RNAi THERAPEUTICS MARKET (2ndEDITION) 2019-2030

Dissertation submitted in partial fulfillment of the requirement for the degreeof

BACHELOR OF TECHNOLOGY

IN

BIOTECHNOLOGY

By

SAESHA VERMA 151851

UNDER THE GUIDANCE OF

Mr. Gaurav Chaudhary Mrs. Simriti Gupta

Roots Analysis Pvt. Ltd.



JAYPEE UNIVERSITY OF INFORMATION TECHNOLOGY, WAKNAGHAT MAY 2018

CERTIFICATE

This is to certify that the work reported in the B.Tech. academic project report entitled **"RNAi Therapeutics Market (2nd Edition), 2019-2030**" submitted by**Saesha Verma** in partial fulfillment for the award of degree of B.Tech. in Biotechnology from **Jaypee University of Information & Technology, Waknaghat** has been carried out under my supervision. This work has not been submitted partially or wholly to any other University or Institute for the award of any other degree, diploma or such other titles.

Mrs. Simriti Gupta Associate Roots Analysis Pvt. Ltd. Date:

DECLARATION

I hereby declare that the work reported in the B.Tech. academic project report entitled **"RNAi therapeutics Market(2nd Edition),2019-2030"** submitted at **Jaypee University of Information Technology, Waknaghat**is an authentic record of my work carried out under the supervision of **Mr. Gaurav Chaudhary** and **Mrs. Simriti Gupta**. I have not submitted this work elsewhere for any other degree or diploma.

Saesha Verma (151851) Department of Biotechnology & Bioinformatics JUIT, Waknaghat

Certified that the above statement made by the student is correct to the best of our knowledge and belief. Roots Analysis owns the copyright of the findings presented in this report. Under no circumstances should this information be shared with other third parties without the prior consent of the company.

Mrs. Simriti Gupta Associate Roots Analysis Pvt. Ltd.

ACKNOWLEDGEMENT

This project is an outcome of continual work over and intellectual support from numerous sources. Therefore, I would like to express my sincere thanks to the people who have helped me the most throughout my project.

I owe my deepest gratitude toMr. Gaurav Chaudhary, CEO, for providing me an opportunity to do internship at their prestigious organization. I am very grateful toMrs. Simriti Gupta for making it possible to carry out this project. Without hercontinuous optimism, enthusiasm, encouragement and support, this study may not have been accomplished as desired.Furthermore, I would also like to acknowledge with much appreciation the crucial role my esteemed advisors Mrs. Rupali Chaudharyfor herextremely valuable insightsand direction at crucial points during the course of my project.

At last but not the least I am deeply grateful to all the members of Roots Analysis whorendered their help during the course of my training and my parents for their motivation, continual support and encouragement at all the stages of my life.

Saesha Verma (151851)

TABLE OF CONTENTS

PageNumber

	List of Figures	1-2
	List of ABBREVIATIONS	3
	ABSTRACT	4
	CHAPTER-1	5-6
	COMPANY PROFILE	
1.1	Company Overview	
1.2	Research Methodology	
	CHAPTER-2	7-13
	INTRODUCTION	
2.1	Chapter Overview	
2.2	Discovery of RNAi	
2.3	Mechanism of RNAi	
2.4	Types of RNAi molecules and their mode of action	
2.5	Applications of RNAi	
2.6	Advantages and Disadvantages of RNAi	
	CHAPTER-3	14-18
	MARKET OVERVIEW	
3.1	Chapter Overview	
3.2	Overall Market Landscape	
3.3	Pipeline Building	

	CHAPTER-4	19-20
	TECHOLOGY PLATFORMS AND DELIVERY SYSTEM	
4.1	Chapter Overview	
4.2	Database Building	
	CHAPTER-5	21-26
	CLINICAL TRAIL ANALYSIS	
5.1	Chapter Overview	
5.2	Pipeline Building	
5.3	Data Analysis	
	CHAPTER-6	27-30
	PROMOTIONAL ANALYSIS	
6.1	Chapter Overview	
6.2	Channels used for Promotional Analysis	
6.3	Promotional Analysis: Onpattro	
	CHAPTER-7	31-33
	PARTNERSHIPS AND COLLABORATIONS	
7.1	Chapter Overview	
7.2	Types of Partnerships and Collaborations	
7.3	Database Building	
	CHAPTER-8	34-35
	PATENT ANALYSIS	
8.1	Chapter Overview	
8.2	Database Building	

	CHAPTER-9	36-38
	VC FUNDING	
9.1	Chapter Overview	
9.2	Types of Funding	
9.3	Database Building	
	CHAPTER-10	39-41
	SERVICE PROVIDERS	
10.1	Chapter Overview	
10.2	Types of Service Providers	
10.3	Database Building	
	CHAPTER-11	42-47
	ADDITIONAL PROJECTS	
11.1	ADDITIONAL PROJECTS Biopharma CMO	
11.1 11.1.1	ADDITIONAL PROJECTS Biopharma CMO Demand Collation	
11.1 11.1.1 11.1.2	ADDITIONAL PROJECTS Biopharma CMO Demand Collation Logo Landscape	
11.1 11.1.1 11.1.2 11.1.3	ADDITIONAL PROJECTSBiopharma CMODemand CollationLogo LandscapeAppendix Building	
11.1 11.1.1 11.1.2 11.1.3 11.2	ADDITIONAL PROJECTS Biopharma CMO Demand Collation Logo Landscape Appendix Building Medical Device CMO	
11.1 11.1.1 11.1.2 11.1.3 11.2 11.2.1	ADDITIONAL PROJECTS Biopharma CMO Demand Collation Logo Landscape Appendix Building Medical Device CMO Primary Research	
11.1 11.1.1 11.1.2 11.1.3 11.2 11.2.1 11.2.1 11.3	ADDITIONAL PROJECTS Biopharma CMO Demand Collation Logo Landscape Appendix Building Medical Device CMO Primary Research Gene Therapy	
11.1 11.1.1 11.1.2 11.1.3 11.2 11.2.1 11.3 11.3	ADDITIONAL PROJECTS Biopharma CMO Demand Collation Logo Landscape Appendix Building Medical Device CMO Primary Research Gene Therapy	
11.1 11.1.1 11.1.2 11.1.3 11.2 11.2.1 11.3 11.3	ADDITIONAL PROJECTS Biopharma CMO Demand Collation Logo Landscape Appendix Building Medical Device CMO Primary Research Gene Therapy Primary Research	

CHAPTER-12	48
FUTURE WORK PLAN	
CHAPTER-13	49
CONCLUSION	
CHAPTER-14	50
REFERENCES	

LIST OF FIGURES

Figure	Constitue.	Page						
Number	Caption	Number						
2.1	Timeline of RNAi development	9						
2.2	Pictorial presentation of various RNAi components	10						
2.3	Overview of RNAi mechanism	12						
3.1	Represents the pipeline of siRNA molecules	15						
3.2	Represents the pipeline of miRNA molecules	16						
3.3	Represents the pipeline of shRNA molecules	16						
3.4	Represents the pipeline of sshRNA molecules	17						
3.5	Provides information on the various parameters captured in the pipeline	18						
4.1	Represents the database of RNAi delivery system and technology platforms	20						
5.1	Represents the pipeline of RNAi molecules	22						
5.2	Represents analysis by trial status	23						
5.3	Represents analysis by phase of development	24						
5.4	Represents analysis by type of RNAi modality in North America	24						
5.5	Represents analysis by type of RNAi modality and phase of development in North America							
5.6	Represents analysis by type of indication and phase of development in North America	25						
6.1	Represents the overview of promotional anlysis using harvey ball	28						
6.2	Represents the product website analysis	29						
6.3	Represents the patient assistance program: AlnylumAssist	30						
6.4	Represents the other reimbursement programs	30						
7.1	Represents the exhaustive database of RNAi partnerships and collaborations	33						

8.1	Represents the list of patent both filed / published	35
9.1	Represents the list of various funding instances.	38
10.1	Represents database of service providers of RNAi	40
11.1	Represents the database of demand	43
11.2	Represents the logo lanscape of biopharma CMO companies	43
11.3	Represents the appendix of Biopharma CMO	44
11.4	Represents the database of company contacts and email ID	45
11.5	Represents the database of company contacts	46
11.6	Represents the draft of a transcript	47

LIST OF ABBREVIATIONS

AMD	Age-related Macular Degeneration
CHS	Chalcone Synthase
СМО	Contract Manufacturing Organization
CPC	Corporative Patent Classification
CRO	Contract Research Organization
DTC	Direct to Consumer
FDA	Food and Drug Administration
mRNA	micro Ribonucleic Acid
RISC	RNA-induced Silencing Complex
siRNA	short interference Ribonucleic Acid
shRNA	short hairpin Ribonucleic Acid

ABSTRACT

The project titled, "*RNAi Therapeutics Market (2nd Edition), 2019-2030*" provides an extensive study of the rapidly growing market of RNAi Therapeutics and provides an outlook of the growing pipeline of RNAi therapeutics. RNAi therapeutic market have been one of the most actively evolving market, with its single drug "Onpattro" in market. RNAi therapeutic market is still in its developing stage. It is the regulatory mechanism that cells use to silence or inhibit gene expression through destruction of specific mRNA molecules. RNAi enable the sequence specific knockdown of target gene. This therapyis anticipated to emerge as viable alternative to conventional treatment option for indications such as age-relatedmacular degeneration (AMD), hepatitis C and various forms of cancer. The scope of this project primarily includes various RNAi based drugs targeting several therapeutic areas such as oncology, genetic disorders and infectious diseases. Several players, including RNAi therapeutic developers, research institutes, contract manufacturing organizations, and government organizations, are playing a critical role in the development and manufacturing of these therapeutics.

During my on-job training, I worked on different modules of the project. These include drafted an introduction on RNAi therapeutics, prepared pipeline of RNAi based drugs, conducted clinical trialanalysis, gathered data related to collaborations and partnerships, analyzed promotional strategies of marketed drug, collated data for patent analysis, VC funding and service providers in RNAi therapeutic domain. Apart from this, I contributed in four additional projects namely, Biopharma CMO, Medical Devices CMO, Gene Therapy and Next Generation Contact Lenses and Visual Prostheses,wherein I gathered information related to demand analysis, prepared logo landscape and gathered contacts for primary research.

COMPANY PROFILE



1.1 Company Overview

Roots Analysis Pvt. Ltd. is a business research and consulting firm, which specializes in providing in-depth business research and consulting services for bio/pharmaceutical industry. Focused on providing an informed and impartial view on key challenges facing the industry, the research is primarily driven by an in-depth analysis covering the following parameters [1]:

- Research and development
- Technology evolution
- Existing market landscape
- Future Commercial potential
- Regulatory concerns
- Regional growth drivers
- Risks and opportunities

The firmhas expertise in analyzing areas that have lacked quality research so far or require more focused understanding within the broader industry. Apart from writing reports on identified areas, the company also provide bespoke research / consulting services dedicated to serve our clients in the best possible way.

The business reports highlight trends ranging from commercial success / potential, technological developments and future outlook built around opportunities and threats.

The companymajorly focus on areas spanning the following domains:

- Therapeutic segments
- Emerging technologies
- Medical devices
- Drug delivery
- Clinical trials

1.2 Research Methodology

The data presented in the reports has been gathered via secondary and primary research. For all our projects, we conduct interviews with experts in the area (academia, industry, medical practice and other associations) to solicit their opinions on emerging trends in the market. This is primarily useful for us to draw out our own opinion on how the market may evolve across different regions and technology segments. Wherever possible, the available data has been checked for accuracy from multiple sources of information.

The secondary sources of information include:

- Annual reports
- Investor presentations
- SEC filings
- Industry databases
- News releases from company websites
- Government policy documents
- Industry analysts' views

INTRODUCTION

2.1Chapter Overview

RNAi therapeutics is an emerging field of therapeutics and in just two decades it got its name imprinted in all spheres of pharmaceutical industry. RNAi is naturally occurring process in eukaryotic cells in which silencing of gene is done through knockdown of specific mRNA molecules. Silencing of gene is due to degradation of RNA into short RNA strands. Thus, based on this natural process of RNAi various big and small pharma industries have built RNAi based therapeutics which will be further used to treat several therapeutic areas such as oncology, genetic disorders and infectious diseases. One of the major advantages of RNAi is that it enables the sequence specific knockdown of a target gene. Indications such as age-related macular degeneration (AMD), hepatitis C and various forms of cancer that are hard to address with the available therapies are being considered as potential areas that are likely to benefit from RNAi based therapeutics. [2]

This chapter provides an exhaustive view over discovery of RNAi, mechanism of RNAi, types of RNAi molecules and their mode of action, application of RNAi and merits and demerits of RNAi. The chapter provides the information about the basic scientific information about the RNAi and how the concept of RNAi is further utilized by various pharma players.

Despite various challenges, such as interference with cellular RNAi components, offtarget effects and ineffective delivery mechanisms for *in vivo* applications, this technology still holds the potential to become a potent new therapeutic class. With some drugs being tested in human trials while others in the preclinical development stage, the industry has already witnessed several ups and downs in its brief history. Although, there are challenges related to RNAi therapeutics, several stakeholders, including service providers, are continuously investing in efforts to combat specific roadblocks.

2.2 Discovery of RNAi

Napoli and Jorgensen, they observed gene silencing in plants via RNAi in late 1980s and early 1990s, was first performed on Petunia. The experiment was conducted with an aim to evaluate whether chalcone synthase (CHS) was the rate-limiting enzyme in anthocyanin biosynthesis pathway. Anthocyanins are responsible for the deep violet colour in petunias. Attempting to enhance the colour of the flowers, the scientists developed transgenic plants containing extra copies of the CHS gene. This unexpectedly resulted in the formation of white flowers with decreased levels of both endogenous and transgenic CHS as compared to the wild type. This led to the hypothesis that introduction of the transgene *co-suppressed* the endogenous CHS gene.

Further this phenomenon of co-suppression, which is known as quelling in fungi was performed by Romano and Macino in *Neurospora Crassa* in 1992 by introduction of homologous RNA.

Major instance in history of RNAi took place when RNAi mechanism was first demonstrated in *C.elegans* in 1998 by Andrew Fire and Craig Mello, which fetch them Nobel Prize in 2006. [3]

Thereafter may advancements take place in the field of RNAi, which aroused the interest of various pharmaceutical industries to manipulate the RNAi mechanism for drug development. Thus, leading to development of various drugs where Onpattro forms the first marketed drug in the history of RNAi.



Figure 2.1 Timeline of RNAi development

2.3 Mechanism of RNAi

RNAi is a natural process of gene silencing in cell. The following molecules are important components of RNAi Mechanism.

- **Double Stranded RNA (dsRNA):** it triggers the mechanism of RNAi and can be both endogenous and exogenous, where endogenous is produced in the nucleus and exogenous is introduced externally into cell.
- miRNA or siRNA: miRNA is ≈19-24 base pair long endogenous ssRNA which is formed from primary mRNA. They work by translational repression.

siRNA is \approx 25 nucleotides long exogenous dsRNA. It acts as guide RNA for mRNA degradation.

• Dicer and Drosha:

Dicer is RNase III endonuclease enzyme that shows specificity towards dsRNA and cleaves it, leaving 3' overhangs of two to three nucleotides and a 5' phosphate. It produces the fragments of 22 nucleotides; therefore, this enzyme is known to initiate the process of RNAi by cleaving dsRNA into siRNA

Drosha is type II RNase III endonuclease enzyme that initiates the process of miRNA cleavage, with domain architecture. It contains three domains: highly conserved central domain (cleavage activity), C- terminal containing two tandem RNaseIII domains (RIIIDa and RIIIDb) and dsRNA binding domain [4]

 RNA Induced Silencing Complex (RISC): It is a multi-ribonucleoprotein complex that incorporates one strand of small interfering RNA (siRNA) or micro RNA (miRNA). RISC uses miRNA or siRNA as template for recognizing mRNA, thereby activating RNase and cleaves it. [5]



Figure 2.2Pictorial presentation of various RNAi components

RNAi is an RNA-dependent, regulatory mechanism of gene silencing. The mechanism of RNAi comprises of a three-step process

Step 1: Processing of dsRNA

The endogenous source of dsRNA is miRNA, formed from its precursor known as primiRNA.There are two steps involved in the maturation of miRNA. The first step involves the formation of pre-miRNA (~70 bp precursor) by Drosha in the nucleus. The second step involves cleavage of the pre-miRNA by Dicer in the cytoplasm to form mature miRNAs (~21-25 bp long). For exogenous dsRNA it is cleaved into siRNA by Dicer in cytoplasm.

Step 2: Assembly of RISC complex

The siRNA or miRNA molecules are recognized by the RISC complex. Ago, the most basic proteins, are highly conserved members of the RISC. The Ago protein consists of two homologous regions, the PAZ domain and the PIWI domain. According to the structural analysis of Ago, it appears that the PAZ domain specifically recognizes the unique structure of two 3' nucleotides overhangs of siRNA while the PIWI domain is the functional domain of the protein. This domain displays RNaseH-like activity Activation of the RISC complex is an ATP dependent process as unwinding of the siRNA duplex requires energy. Only the single stranded siRNA joins the active form of the RISC. The loaded strand acts as a guide to identify and bind to the target mRNAs via Watson-Crick base pairing. The other strand is either discarded or cleaved during the loading process. The strand that has a lower thermal stability of the base at the 5' end is usually loaded onto the RISC.

