

研究报告

小核酸药物行业图谱¹

科创金融研究中心

朱雅姝 胡杏

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一、引言

mRNA

mRNA

2015

2025

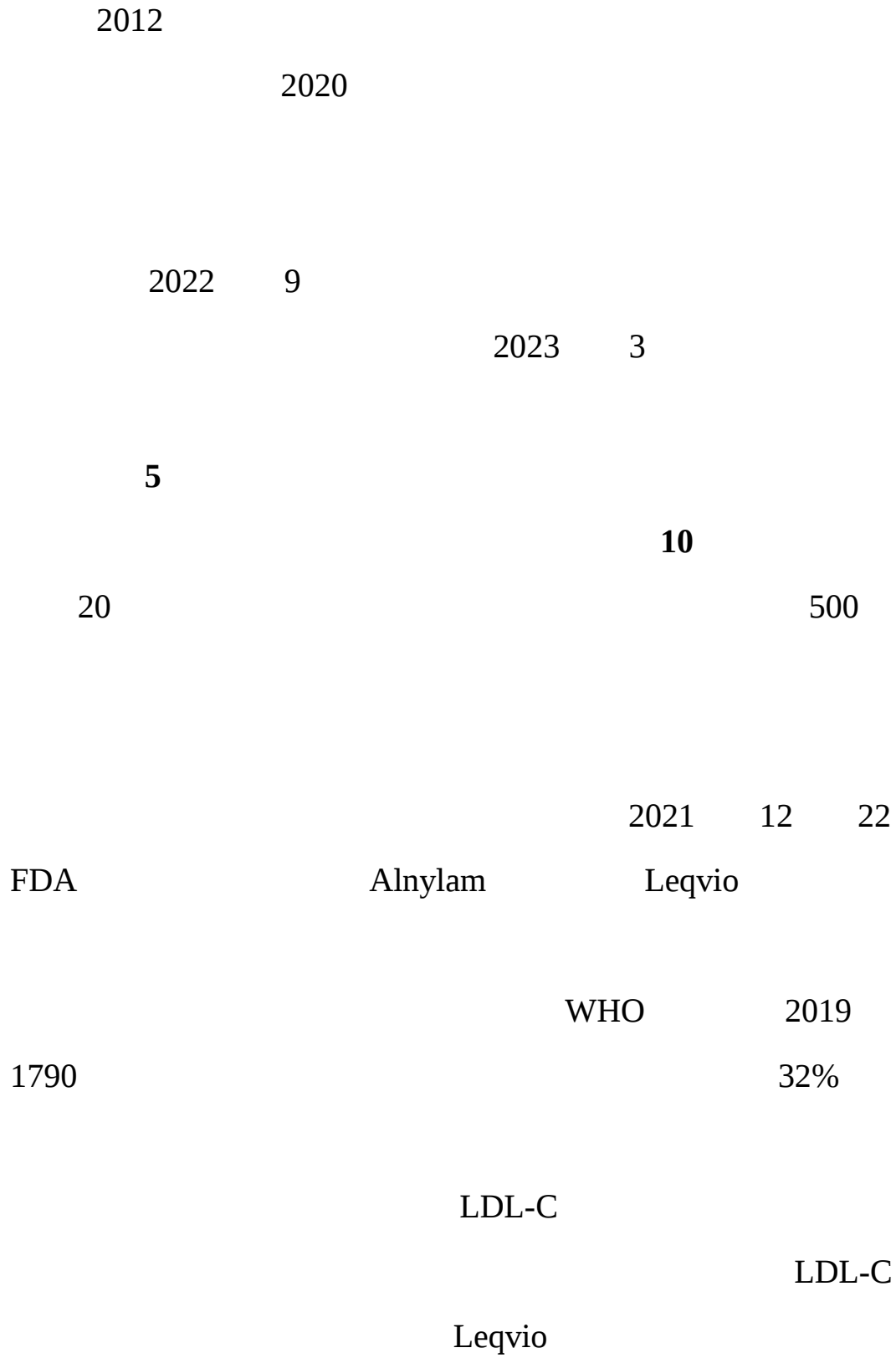
2017

RNA

T

CAR-T

2022



二、小核酸药物概念

1957 Francis Crick

DNA

RNA

RNA

DNA

DNA

RNA

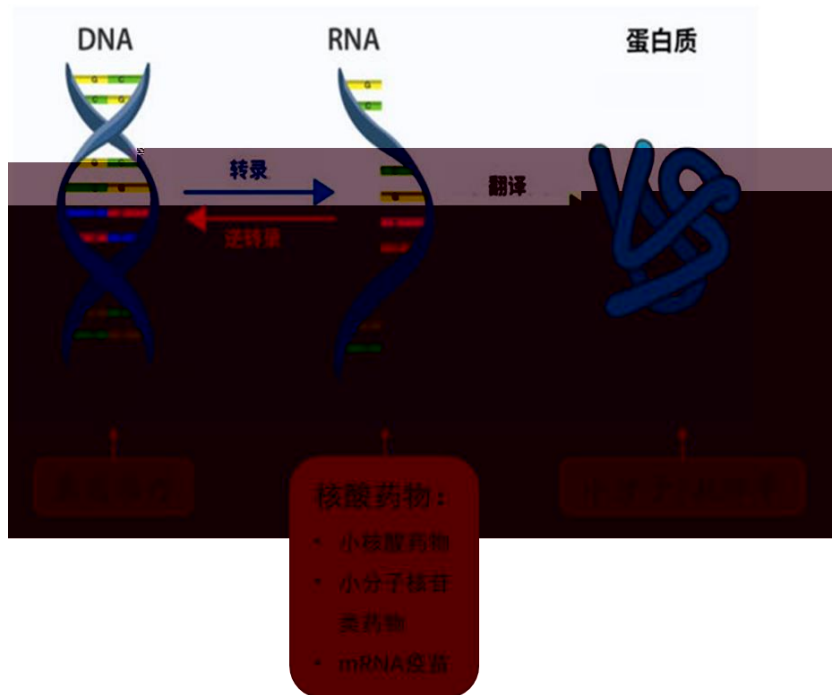
DNA

4

/

RNA

20



2-1

DNA RNA

mRNA

mRNA

1

30nt

RNA

2

DNA RNA

3 mRNA

mRNA 2

mRNA

2-1

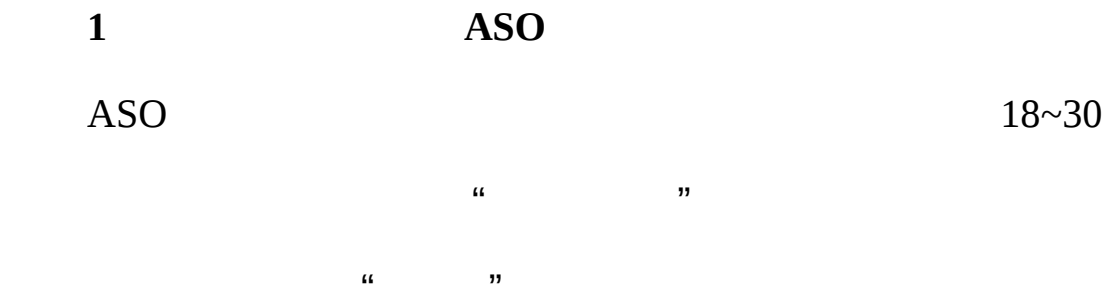
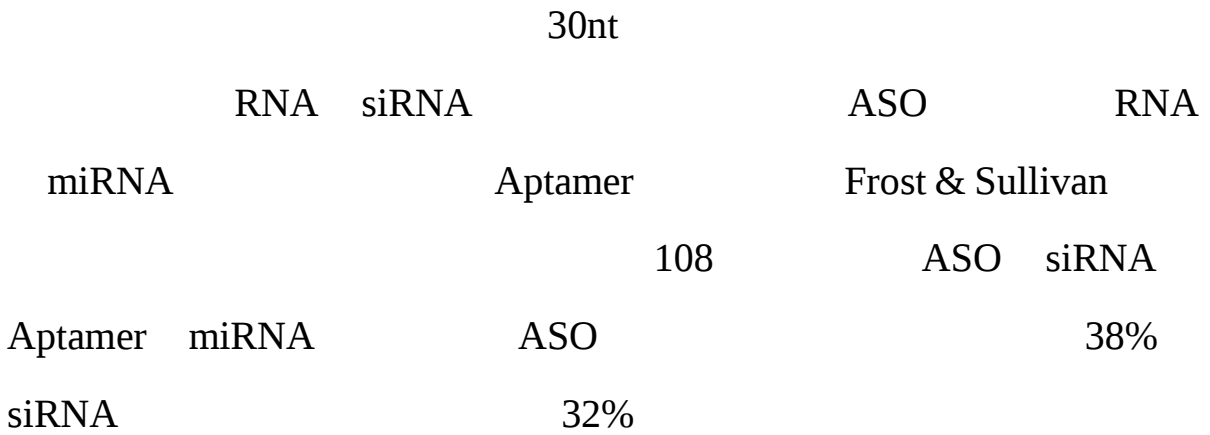
	30nt	RNA		Spinraza

