RNAi THERAPEUTICS MARKET (2nd EDITION) 2019-2030

Dissertation submitted in partial fulfillment of the requirement for the degreeof

BACHELOR OF TECHNOLOGY

IN

BIOTECHNOLOGY

By

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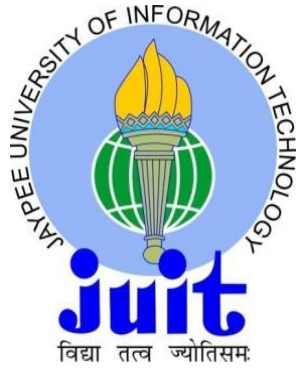
151851

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.

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Department of Biotechnology & Bioinformatics
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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)

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LIST OF ABBREVIATIONS

AMD	Age-related Macular Degeneration
CHS	Chalcone Synthase
CMO	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.

CHAPTER 1

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

CHAPTER 2

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, off-target 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.

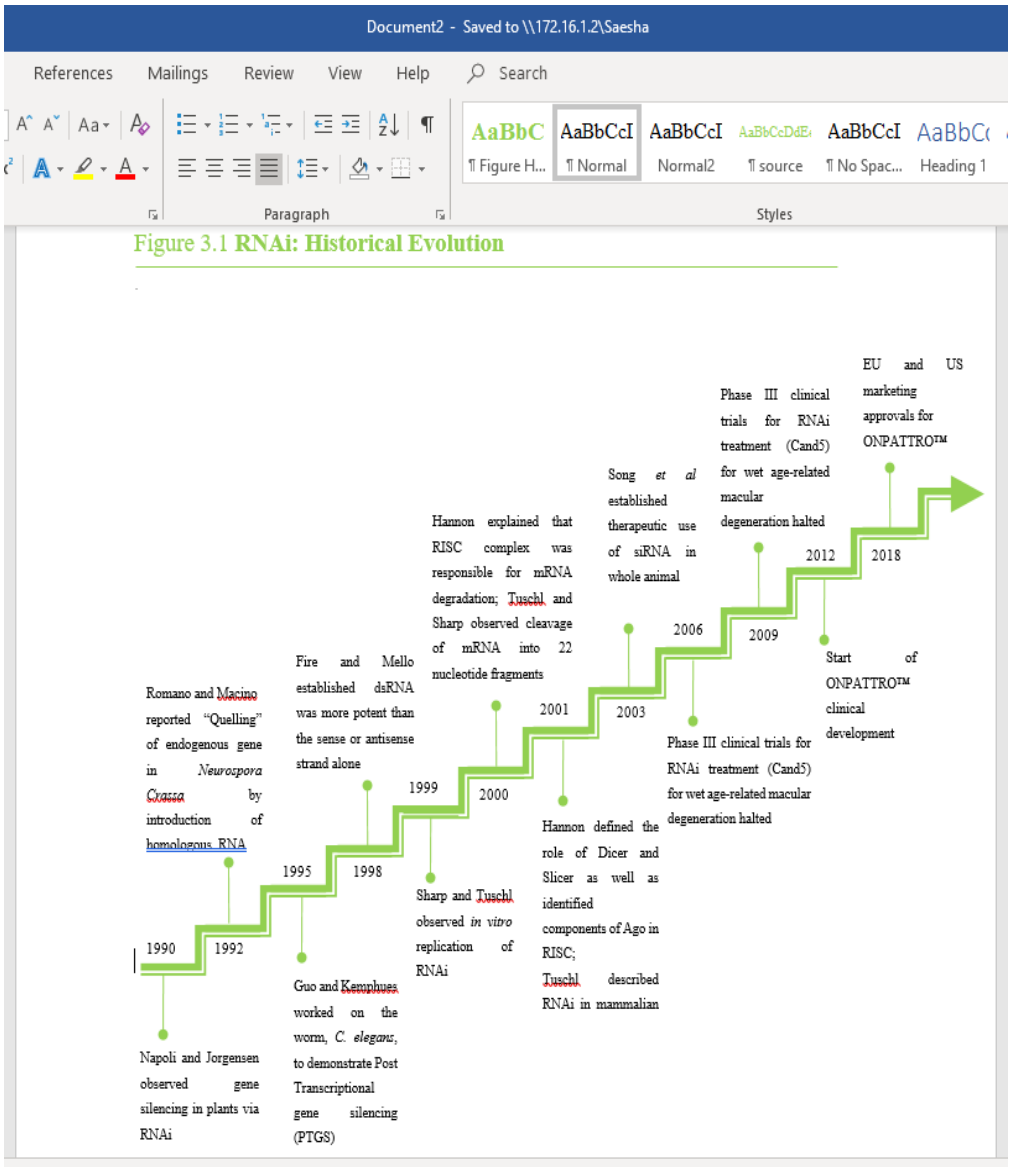


Figure 2.1 Timeline of RNAi development

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 ≈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]

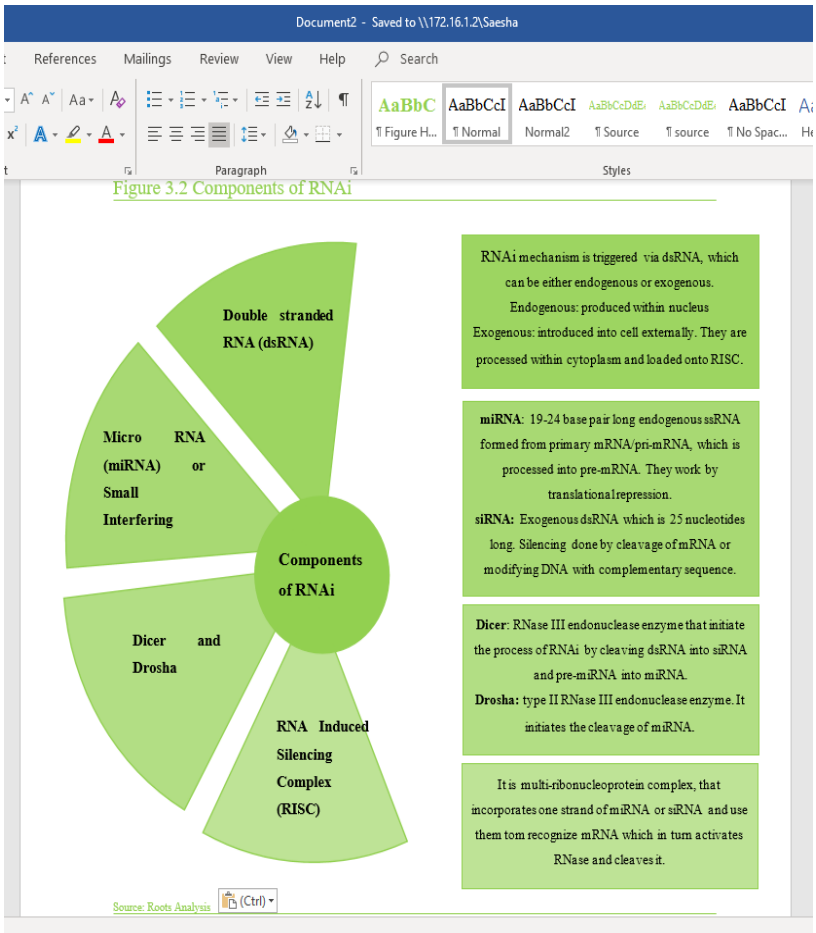


Figure 2.2 Pictorial presentation of various RNAi components

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 pri-miRNA.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]

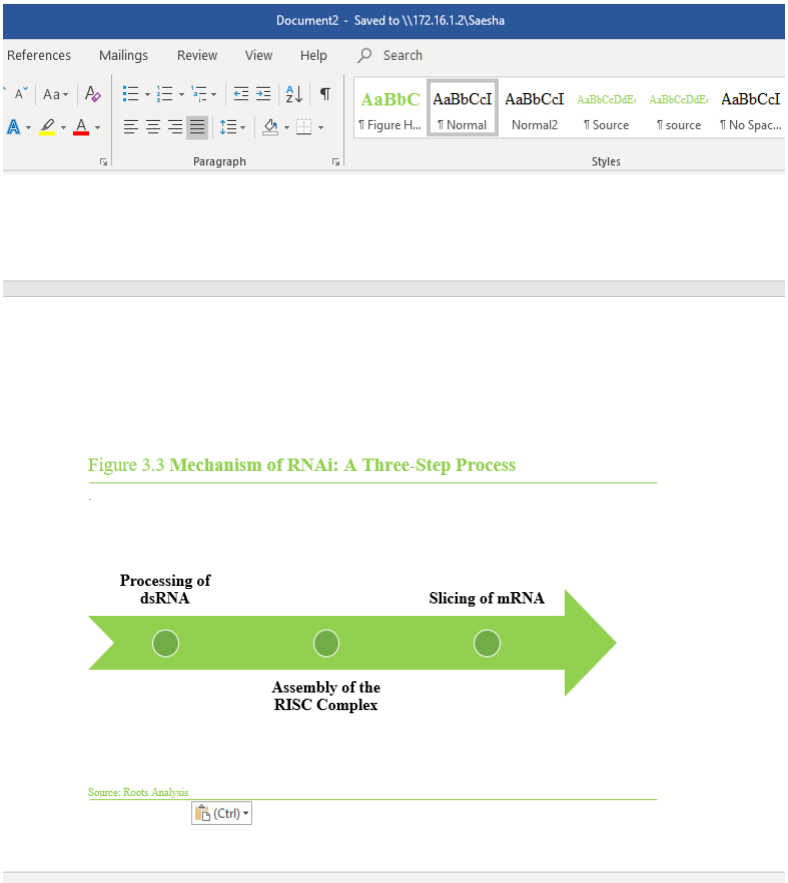


Figure 2.3 Overview of RNAi mechanism

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. Th e 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

CHAPTER 3

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.

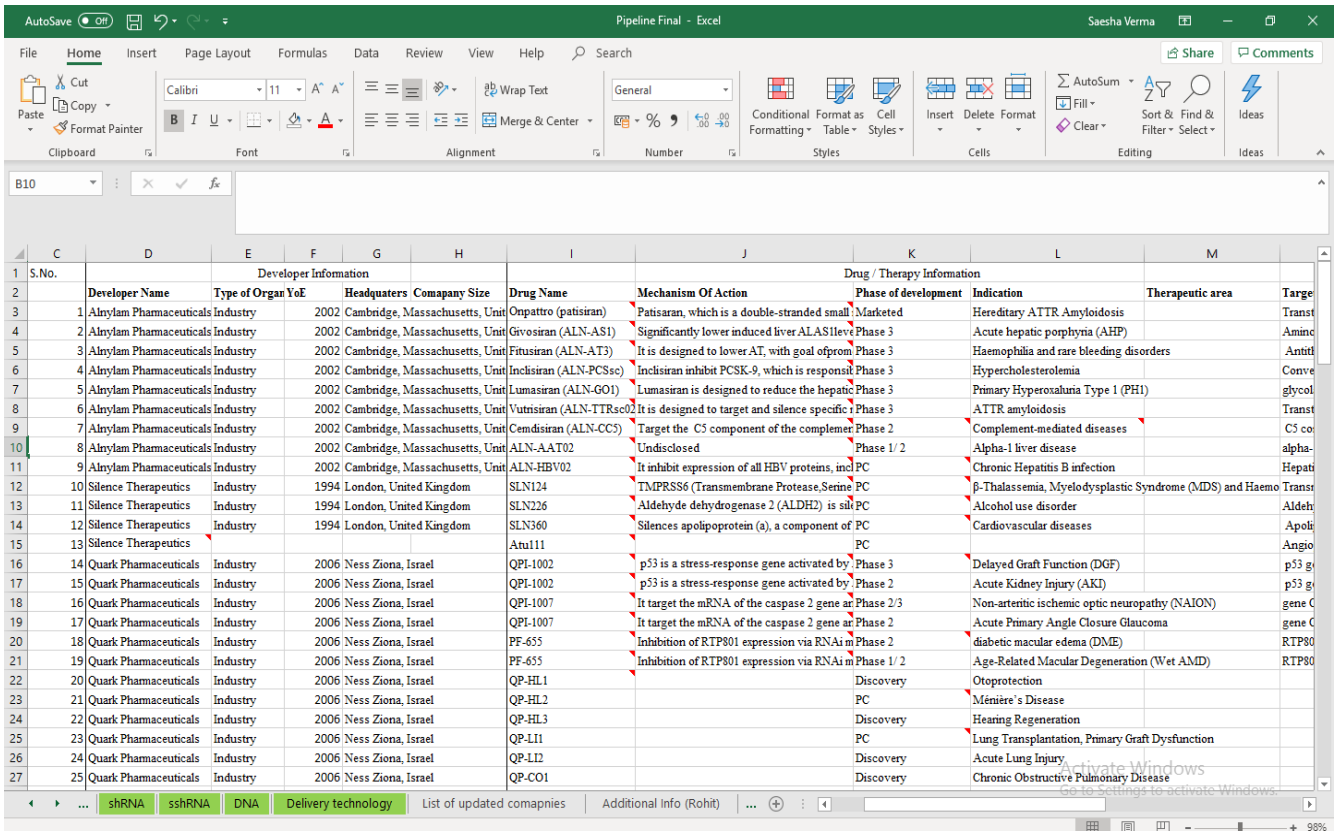
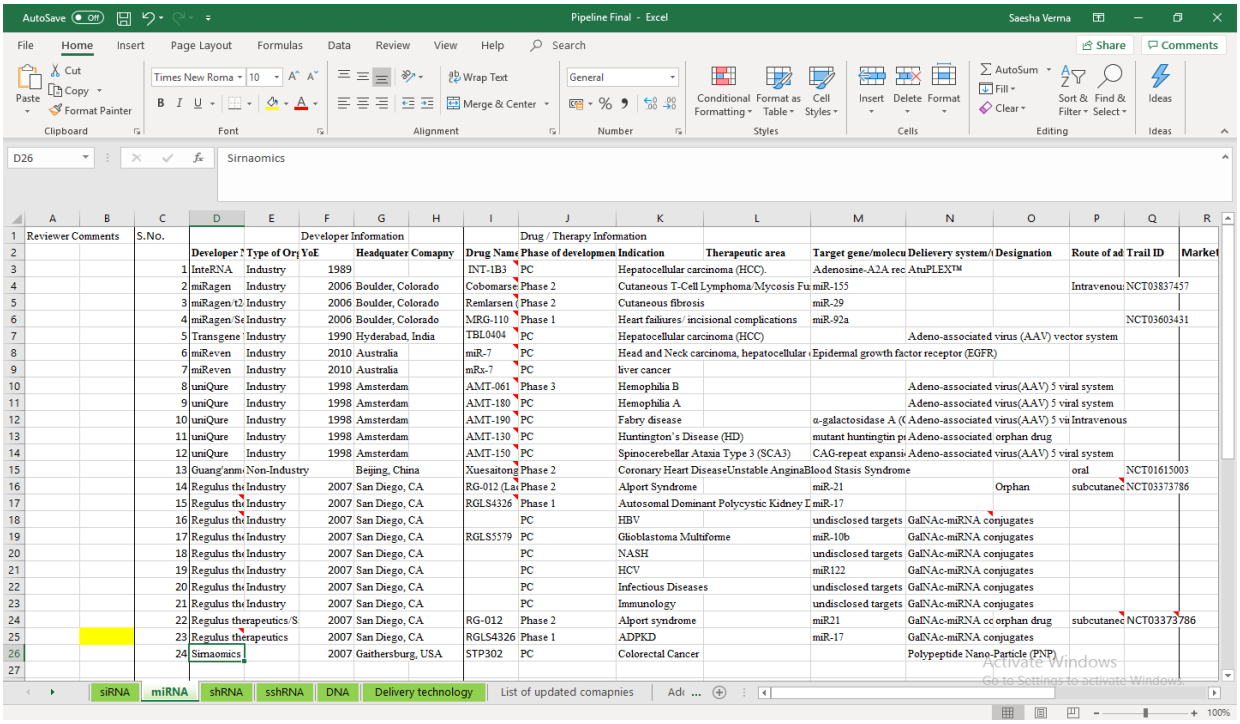
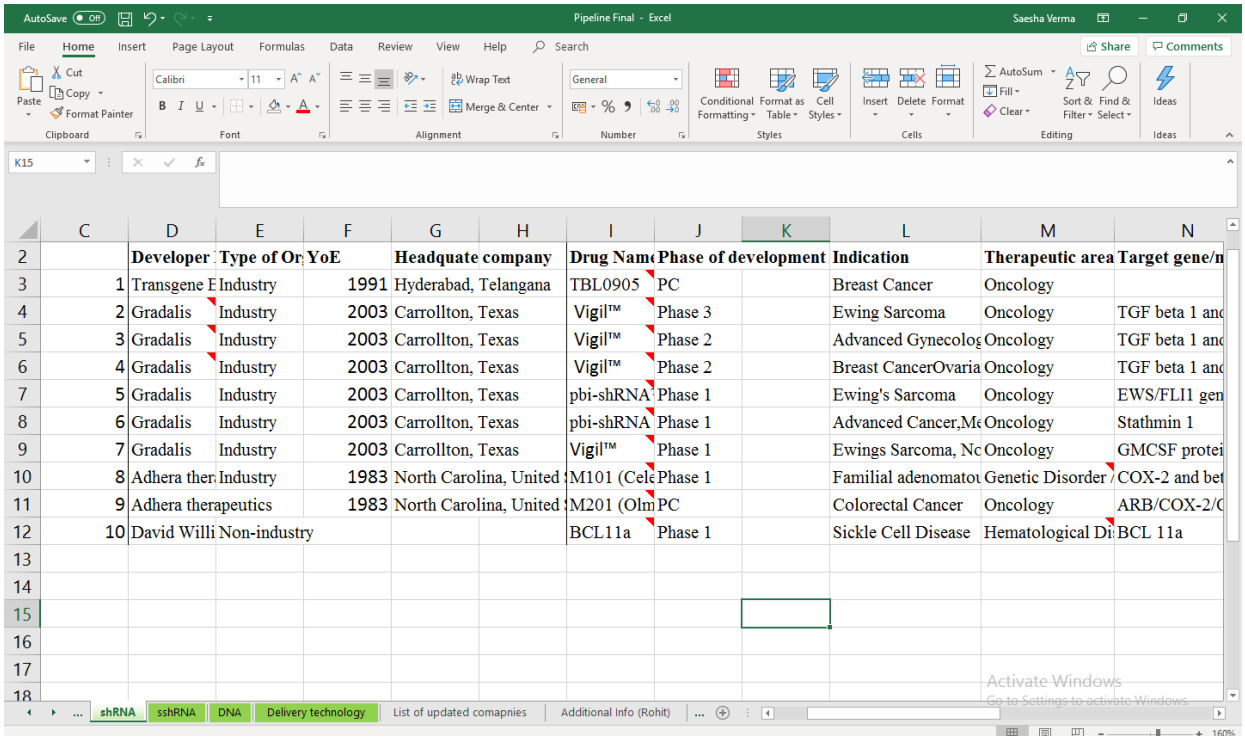