Step 3: Slicing of mRNA

Integration of the siRNA into the active RISC complex enables it to identify and hybridize to the target mRNA. This ultimately leads to the degradation of mRNA into smaller fragments. The almost perfect base pairing is sufficient for endonucleolytic cleavage in the middle of target complementary region that occurs at ten nucleotides upstream of the nucleotide paired with the 5' end of the guide siRNA. The catalytic activity of the RISC depends on the intact guiding strand present with it. Cellular exonucleases degrade the cleaved transcripts. [6]

Document2 - Saved to \\172.16.1.2\Saesha												
References M	ailings Review View	Help	∠ Search									
` A ` Aa - A _⊘	≣ • }≣ • '₹ • € ₹ 4	t ¶	AaBbC AaBbCcI AaBbCcI AaBbCcDdE(AaBbCcDdE(AaBbCcDdE(AaBbCcDdE)									
<u>A</u> • <u>A</u> • <u>A</u> •	≣≡≡≣ \$≣- &-	•	Tipure H TiNormal Normal2 TiSource Tisource TiNo Spac									
Fa	Paragraph	G.	i Styles									



Figure 2.3 Overview of RNAi mechanism

2.1Applications of RNAi

- **FunctionalGenomics:** The advantages of RNAi technology in functional genomics is that it provides specificity and efficacy in silencing members of a single or multiple gene families. However, since RNAi is a homology-dependent process a carefully selection of a unique or conserved region of the target gene ensures that a specific member of a multiple gene family can be silenced [7]
- Therapeutics: RNAi technology offers the promise of being able to treat diseases that are characterised by abnormal gene functions. It targets a disease at post-transcriptional level, thus is a highly selective technology. The most common therapeutic areas that have captured the focus of both research institutions and companies are neurogenerative disorders, oncology and viral diseases.
- **Biotechnology:** RNAi is not just limited to therapeutics; it is being used in the field of biotechnology. RNAi has proven to be a powerful approach for silencing genes to

improve agronomic traits in crop plants. The approach has been used to target specific plant genes for improved traits such as modified oil content in soybeans, increased lysine content in corn, and reduced caffeine content in coffee and to provide resistance to numerous viral diseases. [8]

2.4Advantages and Disadvantages of RNAi

ADVANTAGES [9]

- Highly specific target disease specific allele
- Highly potent in comparison to other oligonucleotide mechanisms
- Efficient in gene knockdown as compared other nucleotide mechanisms
- Stable and long-term silencing is achieved by shRNA
- RNAi type screening and mutations can be identified easily
- Can downregulate expression of any gene

DISADVANTAGES

- Can compete with endogenous RNAs as dependent on miRNA processing
- Exogenous dsRNA can induce innate immune response.
- Microarray technology show that siRNA can show off-target silencing of large no. of genes
- Since it is gene suppressing technology therefore regulatory mechanism cannot be identified
- Improper target recognition can result in toxicity

MARKET OVERVIEW

3.1Chapter Overview

The use of RNAi for therapeutic purposes can be traced back to late 1990s. Now RNAi therapeutics is an emerging class of therapeutics in the pharmaceutical market with several molecules being developed across several therapeutic areas. Although there is only one approved molecule i.e. Onpattro, there are many RNAi based drugs that are in its late clinical and preclinical phase. In coming years RNAi therapeutics will form an integral part of pharmaceuticals industries targeting various therapeutics areas including rare diseases.

3.2 Overall Market Landscape

RNAi Therapeutics have shown positive clinical results and potential to treat life threatening diseases, such as cancer, autoimmune disorders and infectious diseases. RNAi Therapeutic industry player have intruded various molecular domain of RNAi i.e. siRNA, miRNA, shRNA, sshRNA and DNA. Various pharmaceuticals giants are working on different molecules of RNAi and thus developing their pre-clinical and clinical pipeline. The therapeutic benefits of RNAi have outweighed the drawbacks associated with the it that primarily comprise complex, time consuming and tedious manufacturing processes. This domain has attracted several research institutes and companies to invest time and money. In order to meet the growing demand of increased number of clinical trials and improve the manufacturing processes, more and more organizations are contributing to the space by setting-up capabilities to manufacture cell-based therapies. In this project, we identified over several organizations, including industry stakeholders and academic players that are actively involved in the production of RNAi based therapeutics.

3.3Pipeline Building

Pipeline is a list of drugs or molecules that have been gathered from multiple sources, such as public records and company websites (including investor presentations). It governs the structure of the overall report and acts as the most important aspect in the process of drafting the report insights. Hence, it must be robust, exhaustive and finely structured, in order to produce accurate analysis.

In our study, we have found that different companies are developing RNAi products using different types of RNAi modalities. Based on this, our pipeline has been segmented into four subclasses i.e. siRNA, miRNA, shRNA and sshRNA.

A	utoSave 🤅	•₩ 8 % • ~	÷				Pip	eline Final - Excel		Saesha Ve	rma 🖻 — 🖸	v ×
File	e Ho	me Insert Pag	je Layout 🛛 Fi	ormulas	Data	Review View	Help 🔎 Search				🖻 Share 🛛 🖓 Con	nments
Pas	te Clipboa	t Calibri py • rmat Painter rd 5	• 11 <u>U</u> • ⊞ • Font	• A^ A*	==	= ≫ - 80 V = 5 5 E ⊠ N Alignment	Vrap Text Gen Merge & Center マ rs	v % 9 50 00 Number r₂ Styles	t as Cell Insert	Cells Edit	Sort & Find & Filter * Select * Ideas	
B10		• I X V	Jx									^
	с	D	F	F	G	н	1	J	к	1	м	
1 5	No.		Devel	loper Informa	ation			1	Drug / Therapy Informat	ion		
2		Developer Name	Type of Organ	YoE	Headouaters	Comanany Size	Drug Name	Mechanism Of Action	Phase of development	Indication	Therapeutic area	Targe
3	1	Alnylam Pharmaceutical	ls Industry	2002	Cambridge, N	Massachusetts, Unit	Onpattro (patisiran)	Patisaran, which is a double-stranded smal	Marketed	Hereditary ATTR Amyloidosis		Transt
4	2	Alnylam Pharmaceutical	ls Industry	2002	Cambridge, N	Massachusetts, Unit	Givosiran (ALN-AS1)	Significantly lower induced liver ALAS11ev	Phase 3	Acute hepatic porphyria (AHP)		Amine
5	3	Alnylam Pharmaceutical	ls Industry	2002	Cambridge, N	Massachusetts, Unit	Fitusiran (ALN-AT3)	It is designed to lower AT, with goal ofpror	n Phase 3	Haemophilia and rare bleeding dis	sorders	Antitl
6	4	Ainviam Pharmaceutical	ls Industry	2002	Cambridge, N	Massachusetts, Unit	Inclisiran (ALN-PCSsc)	Inclisiran inhibit PCSK-9, which is respons	it Phase 3	Hypercholesterolemia		Conve
7	5	Alnylam Pharmaceutical	ls Industry	2002	Cambridge, N	Massachusetts, Unit	Lumasiran (ALN-GO1)	Lumasiran is designed to reduce the hepat	c Phase 3	Primary Hyperoxaluria Type 1 (PH	11)	givcol
8	6	Alnylam Pharmaceutical	ls Industry	2002	Cambridge, M	Massachusetts, Unit	Vutrisiran (ALN-TTRsc0)	It is designed to target and silence specific	Phase 3	ATTR amyloidosis		Transt
9	7	Alnylam Pharmaceutical	ls Industry	2002	Cambridge, N	Massachusetts, Unit	Cemdisiran (ALN-CC5)	Target the C5 component of the compleme	Phase 2	Complement-mediated diseases		C5 co
10	8	Alnylam Pharmaceutical	ls Industry	2002	Cambridge, N	Massachusetts, Unit	ALN-AAT02	Undisclosed	Phase 1/2	Alpha-1 liver disease		alpha-
11	9	Alnylam Pharmaceutical	ls Industry	2002	Cambridge, N	Massachusetts, Unit	ALN-HBV02	It inhibit expression of all HBV proteins, in	PC	Chronic Hepatitis B infection		Hepati
12	10	Silence Therapeutics	Industry	1994	London Uni	ted Kingdom	SLN124	TMPRSS6 (Transmembrane Protease Serin	PC	β-Thalassemia Myelodysplastic	Syndrome (MDS) and Haem	o Transr
13	11	Silence Therapeutics	Industry	1994	London Uni	ted Kingdom	SLN226	Aldehvde dehvdrogenase 2 (ALDH2) is si	I PC	Alcohol use disorder	- ,	Aldeh
14	12	Silence Therapeutics	Industry	1994	London, Uni	ted Kingdom	SLN360	Silences apolipoprotein (a), a component o	f PC	Cardiovascular diseases		Apoli
15	13	Silence Therapeutics	•				Atu111		PC			Angio
16	14	Ouark Pharmaceuticals	Industry	2006	Ness Ziona.	Israel	OPI-1002	p53 is a stress-response gene activated by	Phase 3	Delayed Graft Function (DGF)		p53 g
17	15	Quark Pharmaceuticals	Industry	2006	Ness Ziona	Israel	OPI-1002	p53 is a stress-response gene activated by	Phase 2	Acute Kidney Injury (AKI)		p53 g
18	16	Quark Pharmaceuticals	Industry	2006	Ness Ziona	Israel	OPI-1007	It target the mRNA of the caspase 2 gene a	Phase 2/3	Non-arteritic ischemic optic neuro	mathy (NAION)	gene (
19	17	Quark Pharmaceuticals	Industry	2006	Ness Ziona.	Israel	OPI-1007	It target the mRNA of the caspase 2 gene a	r Phase 2	Acute Primary Angle Closure Gla	ucoma	gene C
20	18	Quark Pharmaceuticals	Industry	2006	Ness Ziona	Israel	PF-655	Inhibition of RTP801 expression via RNAi	m Phase 2	diabetic macular edema (DME)		RTP80
21	19	Quark Pharmaceuticals	Industry	2006	Ness Ziona	Israel	PF-655	Inhibition of RTP801 expression via RNAi	m Phase 1/2	Age-Related Macular Degeneration	on (Wet AMD)	RTP80
22	20	Quark Pharmaceuticals	Industry	2006	Ness Ziona	Israel	OP.HL1		Discovery	Otoprotection	(((((((((((((((((((((((((((((((((((((((
23	20	Quark Pharmaceuticals	Industry	2006	Ness Ziona	Israel	OP_HI 2		PC	Ménière's Disease		
24	21	Quark Pharmaceuticals	Industry	2006	Ness Ziona	Israel	OP HI 3		Discovery	Hearing Pegeneration		
25	22	Quark Thannaceuticals	Industry	2000	Noss Ziona	Israel	OPIII		Discovery	Lung Transplantation Drimog: Gr	aft Druction	
25	23	Quark Thannaceuticals	Industry	2000	Ness Zione	Israel	OP LD		Discourses	A sute Lung Initiation, Filmary Of	an Dystancaon	
20	24	Quark Pharmaceuticals	Industry	2000	Ness Ziona,	Istael	OP CO1		Discovery	Chronic Obstructive Pulyate	Vindows	
21	25	Quark Fnamaceuticais	mausay	2006	ivess Ziona,	ISTACI	Qr-COI		Discovery	Go to Setting	nsease as to activate Windows	
•	· • ·	. shRNA sshRNA	A DNA	Delivery teo	hnology	List of updated	comapnies Additi	ional Info (Rohit) 🕂 🗄 🖣				Þ

Figure 3.1Represents the pipeline of siRNA molecules

Au	oSave 💽 Off		2.6	- =						Pipeline F	ïnal - Excel				Saesha Verm	a 🖽	- e	9 ×
File	Home	Insert	Pag	e Layout	Formulas	Data	Review	v View	Help	♀ Search						ය Share	2 🖵 Cor	mments
Paste	Clipboard	ainter rs	Times N B I	lew Roma → U → Font f= Siri	10 - A^ - <u>A</u> - <u>A</u>	A" =	= = *	≷ب وي ≣ ع≣ ₪ Alignment	Wrap Text Merge & Cer	General ™ × %	• 00 00 F nber 5₂	Conditional Format as Formatting • Table • Styles	Cell Insert De Styles * C	lete Format ells	∑ AutoSum ▼ / ☑ Fill ▼ S ⊘ Clear ▼ F Editing	ort & Find & ilter + Select	ldeas Ideas	
	A E	в	с	D	E	F	G	н	1	J	к	L	м	N	0	Р	Q	R A
1 Re	viewer Commer	nts S.M	No.		I	Developer	Information			Drug / Therapy Info	mation							
2				Developer I	Type of Org Y	íoE	Headquater	Comapny	Drug Name	Phase of developmen	Indication	Therapeutic area	Target gene/molecu	Delievery system	n/(Designation	Route of ad	Trail ID	Market
3			1	InteRNA	Industry	1989			INT-1B3	PC	Hepatocellular car	rcinoma (HCC).	Adenosine-A2A rec	AtuPLEXTM				
4			2	miRagen	Industry	2006	Boulder, Co	olorado	Cobomarse	Phase 2	Cutaneous T-Cell	Lymphoma/Mycosis Fu	a miR-155			Intravenou	NCT038374	57
5			3	miRagen/t2	Industry	2006	Boulder, Co	olorado	Remlarsen	Phase 2	Cutaneous fibrosi	is	miR-29					
6			4	miRagen/Se	Industry	2006	Boulder, Co	olorado	MRG-110	Phase 1	Heart failiures/ inc	cisional complications	miR-92a				NCT036034	31
7			5	Transgene	Industry	1990	Hyderabad	India	TBL0404	PC	Hepatocellular car	rcinoma (HCC)		Adeno-associate	ed virus (AAV) ve	ctor system		
8			6	miReven	Industry	2010	Australia		miR-7	PC	Head and Neck ca	arcinoma, hepatocellular	Epidermal growth fa	tor receptor (EGI	FR)			
9			7	miReven	Industry	2010	Australia		mRx-7	PC	liver cancer			• •	Í			
10			8	uniOure	Industry	1998	Amsterdam		AMT-061	Phase 3	Hemophilia B			Adeno-associate	ed virus(AAV) 5 v	iral system		
11			9	uniOure	Industry	1998	Amsterdam		AMT-180	PC	Hemophilia A			Adeno-associate	ed virus(AAV) 5 v	iral system		
12			10	uniOure	Industry	1998	Amsterdam		AMT-190	PC	Fabry disease		a-galactosidase A (Adeno-associate	ed virus(AAV) 5 v	i Intravenou	s	
13			11	uniOure	Industry	1998	Amsterdam		AMT-130	PC	Huntington's Dise	ease (HD)	mutant huntingtin p	Adeno-associate	ed orohan drug			
14			12	uniOure	Industry	1998	Amsterdam		AMT-150	PC	Spinocerebellar A	taxia Type 3 (SCA3)	CAG-repeat expansi	Adeno-associate	d virus(AAV) 5 v	iral system		
15			13	Guang'anm	Non-Industr	v	Beijing, Chi	ina	Xuesaitong	Phase 2	Coronary Heart D	iseaseUnstable Anginal	Blood Stasis Syndrom	e		oral	NCT016150	03
16			14	Regulus the	Industry	2007	San Diego	CA	RG-012 (La	Phase 2	Alport Syndrome		miR-21		Omhan	subcutaned	NCT033737	86
17			15	Regulus the	Industry	2007	San Diego	CA	RGL \$4326	Phase 1	Autosomal Domin	ant Polycystic Kidney	miR-17		p			
18			16	Regulus the	Industry	2007	San Diego	CA		PC	HBV		undisclosed targets	GaINA c-miRNA	conjugates			
19			17	Regulus the	Industry	2007	San Diego	CA	RGL \$5579	PC	Glioblastoma Mult	tiforme	miR-10b	GaINAc.miRNA	conjugates			
20			18	Regulate the	Industry	2007	San Diego	CA		PC	NASH		undisclosed targets	GaINAc.miRNA	conjugates			
21			19	Regulus the	Industry	2007	San Diego	CA		PC	HCV		miR122	GalNAc-miRNA	conjugates			
22			20	Remine the	Industry	2007	San Diego,	CA		PC	Infections Disease		undisclosed targets	GaINAc miRNA	conjugates			
22			20	Regulus the	Industry	2007	San Diago	CA		PC	Immunology		undisclosed targets	GaINA a miPNA	conjugates			
24			21	Regulus the	eraneutice/S	2007	San Diego,	CA	PG-012	Phase 2	Alport syndrome		miP21	GalNAc miRNA	conjugates	cuboutana	NCT02272	796
24			22	Regulus the	erapeutics/5	2007	San Diego,	CA	RG-012	Phase 1	ADPED		miR_17	GalNAc-miRNA	ce ofpnan urug	subcutaries	NC105575	/00
25			23	Simoomi	erapeudos	2007	Gaithershi	on TISA	STD202	Prinase I	Colorectal Courses		nnx-17	Polynontide N	o Portiolo (P)TP)			
27			24	Sumaomics		2007	Gatthersbur	is, USA	51P502	10	Colorectal Cancer			i olypepude Nan	Activate W	indows		
4	► si	IRNA	miRNA	shRNA	sshRNA	DNA	Deliver	y technolo	gy List	of updated comap	nies Adc				Gb to Settings	to activate	Window	
															# =	四	1	+ 100%