DNA

RNA



mRNA



RNA

ASO

mRNA



mRNA

ASO

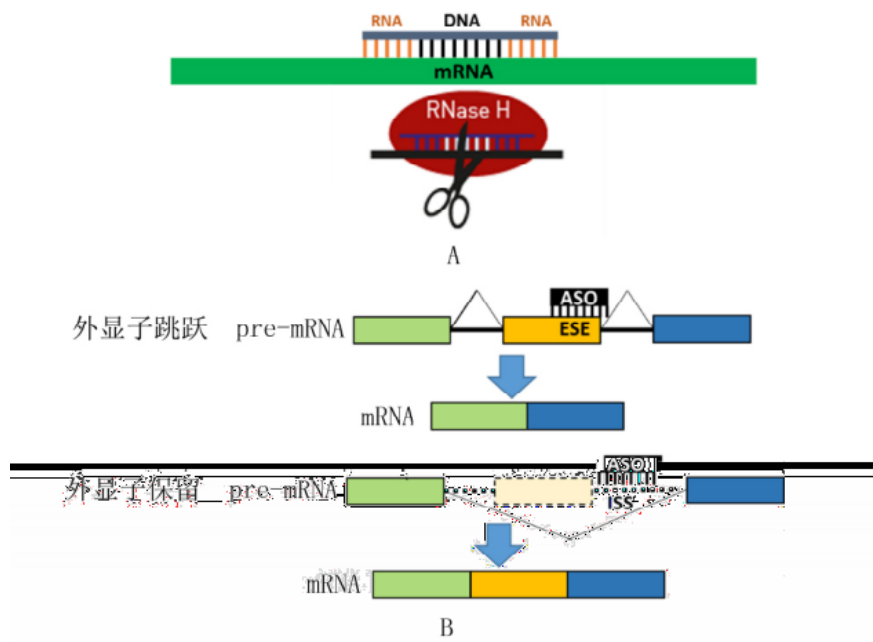
mRNA

mRNA

➤ mRNA ASO mRNA
RNaseH mRNA

➤ DNA pre-mRNA mRNA
pre-mRNA RNA

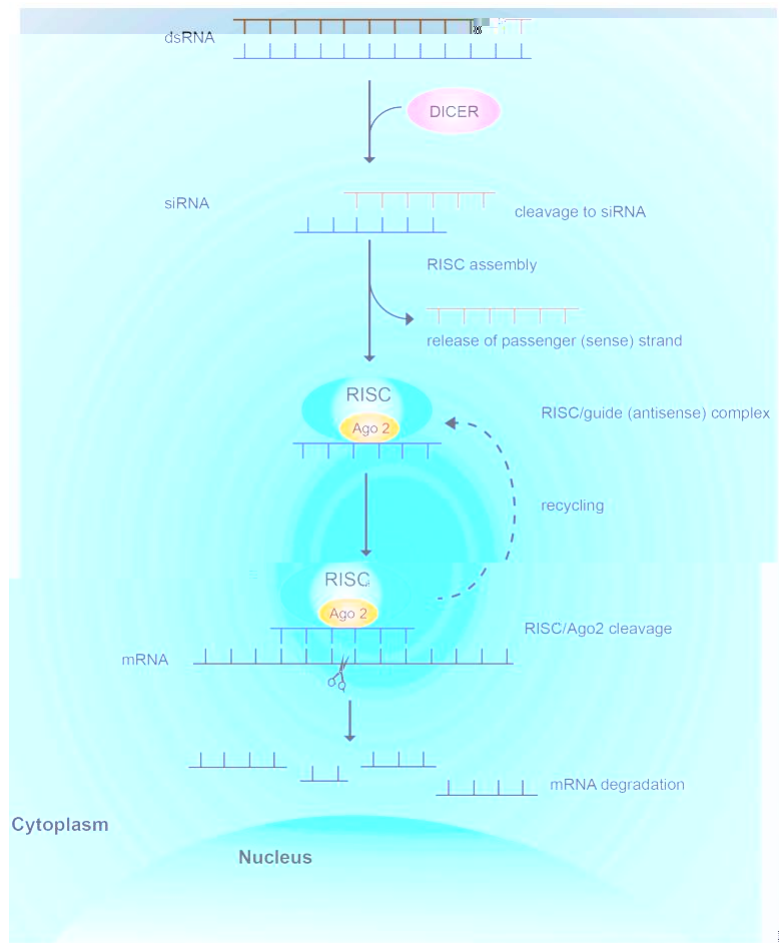
ASO
➤ uORF
mRNA ASO uORF



2-2

2 RNA siRNA

RNA Small interfering RNA siRNA 19-
23 RNA
siRNA RNAi
RNA dsRNA
Dicer 21~23
RNA siRNA siRNA Ago2
siRNA RNA
RISC mRNA



2-3 siRNA

3 RNA miRNA

RNA microRNA, miRNA 22

RNA / mRNA

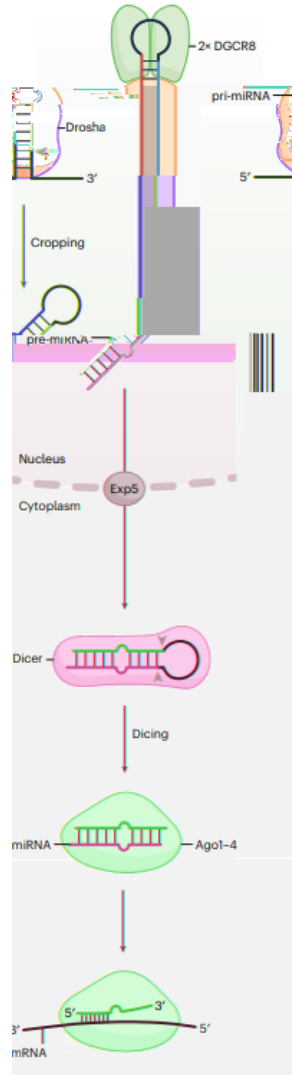
miRNA

miRNA pri-miRNA Drosha

miRNA pre-miRNA Dicer

miRNA RNA RISC

mRNA



2-4 miRNA

4

Aptamer

“ ”

