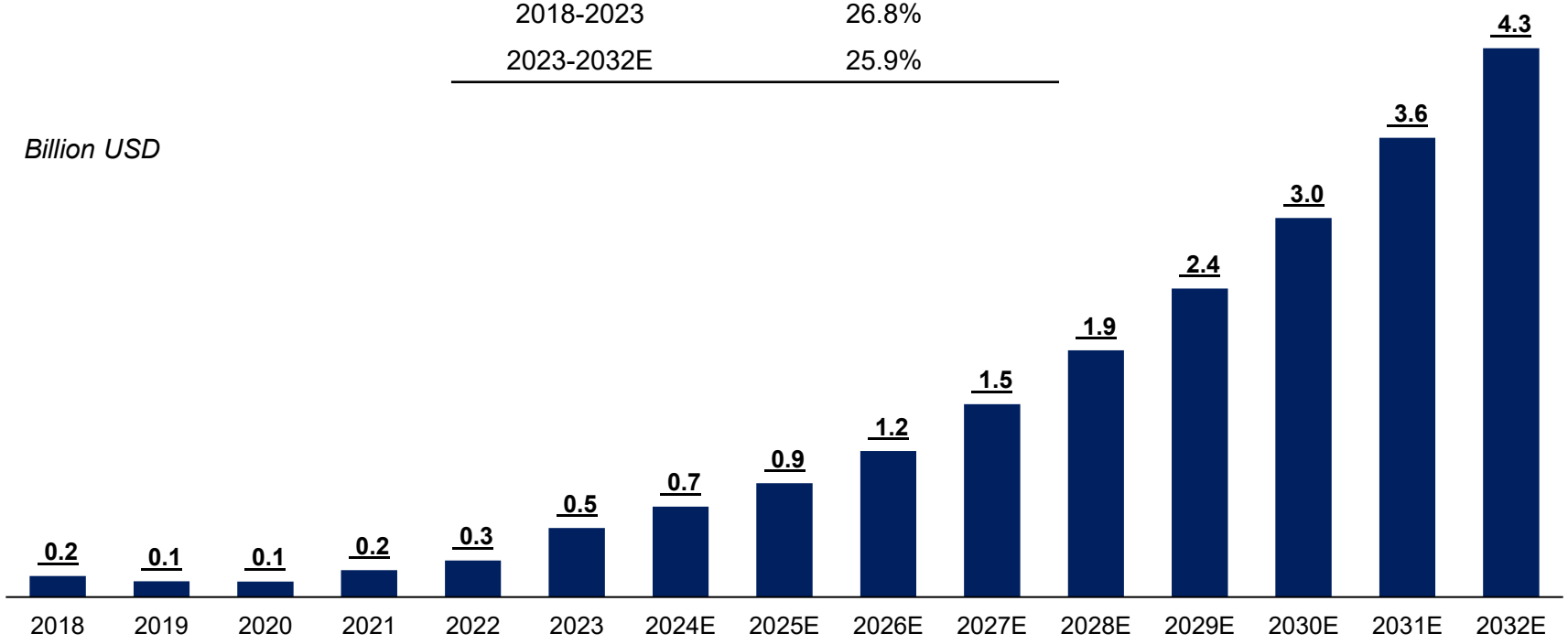
Source: Annual Report, Expert Interview, Public Information, Frost & Sullivan Analysis

China Peptide CRDMO Market Size, 2018-2032E

- China peptide CRDMO market size fluctuates between 2018 and 2023, rising to 0.5 billion USD in 2023. China CRDMO market size is expected to grow at a CAGR of 25.9% between 2023 and 2032, reaching 4.3 billion USD in 2032.

China Peptide CRDMO Market Size, 2018-2032E

	CAGR
2018-2023	26.8%
2023-2032E	25.9%



Note: Cosmetic peptides are not included.