Figure 3.2 Represents the pipeline of miRNA molecules

Aut	oSave 💽	8	। ७- ९- -					Pipeline Final - E	Excel				Saesha Verma 🖪	- 0 ×
File	Home	In	sert Page Lay	yout Formulas	s Data Re	view View	Help 🔎 S	earch					🖻 Sh	are 🛛 🖓 Comments
Paste	X Cut Copy → ≪ Format P	ainte	Calibri B I U √	• 11 • A^		- 200 v 200 v 20	rap Text erge & Center र	General	- -0 _00 C -0 →0 Fr	Condition ormattin	nal Format as Ce Ig * Table * Style	II Insert Delete Format	∑ AutoSum * A Z V / Fill * Sort & Fin- Sort & Filter * Sele	d & Ideas
	Clipboard		5	Font	51	Alignment	5	Number	Gi I		Styles	Cells	Editing	Ideas 🔺
K15	Ť		X V Jx											~
	С		D	E	F	G	Н	1	J		К	L	М	N
2			Developer	Type of Or	YoE	Headquate	company	Drug Nam	Phase	of de	evelopment	Indication	Therapeutic area	Target gene/n
3		1	Transgene H	Industry	1991	Hyderabad,	Telangana	TBL0905	PC			Breast Cancer	Oncology	
4		2	Gradalis	Industry	2003	Carrollton,	Texas	Vigil™	Phase ?	3		Ewing Sarcoma	Oncology	TGF beta 1 and
5		3	Gradalis	Industry	2003	Carrollton,	Texas	Vigil™	Phase 2	2		Advanced Gynecolog	Oncology	TGF beta 1 and
6		4	Gradalis	Industry	2003	Carrollton,	Texas	Vigil™	Phase 2	2		Breast CancerOvaria	Oncology	TGF beta 1 and
7		5	Gradalis	Industry	2003	Carrollton,	Texas	pbi-shRNA	Phase	1		Ewing's Sarcoma	Oncology	EWS/FLI1 gen
8		6	Gradalis	Industry	2003	Carrollton,	Texas	pbi-shRNA	Phase	1		Advanced Cancer,Me	Oncology	Stathmin 1
9		7	Gradalis	Industry	2003	Carrollton,	Texas	Vigil™	Phase 2	1		Ewings Sarcoma, No	Oncology	GMCSF protei
10		8	Adhera ther	Industry	1983	North Caro	lina, United	M101 (Cel	Phase	1		Familial adenomator	Genetic Disorder	COX-2 and bet
11		9	Adhera ther	apeutics	1983	North Caro	lina, United	M201 (Olm	PC			Colorectal Cancer	Oncology	ARB/COX-2/C
12	:	10	David Willi	i Non-industr	ry			BCL11a	Phase	1		Sickle Cell Disease	Hematological Di	BCL 11a
13														
14														
15														
16														
17													Activate Window	
18				Data Data		Link of undefined		additional lafe (Da	- 1. Tax	0			Go to Settings to activ	ate Windows.
•	' sl	nKN	SSNKIVA	DINA Deliver	y technology	List of updated	omaphies	additional into (Ro)nic)	+	: 4			Þ

Figure 3.3 Represents the pipeline of shRNA molecules

Auto	Save 💽 🖁	9· @· •				Pipeline	Final - Excel				Saesha Verma	B –	o ×
File	Home Inser	rt Page Layou	t Formulas	Data Review	View Help	♀ Search						🖻 Share 🛛 🖓 G	Comments
Paste *	K Cut Copy → ダ Format Painter Clipboard 5	Calibri B I U +	• 11 • A° A″ ⊞ •		e ab Wrap Text →= I Merge & C ignment	enter + E N		Conditional Format a Formatting * Table * Styles	as Cell Insert Styles * *	Delete Format Cells	∑ AutoSum * Ac Fill * Z Clear * Filt Editing	t & Find & Idea er * Select *	is as A
K16	K16 • : × ✓ fr												
	D	E	F	G	н	I.	J	K	L	М	Ν	0	1
1			Developer	Information			Drug / Th	erapy Inform	ation				
2	Developer	Type of O	YoE	Headquate	company	Drug Nam	Phase of	developmen	Indication	Therapeu	it Target ge	ne/molecul	e/orga
3	Somagenics	Industry	1997	Santa Cruz,	CA	SG220	PC		Hepatitis C	virus (HCV	V Conserved	region with	in the i
4	Somagenics	Industry	1997	Santa Cruz,	CA	SG273	PC		Hepatitis C	virus (HCV	V Conserved	region with	in the i
5	Somagenics	Industry	1997	Santa Cruz,	CA	NA	PC		Diabetic W	ound Heali	n Prolyl hyd	roxylase do	main-c
6													
7													
8													
9													
10													
11													
12													
13													
14													
15											Activate Wir	dows	
16	shRNA	sshRNA DN	IA Delivery tec	hnology List of	updated comapni	es Additiona	l Info (Rohit)	(+) ; (1		Go to Settings to	activate Windo	

Figure 3.4 Represents the pipeline of sshRNA molecules

For building a pipeline, several parameters were selected with respect to the scope of the project. RNAi therapeutics market is a drug-based project, hence all the industry, non-industry players involved in development of RNAi based therapeutics were captured along with some of the basic information about the drug developer. For example, the founding year of the company, total number of employees in the company, and their headquarters. Other key parameters that were captured in the project are listed below:

- Drug name
- Mechanism of Action
- Phase of development
- Indication
- Therapeutic area
- Target gene / molecule / organ
- Delivery system / technology
- Designation of drug
- Route of administration
- Trail ID
- Phase wise distribution of indication for each drug

,	AutoSave 💽 🖁	७ • €• =			Pipeline Final -	Excel				Saesha V	′erma 🗈	- 0	×
Fi	le Home Ins	ert Page Layout Formu	las Data Review	v View Help 🔎	Search						🖻 Share	🖓 Com	ments
Pa	Clipboard	Calibri 11 B I ⊔ +		Image: Second	General	Conditional For Formatting Ta	mat as Cell ıble • Styles •	Insert	Delete Format Cells	∑ AutoSum ↓ Fill * ♦ Clear * Ed	Sort & Find & Filter + Select +	Ideas	~
B1	0 - :	× √ f*											^
1	к	L	м	N	0	P		Q	R	S	т	U	V 🔺
1	ug / Therapy Informati	on											
2	Phase of development	Indication	Therapeutic area	Target gene/molecule/organ		Delievery system/technolo	gy	Designation	Route of admiistr	ra Trial ID	Marketed	Phase III F	Phase I
3	Marketed	Hereditary ATTR Amyloidosis		Transthyretin (TTR)		Enhanced Stabilization Che	emistry (ESC)-	(Breakthrou	Subcutaneous	NCT03862807	Hereditary ATTE	Amyloidosi	s
4	Phase 3	Acute hepatic porphyria (AHP)		Aminolevulinic acid synthase	1 (ALAS1)	Enhanced Stabilization Che	emistry (ESC)-(Breakthrou	Subcutaneous	NCT03338816		Acute hepat	tic porp
5	Phase 3	Haemophilia and rare bleeding dis	orders	Antithrombin (AT)		Enhanced Stabilization Che	emistry (ESC)-	Orphan dru	Subcutaneous	NCT03549871		Haemophiliz	and ra
6	Phase 3	Hypercholesterolemia		Convertase subtilisin kexin typ	pe 9 (PCSK9)	Enhanced Stabilization Che	emistry (ESC)-4	Orphan dru	Subcutaneous	NCT03397121		Hypercholes	steroler
7	Phase 3	Primary Hyperoxaluria Type 1 (PH	1)	glycolate oxidase (GO)		Enhanced Stabilization Che	emistry (ESC)-	Breakthrou	Subcutaneous	NCT03681184		Primary Hyp	veroxalu
8	Phase 3	ATTR amyloidosis		Transthyretin (TTR)		Enhanced Stabilization Che	emistry (ESC)-	Orphan dru	Subcutaneous	NCT03759379		Transthyreti	in-medi
9	Phase 2	Complement-mediated diseases		C5 component of the complem	nent pathway	Enhanced Stabilization Che	emistry (ESC)-	GaINAc	Subcutaneous	NCT03841448			
10	Phase 1/2	Alpha-1 liver disease		alpha-1 antitrypsin (AAT)		Enhanced Stabilization Che	emistry (ESC)-(GaiNAc	Subcutaneous	NCT03767829			
11	PC	Chronic Hepatitis B infection		Hepatitis B virus (HBV) genon	ne	Enhanced Stabilization Che	emistry (ESC)-	GalNAc	Subcutaneous				
12	PC	β-Thalassemia, Myelodysplastic S	yndrome (MDS) and Haen	n Transmemebrane protein serin	e-6 (TMPRSS66)	GalNAc-siRNA Platform te	chnology	Orphan dru	Subcutaneous				
13	PC	Alcohol use disorder		Aldehyde Dehydrogenase 2 (A	ALDH2)	GalNAc-siRNA Platform te	chnology		Subcutaneous				
14	PC	Cardiovascular diseases		Apolipoprotein (a)		GalNAc-siRNA Platform te	chnology		Subcutaneous				
15	PC			Angiopoietin2								Delayed Gra	aft Func
16	Phase 3	Delayed Graft Function (DGF)		p53 gene				Orphan Dr	Intravenous	NCT03510897			
17	Phase 2	Acute Kidney Injury (AKI)		p53 gene				Orphan Dr	Intravenous	NCT02610283		Non-arteritic	c ischer
18	Phase 2/3	Non-arteritic ischemic optic neuro	pathy (NAION)	gene Caspase 2				Orphan Dr	intravitreal	NCT02341560			
19	Phase 2	Acute Primary Angle Closure Glau	icoma	gene Caspase 2				Orphan Dr	intravitreal	NCT01965106			
20	Phase 2	diabetic macular edema (DME)		RTP801		BiFAR™ target discovery	platform		intravitreal	NCT01445899			
21	Phase 1/2	Age-Related Macular Degeneratio	n (Wet AMD)	RTP801		BiFAR™ target discovery	platform		intravitreal	NCT00713518			
22	Discovery	Otoprotection											
23	PC	Ménière's Disease											
24	Discovery	Hearing Regeneration											
25	PC	Lung Transplantation, Primary Gra	ift Dysfunction										
26	Discovery	Acute Lung Injury											
27	Discovery	Chronic Obstructive Pulmonary D	isease										
28	Discovery	Myocardial Infarction								Activate	Windows		
29	Discovery	Chemotherany Induced Alonecia								Go to Settir	ngs to activate	Windows.	
	siRNA	miRNA shRNA sshR	NA DNA Deliver	y technology List of upd	lated comapnies	Ad: 🕂 🗄 🖪							Þ
											<u> </u>	-	+ 96%

Figure 3.5Provides information on the various parameters captured in the pipeline

TECHNOLOGY PLATFORM AND DELIVERY SYSTEM

4.1Chapter Overview

For a RNAi therapeutic platform to be effective, it requiresspecific, stable and potent RNAi compounds and the ability to deliver these compounds to the target tissues. Delivery of RNAi molecule into the host is most challenging task of RNAi Therapeutics. Therefore, to overcome such roadblocks, different industry players have come up with different technologies and delivery platforms to enhance the efficacy of RNAi therapeutics. This chapter provides detailed information on various technology platforms and delivery systems that are being developed or licensed by various companies active in the RNAi therapeutic market.

4.2Database Building

Database is similar to the pipeline, the only difference is that it is a list of companies / devices / technologies, whereas pipeline is a list of drugs / molecule, both have been created from multiple sources such as public records, survey and company website (including investor presentation)It governs the structure of the overall report and acts as the most important aspect in the process of drafting the report insightsHence, it must be robust, exhaustive and finely structured, in order to produce accurate analysis.

Here, for the purpose of collating data related to technology platforms and delivery system, we have built the database of various technologies and delivery system which have been developed and licensed by different companies.

AL	itoSave 💽 Off	u 19	C1 * *			i	Pipeline Final - Excel		Saesha Verma	6 – 0 ×
File	Home	Insert	Page Layout	Formulas Da	ta Review V	iew Help 🔎 Sear	ch			🖻 Share 🛛 🖓 Comments
Past	Le Clipboard	Painter 5	nes New Roma ▼ I U ▼ ∰ Font	10 • A A A	Ē ☴ ☴ ॐ • Ē ☴ ☴ ☶ ☶ Alignm	وی Wrap Text ه Merge & Center ۲۰ ه nent آی	ieneral ▼ ₩ ~ % 9 50 00 Number 5 Style	nat as Cell ble * Styles * Cells	Trat → Clear → Filter Editing	x Find & Ideas
123	•	: × v	f _x							^
	D	E	F	G	Н	I	J	К	L	M
1			Developer	Information			Technology information			
2	Developer	Type of or	rş YoE	Headquaters	Company size	Name	Mode of Action	Molecules that it can deli	Organ /cells	Therapeutic area
3	Polyplus- t	Industry	2001	Eastern France	11-50 employee	jetPRIME®		STICKY SIRNAs, DNA, siR	Adherent cell line	
4	Polyplus- t	Industry	2001	Eastern France	11-50 employee	INTERFERin®		siRNA, miRNA (microRNA	Adherent and suspensio	n cells
5	PCI Biotec	Industry	2000	Oslo, Norway	2-10 employees	fimaNAc		mRNA and siRNA		
6	Aro Biothe	Industry	2017	Philadelphia, Pe	e 2-10 employees	Centyrin siRNA	cMET receptor and the epidermal	silencing RNAs (siRNAs) a	muscle, CNS, and immu	ne cells.
7	Genevant	Industry	2017	Buraby, Canada	11-50 employee	(LNP)	EPR, increased circulation half-	siRNA	liver	
8	Bioasis	Industry			2-10 employees	xB3™ platform techn	ology	Abs, siRNA, enzymes and o	Brain	
9	20Med The	Industry	2011	Netherlands	2-10 employees	Nanogel Targeted drug	siRNA are loaded onto the nanoge	siRNA, miRNA, mRNA, DN	cancer therapy	
10	TriPhos Th	Industry			2-10 employees	siRNN platform	Negative charge on the backbone	siRNA	tumor cells, T cells, B o	ells, Macrophage, neur
11	Avidity Nar	Industry	2012	La Jolla CA	11-50 employee	Antibody Oligonucleo	AOCs combine the tissue selective	oligonucleotides siRNAs	Heart	
12	Arcturus Th	Industry		San Diego, CA	51-200 employe	Lipid-enabled and Uni	ockedNucleomonomer Agent mod	siRNA, mRNA, DNA	hepatocytes and stellate	e cellsmuscle cells, lun
13	Alnylam D	Industry				GalNAc	Receptor- mediated endocytosis.	siRNA	Liver, CNS, solid tumor	urs& other tissues
14	Mirus	Industry			11-50 employee	TransIT-X2® Dynami	Delivery System	plasmid DNA, siRNA/miRN	HeLa cells, Normal hur	nan dermal fibroblasts (
15	Mirus	Industry			11-50 employee	TransIT-TKO® Transf		siRNA and plasmid DNA	mammalian cells	
16	Mirus	Industry			11-50 employee	TransIT-siOUEST® T	ansfection Reagent	siRNA	mammalian cells	
17	Mirus	Industry			11-50 employee	TransIT®-2020 Reage	nt	shRNA	Human umbilical vein e	ndothelial cells (HUVE
18	Mirus	Industry			11-50 employee	TransIT®-LT1 Transfe	ction Reagent	shRNA	Human Induced Pluripo	tent Stem Cells (iPSCs
19	Arbutus Bio	Industry	2007	Warminster, Pe	151-200 employe	Marqibo®			•	
20	Rxi Therape	Industry	2011	Marlborough, M	111-50 employee	sd-rxRNA	sd-rxRNAs are hybrid oligonucleo	mRNA and IncRNA	skin, retina, lung, spinal	cord and liver
21										
22										
23									A ctivato Mine	lows
24									Go to Sottings to	stivato Windows
4	• 9	iRNA miR	RNA shRNA	sshRNA DN	A Delivery tech	List of updated	l comapnies 🛛 Adt 📖 🕀 🗄 📢		Go to Settings to	Ictivate windows.
										- 130%

Figure 4.1Represents the database of RNAi delivery system and technology platforms

For building the database various parameters were taken into consideration with respect to scope of the report. The information regarding various platforms and delivery system was collated based on the various parameters listed below:

- Name of the technology
- Mode of action
- Molecules it can deliver
- Target organ / cell
- Therapeutic area
- Route of administration

In addition to this, basic company information was also collated which includes type of organization, year of establishment, headquarters and company size.

Thus, such collated data forms the ground for conducting intuitive analysis and report building.