20-

100

DNA RNA

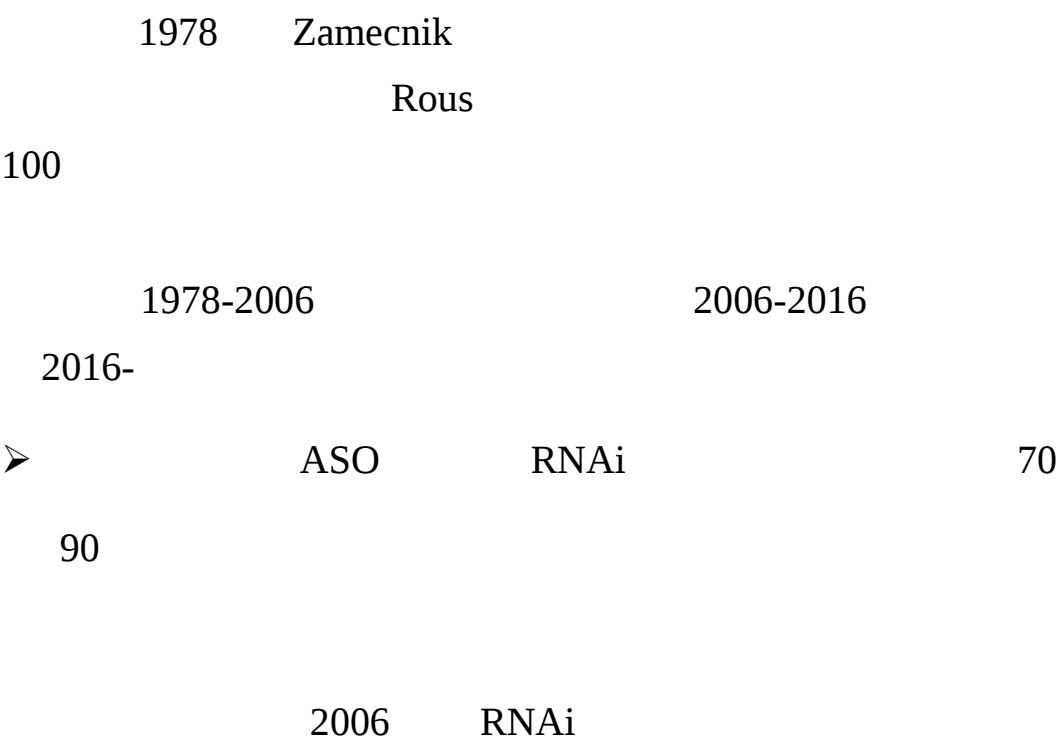
1

2

3

	✓ ✓ siRNA	✓	✓ miRNA	✓
		5 siRNA		1

三、小核酸药物产业化



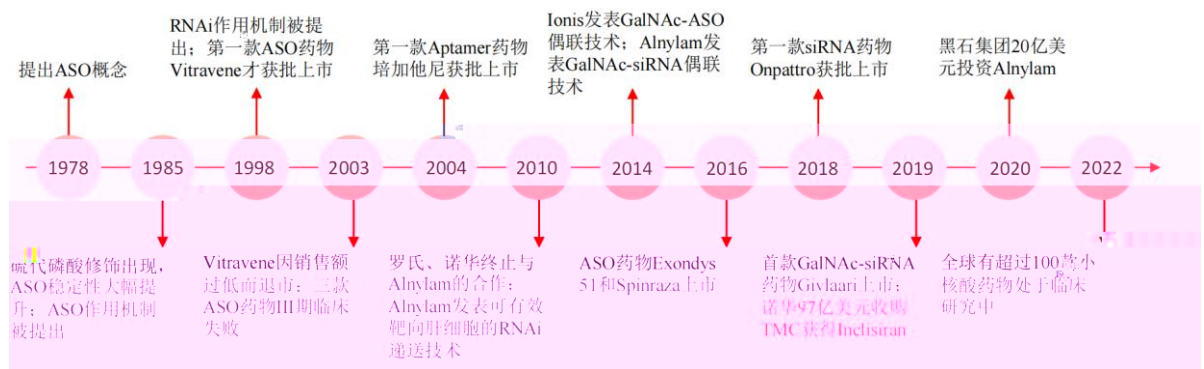


2005

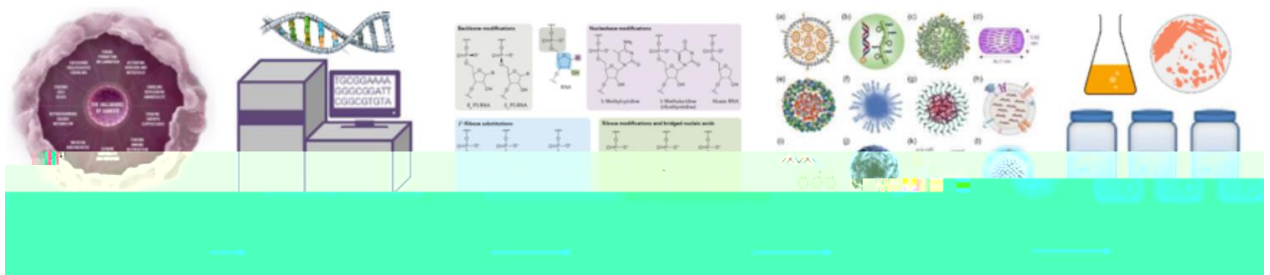
2016



2016

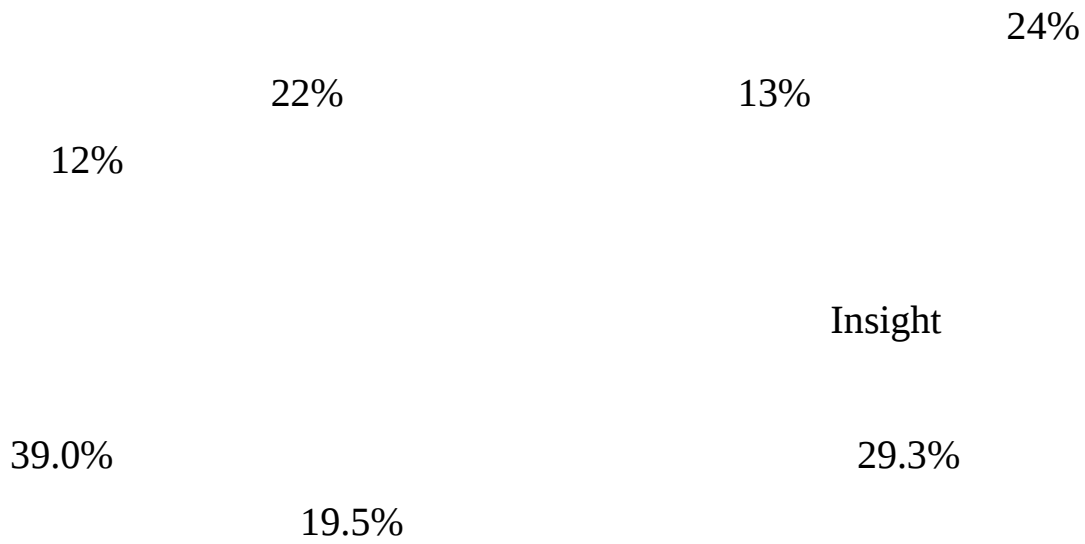


3-1



3-2

1



2

RNA

GC

35%-55%

A T

3

4

5

1

2

CDMO

1

RNA

mRNA

2



Merck

Thermo Fisher

Danaher
GE Healthcare



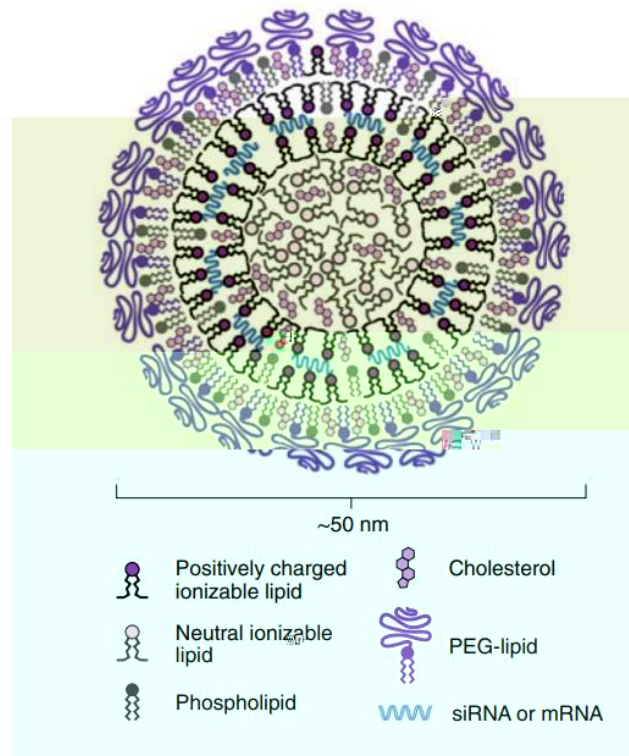
2 -0-

LNP N- Lipid Nanoparticle
LNP GalNac (GalNac)

➤ LNP

LNP RNA
RNA
RNA RNA LNP

LNP FDA
siRNA mRNA Alnylam
Patisiran LNP siRNA LNP
Arbutus Moderna
CureVac BioNtech Alnylam
Moderna BioNtech
mRNA
LNP