Figure 3.1 Represents the pipeline of siRNA molecules



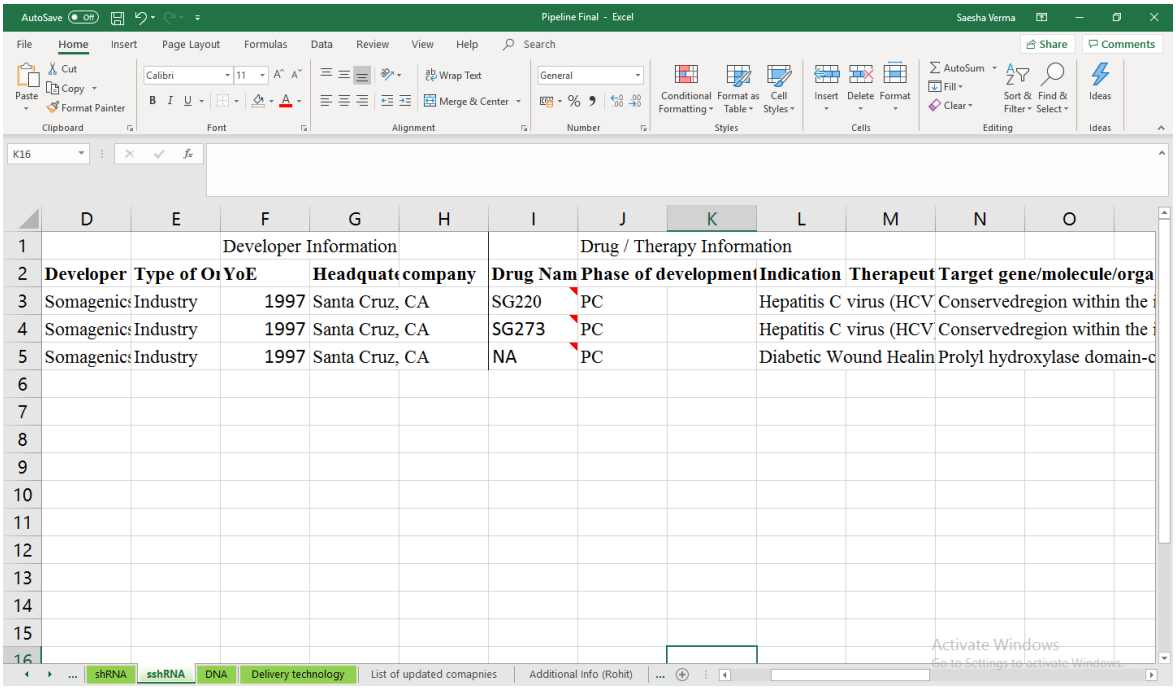
Reviewer Comments	S.No.	Developer Information				Drug / Therapy Information								
		Developer	Type of Org	YoE	Headquater	Company	Drug Name	Phase of development	Indication	Therapeutic area	Target gene/molecu	Delivery system/	Designation	Route of ad	Trail ID	Market
	1	InteRNA	Industry	1989			INT-1B3	PC	Hepatocellular carcinoma (HCC).		Adenosine-A2A rec	AtuPLEX™				
	2	miRagen	Industry	2006	Boulder, Colorado		Cobomarse	Phase 2	Cutaneous T-Cell Lymphoma/Mycosis Fu		miR-155			Intravenou	NCT03837457	
	3	miRagen/t2	Industry	2006	Boulder, Colorado		Remlarsen	Phase 2	Cutaneous fibrosis		miR-29					
	4	miRagen/Se	Industry	2006	Boulder, Colorado		MRG-110	Phase 1	Heart failiures/ incisional complications		miR-92a				NCT03603431	
	5	Transgene	Industry	1990	Hyderabad, India		TBL0404	PC	Hepatocellular carcinoma (HCC)			Adeno-associated virus (AAV) vector system				
	6	miReven	Industry	2010	Australia		miR-7	PC	Head and Neck carcinoma, hepatocellular		Epidermal growth factor receptor (EGFR)					
	7	miReven	Industry	2010	Australia		mRx-7	PC	liver cancer							
	8	uniQure	Industry	1998	Amsterdam		AMT-061	Phase 3	Hemophilia B			Adeno-associated virus(AAV) 5 viral system				
	9	uniQure	Industry	1998	Amsterdam		AMT-180	PC	Hemophilia A			Adeno-associated virus(AAV) 5 viral system				
	10	uniQure	Industry	1998	Amsterdam		AMT-190	PC	Fabry disease		α-galactosidase A ((	Adeno-associated virus(AAV) 5 vi		Intravenous		
	11	uniQure	Industry	1998	Amsterdam		AMT-130	PC	Huntington's Disease (HD)		mutant huntingtin pi	Adeno-associated	orphan drug			
	12	uniQure	Industry	1998	Amsterdam		AMT-150	PC	Spinocerebellar Ataxia Type 3 (SCA3)		CAG-repeat expansi	Adeno-associated virus(AAV) 5 viral system				
	13	Guang'anm	Non-Industry		Beijing, China		Xuesaitong	Phase 2	Coronary Heart DiseaseUnstable Angina	Blood Stasis Syndrome				oral	NCT01615003	
	14	Regulus the	Industry	2007	San Diego, CA		RG-012 (La	Phase 2	Alport Syndrome		miR-21		Orphan	subcutanec	NCT03373786	
	15	Regulus the	Industry	2007	San Diego, CA		RGLS4326	Phase 1	Autosomal Dominant Polycystic Kidney D		miR-17					
	16	Regulus the	Industry	2007	San Diego, CA			PC	HBV		undisclosed targets	GalNAc-miRNA conjugates				
	17	Regulus the	Industry	2007	San Diego, CA		RGLS5579	PC	Glioblastoma Multiforme		miR-10b	GalNAc-miRNA conjugates				
	18	Regulus the	Industry	2007	San Diego, CA			PC	NASH		undisclosed targets	GalNAc-miRNA conjugates				
	19	Regulus the	Industry	2007	San Diego, CA			PC	HCV		miR122	GalNAc-miRNA conjugates				
	20	Regulus the	Industry	2007	San Diego, CA			PC	Infectious Diseases		undisclosed targets	GalNAc-miRNA conjugates				
	21	Regulus the	Industry	2007	San Diego, CA			PC	Immunology		undisclosed targets	GalNAc-miRNA conjugates				
	22	Regulus therapeutics/S		2007	San Diego, CA		RG-012	Phase 2	Alport syndrome		miR21	GalNAc-miRNA cc	orphan drug	subcutanec	NCT03373786	
	23	Regulus therapeutics		2007	San Diego, CA		RGLS4326	Phase 1	ADPKD		miR-17	GalNAc-miRNA conjugates				
	24	Simaomics		2007	Gaithersburg, USA		STP302	PC	Colorectal Cancer			Polypeptide Nano-Particle (PNP)				

Figure 3.2 Represents the pipeline of miRNA molecules



	Developer	Type of Or	YoE	Headquate	company	Drug Nam	Phase of development	Indication	Therapeutic area	Target gene/n
1	Transgene E	Industry	1991	Hyderabad, Telangana		TBL0905	PC	Breast Cancer	Oncology	
2	Gradalis	Industry	2003	Carrollton, Texas		Vigil™	Phase 3	Ewing Sarcoma	Oncology	TGF beta 1 and
3	Gradalis	Industry	2003	Carrollton, Texas		Vigil™	Phase 2	Advanced Gynecolog	Oncology	TGF beta 1 and
4	Gradalis	Industry	2003	Carrollton, Texas		Vigil™	Phase 2	Breast CancerOvaria	Oncology	TGF beta 1 and
5	Gradalis	Industry	2003	Carrollton, Texas		pbi-shRNA	Phase 1	Ewing's Sarcoma	Oncology	EWS/FLI1 gen
6	Gradalis	Industry	2003	Carrollton, Texas		pbi-shRNA	Phase 1	Advanced Cancer,Me	Oncology	Stathmin 1
7	Gradalis	Industry	2003	Carrollton, Texas		Vigil™	Phase 1	Ewings Sarcoma, Nc	Oncology	GMCSF protei
8	Adhera ther	Industry	1983	North Carolina, United		M101 (Cele	Phase 1	Familial adenomatou	Genetic Disorder	COX-2 and bet
9	Adhera therapeutics		1983	North Carolina, United		M201 (Olm	PC	Colorectal Cancer	Oncology	ARB/COX-2/C
10	David Willi	Non-industry				BCL11a	Phase 1	Sickle Cell Disease	Hematological Di	BCL 11a

Figure 3.3 Represents the pipeline of shRNA molecules



	D	E	F	G	H	I	J	K	L	M	N	O
1			Developer Information				Drug / Therapy Information					
2	**Developer**	**Type of Or**	**YoE**	**Headquate**	**company**	**Drug Nam**	**Phase of development**		**Indication**	**Therapeut**	**Target gene/molecule/orga**	
3	Somagenics	Industry	1997	Santa Cruz, CA		SG220	PC		Hepatitis C virus (HCV		Conservedregion within the i	
4	Somagenics	Industry	1997	Santa Cruz, CA		SG273	PC		Hepatitis C virus (HCV		Conservedregion within the i	
5	Somagenics	Industry	1997	Santa Cruz, CA		NA	PC		Diabetic Wound Healin		Prolyl hydroxylase domain-c	

Figure 3.4 Represents the pipeline of sshRNA molecules

For building a pipeline, several parameters were selectedwith 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

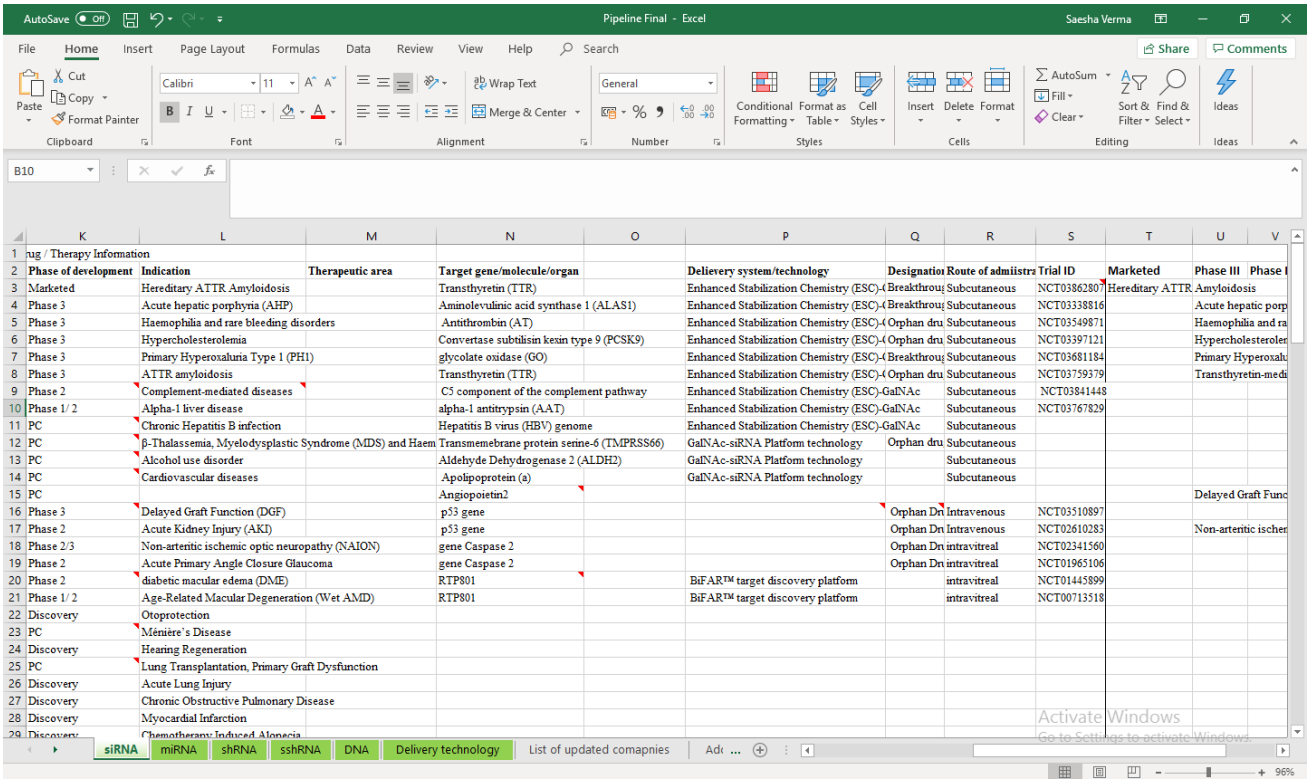


Figure 3.5 Provides information on the various parameters captured in the pipeline