CLINICAL TRIAL ANALYSIS

5.1Chapter Overview

A clinical trial is a type of research that is done to study a test or treatment given to people. Clinical trials study how safe and helpful tests and treatments are. If found safe and efficacious, they may receive approval from the regulatory agency and subsequently enter the market. Clinical trials can evaluate many things, such as [10]

- New drugs not yet approved by the U.S. FDA (Food and Drug Administration)
- New uses of drugs already approved by the FDA
- New ways to give drugs, such as in pill form
- Use of alternative medicines, such as herbs and vitamins
- New tests to find and track disease
- Drugs or procedures that relieve symptoms

The chapter provides an elaborative analysis of clinical trials of the molecules enlisted in the pipeline above. There are more than 100 molecules currently in trials and we have done the analysis of these trials depending on various parameters.

Such analysis provides exhaustive view of the market in terms of clinical trials, thereby giving an elaborative and analytical information of the molecules currently in different phases of clinical studies.

5.2Data Collection

The data was gathered for the RNAi molecules presented in the pipeline that are currently in the clinical stages of development. The data was extracted from *www.clinicaltrails.gov*, which is a repository of publicly funded clinical studies occurring across the globe. This registry is run by United States National Library of Medicine (NLM) at National Institute of Health (NIH). [11]

Therefore, all the available trials were extracted in order to perform exhaustive analysis.

,	AutoSave 💽 Of		9• °° •	:				RNA	-Clinical Trail	Analysis ([trugs) - SG E	dit - 2 - Excel					5	aesha Vern	na 🖽	- 6	×
Fi	ile Home	Insert	Page La	yout Forn	nulas (Data Rev	view Vie	w Help	𝒫 Searce	h									암 Shar	e 🖓 🖓 Con	nments
Pa	Cut	Painter	Calibri B I U	• 11 • • ⊞ • Font	A* A* * <u>A</u> *	= = <u>=</u>	≫~ ⊡ ⊡ [ab Wrap Text Merge & Ce	enter + Eg	eneral • % 9 Numb	v 1 €0 .00 20 €0	Conditiona Formatting	I Format a • Table • Styles	as Cell Styles *	Insert *	Delete Forma	∑ Aut ↓ Fill ∳ Clea	oSum * , ir* i Editin	AZV Sind & fort & Find & filter * Select	k Ideas	
R3	×	: ×	√ f×	20																	^
1		с	D	E	F	G	н	1	J		К	L	M	N	0	P	Q	R	S AT	T	U 🔺
1	NCTNING		1	2 :	5	4 5	b Chatur	Church Doorseld	Candiblana	8	9 71	10	11	1.		13 14	15	1 Constitution	6 1/	18	Church I. F
2	NCTNUMber		rype o	Oreattra	Detisiren	Acronym in Dationts	Netwotre	No Desults A	Amulaidasi	ic Comili	Constin Di	Drug Dati	Juccome	Sponsor/	Gender	Age	Phases	Enrolline	r Funded B	study Typ	Interve
2	NCT01617967			Onpattro	Safety a	nd Tolerabil	Complete	Has Results	TTR-mediat	tod Amvl	Genetic Di	Drug: Pati /	werage c	Alnylam		18 Vears	Phase 3	2	9 Industry	Interventi	Interve
5	NCT02510261		SIRNA	Onpattro	The Stud	ly of an Inve	Enrolling	No Results A	Amyloidosi	ic Any	Genetic Di	Drug: Pati 9	afety and	Alnylam		18 Vears 1	(Phase 2	21	1 Industry	Interventi	Interve
6	NCT02939820		ciRNIA	Onpattro	Evnanda	d Accoss Dr	Approved	No Results A	TTR-mediat	ted Amvl	Genetic Di	Drug: natici	iran (ALN	Alnylam		18 Vears	NA	null	Industry	Expanded	Access
7	NCT01960348		SIRNA	Onpattro		The Study	Complete	Has Results	TTR-mediat	ted Amyl	Genetic Di	Drug: nati I	Andified	Alnylam		18 Vears 1	Phase 3	22	5 Industry	Interventi	Allocat
8	NCT01961921		siRNA	Onpattro	The Stud	iv of ALN-TI	Complete	Has Results	TTR-mediat	ted Amyl	Genetic Di	Drug: ALN 1	he Numb	ΔInvlam	ΡΔΙΙ	18 Years t	(Phase 2	2	7 Industry	Interventi	Interve
9	NCT02053454		SIRNA	Onnattro	A Study	of the Safet	Complete	No Results A	Transthyre	tin (TTR)	Genetic Di	Drug: nati 1	the prope	Alnylam	ΡΔΙΙ	20 Vears 1	Phase 1	1	2 Industry	Interventi	Allocat
10	NCT01559077		siRNA	Onpattro	Trial to F	valuate Saf	Complete	No Results A	TTR-mediat	ted Amvl	Genetic Di	Drug: ALN 1	he propo	ΔInvlam	PΔII	18 Years t	(Phase 1	1	7 Industry	Interventi	Allocat
11	NCT03759379		SIRNA	Onpattro	HELIOS-A	A: A Study o	Recruiting	No Results A	Amyloidos	is. Hered	Genetic Di	Drug: Pati (hange fr	Alnylam	PAII	18 Years 1	Phase 3	16	0 Industry	Interventi	Allocat
12	NCT02949830		siRNA	Givosirar	A Study	to Evaluate	Active. no	No Results A	Acute Inter	mittent	Metabolic	Drug: givo 1	he safet	Alnylam	PAII	18 Years	Phase 1	1	7 Industry	Interventi	Interve
13	NCT02452372		SIRNA	Givosirar	A Phase	1 Study of G	Complete	No Results A	Acute Inter	mittent	Metabolic	Drug: givo 1	he safety	Alnylam	PAIL		Diseas 1	- 4	0 Industry	Interventi	Allocat
14	NCT03338816		siRNA	Givosirar	ENVISIO	N: A Study t	Active. no	No Results A	Acute Hepa	atic Porpl	Ophthalm	Drug: Give 1	he annua	Alnylam	PAII	Saesha Ver	ma: tiseases ordi	, 9	4 Industry	Interventi	Allocat
15	NCT03505853		SIRNA	Givosirar	A Study	to Investiga	Complete	No Results A	Acute Inter	mittent	Metabolic	Drug: Give F	Profile of	Alnylam	PAII	are-diseases	acute-	1	0 Industry	Interventi	Interve
16	NCT03417245		siRNA	Fitusiran	(A Study	of Fitusiran	Recruiting	No Results A	Hemophilia	A Hem	Genetic Di	Drug: fitus	Annualize	Genzyme	, Male	intermittent	-porphyria/	12	0 Industry	Interventi	Allocat
17	NCT03417102		siRNA	Fitusiran	(A Study	of ATLAS-IN	Recruiting	No Results A	Hemophilia	AlHem	Genetic Di	Drug: fitus	Annualize	Genzyme	. Male	12 years a	r Phase 3	5	4 Industry	Interventi	Allocat
18	NCT03549871		siRNA	Fitusiran	(A Study	of ATLAS-PP	Recruiting	No Results A	Hemophilia	а .	Genetic Di	Drug: Fitu A	Annualize	Genzyme	, Male	12 Years	Phase 3	7	0 Industry	Interventi	Interve
19	NCT03159416		siRNA	Inclisiran	A Study	of Inclisiran	Complete	No Results A	Renal Impa	irment	Renal Diso	Drug: Incli F	harmaco	The Med	All	18 Years	Phase 1	3	1 Industry	Interventi	Allocat
20	NCT03060577		siRNA	Inclisiran	An Exter	nsion Trial o	Active, no	No Results A	Atheroscle	rotic Car	Metabolic	Drug: Incli F	Percentag	The Med	icAll	18 Years a	Phase 2	49	0 Industry	Interventi	Allocat
21	NCT03851705		siRNA	Inclisiran	A Study	of ORION-5	Recruiting	No Results A	Renal Impa	irment	Renal Diso	Drug: Incli F	Percent C	The Med	icAll	18 Years t	Phase 2	4	5 Industry	Interventi	Allocat
22	NCT03814187		siRNA	Inclisiran	Trial to A	s ORION-8	Not yet re	No Results A	ASCVD Ele	vated Ch	Metabolic	Drug: Incli F	roportio	The Med	icAll	18 Years	Phase 3	370	0 Industry	Interventi	Interve
23	NCT02314442		siRNA	Inclisiran	A Phase	1 Study of a	Complete	No Results A	Hyperchole	esteroler	Metabolic	Drug: ALN 1	he safet	Alnylam	PAII	18 Years	Phase 1	7	0 Industry	Interventi	Allocat
24	NCT03399370		siRNA	Inclisiran	Inclisirar	ORION-10	Active, no	No Results A	ASCVD Ele	vated Ch	Metabolic	Drug: Incli F	Percentag	The Med	All	18 Years	Phase 3	156	1 Industry	Interventi	Allocat
25	NCT03400800		siRNA	Inclisiran	Inclisirar	ORION-11	Active, no	No Results A	ASCVD Ele	vated Ch	Metabolic	Drug: Incli F	Percentag	The Med	icAll	18 Years	Phase 3	161	7 Industry	Interventi	Allocat
26	NCT03397121		siRNA	Inclisiran	Trial to E	v ORION-9	Active, no	No Results A	Heterozygo	ous Famil	Metabolic	Drug: Incli F	Percentag	The Med	All	18 Years	Phase 3		2 Industry	Interventi	Allocat
27	NCT02963311		siRNA	Inclisiran	A Study	of ORION-2	Complete	No Results A	Homozygou	us Famili	Metabolic	Drug: ALN F	Percentag	The Med	icAll	12 Years	Phase 2	vate W	4 Industry	Interventi	Interve 🚽
	< • -	Charts-Tri	ials Char	ts-Patients	Sheet4	Sheet5	Geograph	y Combin	ed Year	Status	Phases	🕀 :	•				Gote	Settings	to activat	s Windows	•

Figure 5.1 Represents the pipeline of RNAi molecules

For data collection, several keywords were used that will cover the overall scope of the report. These were the uniquely formed keywords into order to extract most accurate data from the *www.clinicaltrails.gov*. Below is the list of the keywords used during collating data:

- siRNA / short interference RNA; "siRNA" or "short interference RNA"
- miRNA / microRNA; "miRNA" or "microRNA"
- shRNA / short hairpin RNA; "shRNA" or "short hairpin RNA"
- sshRNA / synthetic short hairpin RNA; "sshRNA" or "ssynthetic short hairpin RNA"
- RNAi / RNA interference; "RNAi" or "RNA interference"

Trials obtained from each keyword was downloaded and all the trials were collated into a single sheet where further analysis were done.

5.3 Data Analysis

The collated data was further utilized for performing analysis. Analysis are performed in order to procure the detailed examination of the various parameters. For clinical trial analysis, we have taken into consideration various parameters and on that basis, analysis is performed. Therefore, these analyses are performed on following basis

- Geography
- No. of trials
- No. of patients
- Year of trials
- Status of trials
- Phases of trials

	AutoSave 💽)• @	÷				RNAi-Clini	al Trail Ana:	alysis (Drugs) - SG E	dit-2 - Exce	I			
ł	ile Home	e Insert	Pag	e Layout	Formula	5 Data	Review View H	lelp 🔎	Search						
F	Cut	-	Calibri B I	- - U - []]	11 • A^	≡	≡ ≡ ≫ • åb Wrap ≡ ≡ € 至 ⊞ Merg	Text e & Center	Gener	ral ▼	Condition	al Format as	Cell Inser	t Delete	Format
	Clinboard	at Fairner		Font		5	Alignment		r.	Number 5	ronnatun	Styles	yies ·	Cells	
	coproting						. ang the second second					54745			
Ľ	3 *			f _x											
_		A		В	С	D	E	F	G	Н		1		J	K
2							Status	Count		Status		Count of Stat			
4	Row Labels		- Coun	t of Status		1	Completed	61		Completed		count of stat	61		
5	Active, not r	recruiting		18		2	Recruiting	28		Recruiting			28		
6	Approved fo	or marketing	z	1		3	Active, not recruiting	18		Active, not recr	uiting		18		
7	Available			1		4	Enrolling by invitation	3		Enrolling by inv	itation		3		
8	Completed			61		5	Not yet recruiting	4		Not yet recruiti	ng		4		
9	Enrolling by	invitation		3		6	Available	1		Available			1		
10	Not yet recr	uiting		4		7	Approved for marketing	1		Approved for m	arketing		1		
11	Recruiting			28											
12	Grand Total			116											
13							Count of Statu	S							
14							4, 3% 1, 1%								
15	-						3, 3% 1, 1%								
16						18	15%	• Co	mpleted						
1/	-						, 12/0	Re	ruiting						
18								Ac	rive not reci	ruiting					
20							61,	53%	olling by inv	vitation					
21								= No	t vet recruit	ing					
22						28	3, 24%	- 44	silabla						
23								I AV	maple						
24								II Ap	proved for n	narketing					
25															
26															
27															
28															
	< →	Charts-Pa	tients	Sheet4	Sheet5	Geograp	hy Combined Year	Status	Phases	siRNA mi	🕂				

Figure 5.2Represents Analysis by trial status

The above donut graph presents the distribution of clinical trials on the basis of trial status.

AutoSave 💽	出 り・ペ・ -				RN	Ai-Clinical	Trail Analysis (Drugs) - SG Ed	it - 2 - Excel					Saes	ha Verma	æ
File Home	Insert Page La	yout F	ormulas	Data Review	View Help	ЯS	earch									合 Share
Paste Cut Paste Clipboard	ter	• 11 • ⊞ • Font	• A° A`		+ ₽₽ Wrap Text	Center ▼	General 🚰 👻 % Numb	• 9 50 -00 per 5	Conditional Format a Formatting ~ Table ~ Styles	as Cell Styles *	Insert *	Delete Čells	Format	∑ AutoSu ➡ Fill * � Clear *	m * AS Z Sort Filte Editing	& Find & r * Select *
A11 -	$\times \checkmark f_x$															
A	В	С	D	E	F	G	Н	- I -	J	к	L	М	1	N	0	Р
3 Row Labels 💌	Count of Phases			Phases	Count of Phases											
4 Phase 1	38			Phase 1	38											
5 Phase 1 Phase 2	17			Phase 2	36											
6 Phase 2	36			Phase 3	21					Cour	nt of Ph	lases				
7 Phase 2 Phase 3	2			Phase 1 Phase 2	17											
8 Phase 3	21			Phase 2 Phase 3	2									Pha	- 1	
9 NA	2			Grand Total	116							38, 17%				
10 Grand Total	116													- The	2	
11				Phases	Count of Phases									- 118	5H 2	
12				Phase 1	38											
13				Phase 1 Phase 2	17								36.16%	- Pha	se 3	
14				Phase 2	36				116, 505	70						
15				Phase 2 Phase 3	2									= Pha	se 1 Phase 2	
16				Phase 3	21											
17				Grand Total	116							21, 9	9%	= Pha	se 2 Phase 3	
18											2, 1947,	, 7%				
19														- Gra	nd Total	
20																
21																
22																
23																
24																
25																
26																
27																
28														Activa	te Win	dows
29														Gatas	stringer to	activatal
 Image: Characteristic Characteristic	arts-Patients Sh	neet4 S	heet5 0	Geography Com	bined Year	Status	Phases	siRNA mil	🕂 : 🖣						standa to	activate i

Figure 5.3 Represents analysis by phase of development

The above donut chart shows the phase wise split of the number of trials at a global level.

A	utoSave 💽 🛱	り・ ペ・・				RNAi-Clini	cal Trail Ana	lysis (Drugs) - SG Ed	it - 2 - Excel				Saesha Veri	na 🖽	_
File	Home Ins	ert Page Layout	Formulas	Data I	Review View	r Help 🔎	Search							යි Share	PC
Pas	te Cut ⊘ Copy ~ ⊘ Format Painter Clipboard	Calibri B I ∐ → I Fai Font	• 11 • A^ /	× = = = • = = = = =	≡ ॐ - at	े Wrap Text Merge & Center t	• Genera	al v % 9 58 38 Number 5	Conditional Formatting +	Format as Cell Table * Styles * Styles	Insert De	ells	∑ AutoSum ▼ ↓ Fill ▼ ♦ Clear ♥ Edition	AZY Sort & Find & Filter * Select *	Ideas
AP	15 👻 i	× ✓ fx													
	С	D	E	F	G	Н	1.1	J	К	L	М	N	0	Р	C
1															
2	Туре	of RNAi molecu	ile												
3											0.18%				
4												- 0.03%			
5	North Bow Jabola	America	Amorica								3.66%		= siF	NA	
7			America		ciRNA	11506 44									
8	miRNA	4			shRNA	437.9976							shl	RNA	
9	shRNA	437.997619			DNA	21									
10	siRNA	11506.4383			miRNA	4									
11	Grand Total	11969.436			Grand To	t 11969.44							= Dr	A	
12															
13											96.13%		= mi	RNA	
14															
15															
17															
18															
19															
20													Activate W	/indows	Mindou
4	Charts	-Patients Sheet4	Sheet5	Geography	Combined	Year Status	Phases	siRNA mil	🕀 🗄	•			Go to setting		14 Hidov

Figure 5.4Represents analysis by type of RNAi modality in North America

The above donut chart presents the distribution of clinical trials conducted in of North America based on type of RNAi modality. Similar analyses were performed for Europe, Asia-Pacific and Rest of the world.