3-3 LNP

➤ GalNac

GalNac

Alnylam

GalNac

GalNac

siRNA

Givosiran 2019

Inclisiran

2020

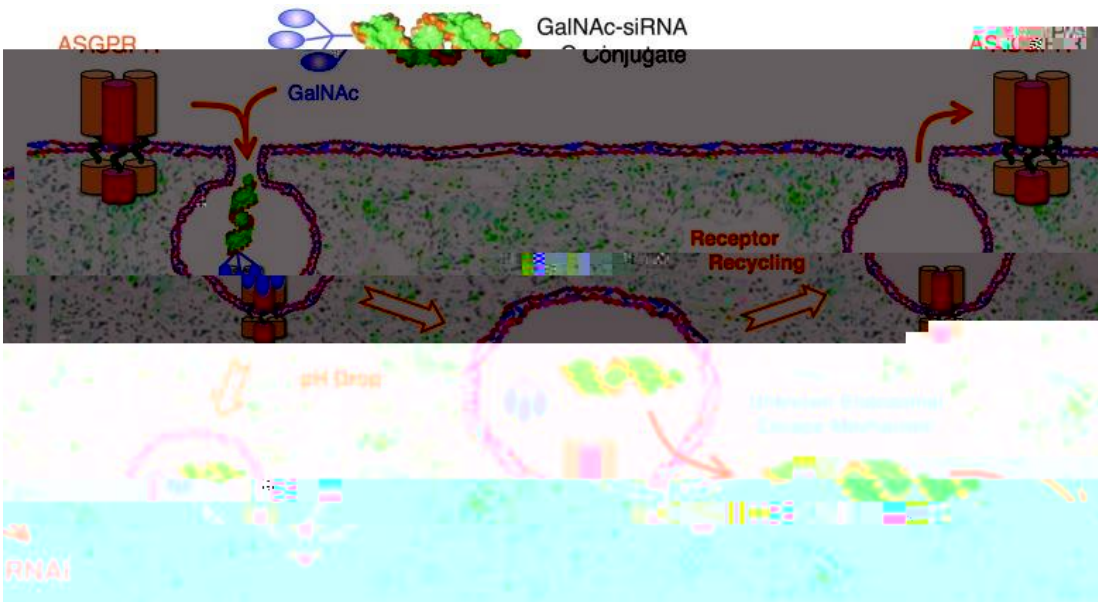
Lumasiran 2020

GalNac

3

ASGPR

GalNac



3-3 GalNAc-siRNA

GalNac

GalNac

3-2

RNA			ASO siRNA	

LNP	RNA RNA		mRNA siRNA LNP GalNac	LNP Arbutus Moderna CureVac BioNtech Alnylam
GalNac	ASGPR		5 siRNA 4 GalNac	Alnylam GalNac

CDMO

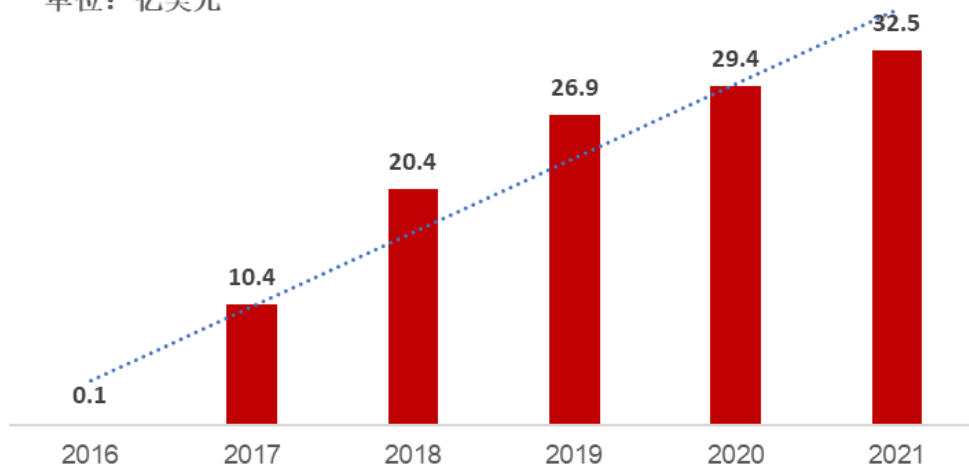


3-4

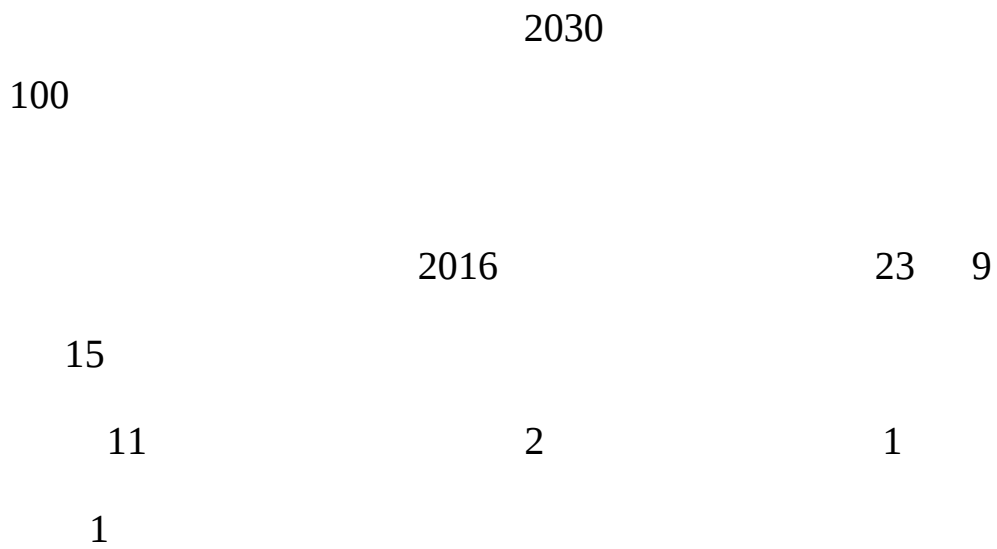
四、小核酸药物的市场

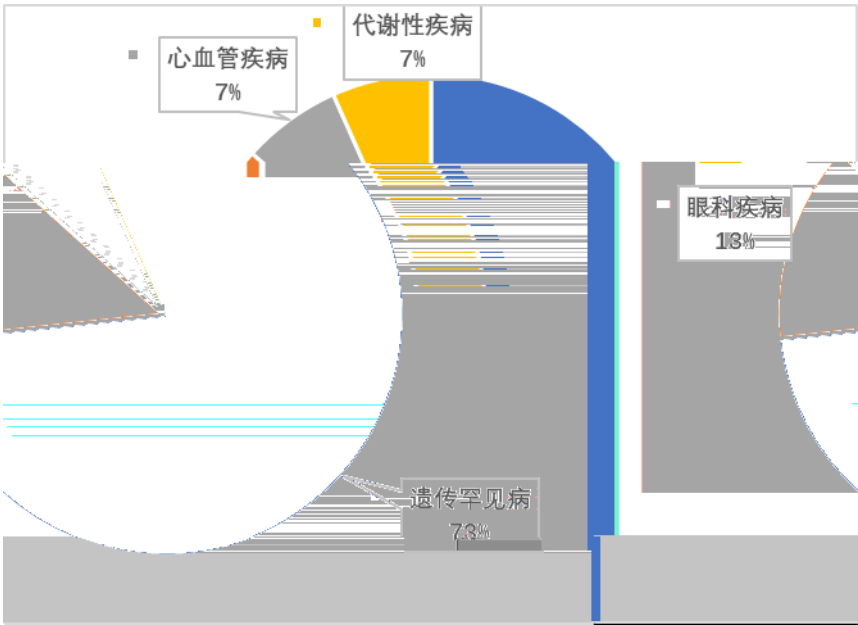
		2016	ASO
2016	0.1	2021	32.5
	217.8%		
		2025	
100			

单位：亿美元



4-1 2016-2021





4-2 2023 9

4-1

ASO	Vitravene	Novartis/Ionis	CMV UL123		1998	Naked
	Kynamro	Kastle/Ionis	ApoB-100		2013	Naked
	Exondys	Sarepta	DMD exon 51		2016	Naked

	Spinraze	Ionis/Biogen	SMN2 exon 7		2016	Naked
	Tegsedi	Ionis	TTR		2018	Naked
	Waylivra	Ionis	APOC3		2019	Naked
	Vyondys 53	Sarepta	DMD exon 53		2019	Naked
	Viltepso	Nippon Shinyaku	DMD exon 53		2020	Naked
	Amondys 45	Sarepta	DMD exon			