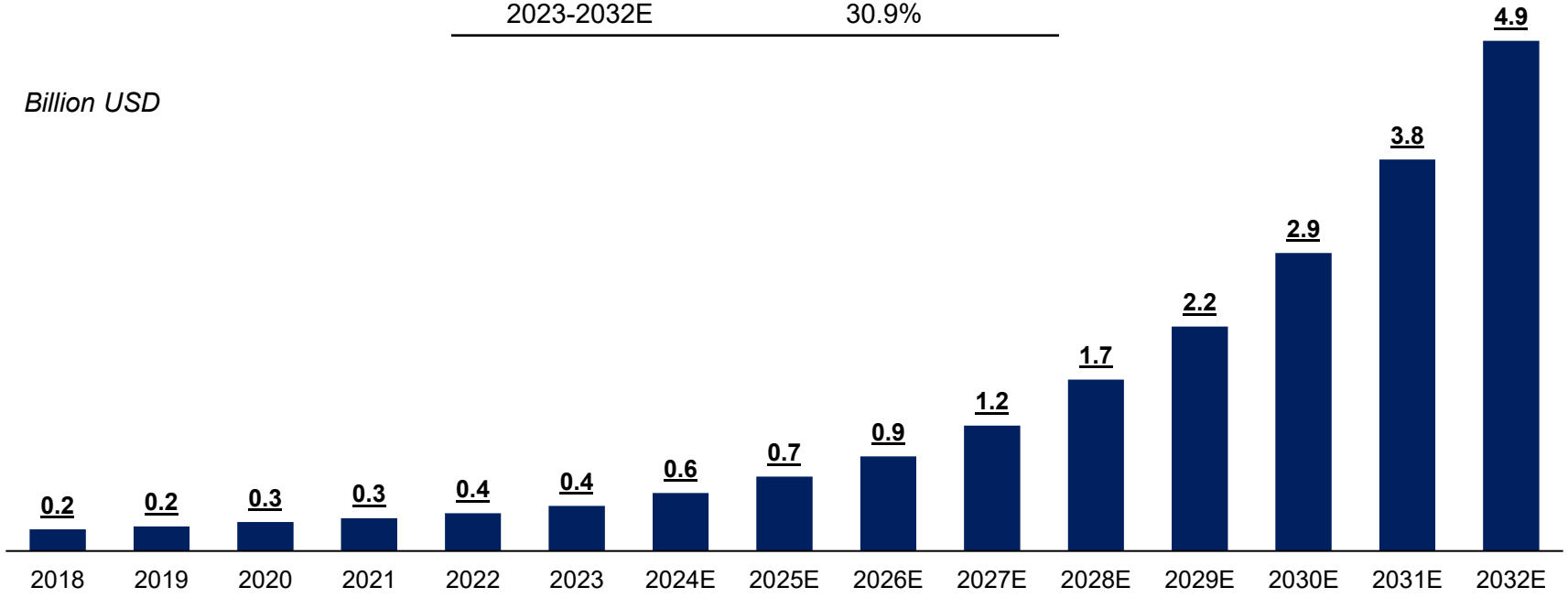
Source: Annual Report, Expert Interview, Public Information, Frost & Sullivan Analysis

US Peptide CRDMO Market Size, 2018-2032E

- The U.S. peptide CRDMO market size grew from 0.2 billion USD in 2018 to 0.4 billion USD in 2023.The U.S. peptide CRDMO market size is expected to grow at a CAGR of 30.9% between 2023 and 2032, reaching 4.9 billion USD in 2032.

US Peptide CRDMO Market Size, 2018-2032E

	CAGR
2018-2023	16.0%
2023-2032E	30.9%



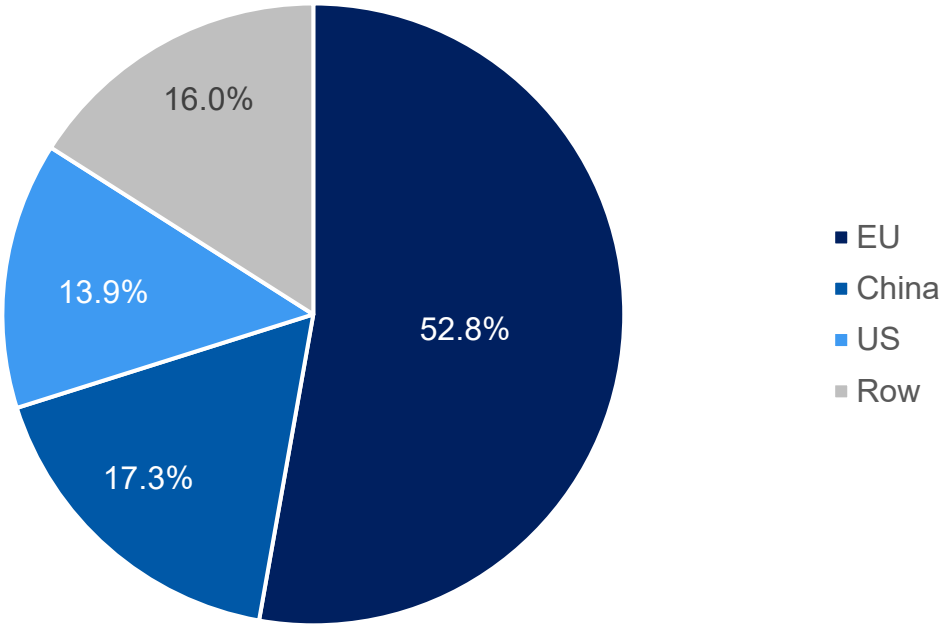
Note: Cosmetic peptides are not included.