Figure 5.5Represents analysis by type of RNAi modality and phase of development in North America

The above bar chart shows the distribution of clinical trials conducted in North America on the basis on type of RNAi modality and phase of development. Similar analysis is performed for Europe, Asia-Pacific and Rest of the world.

9W	RNA View	i-Clinical ⁻ Help (Trail Analysis Q Tell me w	(Drugs) - hat you v	SG Ed vant to	it -v2 - Exce	l I	ll , ll		Sa	aesha Verma	Ē		口 只 Sha	×
eb \ E I	Wrap Text Merge & C	enter 👻	General ♀ % Num	9 €.0 .00	• 00. €.€	Conditiona Formatting	I Format Table	as Cell • Styles •	Insert D	velete Format	∑ Auto ↓ Fill ▼ ♦ Clea	Sum - S r - F Edition	ort & Find & ilter ▼ Select ⊽		~
													5		v
	Q	R	S	Т		U	V	W	х	Y	Z	AA	AB	AC	
				5.3% 5.3% 2.6% 15.8% 13.2% 7.9% 36.8%		6, i 7, . 9, . 3, J 23 9, . 16, . 3, J 23, .	398 33% 55% 65% 1% 4% 4% 5% 6%		3.7% 8.7% 7.4% 18.5% 7.4% 14.8% 11.1% 29.6%		0.0%				
			1	Phase I		Pha	se II		3.7% Phase III		Not Applicable	e			
				Oncology Infectious Hepatolog	Disease y	= Genetic s = Cardiov = Neurolo	Disorders ascular Diso gical Disord	= Ophtha rders = Renal I ers = Others	lmology)isorders	= Metabolic D = Dermatology	isorders v				

Figure 5.6Represents analysis by type of indication and phase of development in North America

The above bar graph provides the phase wise distribution of different indications targeted by RNAi Therapeutics. Through this bar split percentage of different indications can be concluded in different phases.Similar analysis is performed for Europe, Asia-Pacific and Rest of the world.

PROMOTIONAL ANALYSIS

6.1Chapter Overview

Drug developers heavily rely on a number of broadcasting channels, such as direct to consumer (DTC) advertisements, product websites and conferences, to promote their drugs. The importance of such promotions is evident from the fact that the pharmaceutical industry spent close to USD 6.1 billion in DTC advertisements in 2018. [12]

The target individuals for these promotional campaigns are usually consumers (patients), caretakers / caregivers and healthcare professionals (physicians).

- Promotional campaigns offer several advantages to drug developers, end users and physicians, some of which are listed below:
- Better adoption of drug
- Increases interaction of patients with physicians
- Educate patients
- Drive patient compliance

This chapter provides the promotional instance of Onpattro which is the first marketed RNAi Therapeutic drug and gives the brief overview on channels used for promotional campaigns in this report.

6.2 Channels Used for Promotional Campaign

There are several channelsavailable for use by drug developers to promote their products. Some of these channels are mentioned below:

• **Product Websites:** Drug developers often launch separate product websites which provide information related to the drug. The primary objective of the website is to provide vital information regarding indications, efficacy of drug benefits and side effects of drug.

- **Patient Assistance Program:** Such are the programs which are initiated by the drug developers in order to provide financial assistance to patients. For this either drug developers offer co-pay schemes or provide drug free of cost for specified period.
- **Detailing material (face to face sales and promotional activities):** Detailing materials include brochure, leaflets and flyers which also contain information about the drug. The are in addition to the product website.
- **Direct to Consumer (DTC) advertisements:** These are promotional campaign which target consumers directly. Such advertisements take place via television, print media, social media or even radio.
- **Oral / Poster presentation at conferences:** Companies participates in various conferences to present their clinical findings.

AutoSave 💽 🗄 🏸 💍 🗧		Promotional Ana	lysis-RNAi			Saesha Verma 🛛 🗹	-	٥	×
File Home Insert Design Layout I	References Mailings <mark>Review</mark>	View Help 🔎 Sear	ch			년 SI	hare	Commen	ts
abc ====================================	Translate Language	Previous Next Show Comments	Track Changes * Reviewing Pane	Accept Reject	Compare	Block Restrict Authors - Editing	Hide Ink •	CV Assistant	
Proofing Speech Accessibility	Language (Comments	Tracking	G Changes	Compare	Protect	Ink	CV	~
	presents a qualitative ar products, to promote th Figure XX.X Prom	nalysis of the key focus are eir offerings. otional / Marketing S	as chosen by the develop trategy: Product We	ers of aforementioned					
		EXONDYS 51 (eteplirsen) Injection		onpattrog					
	Developer Sar	repta Therapeutics	Jazz Pharmaceuticals	Alnylum					
	Type of product Am	tisense oligonucleotide	single-stranded oligodeoxyribonucleotides	siRNA					
	Approved patient Du segment	chenne muscular dystrophy (DMD)	hepatic veno-occlusive disease (VOD) & hematopoietic stem-cell transplantation (HSCT)	hATTR amyloidosis					
	Year of Approval Seg	ptember 19, 2016	March 30, 2016	August 10, 2018					
	Focus area of promotional m	essages							
	Clinical trail data		•						
	Safety information	0							
	Mechanism of Action	۲		٩					
	Dosage			0					
	Full Harvey ball indicates ma Empty Harvey ball indicates n	ximum focus no focus				tivate Windov			
									Ŧ

Figure 6.1 Represents the overview of promotional anlysis using harvey ball

In the report we have done promotional analysis using Harvey Ball which are the ideograms used for the visual communication of qualitative data.

6.3 Example of Promotional Analysis: Onpattro

In promotional analysis of Onpattro which is first RNAi marketed drug we have provided analysis based on various parameters, such as Product website analysis, patient assistance program, other reimbursement program and safety information. Using these parameters analysis is performed using Harvey ball which gives the pictorial representation of the qualitative data. Also, to make analysis more substantial drug overview is provided on basis of parameters such as

- Developer name
- Type of Drug
- Indication
- Target
- Dosage
- First approval



Figure 6.2 Represents the product website analysis

AutoSave 💽 🗄 🏷 🕈 🕫	Promotional Analysis-RNAi	Saesha Verma 🔳 —	0 X
File Home Insert Design Layout	References Mailings Review View Help 🔎 Search	년 Share 🖓	Comments
abc Image: Check Thesaurus Word Document Avia Check Check Accessibility Proofing Speech Accessibility	Simple Markup Reviewing Pare Net Show Comments Net Compare Language Comments Comments Comments Tracking Tracking Tracking Compare Compare	re Block Restrict Authors Editing Ink * re Protect Ink	CV Assistant CV
Page 17 of 19 1 of 2726 words []8	<page-header></page-header>	Activate Windows Go to Settings to activate Win	dows.

Figure 6.3 Represents the patient assistance program: AlnylumAssist



Figure 6.4 Represents the other reimbursement programs

PARTNERSHIPS AND COLLABORATIONS

7.1Chapter Overview

RNAi therapeutics is a niche area that has found a renewed focus in the past few years. Companies involved in this market are witnessing several collaborations aimed at discovering and developing drugs, delivery systems and technology platforms in order to utilise RNAi as a therapeutic option.

In this chapter, we have provided information on the various partnerships/agreements, related to RNAi therapeutics, which have taken place in the recent past.

7.2Types of Partnerships and Collaborations

Stakeholders in the industry adopt a variety of models to collaborate with other companies; some of these standard models have been briefly described below.

- Acquisition: when one company acquires all of the shares and assets of another company.
- Merger: when two companies combine their business operation and merge into single entity
- **Clinical Trail Agreement:** These are the agreements which occur to perform clinical related to a product candidate with / to a partner company.
- Joint Venture: Instances where two or more companies come together to form a new company.
- Manufacturing and Supply Agreement: Where one company opts the services of other company for manufacturing purposes only.
- **Product Development Agreement:** Where two companies come together for development of product or drug.
- **Product Commercialization Agreement:** Where company comes into an agreement with other companies for commercialization of their product candidate.

- **Product Development and Commercialization Agreement:** In such agreements the companies come into agreement to co-develop and co-commercialize the product candidate.
- Licensing Agreement: In this the licensor company grants exclusive or nonexclusive rights to the licensee company for its proprietary or patented product.
- **R&D Agreement:** These are the research collaborations where companies enter into agreement to conduct R&D studies.

7.3 Data Collection

The data was gathered for various industrial and non-industrial collaborations and partnerships. This data hasbeen collected from multiple sources including public records, surveys, press releases, and company sources. It governs the structure of the overall report and actsas the most important stepin drafting the insights. Hence, it must be robust, exhaustive and finely structured, in order to produce accurate analysis.

Such collated data on Partnerships and Collaborations help us to determine the growth of the RNAi market and arousing interests of different pharma players in field of RNAi Therapeutics.

AutoSave 💽 🖁	9• °° =				Partnerships - RNAi	- Excel			Saesha Verma	= - o ×
File Home Insert	Page Layout	Formulas Da	ita Review	View Help 🔎	Search					🖻 Share 🛛 🖓 Comments
Paste Cut Paste Clipboard	Times New Roma ▼ B I U ▼	10 • A A •		란 Wrap Text 태 Merge & Center	General	Condition Formatting	al Format as Cell g * Table * Styles * Styles	Insert Delete Format	∑ AutoSum * A ↓ Fill * Sort & ☆ Clear * Filter Editing	k Find & Ideas
	(. f									
	√ J× Na	me								Â
C	D	E	F	G	н	l. I	J	к	L	M
1	New addition		Old		updated		Doubt			
2	Partner 1				Partner 2					
3 Name 🔻	Headquaters (Sta 🔻	Headquaters (Cov 👻	Region	Name 🔻	Headquaters (Stat 👻	Headquaters (Cou 👻	Region 👻	Name of Drug	Month /year of colls *	Type of collaboration
4 Benitec Biophama	New South Wales	Australia		Axovant	New York	US	North America	BB-301 / AXO-AAV-OPMD	July, 2018	Licensing Agreement
5 Alnylam Pharmaceuticals	Massachusetts	US	North America	Regeneron	New York	United States	North America		April, 2019	Product Development and C
6 Alnylam Pharmaceuticals	Massachusetts	US	North America	Genzyme, a Sanofi com	pany			patisiran, vutrisiran, and fitu	si October, 2012	Product Development and C
7 Alnylam Pharmaceuticals	Massachusetts	US	North America	Medison Pharma	Petah Tikva	Israel		ONPATTRO®	January, 2019	Manufacturing and Supply 2
8 Alnylam Pharmaceuticals	Massachusetts	US	North America	Vir Biotechnology	California	US	North America	VIR-2218 (ALN-HBV02)	October, 2018	Product Development and C
9 Alnylam Pharmaceuticals	Massachusetts	US	North America	Vir Biotechnology	California	US	North America	4 additional RNAi therapeuti	ic October, 2018	Research Collaboration
10 Alnylam Pharmaceuticals	Massachusetts	US	North America	Ionis Pharmaceuticals	California	US	North America	ALN-AS1	January, 2015	Cross Licensing Agreement
11 Benitec Biophama	New South Wales	Australia		4D Molecular Therapeu	California	US	North America	BB-201	November, 2014	Collaborative Research and I
12 Benitec Biophama	New South Wales	Australia		Circuit Therapeutics	Menlo Park, Californi	US	North America	TT-034	November, 2015	Global Licensing Agreement
13 Biocon	Bangalore	India		Quark Pharmaceuticals	CA	US	North America	QPI-1007	December, 2013	Product development & Cor
14 Regen BioPhama	California	US	North America	Benitec Biophama	New South Wales	Australia		Cancer Vaccines	August, 2013	Technology Licensing
15 Benitec Biophama	New South Wales	Australia		Lonza	Basel	Switzerland		TT-034	October, 2015	Manufacturing Services Age
16 Benitec Biophama	New South Wales	Australia		Biomics Biopharma	Nantong,P.R	China		Hepbama®		Joint Venture
17 Benitec Biophama	New South Wales	Australia		ReNeuron		UK		CTX-Exosome	June, 2015	Research Collaboration
18 Benitec Biophama	New South Wales	Australia		Omnia Biologics	Maryland	US	North America	TT-034	May, 2015	Manufacturing Services Age
19 Benitec Biophama	New South Wales	Australia		Asklepios	North Carolina	US	North America	TT-034	April, 2015	License Agreement
20 Arrowhead Research	Californioa	US	North America	Novartis	Basel	Switzerland			March, 2015	Acquisition Agreement
21 Phio Pharmaceuticals	Massachusetts	US	North America	Glycostem Therapeutic	Kloosterstraat	The Netherlands			March, 2019	Research Collaboration
22 Phio Pharmaceuticals	Massachusetts	US	North America	Karolinska Institutet	Stockholm	Sweden			August, 2019	Research Collaboration
23 Phio Pharmaceuticals	Massachusetts	US	North America	Iovance Biotherapeutic	s				May, 2018	Research Collaboration
24 Phio Pharmaceuticals	Massachusetts	US	North America	MirImmune Inc	Massachusetts	US	North America		January, 2017	Acquisition Agreement
25 Phio Pharmaceuticals	Massachusetts	US	North America	PCI Biotech	Oslo	Norway			April, 2015	Research Collaboration
26 Benitec Biopharma	New South Wales	Australia		CN Bio					March, 2015	Research Collaboration
27 Avidity NanoMedicines	Californioa	US	North America	Sevion Therapeutics	Californioa	US	North America		November, 2014	Research Collaboration
← → Sheet1	Sheet2 Sheet	Sheet4	+			: •				Ectivate windows.
										+ 100%

Figure 7.1 Represents the exhaustive database of RNAi partnerships and collaborations

For building the database we have taken into consideration various parameters which includes the basic company information of both partnering companies. The other parameters that have been taken into consideration are

- Name of Drug
- Month / year of collaboration
- Type of collaboration
- Focus Area of collaboration
- Type of RNAi modality
- Indication
- Therapeutic area
- Financial information

PATENT ANALYSIS

8.1Chapter Overview

Several developments have taken place over the last decade in the field of RNAi therapeutics, wherein industry stakeholders have tried to overcome existing limitations and improve efficacy of therapies / platforms to continuously expand their intellectual capital to sustain long term growth. As a result, several patents have been filed to protect the novel intellectual property generated within this domain. This chapter provides an overview of the already filed / published patents related to RNAi therapeutics. It also attempts to highlight the trends associated with patent type, publication year, regional distribution, surgical procedure, industry type, CPC classification, emerging areas, leading players, valuation and opportunity analysis for the expired patents. For the purpose of analysis, we have considered only those patents that have been filed / published since 2014.

8.2Data Collection

The data containing information on filed / published patents since 2014 by various industrial and non-industrial players have been captured from*www.lens.org*website. The website features data related to the patents filed / published including most of domains (in science). The raw data procured from the website will further be used to carry out analysis which will cover trends associated to patent type, publication year, regional distribution, surgical procedure, industry type, CPC classification, emerging areas, leading players, valuation and opportunity analysis for the expired patents. For such analysis our report covers data since 2014.

Such a database containing information related to patents help us to determine the growth of the research in RNAi therapeutic domain and determine lifespan of RNAi market.