1 Spinzara

Spinzara Ionis/Biogen

SMA ASO 18

2016

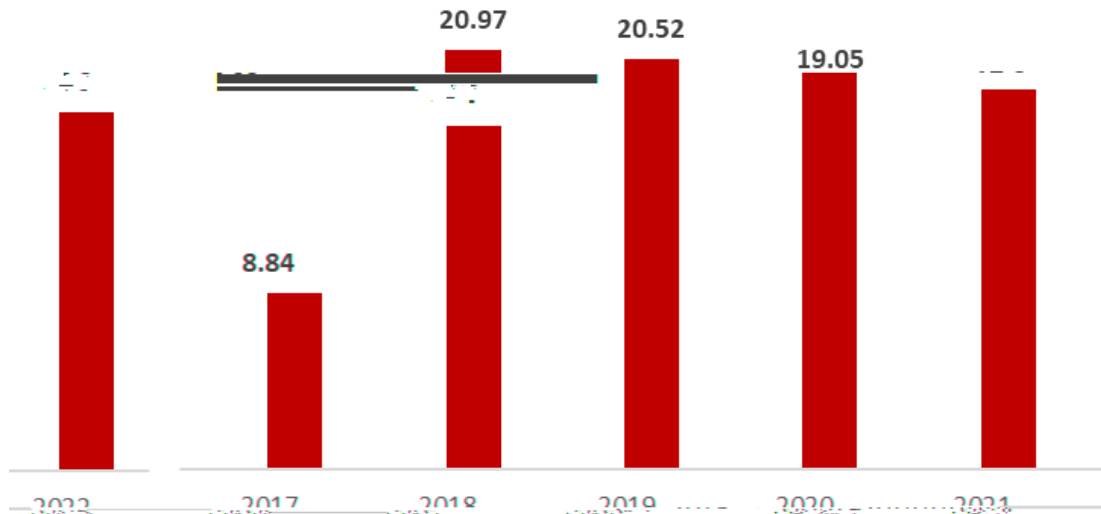
Spinzara

“ ”

2022

17.94

单位：亿美元



4-3 2017-2022 Spinzara

Spinzara

2' -OME

PS

ASO

Spinzara

RNA

2021	12	22	Alnylam	siRNA
Leqvio	FDA			
ASCVD	Leqvio			

PCSK9 mRNA

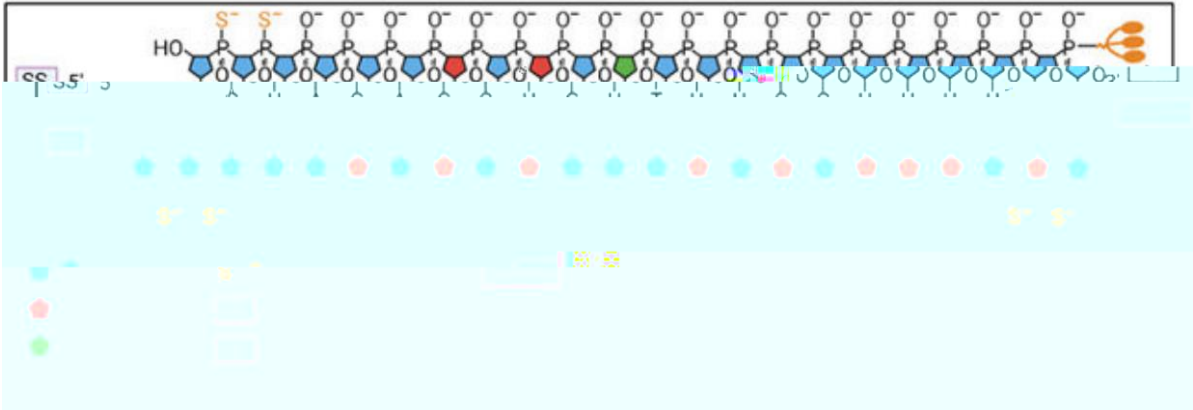
LDL-C

GalNAc

PCSK9

Leqvio

Alynlam ESC



4-5 Leqvio

Leqvio

Leqvio

LDL-C

4-2

		LDL-C			/
		30~50%			

Evolocumab		47~63%		2-8	5718
Leqvio siRNA)	/Alnylam	40~51%	0 3 6 2	20-25	9750 6500

五、小核酸药物产业竞争概况

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1 Alnylam

Alnylam siRNA Alnylam 2002
RNAi 5 siRNA

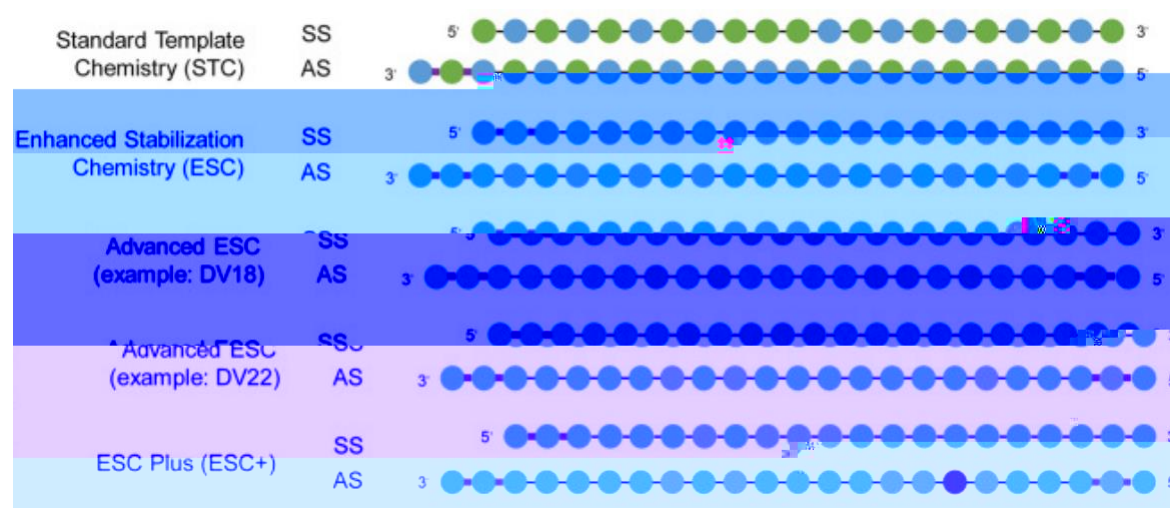
RNAi

DLin-MC3-DMA

GalNac RNAi

GalNac

STC Standard Template Chemistry ESC Enhanced Stability
Chemistry ESC Plus (ESC+)
siRNA Alnylam siRNA
siRNA