Source: Annual Report, Expert Interview, Public Information, Frost & Sullivan Analysis

Peptide CRDMO Market Size, separated by Regions, 2023

- In 2023, the global peptide CRDMO market size reaches 3.1 billion USD, of which the Europe peptide CRDMO market reaches 1.7 billion USD, accounting for 52.8%. China peptide CRDMO market size is 0.5 billion USD, accounting for 17.3% of the global market.

Peptide CRDMO Market Size, separated by EU, China, US, and RoW, 2023



Note: Cosmetic peptides are not included.

Source: Annual Report, Expert Interview, Public Information, Frost & Sullivan Analysis

Competitive Landscape of Global Peptide-focused CRDMO Market, 2023

Company	Main Business Area	Revenue in 2023 (Million USD)	2023 Market Share
Company A	Europe, the U.S., and Asia	431.5	13.8%
Company B	Europe, the Americas, and Asia Pacific	313.6	10.0%
Medtide	China, the United States, Japan, Europe, South Korea, and Australia	47.5	1.5%
Company C	the U.S., China, and Europe	38.6	1.2%
Company D	North America, Australia, South Korea, and MENA region	36.6	1.2%
Company E	Europe, the U.S., and Asia	24.9	0.8%

Note:
1. Company A. Bachem, headquartered in Switzerland. It specializes in the development and production of peptides and oligonucleotides, and its services can be divided into three main categories, Commercial API, chemical manufacturing and control development, research & specialties. Company B. Polypeptide, headquartered in Switzerland. It specializes in the development and manufacturing of synthetic peptides and oligonucleotides used as API or intermediates in therapeutic products. Company C. Ambio, headquartered in the U.S.. It is a full-service peptide manufacturing company. Company D. USV Peptide, headquartered in India. It focuses on peptide NCE, providing manufacturing and regulatory support, generic peptide development/scaling up and commercial production. Company E. BCNpeptides, headquartered in Spain. It is an API manufacturing company, focusing on the GMP manufacturing of bioactive peptides for pharmaceutical, veterinary, and cosmetic applications.
2. Defines the scope of business as being dedicated to peptides based on the fact that peptides account for more than 50% of revenues from the main business.
3. Revenue in 2023 is the revenue generated from peptide in 2023.

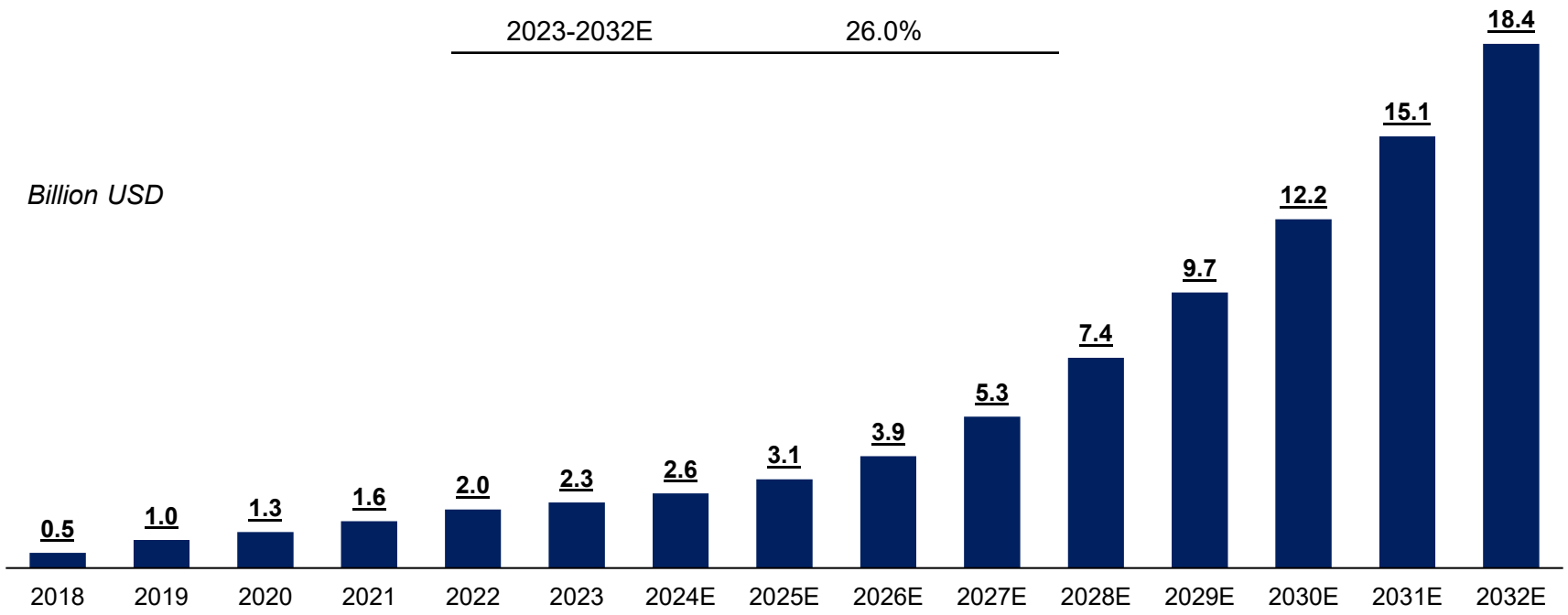
Source: Annual report, Expert interview, Frost & Sullivan analysis