Auto	oSave 💽		9• (?* •			Compiled	Patent List -Published	l & filed - Excel						Si	iesha Vermi	. 🖻	-	٥	х
File	Home	e insert	Page Lay	out Formulas Data Review	v View H	lelp 🔎 S	earch									🖻 Sha	ire 🖓	Comme	nts
Paste	↓ Cut □ Copy ✓ Form Clipboard	/ ▼ nat Painter	Calibri B I <u>U</u> →	• 11 • A [*] A [*] = = = 8 ⊞ • <u>A</u> • <u>A</u> • Font 5	→ ab Wrap → ab Wrap → B Merg Alignment	Text e&Center ▼ ⊊	General	Condit Format	ional Fc ting + - Sty	ormat a Table *	as Cell Styles *	Insert D	Delete Format Cells	∑ Auto ↓ Fill ▼ ♦ Clear	Sum • A Z So • Fi Editing	rt & Find ter * Selec) 4 182 10 :t * 10	eas leas	~
A3546	53 🔻	· : ×	√ f _x	35461															^
4	A	вс	D	E F	G	н	1	J	8	ĸ	L	М	N O	Р	Q	R	s	т	
1																			
2 #	Juris	sdiction Kind	Publicatior Pu	blicatior Title	Applicants	Inventors	URL	Туре	Cited	I Coun C	PC Classific	ations							
3	1 US	B2	US 864256	2014 Methods For Expansion Of Hema	te SCADDEN DAVID	; SCADDEN DAV	IE https://lens.org/05	6-(Granted Pate	int	0 0	:12N5/0647	;;C12N15/113	37;;C12N2310/14	;;C12N2501,	70;;C12Y20	7/11001			
4	2 US	B2	US 863747	2014 Apoptotic Cell-mediated Transfe	ci LI FENGCHUN;;E	S LI FENGCHUN;;	E https://lens.org/10	8-! Granted Pate	int	00	:12N5/0602	;;A61K31/708	38;;A61K35/12;;A	61K39/001;;	A61K2035/1	22;;C12N15	5/113;;C12	N2310/14;;	C12
5	3 WO	A2	WO 2014/	2014 Modified Rnai Agents	ALNYLAM PHARM	A RAJEEV KALLAN	II https://lens.org/11	3- Patent Appli	tati	14 0	12N15/113	;;C0/H21/02;;	;;C12N15/111;;C1	2N2310/14;	C12N2310/	31;;C12N23	10/32;;C1	2N2310/32	1;;0
0	4 05	82	US 862385	2014 Organic Compositions to Treat P	S CHEN JINYUN;;H	CHEN JINYUN;;	H nttps://iens.org/U	4-Granted Pate	int	30	.12N15/113	;;A61K31/713	3;;A61K45/U6;;CU	/H21/U2;;C1	2N2310/14;	C12N2310	/321;;(12)	12310/322;	;01,
1	5 05	A1	US 2014/0	2014 Method For Rapid Identification	C ELEMENTO ULIV	ITELEMENTO ULI	V nttps://iens.org/05	4-, Patent Appli	ati	00	516815/UU;;	C12Q1/68/4;	;;GU1N33/5UU8;;F	3U1N28UU/4	4	C12N2210	/221_012	12210/222	
0	7 110	A1	US 2014/0	2014 Organic compositions to treat P	S HINKLE GREGUR	I HINKLE GREGU	Knups.//iens.org/ou	0 (Patent Appli	.dl	100	.12(115/115	;;A01K31/713 AC1K31/237	5;;A01K45/06;;C0	/HZ1/UZ;;UI	2112310/14;	AC1847/5	/521;;U120	12510/522; 7/64_AC1V	1014
10	2 103	A1	WO 2014/0	2014 Drug Delivery Vehicle Comprision	UNIV NODTH TE	LACKO ANDRAS	https://lens.org/0	1 (Patent Appli	.au	10 /	G1K47/42,,	MUIKJ1/JJ7,,	A01K31/415,,A0	1821/7105,,	401847/342	"HUIK47/J	44,,40184	7/64,,4010	17/1
11	9 11	A1	ALL 2012/2	2014 Compositions And Methods For		MEDZOLIKI ARE) https://lens.org/04	R. Patent Appli	.au ati	0.0	12N15/113	RA61K0/516	,HUIKJI/41J,,HU 51A61K31/AOA	61K31/7103,,	AG1K31/J92	,HUIK4773 5A618317	44,,HUIK4 64-A61K3	1/713-A61	+//
12	10 US	R2	LIS 862911	2014 Methods Of Treating & Meiotic K	IN PELLMAN DAVID	PELIMAN DAVI	D https://lens.org/08	7-1 Granted Pate	nt	0.0	S01N33/501	1 461K31/70	088461K31/710	5-G01N33/	5026G01N	3/57496-4	201N2333	/914G01N	1250
13	11 US	B2	US 863671	2014 Methods And Devices For Drug D	e PRALISNITZ MAR	PRALISNITZ MA	6 https://lens.org/00	R-Granted Pate	nt	15 4	61F9/0017	·· Δ61M37/001	15461M2037/0	023461M2	210/0612	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	5011425555	514,,0014	250
14	12 US	B2	US 865252	2014 Drug Carrier And Drug Carrier Kit	ECNIITSU YOSHIRC	NUTSU YOSHIR	Chttps://lens.org/03	4-(Granted Pate	nt	10 4	61K31/07-	A61K9/0019-	A61K9/127-A61	K9/14-A61K	31/7088-A6	1K38/1833	A61K38/	1841~A61K	38/
15	13 AU	A1	AU 2011/3	2014 Apoptosis-inducing Agent	NITTO DENKO CO	NIITSU YOSHIR	Chttps://lens.org/12	3-Patent Appli	ati	0 4	61K31/713	A61K31/52	A61K31/7088:A	61K31/7105	A61K31/71	1::A61K38/	45::A61K4	5/06::C12N	15/
16	14 US	A1	US 2014/0	2014 Drug Delivery Particle And Metho	d OKADA TAKASHI	OKADA TAKASH	II https://lens.org/14	3- Patent Appli	ati	24	, 61K9/5184	:A61K9/14::A	A61K31/7088;;A6	1K31/713;;A	, 61K47/26;:A	61K47/42;;	A61K48/0	J08::A61K4	8/0
17	15 WO	A1	WO 2014/	2014 Methods For Identifying Diabete	S METANOMICS H	E REIN DIETRICH	https://lens.org/12	2-(Patent Appli	ati	1 (G01N33/503	8;;G01N30/7	206;;G01N33/50	08;;G01N25	00/04::G01M	12500/10;;0	G01N2500	/20;;G01N2	2800
18	16 WO	A1	WO 2014/	2014 Cd25 Pre-selective Combination	Ar UNIV CALIFORNI	ANDERSON JOS	SE https://lens.org/06	4-Patent Appli	ati	14	61K48/005	8;;A61K35/28	3;;A61K47/6901;;	A61K48/005	;C12N5/064	7;;C12N7/0	0;;C12N1	j/1138;;C12	2N15
19	17 US	A1	US 2014/0	2014 Melanoma Treatments	YAO YIHONG;;ST	FYAO YIHONG;;S	Thttps://lens.org/13	7-(Patent Appli	ati	1 0	12N15/113	5;;C12N15/11	13;;C12N2310/11	3;;C12N231)/141;;C12Q	1/6886;;C1	2Q2600/1	06;;C12Q26	00/
20	18 EP	B1	EP 253373	2014 Low-permeability, Laser-activate	d ON DEMAND TH	E COPPETA JONA	Tihttps://lens.org/00	0-Granted Pate	nt	0 4	61F9/0017	;A61F9/008;;	;A61K9/0009;;A6	1K9/0051					
21	19 AU	B2	AU 2008/2	2014 Oligonucleotides For Modulatio	MIRX THERAPEU	MOLLER THORE	E https://lens.org/10	6-! Granted Pate	nt	0 0	12N15/113	1;;C12N15/11	13;;C12N2310/11	3;;C12N231)/141				
22	20 US	B2	US 865325	2014 Short Interfering Rna (sirna) Ana	IC ELMEN JOACHIM	ELMEN JOACHI	Mhttps://lens.org/01	8-: Granted Pate	int	0 0	12N15/113	1;;A61K38/00);;A61K38/09;;A6	1K38/2013;;	A61K38/212	;;A61K38/3	1;;C12N15	/111;;C12N	115/
23	21 US	A1	US 2014/0	2014 Lipid Nano Particles Comprising	C KYOWA HAKKO K	I KUBOYAMA TA	Kihttps://lens.org/05	5-Patent Appli	ati	15 A	61K9/5123	;A61K9/0019	;;A61K31/7088;;	A61K31/712	;A61K31/71	3;;A61K47/	18;;C07C2	11/21;;C12	N15
24	22 AU	B2	AU 2012/2	2014 Powder Conditioning Of Unit Dos	e NOVARTIS AG	BOECKL ANDRE	Vhttps://lens.org/07	2-I Granted Pate	nt	0									
25	23 AU	B2	AU 2007/2	2014 Random Rnai Libraries, Methods	UNIV PENNSYLV	A WANG YONGPI	N https://lens.org/09	6-(Granted Pate	nt	0 0	12N15/108	6;;C12N15/11	11;;C12N15/113;;	C12N15/65;	C12N15/66	;C12N2310	/14;;C12N	2310/53;;C	12N
26	24 US	B2	US 865248	2014 Delivery System For Cytotoxic Dru	g IMMUNOMEDIC	S MCBRIDE WILL	l/https://lens.org/08	5- Granted Pate	nt	3 (07K16/307	5;;A61K31/65	5;;A61K39/3955;	;A61K39/39	583;;A61K47	/595;;A61K	47/6803;;	461K47/685	51;; <i>l</i>
27	25 US	B2	US 863299	2014 Rna Sequence-specific Mediator	s TUSCHL THOMAS	S TUSCHL THOM	Athttps://lens.org/12	3- Granted Pate	nt	11 0	:12N15/113	;;A01K67/033	36;;A01K2207/05	;;A01K2217/	075;;A01K22	27/703;;A0	1K2267/0	3;;A61K38/0	00;;
28	26 US	A1	US 2014/0	2014 Amino Acid Lipids And Uses The	e MARINA BIOTEC	FQUAY STEVEN	C; https://lens.org/07	4-(Patent Appli	ati	12 A	61K47/183	;;A61K9/127;;	;A61K9/1271;;A6	1K9/1272;;A	61K31/7088	;;A61K47/1	8;;A61K47	/22;;A61K4	7/2
29	27 US	B2	US 865835	2014 Methods And Compositions For	TH ROSSI JOHN J;;B	E ROSSI JOHN J;;	B https://lens.org/11	9-4 Granted Pate	nt	10	12N15/113	;;C12N15/111;	1;;C12N2310/14;;	C12N2310/3	3;;C12N231	0/50;;C12N	2310/51;;	C12N2320/	30;;
30	28 AU	A1	AU 2012/3	2014 Poly(vinyl Ester) Polymers For In	VI ARROWHEAD RE	SWAKEFIELD DA	R https://lens.org/13	0-{Patent Appli	ati	0 0	12N15/113	;;A61K31/710	05;;A61K47/58;;O	08F218/04;;	CO8F218/10	;C08F2218	/22;;C12N	2310/14;;C1	L2N
31	29 US	B2	US 863731	2014 Reverse Micelles Based On Phyte	os MAUREL JEAN-CI	J MAUREL JEAN-	CI https://lens.org/15	6-Granted Pate	nt	0 4	A61K9/1075	;;A61K9/0031	l;;A61K9/4858;;A	61K31/7088	;A61K31/71	5;:A61K38/	1816;;A61	K38/28	
32	30 US	A1	US 2014/0	2014 Drug Delivery Compositions And	M BRONICH TATIA	N BRONICH TATI	Al https://lens.org/19	3- Patent Appli	ati	0 4	A61K47/34;;	A61K9/1075;;	;A61K31/704	Go to	Sottings	in active	to Winz	ious	
-	•	Sheet1	+						E .	•				0010	ootunigo				Þ
														III		四	1	+	85%

Figure 8.1 Represents the list of patent both filed / published

For building the database several keywords were used that will cover the overall scope of the report. These were the uniquely formed keywords into order to extract most accurate data from the *lens.org*.

Patents obtained from keyword was downloaded and all the data was collated into a single sheet where further analysis will be done.

Since the data collection was done from 2014 onwards and there were more than 50,000 results obtained.

VC FUNDING

9.1Chapter Overview

In this chapter, we have reviewed how the investor money has funded various companies/researches for development of RNAi therapeutics and technologies. We looked at all the companies identified during the research and extracted information related to investment activities, where available.

Advancements in technologies as well as development of innovative therapeutics have continuously shaped the pharmaceutical industry. Monetary assistance from angel investors, venture capitalists (VCs) and crowd funding schemes from various organisations, along with regulatory assistance from the authorities has allowed the technology driven companies to pace up their research and development activities. RNAi therapeutics has been quite popular with VCs. In our research we have captured an investment / funding from 2014 onwards.

9.2 Types of Funding

There are several ways in which a company may receive financing. For the purpose of this analysis, we have considered the following types of funding:

- **Grant:** Grant is provided by governmental or non-governmental organizations. Usually amount provided by grant is less than the other form of funding. These are basically utilized to carry out the research-based activities
- Seed: These are the early investment that are made into start up. They are highly risky form of investment for investor
- Venture capital Investment: it is a form of equity financing provided by one investor or a group of investors, to growing start-ups that are deemed to possess lucrative growth potential. Progressive rounds of venture capital funding are

denoted as Series A, Series B, Series C, Series D, Series E and so on. Series A funding is provided immediately after seed funding.

- Initial Public offering (IPO): An IPO refers to the instance when a private company offers its stocks / shares to the public for the first time
- Secondary offering: Finances raised throughall public offerings following an IPO are known as secondary offerings.
- Other Equity: All the form of equity that cannot be classified in above categories.
- **Debt financing:** refers to those instances where company take loan either from bank or investor / a group of investors and required to pay back to investor.

9.3 Data Collection

The data was gathered for various funding instances received by the companies (as mentioned in pipeline). This database has been created from multiple sources including public records, surveys, press releases, and company sources. It governs the structure of overall report and acts as the most important aspect in the process of drafting insights. Hence, it must be robust, exhaustive and finely structured, in order to produce accurate analysis.

Such collated data on VC funding help us to determine the growth of the RNAi market and arousing interests of different pharma players in field of RNAi Therapeutics. Increased instances of funding in field of RNAi therapeutics have shown increased growth of RNAi therapeutic market.

٨	utoSave 💽 🖁	9· (? - =				VC funding	Excel		Saesha Verma 🛛 🖻	- 0 ×
Fil	e Home Inser	t Page Layo	out Formulas	Data Review	View Help 🔎	Search			🖒 Share	Comments
Pa	Cut Copy ~ Ste Ste Ste Clipboard 5	Calibri B I U →	11 → A [*] A [*] 11 → A [*] A [*] 11 → A [*] A [*] 1 → A [*] A [*] Font	- = = = ≫ - = = = = = = = = - = = = = = = = = = =	란 Wrap Text 템 Merge & Center → mment	General	Conditional Format as C Formatting * Table * Sty Styles	iell Insert Delete Format Cells	AutoSum * AZY P Fill * Sort & Find & Clear * Filter * Select * Editing	Ideas
A4	• : X	√ f _x	1							^
	В	с	D	E	F	G	Н	I.	J K	L 🔺
1				Opening	Closing					
2	Company Name	Month/Year	Type of Funding	Amount (As per Press R	Amount (As per Press R	Amount (USD)	VC Firm (Investor)	Focus Area		Focus Area C
3									Discovery PC	IND
4	Alnylam Pharmaceuticals	Feburary, 2019	Grant	\$248,000		\$248,000	Advocacy for Impact Grants program.	This annual competitive grants program	n recognizes high-impact proj	ects that address ci
5	Alnylam Pharmaceuticals	January, 2019	Secondary Offering	\$387,500,000		\$387,500,000	Barclays Capital Inc.	Alnylam intends to use the net proceed	ds from this offering for gener	al corporate purpos
6	Alnylam Pharmaceuticals	August, 2018	Grant	Early Access to Medicine	s Scheme (EAMS)		Medicines and Healthcare Products Re	gulatory Agency (MHRA)		
7	Alnylam Pharmaceuticals	November, 2017	Secondary Offering	\$700 million		\$700 million	Goldman Sachs & Co. LLC, J.P. Morgan	Alnylam intends to usethese offering f	for general corporate purpose	s, including clinical
8	Alnylam Pharmaceuticals	May, 2017	Secondary Offering	\$359.4 million		\$359.4 million	Barclays Capital Inc.	Alnylam intends to use these offering f	for general corporate purpose	s, including clinical
9	Alnylam Pharmaceuticals	January, 2015	Secondary Offering	\$450 million		\$450 million	J.P. Morgan Securities LLC and Deutsc	Alnylam intends to use the net proceed	ds from this offering for gener	al corporate purpos
10	Silence Therapeutics	April, 2015	Secondary Offering	£27.3 million			Canaccord Genuity and Peel Hunt are jo	support and expand the Company's pre	e-clinical capabilities and capa	cities
11	Dicema Pharmaceuticals	September, 2018	Secondary Offering	\$100.0 million		\$100.0 million	Citigroup, Leenink Partners and Stifel- je	Dicema intends to use the net proceed	s from this offering for preclin	ical studies and cli
12	Dicema Pharmaceuticals	December, 2017	Secondary Offering	\$40 million		\$40 million	Stifel and Evercore ISI - joint book-runn	Dicema intends to use the net proceed	s from the offering for preclini	cal studies and clin
13	Dicema Pharmaceuticals	January, 2019	IPO	\$92.9 million		\$92.9 million	Jefferies LLC, Leerink Partners LLC, and	1 Stifel, Nicolaus & Company, Incorpora	ated-joint book-running manag	zersRobert W. Baire
14	Arrowhead Research	January, 2018	Secondary Offering	\$60.4 million		\$60.4 million	Jefferies LLC and Barclays Capital Inc	Arrowhead intends to use the net proc	eeds from this offering for ger	neral corporate pur
15	Arrowhead Research	August, 2016	Other Equity	\$45 million		\$45 million	Cantor Fitzgerald & Co.rout Capital LL	and Chardan Capital Markets LLC -Fin	ancial AdvisorsOrbimed, RA	Capital Managemer
16	Arrowhead Research	Feburary, 2014	Secondary Offering	\$104 million		\$104 million	Jefferies LLC, Barclays Capital Inc., and	Arrowhead intends to use the net proc	eeds from this offering for ger	neral corporate purp
17	Simaomics	April, 2019	VC-Series C		\$47 million	\$47 million	CR-CP Life Sciences Fund, Charoen Po	Simaomics plans to use the proceeds to	o support its clinical programs	3
18	Simaomics	May, 2016	VC-Series B		\$10 million	\$10 million	Hong Kong based venture capital firm,	The proceeds will be used to fund clini	cal development	
19	Arbutus Biopharma	January, 2018	VC-Series A		\$116.4 million	\$116.4 million	Roivant Sciences Ltd.	Roivant and Arbutus intend to explore	wY	
20	Arbutus Biophanna	March, 2015	Secondary Offering	\$151.9 million	\$151.9 million	\$151.9 million	Leerink Partners LLC and RBC Capital I	Tekmira anticipates using the net proce	eeds from this offering to deve	alop and advance p
21	Silenseed	July, 2017	Early VC- Series Uni	\$10 million	\$10 million	\$10 million	private investors-undisclosed	Begin a Phase II multicenter trial for its	pancreatic cancer treatment.	
22	Avidity Biosciences	October, 2018	Equity		Undisclosed	Undisclosed	CureDuchenne	Funding will help to advance pre-clinic	al development of p Y	
23	Avidity Biosciences	January, 2017	VC- Series B		\$16 million	\$10 million	Alethea Capital, Alexandria Real Estate	financing round to support the develop	om Y	
24	Avidity NanoMedicines	August, 2014	VC- Series A		\$6 million	\$6 million	Fidelity Biosciences and TPG Biotech F	race Pharmaceuticals, Partner Fund Ma	nagement, L.P. and Y	
25	Phio Pharmaceuticals	October, 2018	Secondary Offering		\$15 million	\$15 million	H.C. Wainwright & Co.	The Company intends to use the net p	roY	
26							-			
27	Celsion Corporation	December, 2018	Others		\$28.5 million	\$28.5 million	New Jersey Economic Development Au	to fund more R&D, expand its workford	e, Yate windows	v
	Sheet1	Sheet2	(+)							MINGOWS.
			-						III II	+ 100%

Figure 9.1Represents the list of various funding instances.