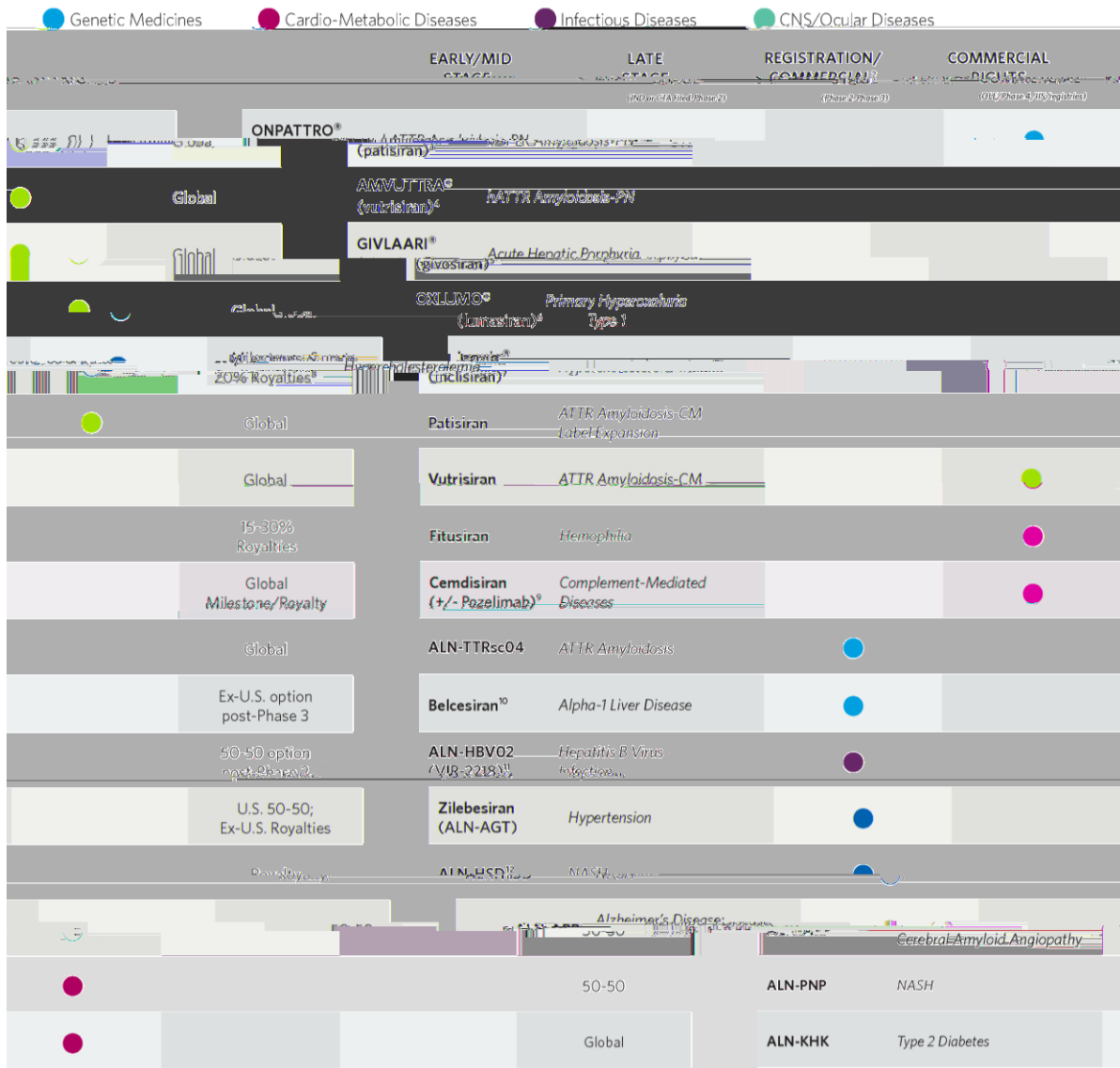


5-1 Alnylam

5-1 Alnylam

STC	2 OH 3 2 2 -F 2 -OMe PS	
ESC	STC 2 -OMe 5 2 PS	
Advanced ESC	ESC 2 -F PS	GalNac-siRNA
ESC+	2 -F GNA	RNAi

Alnylam
(CNS)



5-2 Alnylam

2 Ionis

Ionis 1989 ASO

Ligand Conjugated

Antisense LICA

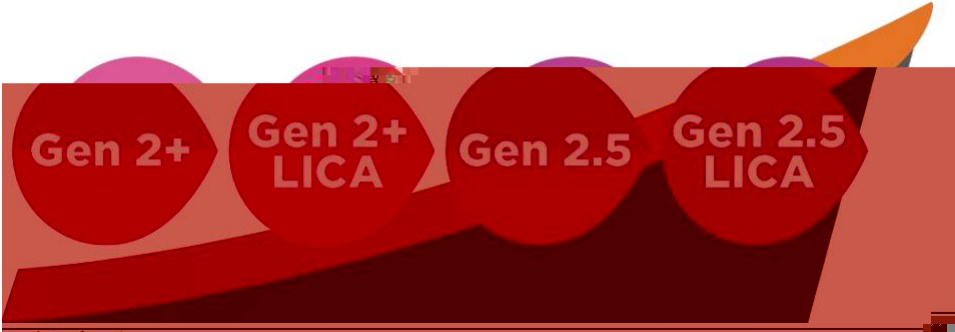
LICA

2

2

2.5

ASO



5-3 Ionis

5-2 Ionis

2	PS MOE	2 -
2.5	cEt 2 4	2 10

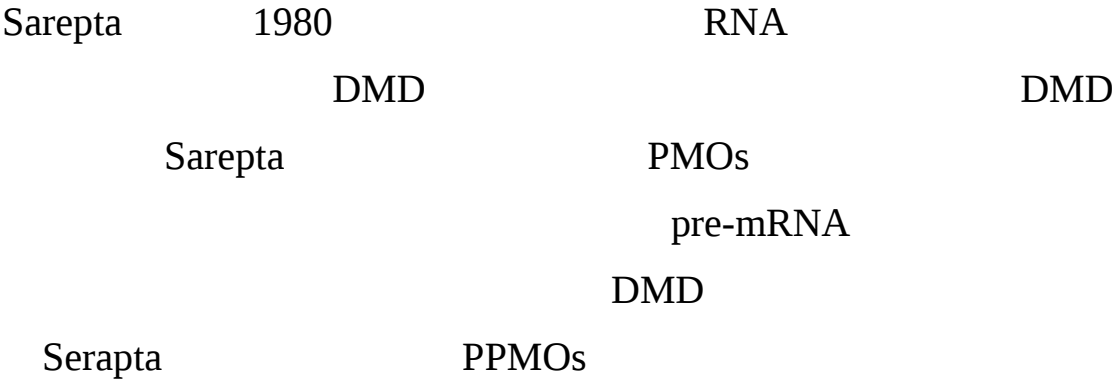
Ionis

GSK



5-4 Ionis

3 Sarepta



5-3 Sarepta

PMOs	RNA	PMO RNA
PPMOs	PMOs	

Program Name	Discovery/Preclinical	Clinical
RNA Targeted Therapies PPMO¹		
SRP-5051 (vesileteplirsen)	Duchenne	
Other Exon Targets ²	Duchenne	
Gene Therapy		
GALGT2 - Nationwide Children's	Duchenne	
GNT 0004 - Genethon	Duchenne	
SRP-9003 (bidridistrogene xeboparvovec)	LGMD2E/R4 β-sarcoglycan	
SRP-9004 (patidistrogene bexoparvovec)	LGMD2B/R2 β-sarcoglycan	
Other LGMD Targets ³	Multiple	Other Targets
Gene Editing		
CAS9 - Duke University	Duchenne	CRISPR/Cas9
CAS9 - Harvard University	Duchenne	CRISPR/Cas9

5-5 Sarepta

5-4

Alnylam	2002	✓	GalNac LNP	
		✓	ESC ESC+	
Ionis	1989	✓	LICA	
		✓	2	2.5
Sarepta	1980	✓		DMD