Global Oligonucleotide Drug CDMO Market, 2018-2032E

- Global oligonucleotide drug CDMO market size continuously grew from 0.5 billion USD in 2018 to 2.3 billion USD in 2023. Global oligonucleotide drug CDMO market size is expected to increase to 18.4 billion USD in 2032.

Global Oligonucleotide Drug CDMO Market size, 2018-2032E

	CAGR
2018-2023	33.8%
2023-2032E	26.0%



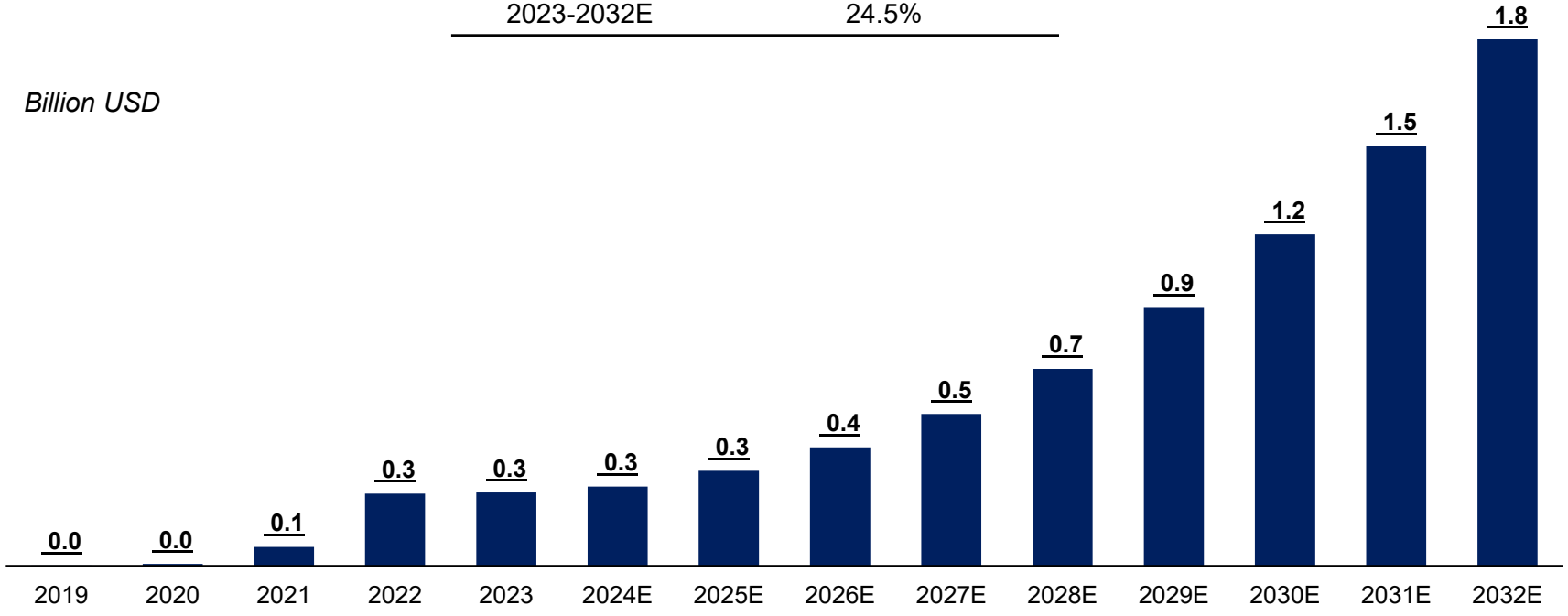
Source: Annual Report, Expert Interview, Public Information, Frost & Sullivan Analysis

China Oligonucleotide Drug CDMO Market, 2019-2032E

- China Oligonucleotide CDMO market size is 1.0 million USD in 2019 and increased to 0.3 billion USD in 2023. China Oligonucleotide CDMO market size is expected to continue expanding and grow to 1.8 billion USD in 2032.