For building the database we have taken into consideration various parameters which includes the basic company information of enlisted companies in pipeline. The other parameters that have been taken into consideration are

- VC Firm (Investor)
- Month / year of funding
- Type of Funding
- Focus Area
- Type of RNAi modality
- Indication
- Financial information (Amount of Funding)

SERVICE PROVIDERS

10.1Chapter Overview

There are several service providers including contract manufacturers and contract researchers worldwide offering RNAi related services. This chapter provides details on these service providers.

10.2Types of Service Providers

Service providers are the organizations, business or individuals that provide their services to others in exchange of payment. [13]

Most of the service providers offer services such as:

- clinical and preclinical synthesis of siRNA, miRNA and shRNA-based vectors,
- development of target libraries of siRNA, miRNA and expression systems,
- validation services and
- high throughput screening services.

Service Provides in pharmaceutical domain are

- Contract Manufacturing Organisations (CMO): A company that offers manufacturing services, with volume capabilities ranging from small amounts for preclinical R&D to larger volumes necessary for clinical trials purposes and commercialization.[14]
- Contract Research Organisations (CRO): A Contract Research Organisation, also called Clinical Research Organization (CRO) is a service organization that provides support to the pharmaceutical and biotechnology industries in the form of outsourced pharmaceutical research services (for both drugs and medical devices). CROs range from large, international full-service organizations to small, niche specialty groups and can offer their clients the experience of moving a new drug or device from its

conception to FDA marketing approval without the drug sponsor having to maintain a staff for these services.[15]

10.3 Database Building

Database contained information regarding various CMO and CROs which provide services to RNAi Therapeutic industries. This database has been created from multiple sources including public records, surveys, press releases, and company sources. It forms the basic structural outline of the overall report and serves as the most important stepin the process of report writing. Hence, it must be robust, exhaustive and finely structured, in order to produce accurate analysis.

Such a database containing information related to the service provides help us to determine the growth of the RNAi market and arousing interests of different pharma players in field of RNAi Therapeutics. Increased instances of service providers in field of RNAi therapeutics have shown increased growth of RNAi therapeutic market.

AutoSa	an 🖸 🛐 🔓 🖓			RNAi service pr	oviders-2 - Excel		Saesha Verma	⊞ – Ø ×
File Paste	Home Insert Page Layout Formu Cut Cut Calibri 11 - M Gropy - B I U A - Font	A^ A' A^ A' A T T T T T T T T T T	Review View R W = $^{\circ}$ · $^{\circ}$ $^{\circ}$ Wra = $^{\circ}$ · $^{\circ}$ Mer Alignment	Help $\label{eq:pressure}$ Search p Text General rge & Center + rge $\label{eq:pressure}$ Nur	Conditional Format as Cell Formating * Table * Styles * Styles	Insert Delete Format Cells	∑ AutoSum * A T Fill * Z Sort & Clear * Filter * Editing	Select + Ideas
D53	▼ : × √ fx							^
C	C D	E	F	G	н	I J	K L	M N (*
4 S.No.	Service Provider	Location	Type of Services	Type of Molecule	Capabilities			
5	1 Abion							
6	2 Agilent Technologies							
7	3 Allele Biotechnology	USA		siRNA; shRNA; miRNA	Allele Biotechnology provides a wide range of serve	ices to the pharmaceutica	al industry. It provides vario	ous RNAi based expression s
8	4 Altogen Labs	USA	CRO	siRNA, shRNA, miRNA	Altogen is a Biotech CRO company which provide v	vide variety of preclinical	l CRO studies, Xenograft a	ad in vivo toxicologystable c
9	5 AMSBIO	UK	CMO	siRNA, miRNA, shRNA	AMSBIO is a research reagents and services provid	<mark>ler</mark> offering siRNA, miRN	A, shRNA plasmids and a l	Dicer siRNA Generation kit.
10	6 Avecia Biotechnology	Milford, MA	CMO	AntisenseSiRNAShRNAMi	Avecia have an over 20 year of experience in oligon	ucleotide development a	nd production, and over 10	00 sequences manufactured
11	7 Biomics Biotechnologies (a GE Unit)	China	CMO	siRNA, shRNA, miRNA	Biomics was established in 2006. The company is ne	ear clinical stage biophan	maceutical company in dev	eloping and commercialising
12	8 Bioneer	Korea	СМО	siRNA, miRNA	Bioneer is a biotech company that provides product	<mark>ts</mark> and technologies in th	e field of molecular biology	Bioneer offers a broad spec
13	9 Biosettia	San Diego Califon	CRO	miRNA, shRNA	Biosettia focuses on the development and commerc	ialization of unique techr	nologies that will provide b	etter solutions for life scienc
14	10 BioSpring	Germany	СМО	siRNA,miRNA	BioSpring is a provider of oligonucleotides includin	<mark>g</mark> siRNAs for RNAi. The	company provides lyophili	ised and ready to use siRNA
15	11 Cell Signaling Technology	USA		siRNA	Cell Signaling focuses on the development of antibo	ody related products. It a	lso offers products for siR!	NA that includes the SignalS
16	12 Cellecta	USA	CRO	shRNA	Cellecta is a CRO providing advanced shRNA and p	e <mark>ptide libraries. The aim</mark>	of the company is to devel	op advanced high-throughp
17	13 Cenix Biosciences	Germany	CRO	siRNA, miRNA	Cenix is a preclinical CRO and technology develops	ient company in the area	of RNAi.It provides a rang	e of in vivo experimental serv
18	14 Creative Animodel	USA	CRO	RNAi	Creative Animodel is a preclinical CRO that provide	<mark>s s</mark> ervices such as PD/PR	C, toxicology and custom at	aimal models. It also provide:
19	15 Dharmacon	USA	CMO	siRNA, miRNA, shRNA	Dharmacon RNAi products encompass the most co	mplete portfolio of innov	ative tools for transient, lor	ag-tem, inducible and in vive
20	16 Eurofins Genomics	UK		siRNA	Eurofins Genomics is a provider of genomics based	<mark>se</mark> rvices that include seq	uencing, genotyping, gene	expression and oligonucleo
21	17 Eurogentec	Belgium	CMO	siRNA	Eurogentec is a leading provider of reliable and inno	vative products and ser	vices to the Life-Science, D	iagnostic and Pharmaceutica
22	18 Exiqon	Denmark	CMO	miRNA	Exiqon is a product manufacturer and service provid	<mark>le</mark> r in the field of life scier	nces. The company offers t	he following products and se
23	19 GeneCopoeia	USA	CMO	shRNA, miRNA	GeneCopoeia is a provider and manufacturer of gen	omics and proteomics pro	oducts and services. In rela	tion to RNAi, it provides pro
24	20 Genecust	UK	CRO	siRNA	Genecust is a CRO which provides genomics based	products and services. I	ts silencing product line co	vers the chemical synthesis
25	21 GeneDesign Inc	China	СМО	siRNA	GeneDesign provides custom synthesis and design	services for nucleic acid	products such as DNA, RI	NA BNA, siRNA and other s
26	22 GenePhama	China	CMO	siRNA, miRNA, shRNA	GenePharmahas established a comprehensive oligor	nucleotide manufacturing	g facility, and provides a wi	de range of open-access tech
27	23 GenScript							
28	24 Mello Biotech					J		
29	25 OriGene Technologies	USA	СМО	shRNA, siRNA, miRNA	OriGene Technologies was founded as a research to	ol company focused on	the creation of the large co	mmercial collection of full-ler
30	26 Phyzat Biopharmaceuticals	Porto, Portugal	CMO/CRO	siRNA	Phyzat Biopharmaceuticals provides RNAi technolo	gy in order to combat se	nous and life threatening d	iseases.It is focused on deve 🖕
()	New CMO-CRO Updated list	Nucleic Acid CMO	-CRO (+)		: 4	•	GO to Setungs to a	Etwate windows.

Figure 10.1Represents database of service providers of RNAi

For building the database we have taken into consideration various parameters which includes the basic company information of enlisted companies in pipeline. The other parameters that have been taken into consideration are

- Type of services
- Type of molecule
- Focus Area
- Capabilities

In the database five new instances of the service providers have been added, thus showing increasing growth of RNAi therapeutic market.

ADDITIONAL PROJECTS

11.1Biopharma CMO

In addition to my project, I have also contributed in another project namely, Biopharma CMO. Following section represents the work that I have been done in this project.

11.1.1Demand Collation

Database was built which contain demand for the top 20 biologics Revenue for 2018.

The database was built on following parameters:

- Drug Name
- Developer of Drug
- Indication
- Price of Drug (Indication specific / generic)
- Dosage Frequency
- Revenues 2013 to 2018

Aut	oSave 💽 🗄 🏷 🤆 🗸 🗸			List of top 20 bio	logics Revenue 2018	- Excel			Saesha Verm	a 🖅 —	o x
File	Home Insert Page Layout Formu	Ilas Data Review	View Help							암 Share	P Comments
Paste *	X Cut Calibri → 11 → Calibri → 11 → S Format Painter Clipboard 5 Font		 → ab Wrap Text = ■ Merge & Alignment 	Gene Center • 🖉 •	ral	Conditional Format as C Formatting Table T Sty Styles	Cell Insert D	Delete Format Cells	∑ AutoSum - ↓ Fill - Si Clear - Fi Editing	ort & Find & liter * Select *	Jdeas
E2	▼ : × ✓ fx Price of Dru	ıg (Indication-specific)									^
1	A B	с	D	E	F	G	н	1	J	к	L A
1	List of top 20 Biologics revenues in 2018	3									
2		Developer of Drug	Indication	Price of Drug (In	Price of Drug (G	Dosage frequency	2013 (millions)	2014 (millions)	2015 (millions)	2016 (millions	2017 (million
				40-mg prefilled pen or syringe for a 40-mg/0.8-	costs £352.14 for a 40-mg prefilled pen or						
3	1 Humira (Adalimumab)	Abbvie	Hidradenitis Supp	ml vial	syringe	160 mg SC on Day 1 (give	\$10659	\$12543	\$14012	\$16078	\$18427
4	2 Humira (Adalimumab)	Abbyle	Uveitis	£92 600 and £318 075 per quality- adjusted life year (OALY)		80 mg SC once, then, afte	\$10659	\$12543	\$14012	\$16078	\$18427
5	3 Eylea (Aflibercept)	Regeneron	Non-proliferative	diabetic retinop	\$600 per 100 mg	vial					
6	4 Eylea (Aflibercept)	Regeneron	Neovascular (We	40 mg/mL, 0.05	\$600 per 100 mg	2 mg (0.05 mL or 50 micro	\$2,105	\$ 2,820	\$4,104	\$4,860	\$ 5,872
7	5 Eylea (Aflibercept)	Regeneron	Macular Edema fo	llowing Retinal '	\$600 per 100 mg	2 mg (0.05 mL or 50 micro	\$2,105	\$ 2,820	\$4,104	\$4,860	\$ 5,872
8	6 Eylea (Aflibercept)	Regeneron	Diabetic Retinopa	thy (DR)	\$600 per 100 mg	2 mg (0.05 mL or 50 micro	\$2,105	\$ 2,820	\$4,104	\$4,860	\$5,872
9	7 Eylea (Aflibercept)	Regeneron	Diabetic Macular	\$1 110 000 per q	\$600 per 100 mg	2 mg (0.05 mL or 50 micro	\$2,105	\$ 2,820	\$4,104	\$4,860	\$ 5,872
10	8 Revlimid (Lenalidomide)	Celgene	Multiple Myelom	2.5 mg is \$21,05	0 for a supply of 2	10 mg PO qDay continuo 1000 mg IV infusion, repeat after 2 week (2 infusions separated by 2 week is 1 course)	\$4,280	\$4,980	\$5,801	\$6,974	\$8,187
				100-mg and 500		Repeat course					
				mg vials of		q24weeks or based on					
				rituximab is		clinical evaluation (but					
				£174.63 and	40 4 11 1	no sooner than 16			Activate W	ndows	
11	9 Kituxan (Rituximab, MabThera	Genetech-a member o	Kneumatoid arthr	£873.15	(10 mg/mL) is \$	weeks)			Go to Settings	to activate W	indows.
4	Sheet1 Sheet2 (+)					E .					Þ
										·····	+ 100%

Figure 11.1 Represents the database of demand

11.1.2Logo Landscape

Logo landscape is pictorial representation of the logos of companies related to biopharma CMO covered in the scope of report.

÷	Logo Landscape - Saved to \\1	72.16.1.2\Saesha	Saesha Verma	E –	٥
Transitions Animations Slide Sho	w Review View Help 🔎 S	earch		🖻 Share 🔤	🖵 Comme
ayout \bullet		A Text Direction *	Arrange Styles - Ø Shape Effects - Styles - Ø Shape Effects -	P Find ↓ Replace → ↓ Select →	Dictate
s Font	G Paragraph		Drawing	Editing	Voice
Example highlights					
This is the default font s This is a two line heade Biopharmaceutical Contr	size for a two line header r ract Manufacturers		40+ companies		
Market Landscape of Emergin	g Biologics				
Type of Biologics	Market Landscape	•	Contract Manufacturing Market Lands	cape	
Antibody Drug Conjugates	4 Recent Approvals: Adcetris®, Kadcyta®, Besponsa® In development	Close to 60% molecules in early phases of development	BECOME AND ALCON DIOSTNERGY	nique dinomoto	44
Cell Therapies	20+ Recent approvals: <u>Xescatae</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approved</u> <u>Approv</u>	More than 65% of cell therapies are use immune cells, primarily, T-cells	Curofins Curofin Cur	ERVICES	65
Gene Therapies	Recent approvals: Luxturma® Invossa ¹ /strinvelis® Approved	Over 50% therapies are being evaluated in various phases of clinical development			51
Biosimilars	Approved Interus Interus Udenvca TM In development	Examples of biologics that have approved biosimilars, Humira®, Enbrel®, Remicade®			39
Note 1: The projected opportunity has been analyzed acr related macular degeneration, retinitis pigmentosa and ot	ross the following segments [A] type of products (contact lenses ther indications) and [D] key geographies (North America, EU5 :	s and visual prostheses). [B] type of contact lens and Asia-Pacific)	es (therapeutic, drug delivery, and diagnostic / monitoring, [C] indications (diabe	etes, glaucoma, age-	

Figure 11.2 Represents the logo lanscape of biopharma CMO companies

11.1.3Appendix

Appendix was prepared in which graphical data was converted into table.

AutoSave 💽 🗄 🏷 🔻		Biopharma CMO app	endix - Read-Only - Saved t	o this PC		Saesha Verma 🗖	- 0 ×
File Home Insert Design	Layout References Ma	ilings Review View Help	𝒫 Search			යි Share	e 🖓 Comments
Cut Copy Paste ✓ Format Painter	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	∷ ≝≠≝≠'≣∗ ≝ ≅ ⊉↓ ¶ ≣ ≡ ≡ ≣ ≌∙ ≜∗ ⊞∗	1. A: AaBbC Chapter H 1 Figure H	1.1. A. 1.1.1 Level 1 Level	2 Level 3 Level	.1. 1.1.1.1.1. ✓ <	Dictate
Clipboard 5	Font 12	Paragraph 🕞		Style	5	5 Editing	Voice 🔺
	Europe	99	41				*
	North America	86	36				
	Asia	49	21				
	Australia	5	2				
	Table 22.3 Biopharmace Headquarters (Country	utical CMO: Distribution by	Location of				
	S. No. Location of Head	quarters	Distribution				
	North America		86				
	1 US		77				
	2 Canada		8				
	3 Mexico		1 00				
	4 IIK		18				
	5 Spain		7				
	6 Germany		20				
	Copyright © 2019 Roots Analysis Private Li	miled		Page 3			
	S. No. Location of Head	quarters	Distribution			Activate Windows	
	7 Belgium		2			Go to Settings to activate	
	8 The Netherlands		7			GO to Settings to activate	 ■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■
Page 1 of 10	0 Kronze		11			01 🖬 🗛	+ 100%

Figure 11.3 Represents the appendix of Biopharma CMO

11.2Medical Device CMO

In this project, I worked on identifying contacts for primary research.