CHAPTER 4

TECHNOLOGY PLATFORM AND DELIVERY SYSTEM

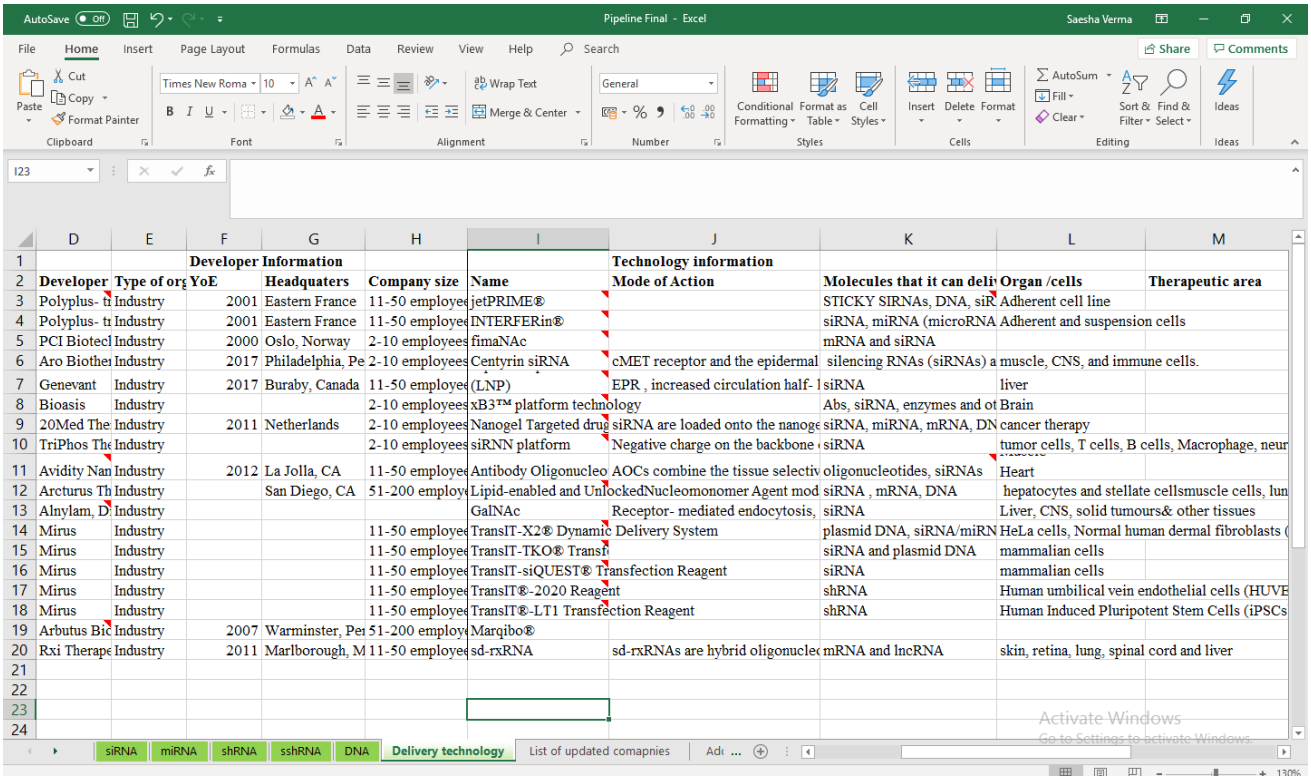
4.1Chapter Overview

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.



	Developer Information					Technology information			
Developer	Type of org	YoE	Headquaters	Company size	Name	Mode of Action	Molecules that it can deli	Organ /cells	Therapeutic area
Polyplus- tr	Industry	2001	Eastern France	11-50 employee	jetPRIME®		STICKY SIRNAs, DNA, siR	Adherent cell line	
Polyplus- tr	Industry	2001	Eastern France	11-50 employee	INTERFERin®		siRNA, miRNA (microRNA	Adherent and suspension cells	
PCI Biotecl	Industry	2000	Oslo, Norway	2-10 employees	fimaNAc		mRNA and siRNA		
Aro Biother	Industry	2017	Philadelphia, Pe	2-10 employees	Centyrin siRNA	cMET receptor and the epidermal	silencing RNAs (siRNAs) a	muscle, CNS, and immune cells.	
Genevant	Industry	2017	Buraby, Canada	11-50 employee	(LNP)	EPR , increased circulation half- l	siRNA	liver	
Bioasis	Industry			2-10 employees	xB3™ platform technology		Abs, siRNA, enzymes and ot	Brain	
20Med The	Industry	2011	Netherlands	2-10 employees	Nanogel Targeted drug	siRNA are loaded onto the nanoge	siRNA, miRNA, mRNA, DN	cancer therapy	
TriPhos The	Industry			2-10 employees	siRNN platform	Negative charge on the backbone	siRNA	tumor cells, T cells, B cells, Macrophage, neur	
Avidity Nan	Industry	2012	La Jolla, CA	11-50 employee	Antibody Oligonucleo	AOCs combine the tissue selectiv	oligonucleotides, siRNAs	Heart	
Arcturus Th	Industry		San Diego, CA	51-200 employ	Lipid-enabled and Unlocked	Nucleomonomer Agent mod	siRNA , mRNA, DNA	hepatocytes and stellate cellsmuscle cells, lun	
Alnylam, D	Industry				GalNAc	Receptor- mediated endocytosis,	siRNA	Liver, CNS, solid tumours& other tissues	
Mirus	Industry			11-50 employee	TransIT-X2® Dynamic	Delivery System	plasmid DNA, siRNA/miRN	HeLa cells, Normal human dermal fibroblasts (	
Mirus	Industry			11-50 employee	TransIT-TKO® Transf		siRNA and plasmid DNA	mammalian cells	
Mirus	Industry			11-50 employee	TransIT-siQUEST® Transfection Reagent		siRNA	mammalian cells	
Mirus	Industry			11-50 employee	TransIT®-2020 Reagent		shRNA	Human umbilical vein endothelial cells (HUVE	
Mirus	Industry			11-50 employee	TransIT®-LT1 Transfection Reagent		shRNA	Human Induced Pluripotent Stem Cells (iPSCs	
Arbutus Bic	Industry	2007	Warminster, Pe	51-200 employ	Marqibo®				
Rxi Therape	Industry	2011	Marlborough, M	11-50 employee	sd-rxRNA	sd-rxRNAs are hybrid oligonucle	mRNA and lncRNA	skin, retina, lung, spinal cord and liver	

Figure 4.1 Represents 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.

CHAPTER 5

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

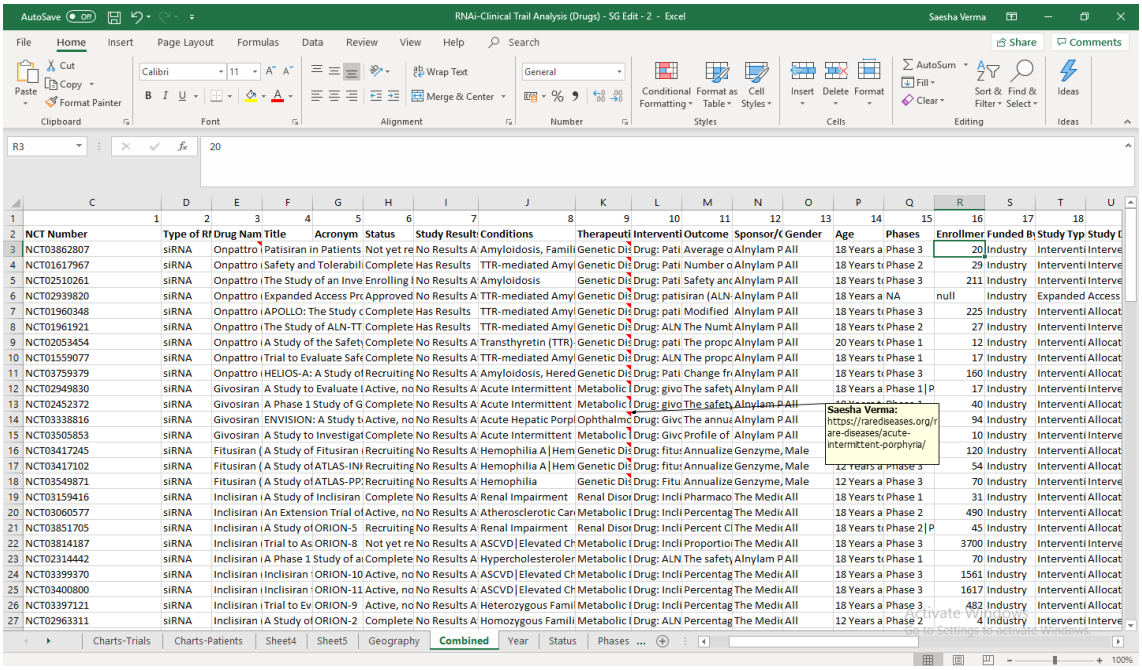
The chapter provides an elaborative analysis of clinical trials of the molecules enlisted in the pipeline above. There are more than 100 molecules currently in trials and we have done the analysis of these trials depending on various parameters.

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.



NCT Number	Type of Rf	Drug Nam	Title	Acronym	Status	Study Result	Conditions	Therapeuti	Interventi	Outcome	Sponsor/C	Gender	Age	Phases	Enrollmer	Funded By	Study Typ	Study D
NCT03862807	siRNA	Onpattro	Patisiran in Patients		Not yet re	No Results A	Amyloidosis, Famili	Genetic Dis	Drug: Pati	Average o	Alnylam P	All	18 Years a	Phase 3	20	Industry	Interventi	Interve
NCT01617967	siRNA	Onpattro	Safety and Tolerabil		Complete	Has Results	TTR-mediated Amy	Genetic Dis	Drug: Pati	Number o	Alnylam P	All	18 Years t	Phase 2	29	Industry	Interventi	Interve
NCT02510261	siRNA	Onpattro	The Study of an Inve		Enrolling I	No Results A	Amyloidosis	Genetic Dis	Drug: Pati	Safety anc	Alnylam P	All	18 Years t	Phase 3	211	Industry	Interventi	Interve
NCT02939820	siRNA	Onpattro	Expanded Access Pro		Approved	No Results A	TTR-mediated Amy	Genetic Dis	Drug: patisiran (ALN		Alnylam P	All	18 Years a	NA	null	Industry	Expanded Access	
NCT01960348	siRNA	Onpattro	APOLLO: The Study c		Complete	Has Results	TTR-mediated Amy	Genetic Dis	Drug: pati	Modified	Alnylam P	All	18 Years t	Phase 3	225	Industry	Interventi	Allocat
NCT01961921	siRNA	Onpattro	The Study of ALN-TT		Complete	Has Results	TTR-mediated Amy	Genetic Dis	Drug: ALN	The Numb	Alnylam P	All	18 Years t	Phase 2	27	Industry	Interventi	Interve
NCT02053454	siRNA	Onpattro	A Study of the Safety		Complete	No Results A	Transthyretin (TTR)	Genetic Dis	Drug: pati	The propc	Alnylam P	All	20 Years t	Phase 1	12	Industry	Interventi	Allocat
NCT01559077	siRNA	Onpattro	Trial to Evaluate Safe		Complete	No Results A	TTR-mediated Amy	Genetic Dis	Drug: ALN	The propc	Alnylam P	All	18 Years t	Phase 1	17	Industry	Interventi	Allocat
NCT03759379	siRNA	Onpattro	HELIOS-A: A Study of		Recruiting	No Results A	Amyloidosis, Hered	Genetic Dis	Drug: Pati	Change fr	Alnylam P	All	18 Years t	Phase 3	160	Industry	Interventi	Allocat
NCT02949830	siRNA	Givosiran	A Study to Evaluate I		Active, no	No Results A	Acute Intermittent	Metabolic	Drug: givo	The safety	Alnylam P	All	18 Years a	Phase 1| P	17	Industry	Interventi	Interve
NCT02452372	siRNA	Givosiran	A Phase 1 Study of G		Complete	No Results A	Acute Intermittent	Metabolic	Drug: givo	The safety	Alnylam P	All			40	Industry	Interventi	Allocat
NCT03338816	siRNA	Givosiran	ENVISION: A Study t		Active, no	No Results A	Acute Hepatic Porp	Ophthalmc	Drug: Givc	The annua	Alnylam P	All			94	Industry	Interventi	Allocat
NCT03505853	siRNA	Givosiran	A Study to Investigat		Complete	No Results A	Acute Intermittent	Metabolic	Drug: Givc	Profile of	Alnylam P	All			10	Industry	Interventi	Interve
NCT03417245	siRNA	Fitusiran	A Study of Fitusiran		Recruiting	No Results A	Hemophilia A| Hem	Genetic Dis	Drug: fitus	Annualize	Genzyme,	Male			120	Industry	Interventi	Allocat
NCT03417102	siRNA	Fitusiran	A Study of ATLAS-INH		Recruiting	No Results A	Hemophilia A| Hem	Genetic Dis	Drug: fitus	Annualize	Genzyme,	Male			54	Industry	Interventi	Allocat
NCT03549871	siRNA	Fitusiran	A Study of ATLAS-PP		Recruiting	No Results A	Hemophilia	Genetic Dis	Drug: Fitu	Annualize	Genzyme,	Male	12 Years a	Phase 3	70	Industry	Interventi	Interve
NCT03159416	siRNA	Inclisiran	A Study of Inclisiran		Complete	No Results A	Renal Impairment	Renal Disor	Drug: Incli	Pharmaco	The Medic	All	18 Years t	Phase 1	31	Industry	Interventi	Allocat
NCT03060577	siRNA	Inclisiran	An Extension Trial of		Active, no	No Results A	Atherosclerotic Car	Metabolic	Drug: Incli	Percentag	The Medic	All	18 Years a	Phase 2	490	Industry	Interventi	Allocat
NCT03851705	siRNA	Inclisiran	A Study of ORION-5		Recruiting	No Results A	Renal Impairment	Renal Disor	Drug: Incli	Percent Cl	The Medic	All	18 Years t	Phase 2| P	45	Industry	Interventi	Allocat
NCT03814187	siRNA	Inclisiran	Trial to Ass ORION-8		Not yet re	No Results A	ASCVD| Elevated Ch	Metabolic	Drug: Incli	Proportio	The Medic	All	18 Years a	Phase 3	3700	Industry	Interventi	Interve
NCT02314442	siRNA	Inclisiran	A Phase 1 Study of a		Complete	No Results A	Hypercholesterolen	Metabolic	Drug: ALN	The safety	Alnylam P	All	18 Years t	Phase 1	70	Industry	Interventi	Allocat
NCT03399370	siRNA	Inclisiran	Inclisiran	ORION-10	Active, no	No Results A	ASCVD| Elevated Ch	Metabolic	Drug: Incli	Percentag	The Medic	All	18 Years a	Phase 3	1561	Industry	Interventi	Allocat
NCT03400800	siRNA	Inclisiran	Inclisiran	ORION-11	Active, no	No Results A	ASCVD| Elevated Ch	Metabolic	Drug: Incli	Percentag	The Medic	All	18 Years a	Phase 3	1617	Industry	Interventi	Allocat
NCT03397121	siRNA	Inclisiran	Trial to Ev ORION-9		Active, no	No Results A	Heterozygous Famil	Metabolic	Drug: Incli	Percentag	The Medic	All	18 Years a	Phase 3	482	Industry	Interventi	Allocat
NCT02963311	siRNA	Inclisiran	A Study of ORION-2		Complete	No Results A	Homozygous Famili	Metabolic	Drug: ALN	Percentag	The Medic	All	12 Years a	Phase 2	4	Industry	Interventi	Interve