China Oligonucleotide Drug CDMO Market size, 2019-2032E

	CAGR
2019-2023	300.1%
2023-2032E	24.5%



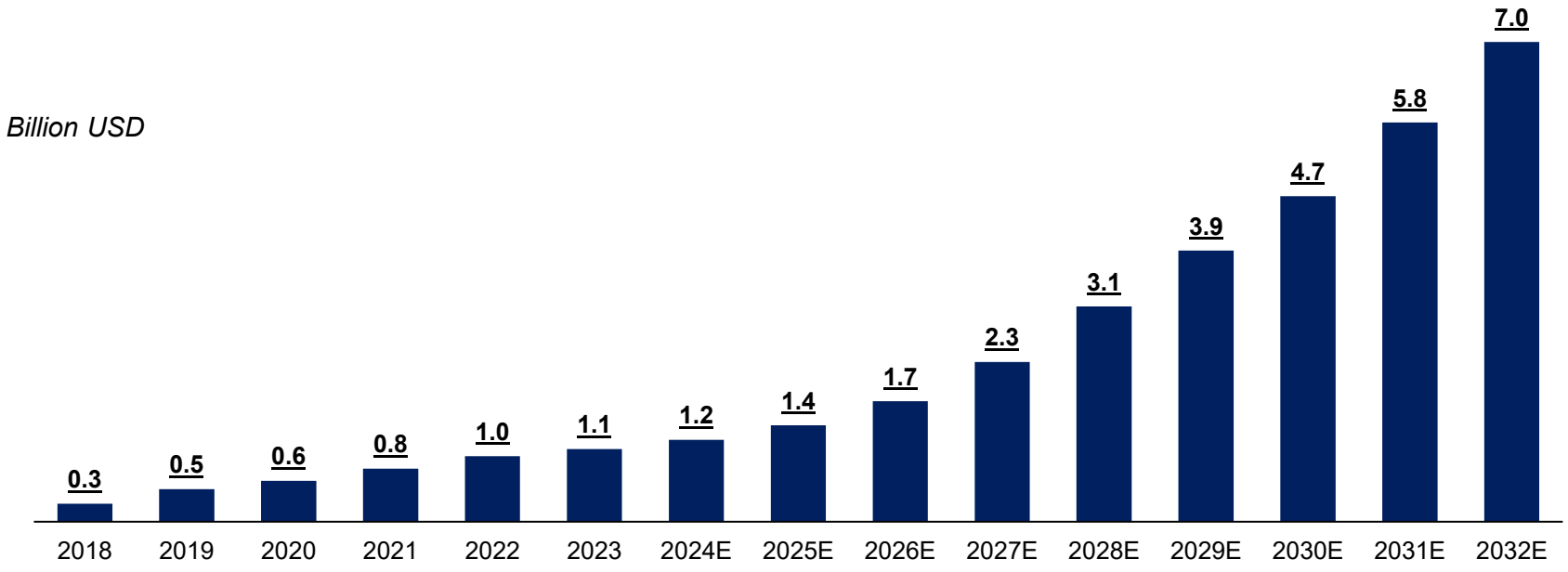
Source: Annual Report, Expert Interview, Public Information, Frost & Sullivan Analysis

US Oligonucleotide Drug CDMO Market, 2018-2032E

- The U.S. oligonucleotide drug CDMO market size continuously grew from 0.3 billion USD in 2018 to 1.1 billion USD in 2023. The U.S. oligonucleotide drug CDMO market size is expected to increase to 7.0 billion USD in 2032.