		✓	PMO	PPMO
--	--	---	-----	------

()
1

2007

2013

Life Technologies Corporation

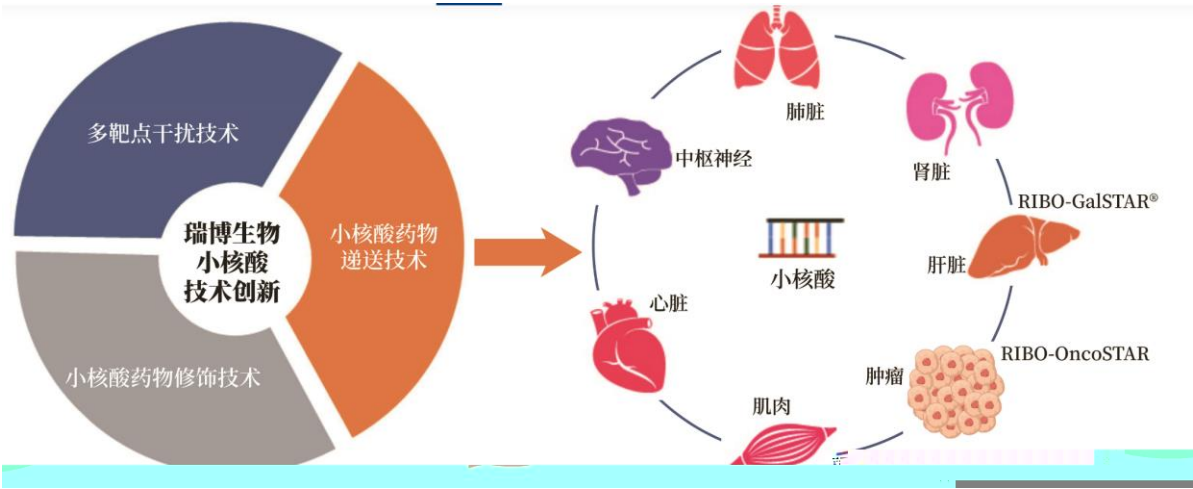
GalNAc

RIBO-GalSTAR

RIBO-

OncoSTAR

RSC2.0



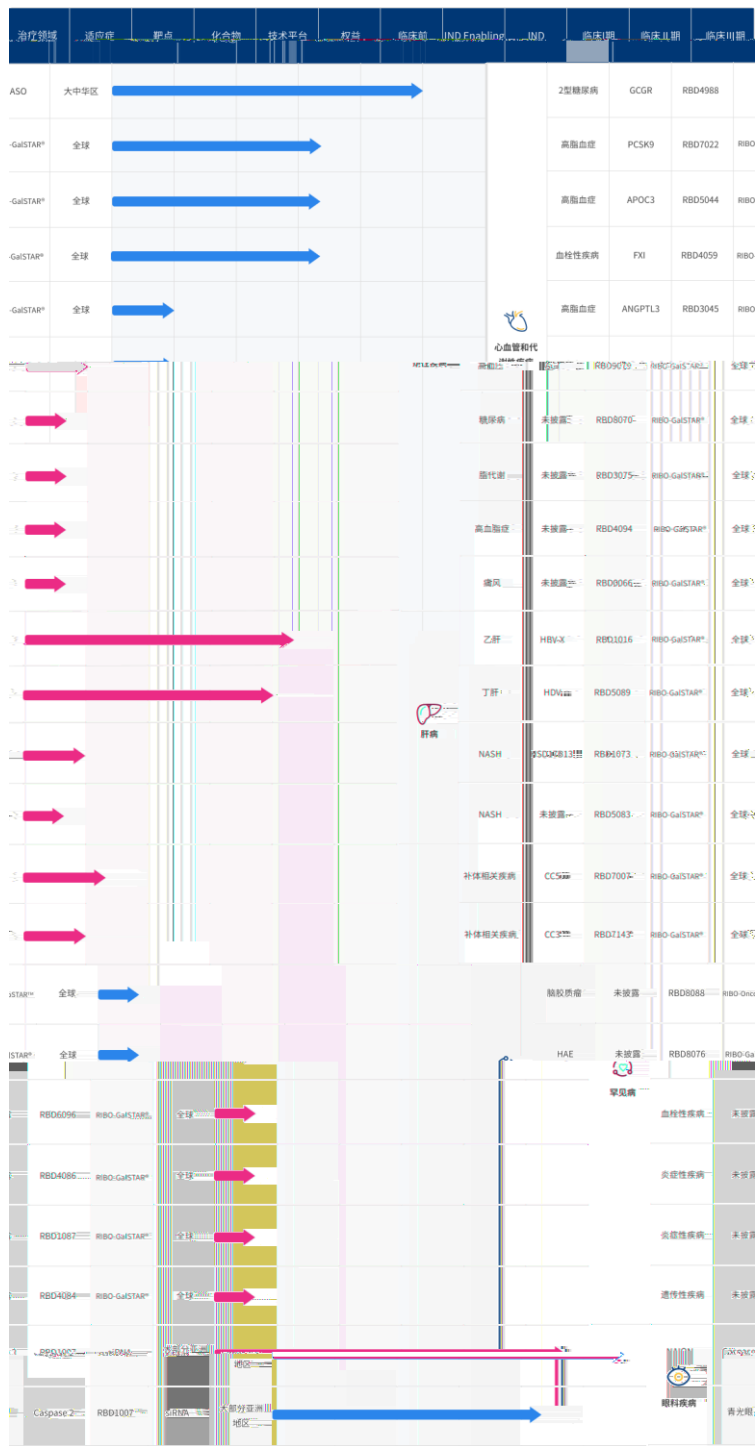
5-6

5-5

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RIBO- GalSTAR		
RIBO- OncoSTAR		
RSC2.0		siRNA /

2012 Quark RBD1007/QPI-
1007 2017 Ionis
ASO



*缺血性视神经病变; *NASH: 非酒精性脂肪性肝炎; *HAE: 遗传性血管性水肿 *NAION: 非动脉炎性前房

siRNA



肿瘤学										
候选药物	靶向基因	适应症	递送平台	临床前	IND 准备	IND	I期	II期	III期	商业权
STP705	TGF-β1/COX-2	isSCC	PNP-IT	美国						全球
		BCC	PNP-IT	美国						全球
STP707	TGF-β1/COX-2	多发性实体瘤	PNP-IV	美国						全球

医学美容										
候选药物	靶向基因	适应症	递送平台	临床前	IND 准备	IND	I期	II期	III期	商业权
STP705	TGF-β1/COX-2	脂肪重塑	PNP-ID	美国						全球

抗病毒物质										
候选药物	靶向基因	适应症	递送平台	临床前	IND 准备	IND	I期	II期	III期	商业权
RV-1730	SARS-CoV-2	新冠病毒疫苗	LNP 肌肉注射	美国						全球

GalAhead™										
候选药物	靶向基因	适应症	递送平台	临床前	IND 准备	IND	I期	II期	III期	商业权
STP122G	因子XI	抗凝剂/血栓性疾病	GalAhead™ 皮下	美国						全球
STP125G	APOC3	高胆固醇血症	GalAhead™ 皮下	美国						全球
STP144G	IL-1β / IL-18	炎症性肠病	GalAhead™							
STP145G	IL-1β / IL-18	炎症性肠病	GalAhead™							
STP146G	IL-1β / IL-18	炎症性肠病	GalAhead™							
STP147G	IL-1β / IL-18	炎症性肠病	GalAhead™							
STP148G	IL-1β / IL-18	炎症性肠病	GalAhead™							
STP149G	IL-1β / IL-18	炎症性肠病	GalAhead™							
STP150G	IL-1β / IL-18	炎症性肠病	GalAhead™							
STP151G	IL-1β / IL-18	炎症性肠病	GalAhead™							
STP152G	IL-1β / IL-18	炎症性肠病	GalAhead™							
STP153G	IL-1β / IL-18	炎症性肠病	GalAhead™							
STP154G	IL-1β / IL-18	炎症性肠病	GalAhead™							
STP155G	IL-1β / IL-18	炎症性肠病	GalAhead™							
STP156G	IL-1β / IL-18	炎症性肠病	GalAhead™							
STP157G	IL-1β / IL-18	炎症性肠病	GalAhead™							
STP158G	IL-1β / IL-18	炎症性肠病	GalAhead™							
STP159G	IL-1β / IL-18	炎症性肠病	GalAhead™							
STP160G	IL-1β / IL-18	炎症性肠病	GalAhead™							
STP161G	IL-1β / IL-18	炎症性肠病	GalAhead™							
STP162G	IL-1β / IL-18	炎症性肠病	GalAhead™							
STP163G	IL-1β / IL-18	炎症性肠病	GalAhead™							
STP164G	IL-1β / IL-18	炎症性肠病	GalAhead™							
STP165G	IL-1β / IL-18	炎症性肠病	GalAhead™							
STP166G	IL-1β / IL-18	炎症性肠病	GalAhead™							
STP167G	IL-1β / IL-18	炎症性肠病	GalAhead™							
STP168G	IL-1β / IL-18	炎症性肠病	GalAhead™							
STP169G	IL-1β / IL-18	炎症性肠病	GalAhead™							
STP170G	IL-1β / IL-18	炎症性肠病	GalAhead™							
STP171G	IL-1β / IL-18	炎症性肠病	GalAhead™							
STP172G	IL-1β / IL-18	炎症性肠病	GalAhead™							
STP173G	IL-1β / IL-18	炎症性肠病	GalAhead™							
STP174G	IL-1β / IL-18	炎症性肠病	GalAhead™							
STP175G	IL-1β / IL-18	炎症性肠病	GalAhead™							
STP176G	IL-1β / IL-18	炎症性肠病	GalAhead™							
STP177G	IL-1β / IL-18	炎症性肠病	GalAhead™							
STP178G	IL-1β / IL-18	炎症性肠病	GalAhead™							
STP179G	IL-1β / IL-18	炎症性肠病	GalAhead™							
STP180G	IL-1β / IL-18	炎症性肠病	GalAhead™							
STP181G	IL-1β / IL-18	炎症性肠病	GalAhead™							
STP182G	IL-1β / IL-18	炎症性肠病	GalAhead™							
STP183G	IL-1β / IL-18	炎症性肠病	GalAhead™							
STP184G	IL-1β / IL-18	炎症性肠病	GalAhead™							
STP185G	IL-1β / IL-18	炎症性肠病	GalAhead™							
STP186G	IL-1β / IL-18	炎症性肠病	GalAhead™							
STP187G	IL-1β / IL-18	炎症性肠病	GalAhead™							
STP188G	IL-1β / IL-18	炎症性肠病	GalAhead™							
STP189G	IL-1β / IL-18	炎症性肠病	GalAhead™							
STP190G	IL-1β / IL-18	炎症性肠病	GalAhead™							
STP191G	IL-1β / IL-18	炎症性肠病	GalAhead™							
STP192G	IL-1β / IL-18	炎症性肠病	GalAhead™							
STP193G	IL-1β / IL-18	炎症性肠病	GalAhead™							
STP194G	IL-1β / IL-18	炎症性肠病	GalAhead™							
STP195G	IL-1β / IL-18	炎症性肠病	GalAhead™							
STP196G	IL-1β / IL-18	炎症性肠病	GalAhead™							
STP197G	IL-1β / IL-18	炎症性肠病	GalAhead™							
STP198G	IL-1β / IL-18	炎症性肠病	GalAhead™							
STP199G	IL-1β / IL-18	炎症性肠病	GalAhead™							
STP200G	IL-1β / IL-18	炎症性肠病	GalAhead™							