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

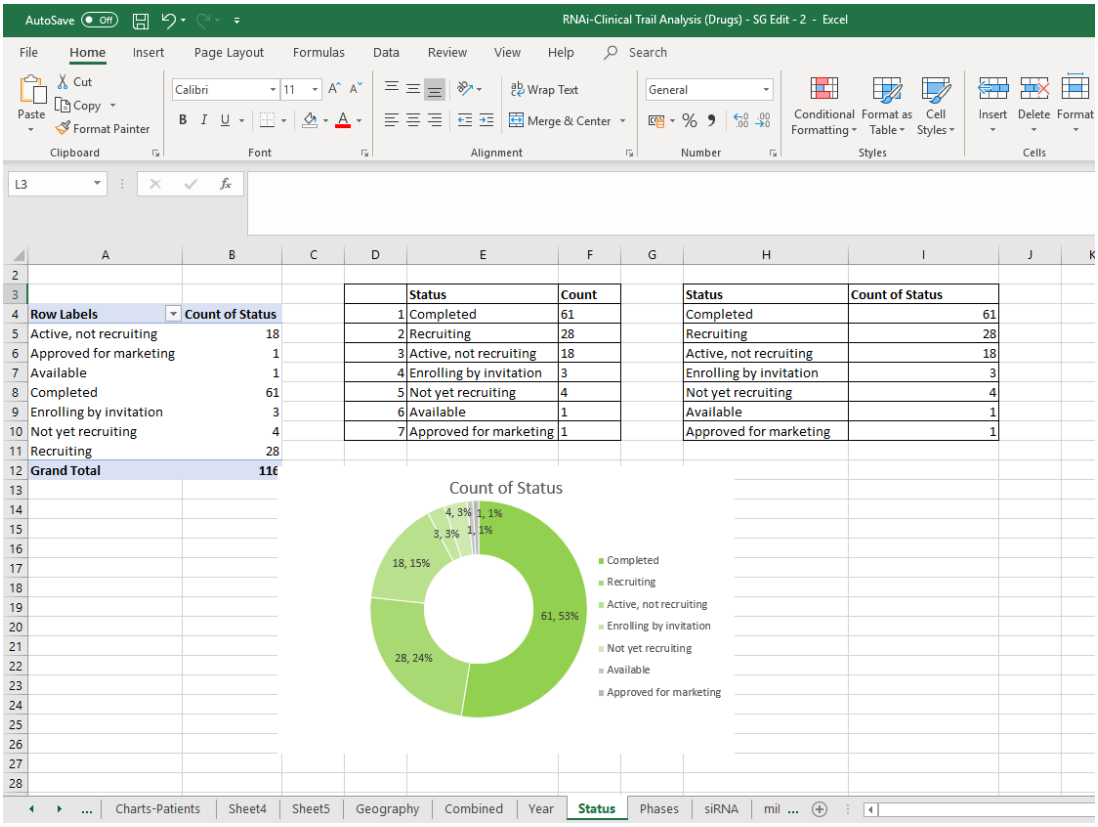
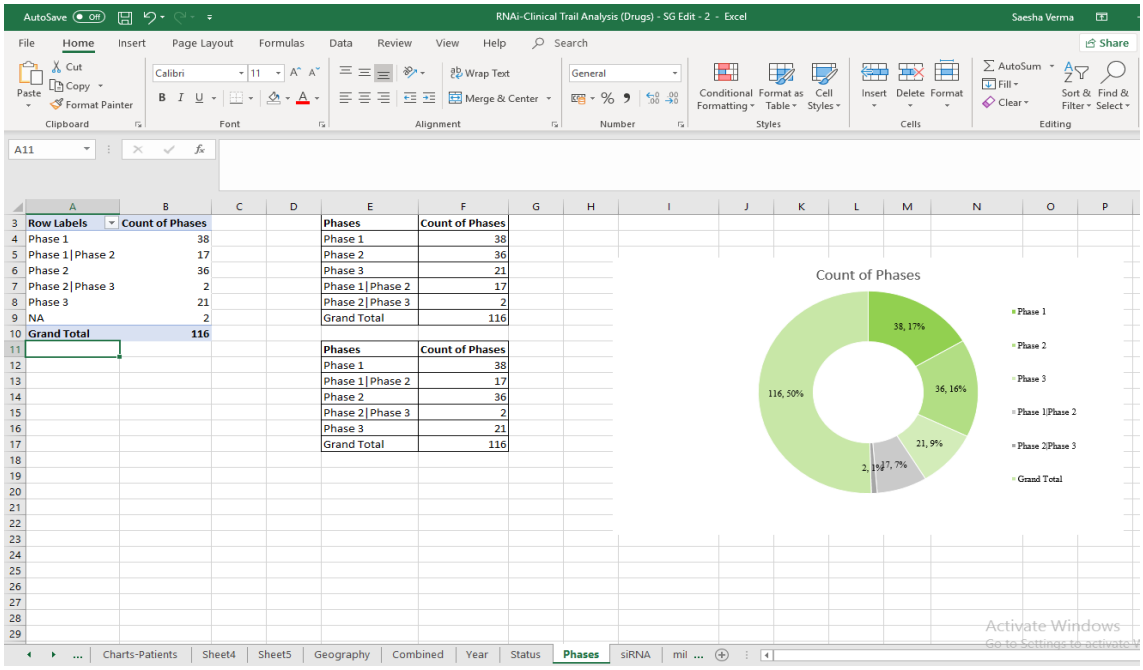


Figure 5.2 Represents Analysis by trial status

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

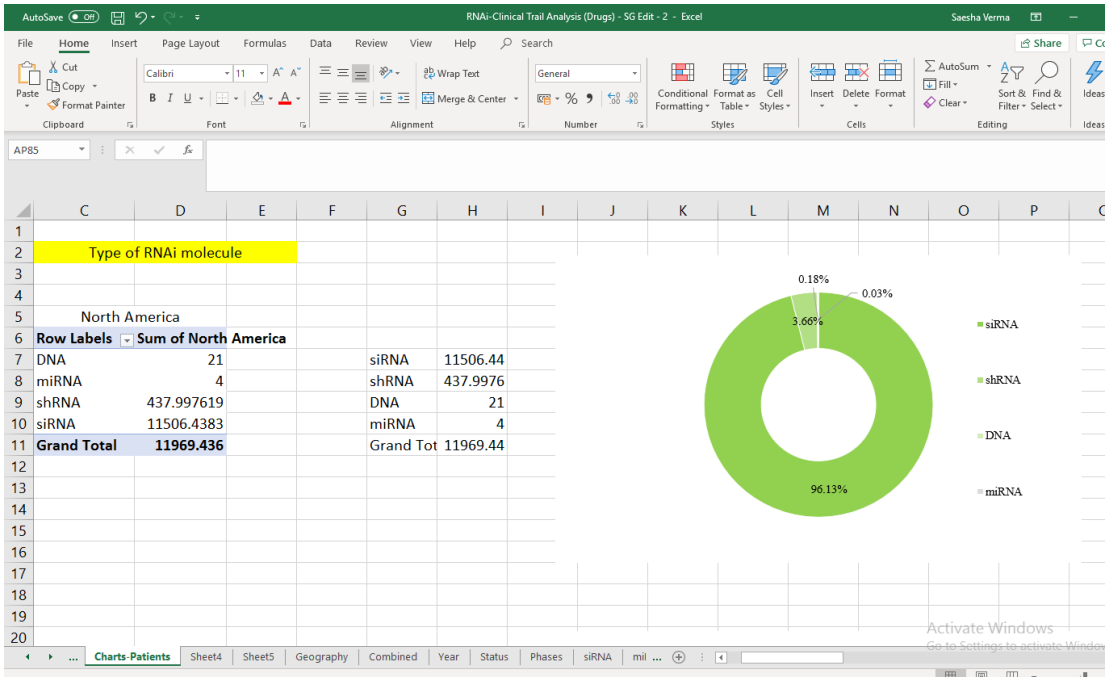


Row Labels	Count of Phases
Phase 1	38
Phase 1|Phase 2	17
Phase 2	36
Phase 2|Phase 3	2
Phase 3	21
NA	2
Grand Total	116

Phases	Count of Phases
Phase 1	38
Phase 1|Phase 2	17
Phase 2	36
Phase 2|Phase 3	2
Phase 3	21
Grand Total	116

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.



Row Labels	Sum of North America
DNA	21
miRNA	4
shRNA	437.997619
siRNA	11506.4383
Grand Total	11969.436

siRNA	11506.44
shRNA	437.9976
DNA	21
miRNA	4
Grand Tot	11969.44

Figure 5.4 Represents 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.

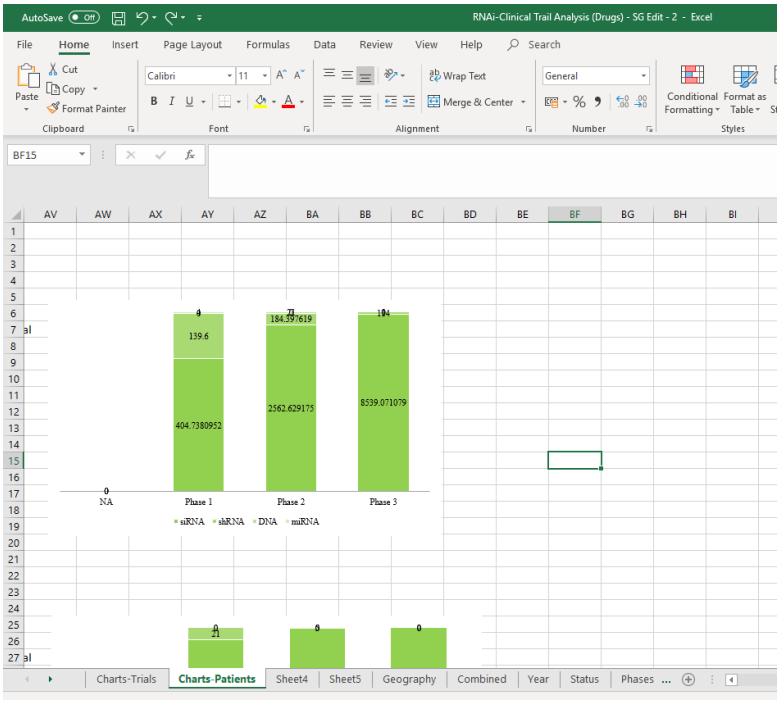


Figure 5.5 Represents analysis by type of RNAi modality and phase of development in North America

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.

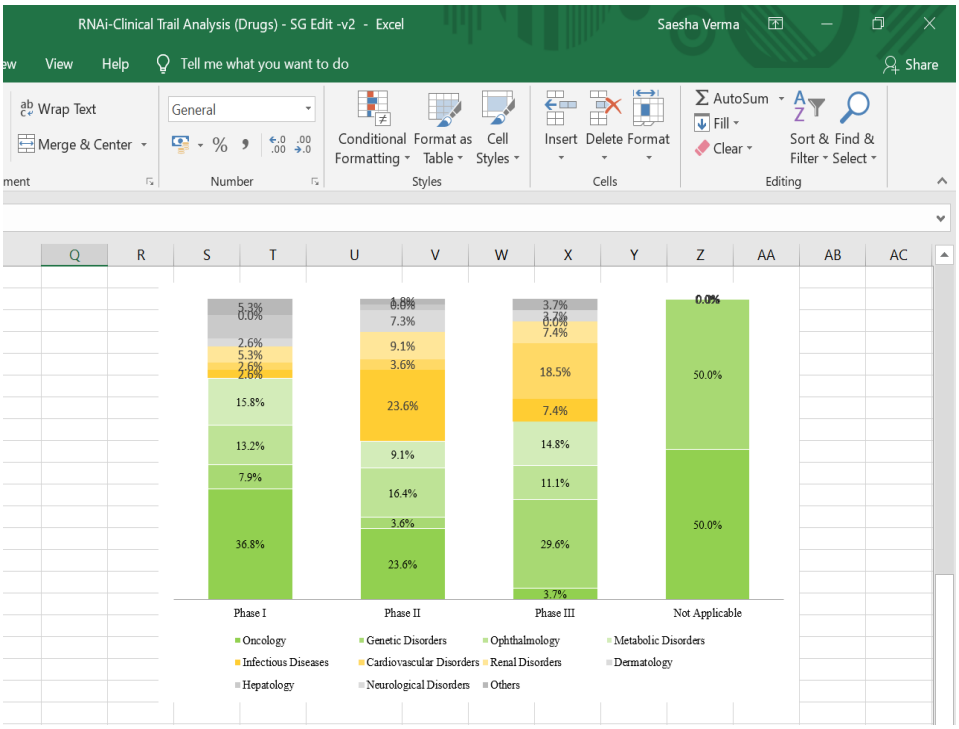


Figure 5.6 Represents analysis by type of indication and phase of development in North America

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.

CHAPTER 6

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.