US Oligonucleotide Drug CDMO Market size, 2018-2032E

	CAGR
2018-2023	32.4%
2023-2032E	23.3%



Source: Annual Report, Expert Interview, Public Information, Frost & Sullivan Analysis

Value Proposition of TIDEs CRDMO

Accelerating R&D Process	• TIDES CRDMOs are typically equipped with cuttingedge R&D and production facilities. These include automated synthesis systems, high-performance liquid chromatographs, ensuring efficient, high-quality and highpurity production of peptide and oligonucleotides. CRDMOs have established streamlined processes for TIDES development, saving time and resources. Additionally, CRDMOs can handle multiple stages of development simultaneously, further expediting the R&D timeline.
Risk Mitigation	• CRDMOs typically maintain teams with extensive experience and expertise in peptide and oligonucleotide R&D, production and quality control. In addition, CRDMOs adhere to stringent regulatory standards and quality control measures to ensure the safety, efficacy, and consistency of the products they manufacture. These CRDMOs provide expertise, resources, and support to navigate complex development processes, ensuring project success. By partnering with CRDMOs, pharmaceutical companies can mitigate risks associated with technical challenges, resource constraints, and regulatory compliance.
Scalability and Flexibility	• TIDES CRDMOs have the ability to seamlessly scale up production as needed, from small-scale research to large-scale commercial batch production. This scalability ensures continuity in the drug development process and acilitates a smooth transition from early development to commercial production.
Cost Control	• The specificity of TIDES drug production process leads to high cost associated with establishing a complete set of hardware facilities solely for TIDES drug R&D and production. CRDMOs offer more flexible capacity and reduce fixed costs for service companies. Compared with self-development and production, TIDES CRDMOs efficiently complete projects through their professional technology and experience, which can help customers save on labor, material and time costs. TIDES CRDMOs provide scale-up production services, leading to lower per-unit production costs.

Sources: Frost & Sullivan Analysis

Growth Drivers of TIDEs CRDMO Market

Unmet Needs in Chronic Disease	• The increasing prevalence of chronic diseases among the aging population, coupled with the rising demand for personalized medicines and precision therapies, underscores the necessity for TIDES drugs. One notable example is GLP-1, a pleiotropic hormone with multifaceted metabolic functions. GLP-1 holds great promise as a candidate for developing pharmacotherapies to address conditions such as obesity, diabetes, and other chronic ailments. In this landscape, TIDES CRDMOs play a pivotal role. They provide essential manufacturing expertise, scale-up capabilities, and regulatory compliance to meet the growing demand for these cutting-edge therapies.
More TIDEs Approvals	• TIDES have indeed established a distinctive therapeutic niche, demonstrating robust momentum because they explore new indications and advance through various stages of research. Notably, an increasing number of peptides are now synthesized chemically rather than relying solely on recombinant methods. For instance, tirzepatide, an exciting GLP-1 analogue, has been developed by Eli Lilly using chemical synthesis.
New Formulations Require Higher Drug Substance Amount & Production Capacity	• Currently, injectables serve as the primary method for administering peptide drugs. However, alternative administration routes, such as oral delivery, are gaining significant attention. The adoption of these alternative forms has the potential to expand the use of peptide drugs into additional disease areas, including inflammation. Oral delivery necessitates larger patient intake compared to injectables. This shift in administration methods requires increased production of drug substances with enhanced capabilities and capacities. CRDMOs play a pivotal role in meeting this demand by offering consistent and reliable supply across the spectrum of low- to high-volume peptide production. Moreover, CRDMOs provide flexibility and tailor development processes to meet the specific requirements of their clients.

Sources: Frost & Sullivan Analysis

Growth Drivers of TIDEs CRDMO Market

Manufacturing Complexity and Technological Advancements	• Given the intricate nature of TIDES APIs synthesis and the stringent quality standards in the pharmaceutical industry, many pharmaceutical and biological companies opt to outsource the production of TIDES drugs to CRDMOs. These CRDMOs possess the necessary technological capabilities and regulatory expertise, driving market growth. Continuous advancements in TIDES synthesis technologies are revolutionizing the efficiency and cost-effectiveness of the manufacturing process. Innovative enzymatic and solid-phase synthesis methods are emerging, making peptide manufacturing increasingly scalable and economical. Notably, some long peptides, such as insulin and GLP-1, that were previously manufactured solely through complex recombinant rDNA processes can now be synthesized using chemical methods. These technological breakthroughs empower peptide CRDMOs to offer pharmaceutical and biological companies a more cost-effective alternative to in-house production.
Outsourcing Strategies of TIDEs Pharmaceutical and biotechnology Companies	• The global TIDES CRDMO services market has experienced consistent growth over the past few years, driven by the expanding global TIDES drug market. Pharmaceutical and biological companies are increasingly turning to CRDMOs to outsource process development and manufacturing. By doing so, these companies can focus on their core competencies, including drug discovery, clinical development, and commercialization. Large pharmaceutical companies, such as Eli Lilly and others, prefer to collaborate with CRDMOs for manufacturing. CRDMOs offer manufacturing capabilities and technologies that may not be available in-house, enabling pharmaceutical companies to produce TIDES drug substances more cost-effectively. Additionally, TIDES drugs represent an emerging therapy, and the leading players in this field are primarily biotech companies. Given their strong propensity for outsourcing, this trend creates significant opportunities for CRDMOs specializing in TIDES drug development and manufacturing.