11.2.1 Primary Research

A Database containing contacts and email IDs of management team of Medical Device CMO companies was prepared.

,	AutoSave 💽	🖫 9° ° • •					MDCM	D contacts Batch 6 AB-	edit - Protec	ted View - Excel	Saesha Verma	⊞ –	٥	×
Fi	ile Home	Insert Page Layout	Formulas	Data	Review	View	Help	✓ Search			ť	Share	🖓 Comme	ents
ſî	PROTECTED VIE	W Be careful—files from th	e Internet can	ontain virus	es. Unless you	need to e	dit, it's safe	er to stay in Protected V	Tiew. En	able Editing				×
112	53 * :	X 🗸 fx												^
		D			E			F		G	Н		1	
2														
3			Not	able to find										
4														_
5														
6	Axcesor		Bot	Adikes			Owner			Greater Milwaukee Area	https://www.linkedin.com/in/bob-adikes-0530028/	boba@a:	xcesor.com	<u>n</u>
7	Axcesor		Sco	tt Loftus			Vice Presid	ent - Development and	Engineering	Milwaukee, Wisconsin	https://www.linkedin.com/in/scott-loftus-a40b3226/	scottl@a	xcesor.con	n
8	Axcesor		Cat	herine Lee			QA/RA M	mager		Ireland	https://www.linkedin.com/in/catherine-lee-b460a5ba/	ocatherin	el@axceso	or.cc
9	BQ+ Medical		Rot	iia Cao			Founder &	President		Shanghai City, China	https://www.linkedin.com/in/ronia-cao-396b2820/		-	
10	BQ+ Medical		Chr	is Han			PM			Songjiang District, Shanghai, Chin	https://www.linkedin.com/in/bqplusmedical-chrishan			
11	Cadence		Ala	n Connor			President a	nd CEO		Charlottesville, Virginia Area	https://www.linkedin.com/in/alandconnor/	alanconr	10r@caden	ice.
12	Cadence		Jim	Gimbel			Director of	Program Management		Greater Pittsburgh Area	https://www.linkedin.com/in/jim-gimbel-0398713/	jimgimb	el@cadenc	ce.co
13	Cadence		Jeff	Kelly			VP and Ger	neral Manager at Cader	nce Inc.	Greater Pittsburgh Area	https://www.linkedin.com/in/kellyjeff/	jeffkelly	@cadence.	.cor
14	Creganna Medical		Mic	hael Tzori			Director of	Operations		San Francisco Bay Area	https://www.linkedin.com/in/michael-tzori-04a9743/	michaelt	zori@te.co	om
15	Creganna Medical		Ma	rco Kurz			Business I	evelopment Manager		Stuttgart Area, Germany	https://www.linkedin.com/in/marcokurz/	marcoku	rz@te.com	1
16	Creganna Medical		Jas	on Bromen			Director of	Advanced Manufactu	ring Engineer	Greater Minneapolis-St. Paul Area	https://www.linkedin.com/in/jason-bromen-5819677/	jasonbro	men@te.c	:om
17	Creganna Medical		Tin	a Donoho			Operations	Manager		Greater Minneapolis-St. Paul Area	https://www.linkedin.com/in/tina-donoho-12a18218/	tinadone	ho@te.co	m
18	Ecomedis medizint	technik	Fra	nk Schiwek			Managing	Partner		Münster, North Rhine-Westphalia	https://www.linkedin.com/in/frank-schiwek-5b887015	5/?trk=pub-p	bmap&origi	inalS
19	Electronic Instrum	entation and Technology (E	IT) Dav	rid Faliskie			President /	Chief Operating Office	r	Leesburg, Virginia	https://www.linkedin.com/in/david-faliskie-b9545550/	david@e	it.com	
20	Electronic Instrum	entation and Technology (E	IT) Jahi	Faieq			Director of	Manufacturing Engine	ening	Washington D.C. Metro Area	https://www.linkedin.com/in/jalil-faieq-1478451/	jalil@eit	.com	
21	Electronic Instrum	entation and Technology (E	IT) Bill	Lingis			Director, B	usiness Development		Greater Pittsburgh Area	https://www.linkedin.com/in/bill-lingis-21750813/	bill@eit.	.com	
22	Gerresheimer		Ma	rcin Raczyńs	ki		Head of Op	erations		Wroclaw, Lower Silesian District, I	https://www.linkedin.com/in/marcinraczynskii/	raczyński	i@gerresh	eim
23	Gerresheimer		Tar	a Bryce			Business I	evelopment Manager		Houston, Texas Area	https://www.linkedin.com/in/tara-bryce-30ab0420/	bryce@g	erresheim	er.c
24	Gerresheimer		Joe	Gauldin			Manufactu	ring Manager		Morganton, North Carolina	https://www.linkedin.com/in/joel-gauldin-30a327101/	gauldin@	ogerreshei	ime
25	Hunt Development	t	Dus	ican Hunt			Operations	Director		Midhurst, West Sussex, United Ki	https://www.linkedin.com/in/duncan-hunt-53344112/	o duncan.h	nunt@hunt	tcor
26	Hunt Development	t	Phil	Brinkley			Production	Operator		Guildford, United Kingdom	https://www.linkedin.com/in/phil-brinkley-5141a0157/	phil.brin	kley@hunt	tcor
27	Hunt Development	t	Tre	vor Hunt			Managing	Director		Guildford, United Kingdom	https://www.linkedin.com/in/trevor-hunt-0bb8a036/?	n trevor.hu	unt@huntc	20m
28	In'Tech Medical		Lau	rent Pruvost			President &	2 CEO			https://intech-medical.com/about/our-history-team	Ipruvost/	@intech-m	nedi
29	In'Tech Medical		Vin	cent Verbrug	ighe		Quality Ma	nager		Polincove, Nord-Pas-de-Calais, Fra	https://www.linkedin.com/in/vincent-verbrugghe-027	vverbrug	ghe@integ	ch-r
30	In'Tech Medical		Ror	nain Ibled			Global Sale	s Director at In'Tech N	fedical	Memphis, Tennessee	https://www.linkedin.com/in/romain-ibled-73339534/	ribled@i	intech-mec	dica
31	Integer		Gre	g Harding			Director of	Operations		Greater Minneapolis-St. Paul Area	https://www.linkedin.com/in/greg-harding-577728/	greg.har	ding@integ	ger. 👻
	< → Ba	itch-6 🕀								4				Þ
Rea	ıdv												+	100%

Figure 11.4 Represents the database of company contacts and email ID

11.3 Gene Therapy

In this project I worked on finding contacts for primary research.

11.3.1 Primary Research

A Database containing contacts of management team of Gene Therapy companies was prepared.

Au	toSave 🤇	• OH)	B 9-0-=			Contact list Set 3-S	V - Protected View - Excel	Saesha Verma	Œ	-	٥	×		
File	Hor	me	insert Page Layout Formulas D	Data I	Review View Help	,			🖻 Share	e 🖓	Comme	nts		
\bigcirc	PROTECT	ED VIEV	V Be careful—files from the Internet can contai	n viruses. I	Unless you need to edit, it's s	afer to stay in Protec	ed View. Enable Editing					>		
66			VulaCar Thereneutic											
Co			Xylocol merapeuto											
al		P	C	D	F		C							
1	A	D	L. L.		C	F	G			-		÷		
2		S. No.	Industry	YoE	Employee Size	Name	Designation	Source						
3		1	AAVogen	2015	2-10 employees	Dr. Buel "Dan" Rod	Founder/Chief Executive Officer	http://aavogen.com/about/						
4		2	AAVogen	2015	2-10 employees	Jade Brown	Business Development Transacti	https://www.linkedin.com/in/iade-brown-mba-0512277/?lipi=um%3A	Ali%3Apag	e%3Ad	flagship	3 54		
5		3	AAVogen	2015	2-10 employees			· · · · · · · · · · · · · · · · · · ·						
6		4	XyloCor Therapeutics	2003	• • • •	Estuardo Aguilar	Chairman and CEO	https://www.advantagene.com/leadership						
7		5	XyloCor Therapeutics	2003		Brain Guzik	Sr. Director Buisness Developmen	https://www.advantagene.com/leadership						
8		6	XyloCor Therapeutics	2003		Andrea Manzanera	Sr. Director, Clinical Research	https://www.advantagene.com/leadership						
9		7	Advaxis	2002	51-200 employees	Kenneth A. Berlin	President and CEO	https://www.advaxis.com/about-us/?pagelink=leadership						
10		8	Advaxis	2002	51-200 employees	Robert G. Petit	EXECUTIVE VICE PRESIDENT A	https://www.advaxis.com/about-us/?pagelink=leadership						
11		9	Advaxis	2002	51-200 employees	Kathy A.	Associate Director Clinical Devel	https://www.linkedin.com/in/kathy-a-87544a1/						
12		10	Allergan (acquired RetroSense Therapeutics)	•	10,001+ employees	Aniket Badkar	adkar Director, Biologics Product Devel (https://www.linkedin.com/in/aniket-badkar-8238006/?lipi=um%3Ali%3Apage%3Ad_flagship3_se							
13		11	Allergan (acquired RetroSense Therapeutics)		10,001+ employees	Amin Szegedi	di Vice President Clinical Developme https://www.linkedin.com/in/armin-szegedi-md-phd-456b555/?lipi=um%3Ali%3Apage%3Ad_t							
14		12	Allergan (acquired RetroSense Therapeutics)		10,001+ employees	Baldo Scassellati Sf	Senior VP, Head Drug Developme	n https://www.linkedin.com/in/baldo-scassellati-sforzolini-593841/?lip	i=um%3Al	i%3Apar	ze%3Ad	fla		
15		13	AlphaVax	1997	51-200 employees	Andrew Graham	VP Development and Technical O	https://www.linkedin.com/in/andrew-graham-b4435a2/						
16		14	AlphaVax	1997	51-200 employees	Peter Young	CEO	https://www.linkedin.com/in/peter-young-b06545/						
17		15	AlphaVax	1997	51-200 employees	Jon Smith	Chief Scientific Officer	https://www.linkedin.com/in/jon-smith-75954611/						
18		16	Amgen	1980	10,001+ employees	Margaret Faul	VP Drug Product Technologies	https://www.linkedin.com/in/margaret-faul-08376a6/?lipi=urn%3Ali9	63Apage%	3Ad_flag	gship3_s	earc		
19		17	Amgen	1980	10,001+ employees	Karla Thatcher Roja	Global Early Clinical Development	t https://www.linkedin.com/in/karla-thatcher-rojas-453239141/						
20		18	Amgen	1980	10,001+ employees	Joyce Chan	Director Business Development	https://www.linkedin.com/in/joyce-chan-2419462/?lipi=um%3Ali%3	Apage%3.4	Ad_flags	hip3_sea	rch		
21		19	Anaerophama Science	2004	11-50 employees	Tetsuya Mishima	CEO	https://www.linkedin.com/in/tetsuya-mishima-b83b96166/?originalS	ubdomain=	jp				
22		20	Anaerophama Science	2004	11-50 employees	Li Wang	Director, Strategic Alliances	https://www.linkedin.com/search/results/people/?facetCurrentComp	any=%5B9	%2212492	255%22%	65D		
23		21	Anchiano Therapeutics	2004	11-50 employees	Frank G. Haluska	President and Chief Executive Off	ñ https://www.anchiano.com/leadership-2/						
24		22	Anchiano Therapeutics	2004	11-50 employees	Ron Knickerbocker	Senior Vice President of Clinical I	https://www.anchiano.com/leadership-2/						
25		23	Anchiano Therapeutics	2004	11-50 employees	Sean Daly	Vice President of Clinical Operation	https://www.anchiano.com/leadership-2/						
26		24	AnGes	1999	36 (as of December 31, 20	Ei Yamada	President and Chief Executive Off	ä http://www.anges.co.jp/en/company/comp_member.html						
27		25	AnGes	1999	37 (as of December 31, 20	l Akihiko Murakami	Director, Production Control Dept	t https://www.linkedin.com/in/akihiko-murakami-48706a71/?lipi=um%	3Ali%3Ap	age%3A	d_flagshi	ip3_		
28		26	AnGes	1999	38 (as of December 31, 20	Nobuhiro Tanaka	Director of CMC Regulatory & Qu	u https://www.linkedin.com/in/宣博-田中-bb334643/?locale=en_US						
29		27	Apic Bio	2017	2-10 employees	John Reilly	Co-Founder and Chief Executive	Chttps://www.apic-bio.com/john-reilly/						
30		28	Apic Bio	2017	2-10 employees	Scott Loiler	Chief Technology Officer	https://www.apic-bio.com/scott-loiler/ Activate Wir	ιdφws					
21		10	Anin Ria	2017	2.10 emplotrees	Inlia Harran	Senior Director Remulatory Affair	n https://www.linkadin.com/in/mlia.hagan.6285467/?linimim?4241943	Anore9624	Ad flage	hing can	mh '		
		Sne	eti (†					[4]						

Figure 11.5Represents the database of company contacts

11.4 Next Generation Ophthalmic Lens

In this project I worked on preparing transcript.

11.4.1 Transcript

Transcript is the written format of the telephonic interview which took place between the Client and Roots Analysis Team.



Figure 11.6 Represents the draft of a transcript

FUTURE WORK PLAN

During my on-job training period, I have collated the data for the above mentioned topics, which in coming weeks will be drafted into word documents. In addition to above mentioned work, our future work prospects are as follows :

- Comprehensive profiles of marketed and mid to late stage clinical products (phase II/III or above); each profile features an overview of the therapy, its mechanism of action, dosage information, details on the cost and sales information (*wherever available*), clinical development plan, and key clinical trial results.
- Development and sales potential based on target consumer segments, likely adoption rate and expected pricing.
- An overview of the most commonly targeted therapeutic indications and details on the RNAi therapeutics that are being developed against them.
- An overview will be provided on use of miRNAs as potential biomarkers and list of several miRNA biomarkers under investigation. In addition, information will be provided on the pipeline of diagnostic kits that have already been approved or are under development.
- SWOT analysis of the RNAi therapeutics market, giving strategic insights to the major factors that are likely to drive future growth whilst also highlighting the weaknesses and threats that may negatively impact the industry's evolution will be conducted.
- A summary of overall report will be provided. A recap of the key takeaways and our independent opinion based on the research and analysis will be described.
- An executive summary of the report will be provided which will offers a high level view on where the RNAi therapeutics market is headed in the mid-long term.

CONCLUSION

The discovery of RNAi has revolutionised the study of gene regulation and paved the way for the development of a novel class of therapeutics capable of supressing the expression of a diseased/altered gene. Further, RNAi therapeutics silences the gene-of-interest by regulating the mRNA levels of the disease-causing gene via a sequence specific process.

In this project, we will conduct in length market study and analysis in the domain of RNAi therapeutic. Various aspects related to RNAi therapeutics market have taken into consideration, namely partnerships and funding in RNAi, clinical trials and patent analysis of RNAi that boost its research aspect to the market domain and many more such analysis are to be included.

Through this training, I am able to build business acumen in the biopharmaceutical industries. This training helped me create an analytical sense of biopharmaceutical market. Also, through this training, I was able to enhance my interpersonal skills. Overall, this training helped me to escalate my technical, analytical and interpersonal skills, thereby emerging as better professional.

REFERENCES

- 1. https://rootsanalysis.com/about-us.html
- 2. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1978219/
- 3. https://mmbr.asm.org/content/67/4/657
- 4. https://www.nature.com/articles/cr201619
- 5. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2727154/
- 6. https://www.ncbi.nlm.nih.gov/pubmed/15103066
- https://www.intechopen.com/books/functional-genomics/rnai-towardsfunctional-genomics-studies
- https://www.news-medical.net/life-sciences/RNA-interference-inbiotechnology.aspx
- http://americandrugdiscovery.com/rnai-type-screens-advantages-anddisadvantages/
- 10. https://www.nccn.org/patients/resources/clinical_trials/explanation.aspx
- 11. https://clinicaltrials.gov/
- 12. https://www.mmm-online.com/home/channel/commercial/dtc-pharma-ad-spending-slipped-4-6-in-2017-kantar/
- 13. http://www.businessdictionary.com/definition/service-provider.html
- 14. https://www.contractpharma.com/contents/view_glossary/2012-02-27/contractmanufacturing-organization-cmo-
- 15. https://www.pharma-iq.com/glossary/contract-research-organisation-cro