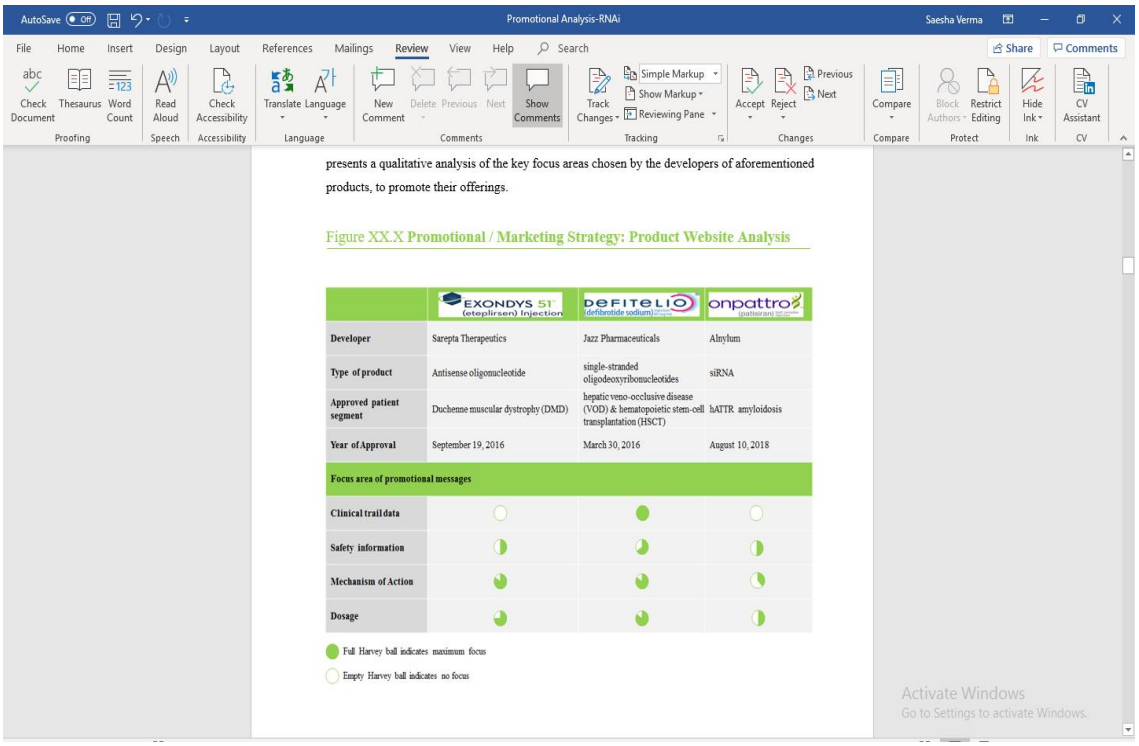


Figure 6.1 Represents the overview of promotional anlysis using harvey ball

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

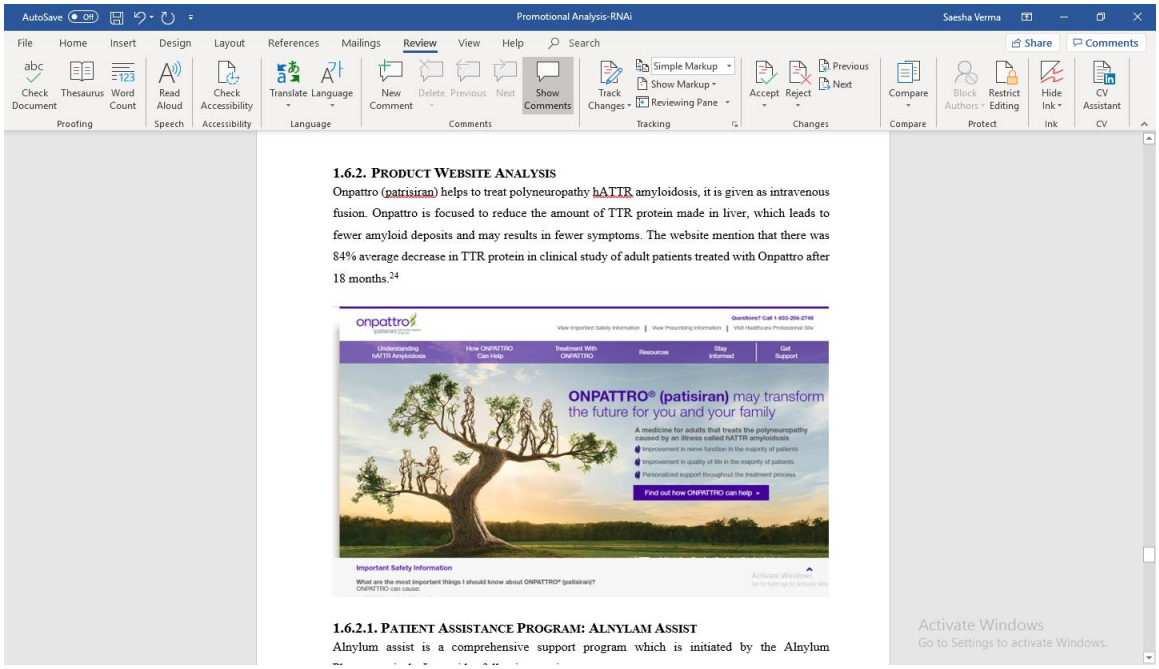


Figure 6.2 Represents the product website analysis

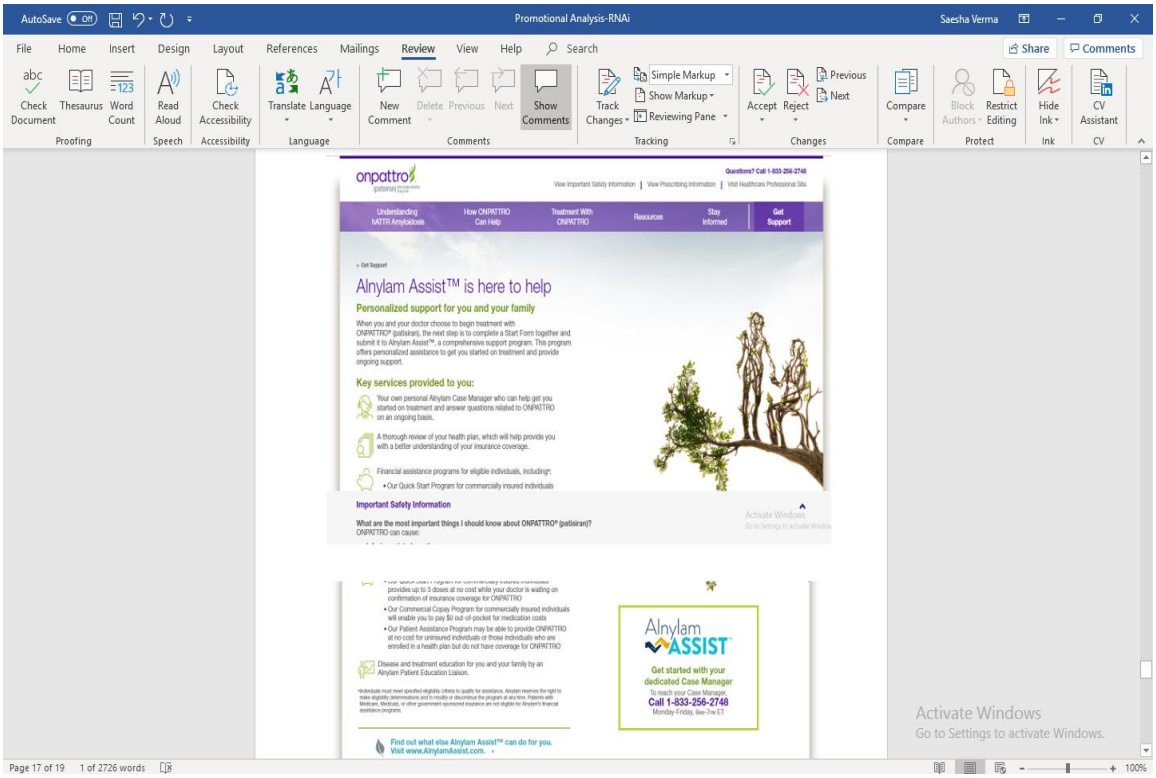


Figure 6.3 Represents the patient assistance program: AlnylumAssist

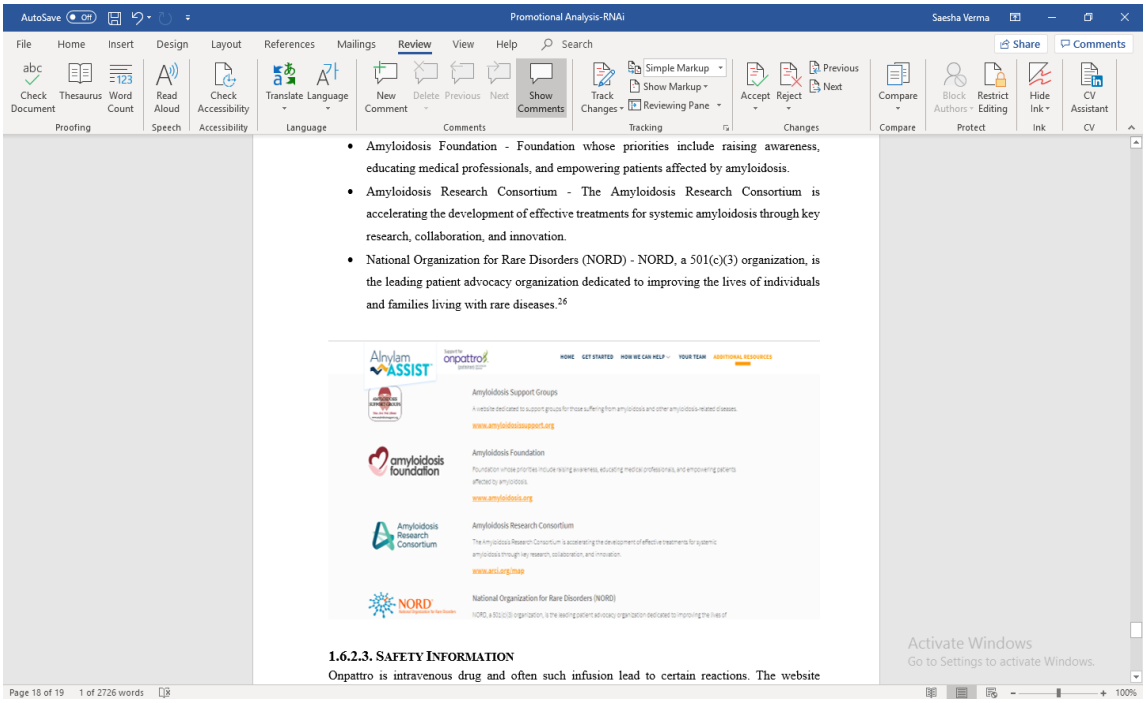


Figure 6.4 Represents the other reimbursement programs

CHAPTER 7

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.

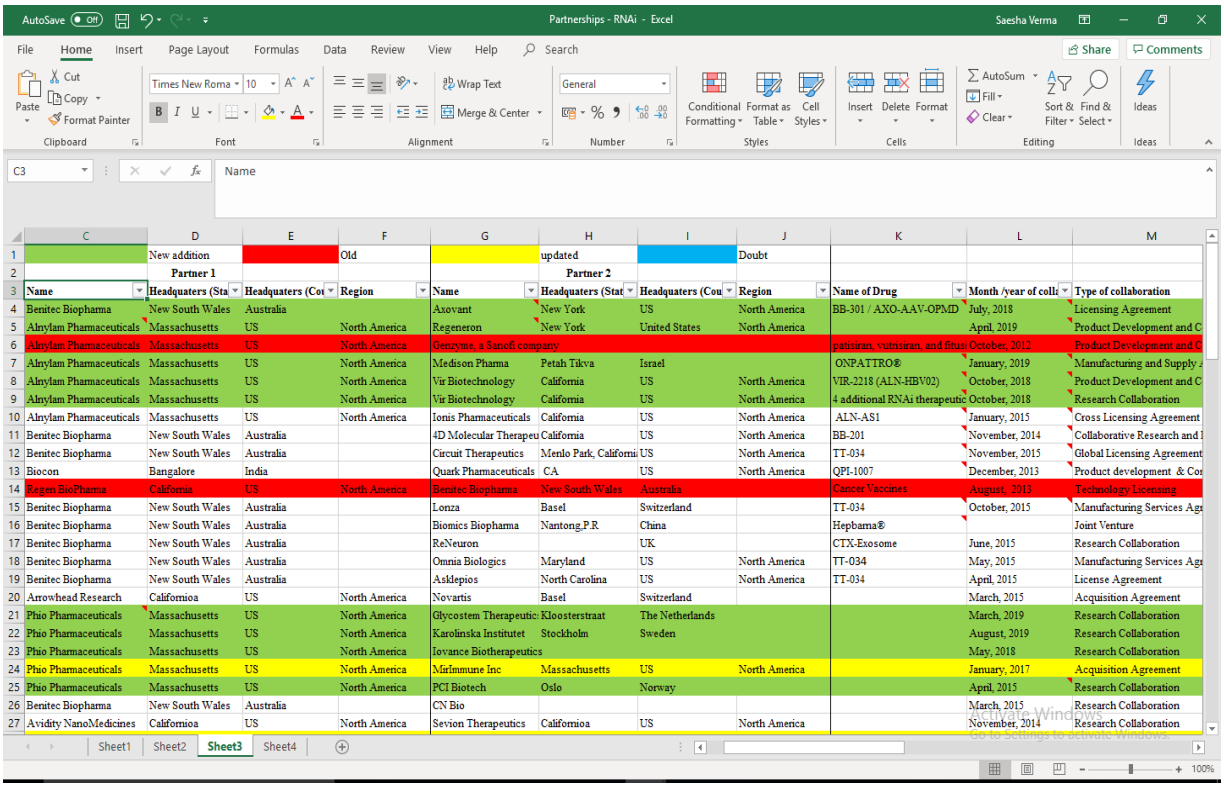
- **Acquisition:** when one company acquires all of the shares and assets of another company.
- **Merger:** when two companies combine their business operation and merge into single entity
- **Clinical Trail Agreement:** These are the agreements which occur to perform clinical related to a product candidate 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 non-exclusive 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.



	C	D	E	F	G	H	I	J	K	L	M
1		New addition		Old		updated		Doubt			
2		Partner 1				Partner 2					
3	Name	Headquaters (Sta	Headquaters (Co	Region	Name	Headquaters (Stat	Headquaters (Cou	Region	Name of Drug	Month /year of colla	Type of collaboration
4	Benitec Biopharma	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 company				patisiran, vutrisiran, and fitus	October, 2012	Product Development and C
7	Alnylam Pharmaceuticals	Massachusetts	US	North America	Medison Pharma	Petah Tikva	Israel		ONPATTRO®	January, 2019	Manufacturing and Supply
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 therapeutic	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 Biopharma	New South Wales	Australia		4D Molecular Therapeu	California	US	North America	BB-201	November, 2014	Collaborative Research and I
12	Benitec Biopharma	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 & Co
14	Regen BioPharma	California	US	North America	Benitec Biopharma	New South Wales	Australia		Cancer Vaccines	August, 2013	Technology Licensing
15	Benitec Biopharma	New South Wales	Australia		Lonza	Basel	Switzerland		TT-034	October, 2015	Manufacturing Services Agr
16	Benitec Biopharma	New South Wales	Australia		Biomics Biopharma	Nantong,P.R	China		Hepbarna®		Joint Venture
17	Benitec Biopharma	New South Wales	Australia		ReNeuron		UK		CTX-Exosome	June, 2015	Research Collaboration
18	Benitec Biopharma	New South Wales	Australia		Omnia Biologics	Maryland	US	North America	TT-034	May, 2015	Manufacturing Services Agr
19	Benitec Biopharma	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 Biotherapeutics					May, 2018	Research Collaboration
24	Phio Pharmaceuticals	Massachusetts	US	North America	MiriImmune 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

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

CHAPTER 8

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.