Sources: Frost & Sullivan Analysis

Future Trends of TIDEs CRDMO Market

Advancement in Complex and Large-Scale Manufacturing	• TIDES drug manufacturing involves various techniques, each customized to the specific characteristics of the TIDES being produced. Due to the diverse nature of TIDES, synthesis methods can vary significantly, resulting in a more complex manufacturing process. Furthermore, the increasing demand for TIDES manufacturing highlights the need for expertise in process scale-up and large-scale production from CRDMOs. These organizations should have the capability to produce TIDES at a large scale, typically achieving GMP batch sizes ranging from hundreds of kilograms to several tons.
Market Scale Expansion	• As the biopharmaceutical sector continues to flourish, the demand for TIDES drugs, as a promising therapeutic modality, is expected to soar. This trend will fuel the expansion of the CRDMO market size globally, driven by the increasing need for outsourcing R&D and manufacturing services for TIDES drugs. Furthermore, the growing demand for personalized medicine and precision therapies, along with the progressive development of therapeutic areas from rare diseases to common chronic diseases, will create more opportunities for the TIDES drug CRDMO market. This evolving landscape underscores the pivotal role that CRDMOs will play in meeting the growing demands of the TIDES drug development and production ecosystem.
Integrated Service	• CRDMOs strategically focus on acquiring differentiated capabilities to enhance their value proposition. One such approach involves adopting the one-stop-shop model, aligning with the trend among major pharmaceutical companies. These companies are consolidating their supplier base and transitioning from outsourcing providers to strategic partners. Leading CRDMOs actively pursue the goal of becoming fully integrated players capable of offering comprehensive services across the entire drug life cycle and supply chain. Their services span from drug substance development to packaging and distribution, covering all key geographical regions. This strategic direction enables CRDMOs to provide enhanced support to their clients and establish long-term, collaborative partnerships that drive mutual success in the dynamic pharmaceutical landscape.
Increasing Specialized Business Range	• The peptide CRDMO market has witnessed a trend towards consolidation, resulting in a decrease in the number of players over the past one or two decades. This consolidation enables companies to specialize in the peptide CRDMO field, allowing them to capture a larger portion of the overall market share and capitalize on synergies within their operations. By concentrating their efforts and resources in this specialized area, these major players can enhance their competitiveness and better meet the evolving needs of their clients in the peptide drugs industry.

Sources: Frost & Sullivan Analysis

Entry Barriers of TIDEs CRDMO Market

Advanced Technologies and Cost for Plant Set-Up	• The development and production of TIDES drugs is highly demanding in terms of technology, equipment and environment, requiring a high degree of technical expertise and sophisticated equipment. In addition, manufacturing complexity of peptides increases exponentially with each added amino acid, requiring the establishment of large GMP compliant manufacturing facilities. These entail significant costs, which escalate further when setting up global sites. TIDES drugs have lengthy R&D cycles, substantial, high investment and high risks. CRDMO companies must allocate substantial capital for equipment acquisition, R&D expenditures, clinical trials, and market expansion.
Stringent Regulations	• The TIDES drug market is subject to stringent regulatory standards, requiring companies to undergo rigorous certification processes and scrutiny before market entry. For instance, manufacturing facilities producing TIDES drugs must adhere to stringent GMP requirements to ensure a clean environment. Also, the increasing stringency of regulations related to commercial manufacturing, poses a key challenge for contract manufacturers. Obtaining GMP certification and building factories is a multi-year process that hinders new entrants from accessing the market.
Experience Accumulation and Capturing Clients	• The synthesis of TIDES drugs generates by-products and impurities, making quality control and purification challenging. This requires extensive experience and knowledge. In addition, TIDES CRDMOs need to build trust with clients. Due to the specificity of TIDES molecules, customers tend to prefer working with experienced and reputable CRDMOs. To compete and attract clients, new TIDES CRDMO players need to build and maintain a large pool of highly qualified talent and acquire expensive and complex technology. Despite differences in molecular structure, peptide and oligonucleotide drugs share many similarities in synthesis, pharmacology, and drug development. Enterprises with peptide related research and production experience have more advantages than new entrants when expanding into the oligonucleotides.
Supply Chain	• The R&D and production of TIDES APIs involves a number of processes, including raw material procurement, manufacturing. Establishing a stable and reliable supply chain is crucial to ensure timely access to key raw materials, such as protected amino acids and nucleoside monomers, that meet quality standards.