5-8

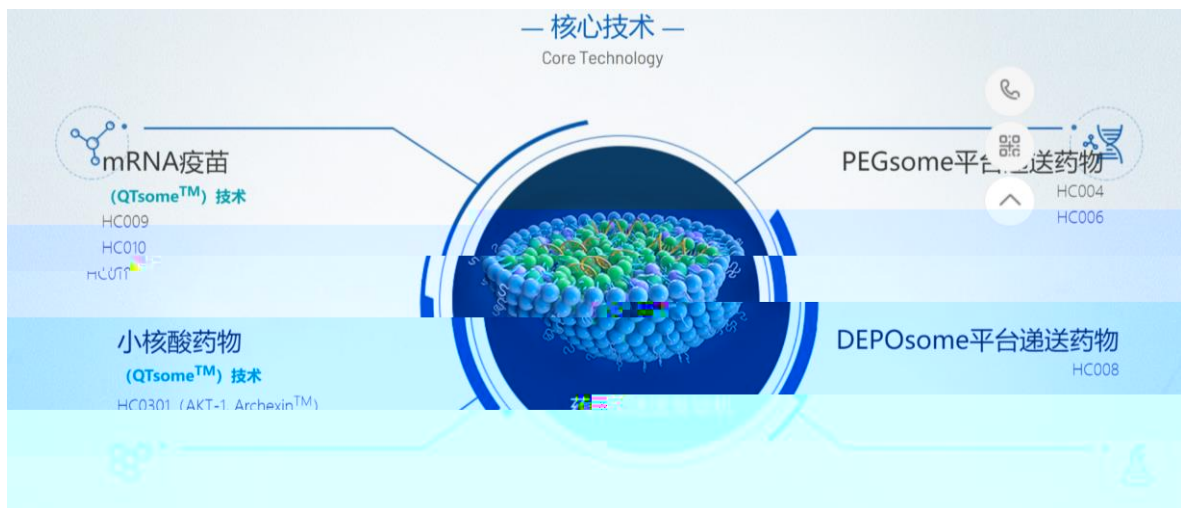
3

2013

mRNA

QTsome™

mRNA



5-9

6

HCO201

核酸创新药管线						
项目代码	靶点	适应症	临床前研究	IND申报	临床I期	临床II期
HC0201	AKT-1	原发性肝癌				
HC0301	AKT-1	原发性肝癌				
HC2101	Anti-miR-21	非小细胞癌				
HC009	加强针	新冠疫苗				
HC010	变异株	新冠多价疫苗				
HC011	肿瘤新生抗原	抗肿瘤				

高端复杂注射剂管线						
项目代码	原研商品名	适应症	实验室开发	工艺技术转移 & 工艺验证	BE研发 & BE试验	ANDA申报
HC007	Abraxane®	肺癌；乳腺癌；胰腺癌等				
HC006	Onivyde®	胰腺癌				
HC008	Exparel®	术后麻醉；神经阻滞镇痛				
HC004	Ambisome®	真菌感染				

5-10

4

2017

RNA saRNA

“ ”

SCAD

GOLD

5-7

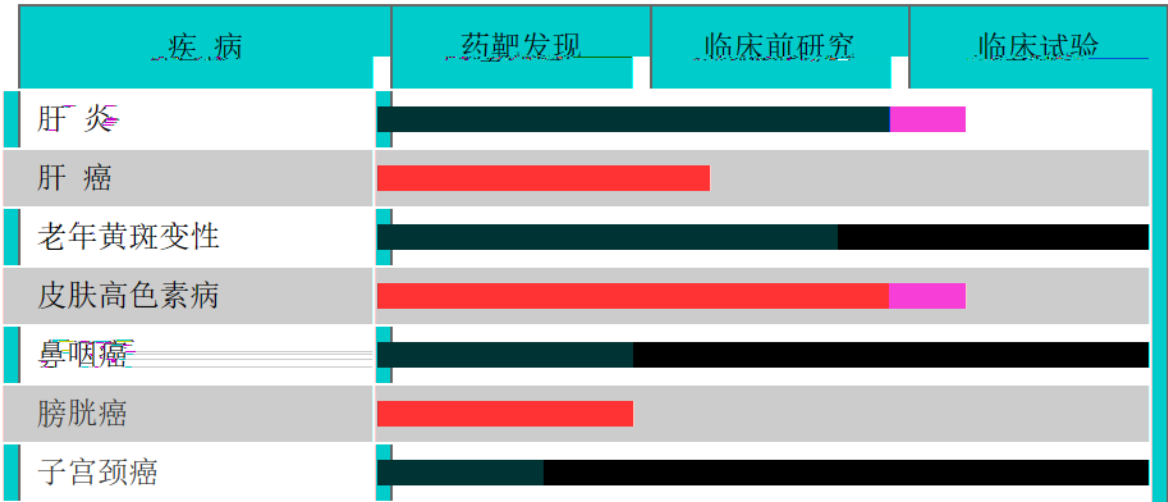
SCAD	RNA	

GOLD		GaINAc
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2006

40



5-12

6

2022

siRNA

ASO

5-8

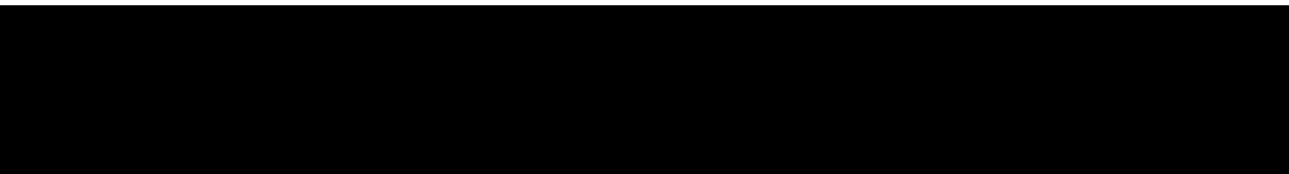


	2007	5 A B C C+ E	✓ ✓ GalNAc RIBO-GalSTAR®
	2007	7 A B C C+ D E IPO	✓ PNP GalNAc ✓ PNP TGF- /COX-2 siRNA
	2013	5 A B C C+ D	✓ QTsome
	2017	2 A A+	✓ saRNA ✓ SCAD GOLD
	2006		✓
	2022	1	✓ siRNA ASO



5-9

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	DNA siRNA ASO mRNA		
	mRNA FNP		
	siRNA miRNA E-migrasome		+
	OFA/iLRP	/	
	RNA LLNs		
	MVP Penetratin		
	-		

六、专业术语解析

DNA

DNA

(exon)

RNA

(intron)

RNA

DNA

open reading frame ORF

1. Zhang, M. and Y. Huang, siRNA modification and delivery for drug development. *Trends Mol Med*, 2022. 28(10): p. 892-893.
2. Migliorati, J.M., J. Jin, and X.B. Zhong, siRNA drug Leqvio (inclisiran) to lower cholesterol. *Trends Pharmacol Sci*, 2022. 43(5): p. 455-456.
3. Kulkarni, J.A., et al., The current landscape of nucleic acid therapeutics. *Nat Nanotechnol*, 2021. 16(6): p. 630-643.
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