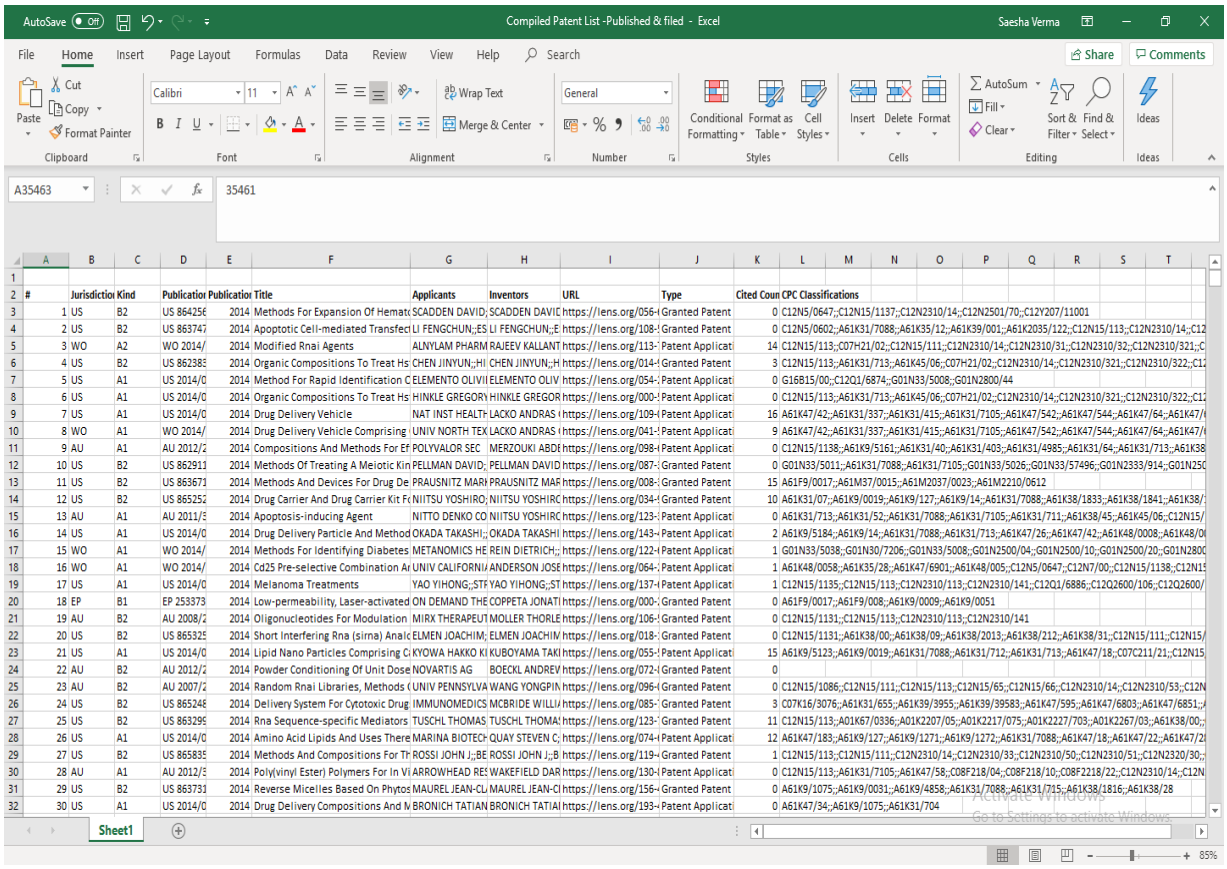


Figure 8.1 Represents the list of patent both filed / published

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.

CHAPTER 9

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

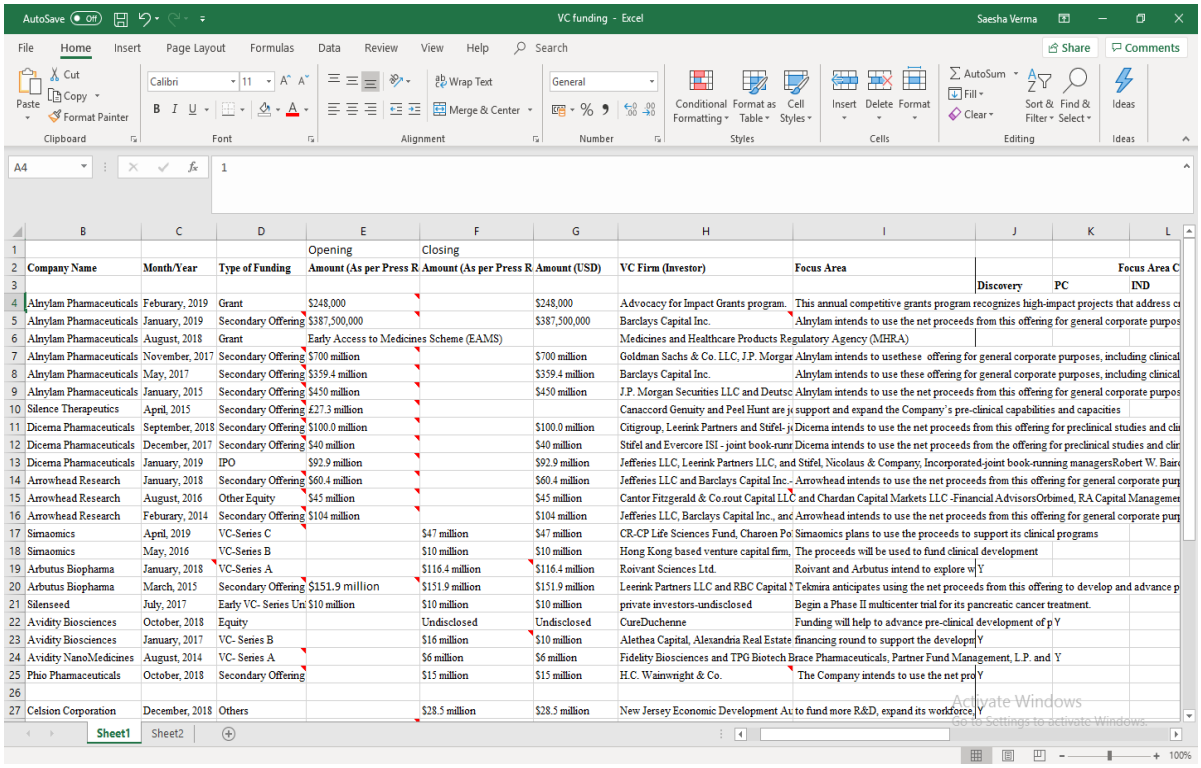
denoted as Series A, Series B, Series C, Series D, Series E and so on. Series A funding is provided immediately after seed funding.

- **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 raisedthroughall 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.



	B	C	D	E	F	G	H	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 recognizes high-impact projects that address cr			
5	Alnylam Pharmaceuticals	January, 2019	Secondary Offering	$387,500,000		$387,500,000	Barclays Capital Inc.	Alnylam intends to use the net proceeds from this offering for general corporate purpos			
6	Alnylam Pharmaceuticals	August, 2018	Grant	Early Access to Medicines Scheme (EAMS)			Medicines and Healthcare Products Regulatory Agency (MHRA)				
7	Alnylam Pharmaceuticals	November, 2017	Secondary Offering	$700 million		$700 million	Goldman Sachs & Co. LLC, J.P. Morgar	Alnylam intends to usethese offering for general corporate purposes, including clinical			
8	Alnylam Pharmaceuticals	May, 2017	Secondary Offering	$359.4 million		$359.4 million	Barclays Capital Inc.	Alnylam intends to use these offering for general corporate purposes, 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 proceeds from this offering for general 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-clinical capabilities and capacities			
11	Dicerna Pharmaceuticals	September, 2018	Secondary Offering	$100.0 million		$100.0 million	Citigroup, Leerink Partners and Stifel- jo	Dicerna intends to use the net proceeds from this offering for preclinical studies and cli			
12	Dicerna Pharmaceuticals	December, 2017	Secondary Offering	$40 million		$40 million	Stifel and Evercore ISI - joint book-runn	Dicerna intends to use the net proceeds from the offering for preclinical studies and clir			
13	Dicerna Pharmaceuticals	January, 2019	IPO	$92.9 million		$92.9 million	Jefferies LLC, Leerink Partners LLC, and Stifel, Nicolaus & Company, Incorporated-joint book-running managersRobert W. Bair				
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 proceeds from this offering for general corporate purp			
15	Arrowhead Research	August, 2016	Other Equity	$45 million		$45 million	Cantor Fitzgerald & Co.rout Capital LLC	and Chardan Capital Markets LLC -Financial 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 proceeds from this offering for general 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 support its clinical programs			
18	Simaomics	May, 2016	VC-Series B		$10 million	$10 million	Hong Kong based venture capital firm,	The proceeds will be used to fund clinical development			
19	Arbutus Biopharma	January, 2018	VC-Series A		$116.4 million	$116.4 million	Roivant Sciences Ltd.	Roivant and Arbutus intend to explore w	Y		
20	Arbutus Biopharma	March, 2015	Secondary Offering	$151.9 million	$151.9 million	$151.9 million	Leerink Partners LLC and RBC Capital M	Tekmira anticipates using the net proceeds from this offering to develop and advance p			
21	Silenseed	July, 2017	Early VC- Series Un	$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-clinical 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 developn	Y		
24	Avidity NanoMedicines	August, 2014	VC- Series A		$6 million	$6 million	Fidelity Biosciences and TPG Biotech	Brace Pharmaceuticals, Partner Fund Management, 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 pro	Y		
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 workforce,	Y		

Figure 9.1 Represents 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)

CHAPTER 10

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

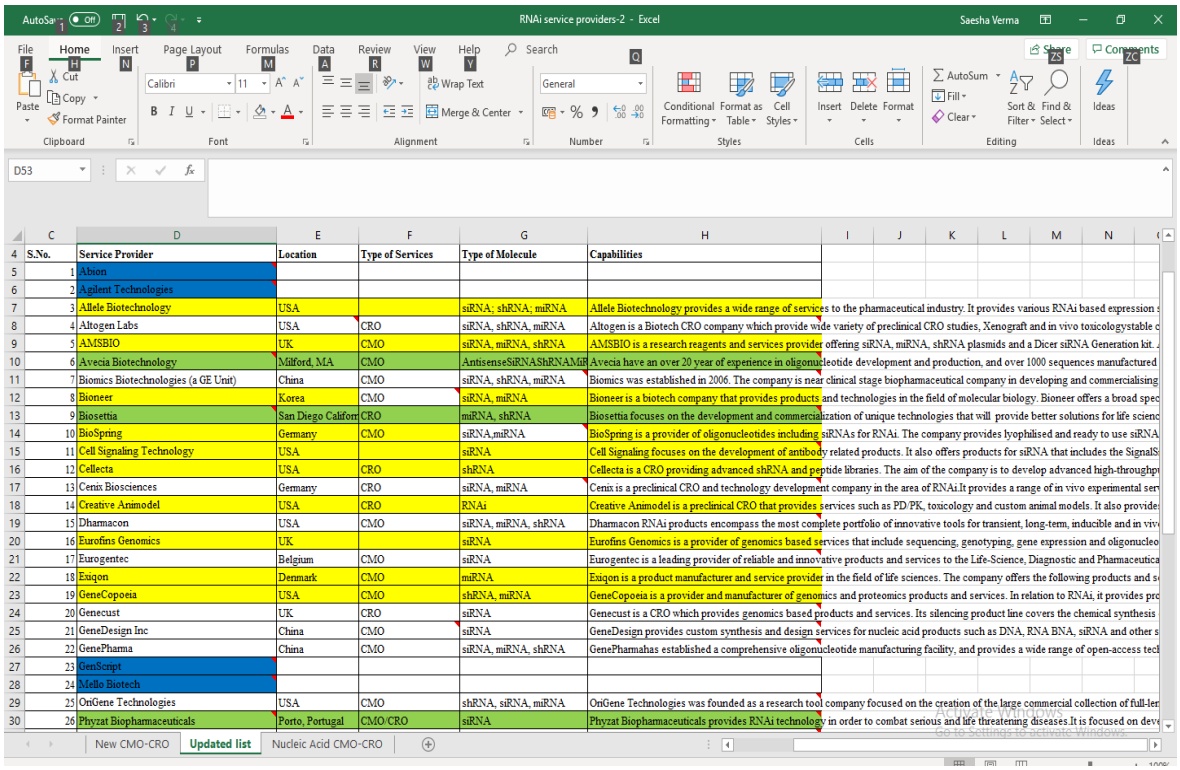
- **Contract Manufacturing Organisations (CMO):**A company that offers manufacturing services, with volume capabilities ranging from small amounts for preclinical R&D to larger volumes necessary for clinical trials purposes and commercialization.[14]
- **Contract Research Organisations (CRO):**A Contract 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.



S.No.	Service Provider	Location	Type of Services	Type of Molecule	Capabilities
1	Abion				
2	Agilent Technologies				
3	Allele Biotechnology	USA		siRNA; shRNA; miRNA	Allele Biotechnology provides a wide range of services to the pharmaceutical industry. It provides various RNAi based expression
4	Altogen Labs	USA	CRO	siRNA, shRNA, miRNA	Altogen is a Biotech CRO company which provide wide variety of preclinical CRO studies, Xenograft and in vivo toxicologystable c
5	AMSBIO	UK	CMO	siRNA, miRNA, shRNA	AMSBIO is a research reagents and services provider offering siRNA, miRNA, shRNA plasmids and a Dicer siRNA Generation kit.
6	Avecia Biotechnology	Milford, MA	CMO	AntisenseSiRNAShRNAMiR	Avecia have an over 20 year of experience in oligonucleotide development and production, and over 1000 sequences manufactured
7	Biomics Biotechnologies (a GE Unit)	China	CMO	siRNA, shRNA, miRNA	Biomics was established in 2006. The company is near clinical stage biopharmaceutical company in developing and commercialising
8	Bioneer	Korea	CMO	siRNA, miRNA	Bioneer is a biotech company that provides products and technologies in the field of molecular biology. Bioneer offers a broad spec
9	Biosettia	San Diego Californ	CRO	miRNA, shRNA	Biosettia focuses on the development and commercialization of unique technologies that will provide better solutions for life scienc
10	BioSpring	Germany	CMO	siRNA,miRNA	BioSpring is a provider of oligonucleotides including siRNAs for RNAi. The company provides lyophilised and ready to use siRNA
11	Cell Signaling Technology	USA		siRNA	Cell Signaling focuses on the development of antibody related products. It also offers products for siRNA that includes the SignalS
12	Cellecta	USA	CRO	shRNA	Cellecta is a CRO providing advanced shRNA and peptide libraries. The aim of the company is to develop advanced high-throughp
13	Cenix Biosciences	Germany	CRO	siRNA, miRNA	Cenix is a preclinical CRO and technology development company in the area of RNAi.It provides a range of in vivo experimental ser
14	Creative Animodel	USA	CRO	RNAi	Creative Animodel is a preclinical CRO that provides services such as PD/PK, toxicology and custom animal models. It also provide
15	Dharmacon	USA	CMO	siRNA, miRNA, shRNA	Dharmacon RNAi products encompass the most complete portfolio of innovative tools for transient, long-term, inducible and in viv
16	Eurofins Genomics	UK		siRNA	Eurofins Genomics is a provider of genomics based services that include sequencing, genotyping, gene expression and oligonucleo
17	Eurogentec	Belgium	CMO	siRNA	Eurogentec is a leading provider of reliable and innovative products and services to the Life-Science, Diagnostic and Pharmaceutica
18	Exiqon	Denmark	CMO	miRNA	Exiqon is a product manufacturer and service provider in the field of life sciences. The company offers the following products and s
19	GeneCopoeia	USA	CMO	shRNA, miRNA	GeneCopoeia is a provider and manufacturer of genomics and proteomics products and services. In relation to RNAi, it provides pro
20	Genecust	UK	CRO	siRNA	Genecust is a CRO which provides genomics based products and services. Its silencing product line covers the chemical synthesis
21	GeneDesign Inc	China	CMO	siRNA	GeneDesign provides custom synthesis and design services for nucleic acid products such as DNA, RNA BNA, siRNA and other s
22	GenePharma	China	CMO	siRNA, miRNA, shRNA	GenePharmahas established a comprehensive oligonucleotide manufacturing facility, and provides a wide range of open-access tech
23	GenScript				
24	Mello Biotech				
25	OriGene Technologies	USA	CMO	shRNA, siRNA, miRNA	OriGene Technologies was founded as a research tool company focused on the creation of the large commercial collection of full-len
26	Phyzat Biopharmaceuticals	Porto, Portugal	CMO/CRO	siRNA	Phyzat Biopharmaceuticals provides RNAi technology in order to combat serious and life threatening diseases.It is focused on deve

Figure 10.1 Represents 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.