Sources: Frost & Sullivan Analysis

Confirmation

- Medtide is one of the most comprehensive peptide-focused CRDMO globally, offering full-cycle services ranging from early-stage discovery, pre-clinical research and clinical development to commercial-stage production.
- Medtide has established world-leading production technology and large-scale production capabilities for peptide drugs.
- Medtide's expertise in peptide drug design, modification, synthesis and production control exceeds competitors.
- Medtide excel in modifying complex antigen peptides ("MAPs"), cyclic peptides (e.g., single-cycle peptides comprising amide bonds, single thioether bonds, and linked disulfide bridge peptides, stapled peptides, bicyclic peptides, and tricyclic peptides), placing us at the forefront of the industry
- The hemostatic gel products of 3D Matrix Japan, Ltd. in collaboration with Medtide enjoys several advantages in safety, convenience, and ease of indication expansion, and has significant market potential.
- The dual benefit of enhanced efficiency and sustainability positions Medtide at the forefront of peptide manufacturing.
- The number of non-insulin peptide drugs that had obtained regulatory approvals reached 76 since 2015 and as of the Latest Practicable Date.
- The percentage of pharmaceutical and biotech companies that outsourced clinical development and production to third party service providers reached approximately 70% in the global peptide drug market in 2023, higher than 30%-40% for biologics.
- Besides TIDES drugs, peptide-oligonucleotide conjugates ("POC"), peptide drug conjugates ("PDC"), and radionuclide drug conjugate ("RDC") drug products are also expected to experience significant growth.
- Oral GLP-1 drugs are expected to experience significant growth in market size and market share, and represent the most active field of future peptide drug development.
- In addition to growth in market size and demand, the global GLP-1 industry has also witnessed the rise of new peptide formulation technologies.
- In terms of barriers to entry, the peptide-focused CRDMO market generally requires high technical expertise.
- The raw materials used by peptide CRDMOs primarily include protected amino acids. The prices of such raw materials remained relatively stable during the Track Record Period.
- Pharmaceutical and biotech companies in Mainland China, including those focused on TIDES related products, experienced a significant slow-down in their NCE development pipelines in 2023 compared to prior years. The healthcare industry experienced a general decline in terms of the amount of financing in recent years, forcing industry players (including our customers) to make strategic adjustments, such as streamlining their pipelines to focus on fewer pipeline products with more potential of commercialization success.
- The generic drug market in Mainland China also witnessed unfavorable development in 2023 due to tighter industry regulation.
- In recent years, the average labor cost in the global CRDMO market, has been steadily increasing as the competition for qualified employees has become more intense.

Sources: Frost & Sullivan Analysis

Confirmation

- The critical raw materials are essential for TIDES CRDMO services, such as Fmoc-L-Ala-OH, Boc-Pro-OH, (R)-DOTA-GA(tBu)4, and rink amide linker. The major raw materials are important to complete the production, such as 2-(1H-Benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate ("HBTU"), 1-Hydroxy-7-azabenzotriazole ("HOAT"), and 2-(5-Norbornene-2-yl)-1,1,3,3- tetramethyluronium tetrafluoroborate ("TDBTU"). The general materials are common chemical materials that are less critical to the overall production processes, including acetone, absolute alcohol, and ethyl acetate.
- Despite the anticipated growth in the GLP-1 drug market, the peptide CRDMO and oligonucleotide CDMO markets in China are experiencing slow growth.
- The intellectual property ownership arrangement is in line with industry norm because other CRDMOs in the industry use similar intellectual property arrangements.
- Consolidation in the industries in which our customers operate may have an impact on such spending as our customers integrate acquired operations, including research and development departments and manufacturing operations.
- Between January 1, 2015 and the Latest Practicable Date, a total of 76 non-insulin peptide drugs received regulatory approval globally. Specifically, during this period, 56 non-insulin peptide drugs were approved in countries or regions outside of China, which included 11 GLP-1 peptide drugs and 45 non-GLP-1 peptide drugs.
- In China, 36 non-insulin peptide drugs were approved, comprising 11 GLP-1 peptide drugs and 25 non-GLP-1 peptide drugs. Among the 36 non-insulin peptide drugs approved in China and 56 approved outside China, 16 drugs were approved in both China and other countries or regions between January 1, 2015 and the Latest Practicable Date.
- Between January 1, 2015 and the Latest Practicable Date, the total number of company-initiated Phase II or Phase III clinical trials for peptide drug pipelines reached 360. The following chart sets forth the distribution by disease area of all company initiated Phase II or Phase III clinical trials for peptide drugs between January 1, 2015 and the Latest Practicable Date.

Sources: Frost & Sullivan Analysis