CHAPTER 11

ADDITIONAL PROJECTS

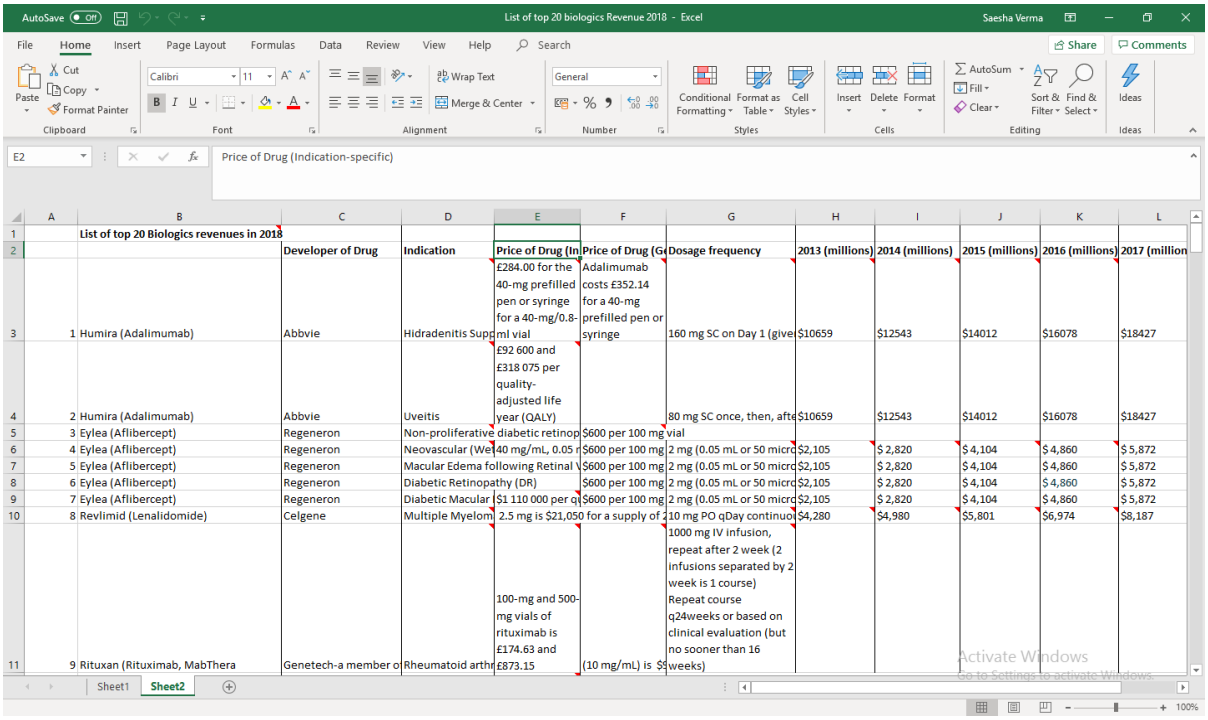
11.1Biopharma CMO

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



		List of top 20 Biologics revenues in 2018										
			Developer of Drug	Indication	Price of Drug (In	Price of Drug (Gl	Dosage frequency	2013 (millions)	2014 (millions)	2015 (millions)	2016 (millions)	2017 (million
3	1	Humira (Adalimumab)	Abbvie	Hidradenitis Supp	£284.00 for the 40-mg prefilled pen or syringe for a 40-mg/0.8-ml vial	Adalimumab costs £352.14 for a 40-mg prefilled pen or syringe	160 mg SC on Day 1 (give	$10659	$12543	$14012	$16078	$18427
4	2	Humira (Adalimumab)	Abbvie	Uveitis	£92 600 and £318 075 per quality-adjusted life year (QALY)		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 (Wet	40 mg/mL, 0.05 r	$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 following Retinal V		$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 Retinopathy (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 $21,050	for a supply of 2	10 mg PO qDay continu	$4,280	$4,980	$5,801	$6,974	$8,187
11	9	Rituxan (Rituximab, MabThera	Genetech-a member o	Rheumatoid arthr	100-mg and 500-mg vials of rituximab is £174.63 and £873.15	(10 mg/mL) is $9	1000 mg IV infusion, repeat after 2 week (2 infusions separated by 2 week is 1 course) Repeat course q24weeks or based on clinical evaluation (but no sooner than 16 weeks)					

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.

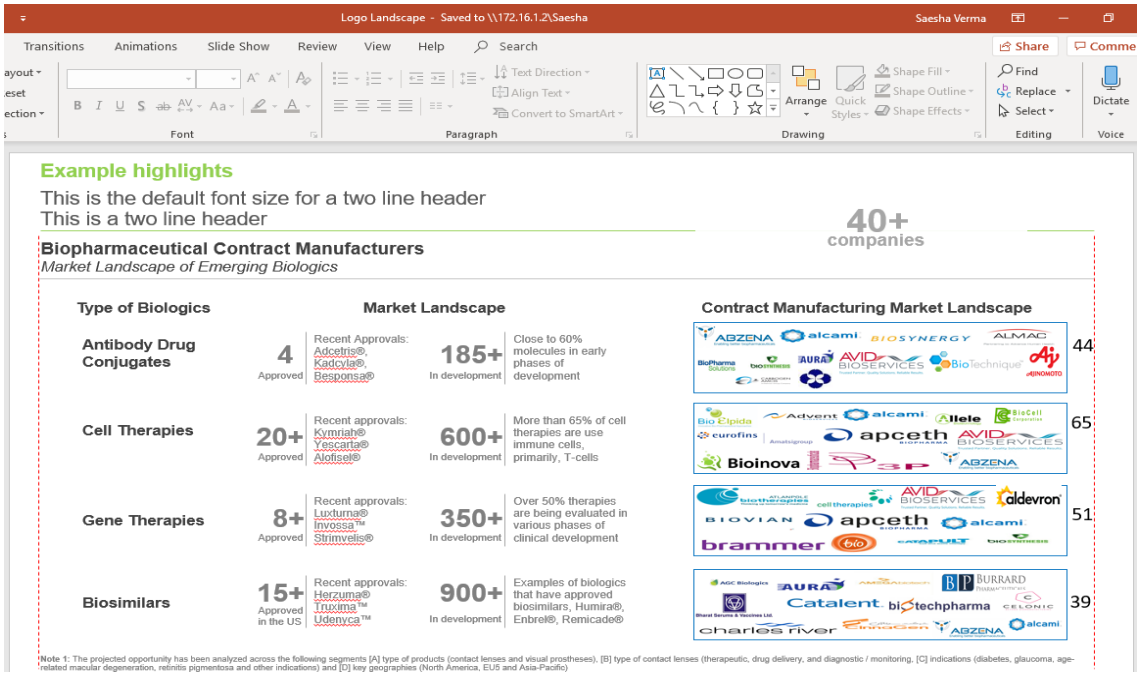
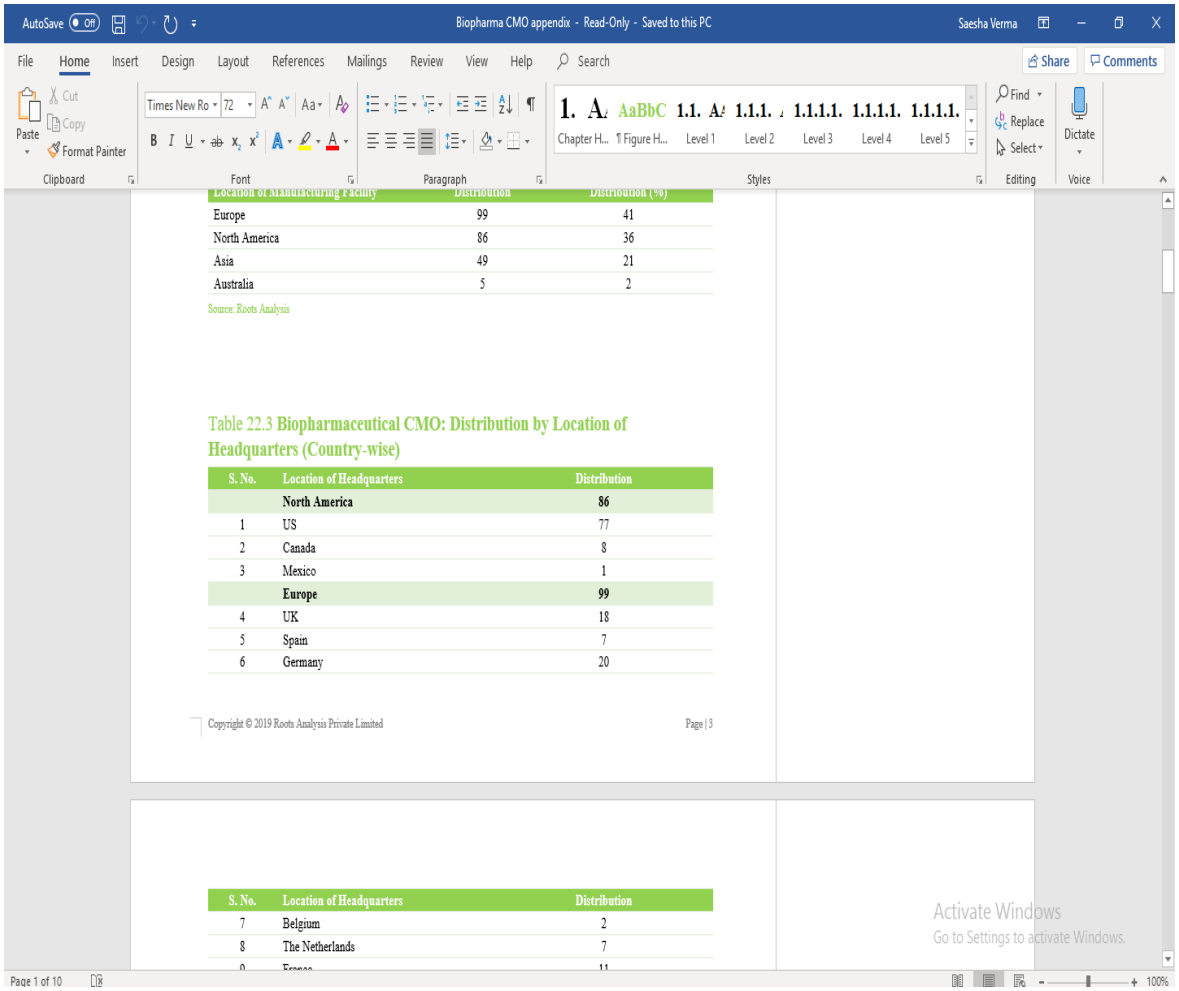


Figure 11.2 Represents the logo lanscape of biopharma CMO companies

11.1.3Appendix

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



Location of Manufacturing Facility	Distribution	Distribution (%)
Europe	99	41
North America	86	36
Asia	49	21
Australia	5	2

Source: Roots Analysis

Table 22.3 **Biopharmaceutical CMO: Distribution by Location of Headquarters (Country-wise)**

S. No.	Location of Headquarters	Distribution
	North America	**86**
1	US	77
2	Canada	8
3	Mexico	1
	Europe	**99**
4	UK	18
5	Spain	7
6	Germany	20

S. No.	Location of Headquarters	Distribution
7	Belgium	2
8	The Netherlands	7

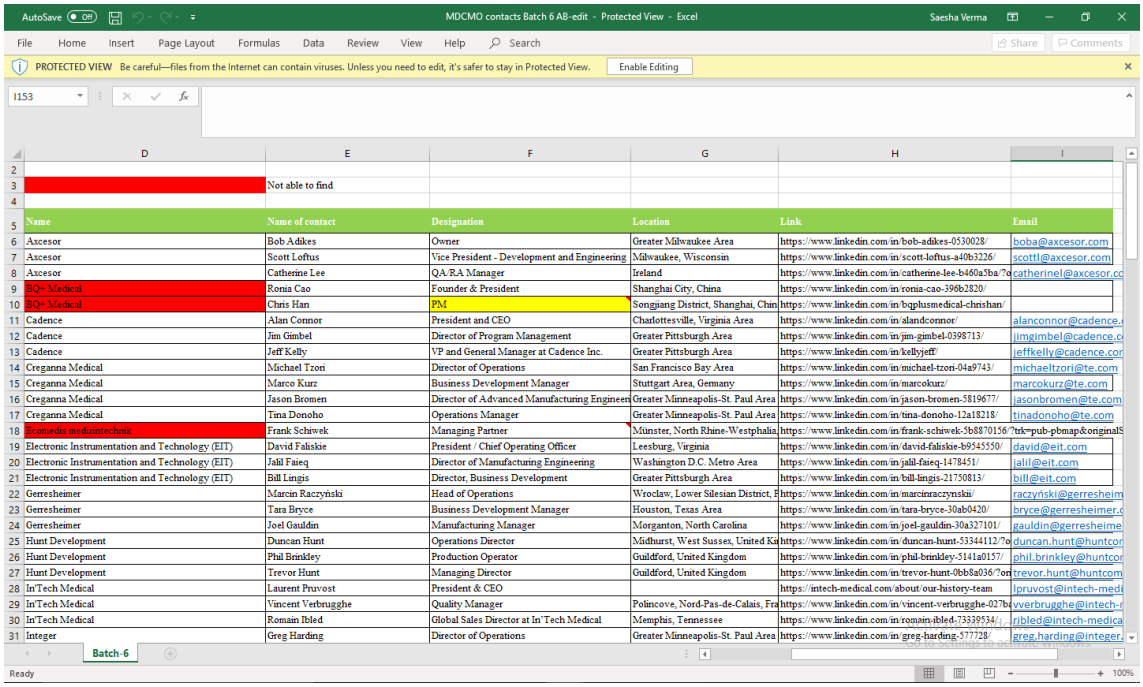
Figure 11.3 Represents the appendix of Biopharma CMO

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.



Name	Name of contact	Designation	Location	Link	Email
Not able to find					
Axcesor	Bob Adikes	Owner	Greater Milwaukee Area	https://www.linkedin.com/in/bob-adikes-0530028/	boba@axcesor.com
Axcesor	Scott Loftus	Vice President - Development and Engineering	Milwaukee, Wisconsin	https://www.linkedin.com/in/scott-loftus-a40b3226/	scottl@axcesor.com
Axcesor	Catherine Lee	QA/RA Manager	Ireland	https://www.linkedin.com/in/catherine-lee-b460a5ba/?o	catherinel@axcesor.co
BQ+ Medical	Ronia Cao	Founder & President	Shanghai City, China	https://www.linkedin.com/in/ronia-cao-396b2820/	
BQ+ Medical	Chris Han	PM	Songjiang District, Shanghai, Chin	https://www.linkedin.com/in/bqplusmedical-chrishan/	
Cadence	Alan Connor	President and CEO	Charlottesville, Virginia Area	https://www.linkedin.com/in/alandconnor/	alanconnor@cadence.c
Cadence	Jim Gimbel	Director of Program Management	Greater Pittsburgh Area	https://www.linkedin.com/in/jim-gimbel-0398713/	jimgimbel@cadence.co
Cadence	Jeff Kelly	VP and General Manager at Cadence Inc.	Greater Pittsburgh Area	https://www.linkedin.com/in/kellyjeff/	jeffkelly@cadence.com
Creganna Medical	Michael Tzori	Director of Operations	San Francisco Bay Area	https://www.linkedin.com/in/michael-tzori-04a9743/	michaeltzori@te.com
Creganna Medical	Marco Kurz	Business Development Manager	Stuttgart Area, Germany	https://www.linkedin.com/in/marcokurz/	marcokurz@te.com
Creganna Medical	Jason Bromen	Director of Advanced Manufacturing Engineeri	Greater Minneapolis-St. Paul Area	https://www.linkedin.com/in/jason-bromen-5819677/	jasonbromen@te.com
Creganna Medical	Tina Donoho	Operations Manager	Greater Minneapolis-St. Paul Area	https://www.linkedin.com/in/tina-donoho-12a18218/	tinadonoho@te.com
Ecomedis medizintechnik	Frank Schiwek	Managing Partner	Münster, North Rhine-Westphalia	https://www.linkedin.com/in/frank-schiwek-5b8870156/?trk=pub-pbmap&originalS	
Electronic Instrumentation and Technology (EIT)	David Faliskie	President / Chief Operating Officer	Leesburg, Virginia	https://www.linkedin.com/in/david-faliskie-b9545550/	david@eit.com
Electronic Instrumentation and Technology (EIT)	Jalil Faieq	Director of Manufacturing Engineering	Washington D.C. Metro Area	https://www.linkedin.com/in/jalil-faieq-1478451/	jalil@eit.com
Electronic Instrumentation and Technology (EIT)	Bill Lingis	Director, Business Development	Greater Pittsburgh Area	https://www.linkedin.com/in/bill-lingis-21750813/	bill@eit.com
Gerresheimer	Marcin Raczyński	Head of Operations	Wroclaw, Lower Silesian District, P	https://www.linkedin.com/in/marcinraczynski/	raczyński@gerresheim
Gerresheimer	Tara Bryce	Business Development Manager	Houston, Texas Area	https://www.linkedin.com/in/tara-bryce-30ab0420/	bryce@gerresheimer.c
Gerresheimer	Joel Gauldin	Manufacturing Manager	Morganton, North Carolina	https://www.linkedin.com/in/joel-gauldin-30a327101/	gauldin@gerresheime
Hunt Development	Duncan Hunt	Operations Director	Midhurst, West Sussex, United Ki	https://www.linkedin.com/in/duncan-hunt-53344112/?o	duncan.hunt@huntcor
Hunt Development	Phil Brinkley	Production Operator	Guildford, United Kingdom	https://www.linkedin.com/in/phil-brinkley-5141a0157/	phil.brinkley@huntcor
Hunt Development	Trevor Hunt	Managing Director	Guildford, United Kingdom	https://www.linkedin.com/in/trevor-hunt-0bb8a036/?or	trevor.hunt@huntcom
InTech Medical	Laurent Pruvost	President & CEO		https://intech-medical.com/about/our-history-team	lpruvost@intech-medi
InTech Medical	Vincent Verbrugghe	Quality Manager	Polincove, Nord-Pas-de-Calais, Fra	https://www.linkedin.com/in/vincent-verbrugghe-027ba	vverbrugghe@intech-r
InTech Medical	Romain Ibled	Global Sales Director at InTech Medical	Memphis, Tennessee	https://www.linkedin.com/in/romain-ibled-73339534/	rjbled@intech-medica
Integer	Greg Harding	Director of Operations	Greater Minneapolis-St. Paul Area	https://www.linkedin.com/in/greg-harding-577728/	greg.harding@integer.

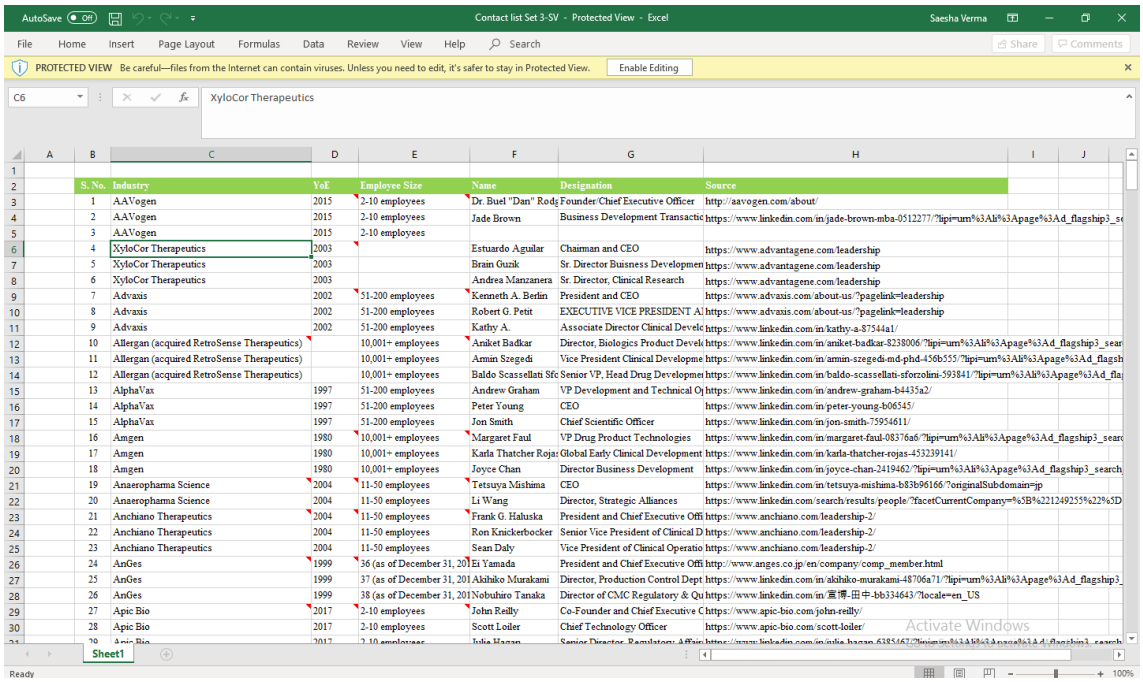
Figure 11.4 Represents the database of company contacts and email ID

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.



S. No.	Industry	YoE	Employee Size	Name	Designation	Source
1	AAVogen	2015	2-10 employees	Dr. Buel "Dan" Rodg	Founder/Chief Executive Officer	http://aavogen.com/about/
2	AAVogen	2015	2-10 employees	Jade Brown	Business Development Transactio	https://www.linkedin.com/in/jade-brown-mba-0512277/?lipi=urn%3Ali%3Apage%3Ad_flagship3_s
3	AAVogen	2015	2-10 employees			
4	XyloCor Therapeutics	2003		Estuardo Aguilar	Chairman and CEO	https://www.advantagene.com/leadership
5	XyloCor Therapeutics	2003		Brain Guzik	Sr. Director Buisness Developmen	https://www.advantagene.com/leadership
6	XyloCor Therapeutics	2003		Andrea Manzanera	Sr. Director, Clinical Research	https://www.advantagene.com/leadership
7	Advaxis	2002	51-200 employees	Kenneth A. Berlin	President and CEO	https://www.advaxis.com/about-us/?pagelink=leadership
8	Advaxis	2002	51-200 employees	Robert G. Petit	EXECUTIVE VICE PRESIDENT A	https://www.advaxis.com/about-us/?pagelink=leadership
9	Advaxis	2002	51-200 employees	Kathy A.	Associate Director Clinical Develc	https://www.linkedin.com/in/kathy-a-87544a1/
10	Allergan (acquired RetroSense Therapeutics)		10,001+ employees	Aniket Badkar	Director, Biologics Product Develc	https://www.linkedin.com/in/aniket-badkar-8238006/?lipi=urn%3Ali%3Apage%3Ad_flagship3_sear
11	Allergan (acquired RetroSense Therapeutics)		10,001+ employees	Armin Szegedi	Vice President Clinical Developme	https://www.linkedin.com/in/armin-szegedi-md-phd-456b555/?lipi=urn%3Ali%3Apage%3Ad_flagsh
12	Allergan (acquired RetroSense Therapeutics)		10,001+ employees	Baldo Scassellati Sfo	Senior VP, Head Drug Developmer	https://www.linkedin.com/in/baldo-scassellati-sforzolini-593841/?lipi=urn%3Ali%3Apage%3Ad_fla
13	AlphaVax	1997	51-200 employees	Andrew Graham	VP Development and Technical Oj	https://www.linkedin.com/in/andrew-graham-b4435a2/
14	AlphaVax	1997	51-200 employees	Peter Young	CEO	https://www.linkedin.com/in/peter-young-b06545/
15	AlphaVax	1997	51-200 employees	Jon Smith	Chief Scientific Officer	https://www.linkedin.com/in/jon-smith-75954611/
16	Amgen	1980	10,001+ employees	Margaret Faul	VP Drug Product Technologies	https://www.linkedin.com/in/margaret-faul-08376a6/?lipi=urn%3Ali%3Apage%3Ad_flagship3_searc
17	Amgen	1980	10,001+ employees	Karla Thatcher Rojas	Global Early Clinical Development	https://www.linkedin.com/in/karla-thatcher-rojas-453239141/
18	Amgen	1980	10,001+ employees	Joyce Chan	Director Business Development	https://www.linkedin.com/in/joyce-chan-2419462/?lipi=urn%3Ali%3Apage%3Ad_flagship3_search
19	Anaeropharma Science	2004	11-50 employees	Tetsuya Mishima	CEO	https://www.linkedin.com/in/tetsuya-mishima-b83b96166/?originalSubdomain=jp
20	Anaeropharma Science	2004	11-50 employees	Li Wang	Director, Strategic Alliances	https://www.linkedin.com/search/results/people/?facetCurrentCompany=%5B%221249255%22%5D
21	Anchiano Therapeutics	2004	11-50 employees	Frank G. Haluska	President and Chief Executive Offi	https://www.anchiano.com/leadership-2/
22	Anchiano Therapeutics	2004	11-50 employees	Ron Knickerbocker	Senior Vice President of Clinical D	https://www.anchiano.com/leadership-2/
23	Anchiano Therapeutics	2004	11-50 employees	Sean Daly	Vice President of Clinical Operatio	https://www.anchiano.com/leadership-2/
24	AnGes	1999	36 (as of December 31, 201	Ei Yamada	President and Chief Executive Offi	http://www.anges.co.jp/en/company/comp_member.html
25	AnGes	1999	37 (as of December 31, 201	Akihiko Murakami	Director, Production Control Dept	https://www.linkedin.com/in/akihiko-murakami-48706a71/?lipi=urn%3Ali%3Apage%3Ad_flagship3_
26	AnGes	1999	38 (as of December 31, 201	Nobuhiro Tanaka	Director of CMC Regulatory & Qu	https://www.linkedin.com/in/宣博-田中-bb334643/?locale=en_US
27	Apic Bio	2017	2-10 employees	John Reilly	Co-Founder and Chief Executive C	https://www.apic-bio.com/john-reilly/
28	Apic Bio	2017	2-10 employees	Scott Loiler	Chief Technology Officer	https://www.apic-bio.com/scott-loiler/

Figure 11.5 Represents 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.

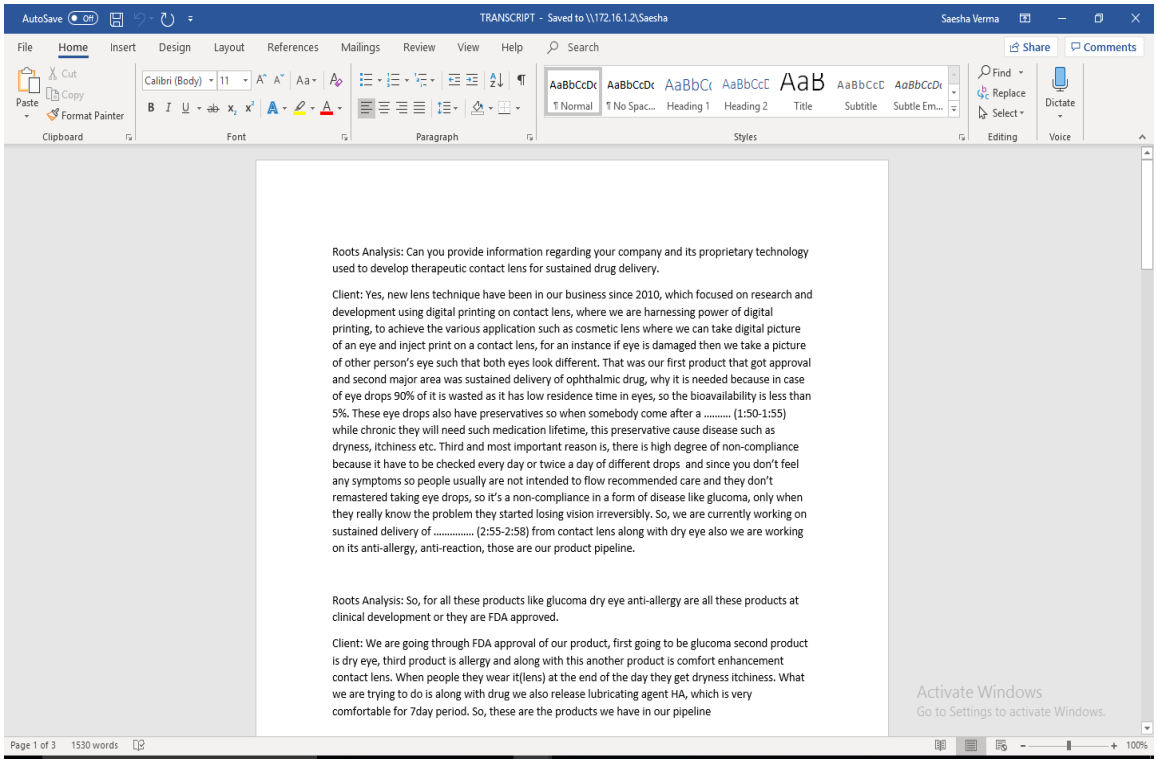


Figure 11.6 Represents the draft of a transcript

CHAPTER 12

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.

CHAPTER 13

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.

CHAPTER 14

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