

RNAI DRUG DELIVERY: TECHNOLOGIES AND GLOBAL MARKETS



BIO076B
June 2014

Usha Nagavarapu
Project Analyst

ISBN: 1-56965-871-4

bcc | Research
Market Forecasting

BCC Research
49 Walnut Park, Building 2
Wellesley, MA 02481 USA
866-285-7215 (toll-free within the USA),
or (+1) 781-489-7301
www.bccresearch.com
information@bccresearch.com

TABLE OF CONTENTS

TOPIC	PAGE NO.
CHAPTER 1 INTRODUCTION	2
STUDY GOALS AND OBJECTIVES	2
REASONS FOR DOING THE STUDY	2
SCOPE OF REPORT	2
INTENDED AUDIENCE	2
METHODOLOGY	3
RELATED BCC RESEARCH REPORTS	3
ANALYST'S CREDENTIALS	3
BCC RESEARCH WEBSITE	3
DISCLAIMER	4
CHAPTER 2 SUMMARY	6
<i>SUMMARY TABLE GLOBAL MARKET FOR RNAI DRUG DELIVERY TECHNOLOGIES, THROUGH 2018 (\$ MILLIONS)</i>	7
<i>SUMMARY FIGURE GLOBAL MARKET FOR RNAI DRUG DELIVERY TECHNOLOGIES, 2013-2018 (\$ MILLIONS)</i>	7
CHAPTER 3 OVERVIEW	10
OVERVIEW	10
WHAT IS RNAI?	12
RNAI AS THERAPY	12
THE PROMISE OF RNAI	13
<i>TABLE 1 VARIOUS TECHNOLOGIES FOR GENE SUPPRESSION</i>	13
RNAI TECHNOLOGY	14
RNAI MECHANISM: HOW DOES IT WORK?	15
WHY SIRNA THERAPEUTICS?	16
SIRNA DELIVERY	18
RNAI DESIGN AND METHODOLOGIES	18
Barriers to Delivery	19
Cellular Uptake and siRNAs	20
SiRNA Delivery and Challenges	20
COMMERCIAL INTEREST	21
LIPOSOME-BASED DELIVERY	22
NONLIPOSOMAL METHODS	22
Nucleic-acid Aptamers	22
Aptamers as Therapeutics	23
<i>TABLE 2 THERAPEUTICALLY TARGETED APTAMERS</i>	24
Aptamers for siRNA Delivery	25
Challenges: Aptamer-siRNA Delivery	26
Commercial Interest for Aptamers	28
Nanotechnology-based Delivery	28
Nanoparticles	29
Advantages	29
<i>TABLE 3 REQUIRED STEPS FOR DEVELOPING EFFECTIVE RNAI DRUG</i>	30
ANTISENSE THERAPY	30
Selected Companies	31

TOPIC	PAGE NO.
CLASSES OF ENDOGENOUS SMALL RNAS	31
siRNA	32
miRNA	33
OUTLOOK	33
CHAPTER 4 RNAI DRUG DELIVERY	36
RNAI DISCOVERED	36
IMPORTANCE OF DELIVERY FOR RNAI THERAPEUTICS	36
DRUG DELIVERY TECHNOLOGIES	37
<i>TABLE 4 ROLE OF DRUG DELIVERY</i>	38
NEED FOR NEW TECHNOLOGIES	38
RNAI DELIVERY-TOOL FOR DRUG DISCOVERY AND DEVELOPMENT	39
siRNA Screening	39
shRNA Screening	40
CHALLENGES TO OVERCOME IN DELIVERING RNAI	40
<i>TABLE 5 DIFFERENT RNAI DELIVERY APPROACHES</i>	41
DIFFERENT DELIVERY TECHNIQUES	41
VECTOR-BASED DELIVERY	41
VECTOR-BASED RNAI FOR IN VIVO RNAI EXPERIMENTS	42
<i>TABLE 6 COMPANIES WITH PLASMID RNAI VECTORS</i>	43
Viral Vectors for Delivery of siRNA	43
<i>TABLE 7 RNAi VIRAL VECTOR DELIVERY METHODS</i>	43
<i>TABLE 8 LENTIVIRAL DELIVERY PRODUCTS AND COMPANIES</i>	44
NONVIRAL SIRNA DELIVERY	44
Hydrodynamic IV Injection	44
Electroporation	44
Carrier-mediated Delivery	45
Lipid-based siRNA Delivery	45
Polymer-Based siRNA Delivery	46
Combined Lipid and Polymer Carriers for a Better siRNA Delivery	47
Peptide-Mediated siRNA Delivery	48
Antibody-Mediated siRNA Delivery	49
Dendrimer-Mediated siRNA Delivery	49
Stem-Cell-Based Delivery	50
Light Controllable Delivery of siRNA	50
PROPRIETARY DELIVERY PLATFORMS	50
SYSTEMIC DELIVERY STRATEGIES	52
<i>TABLE 9 THERAPEUTIC STRATEGIES</i>	52
LOCALIZED DELIVERY	53
Targeted Cellular Delivery	53
EXPRESSION-BASED STRATEGIES	55
RNAI DELIVERY AND IMPACT ON THERAPEUTIC DEVELOPMENTS	56
New Developments	57
Tissue Delivery	58
RNAi as Drugs	59
CURRENT NONBIOLOGICAL DELIVERY VEHICLES FOR SIRNAS	59
Simple Excipients	59

TOPIC	PAGE NO.
<i>TABLE 10 SIMPLE EXCIEPIENTS FOR RNAI DELIVERY</i>	60
TRANSFECTION TECHNIQUES	60
Electroporation	60
Conjugates	60
<i>TABLE 11 CONJUGATES, PEPTIDES, AND PROTEINS, OTHERS</i>	61
Peptides and Proteins	61
Dynamic Polyconjugate Transfection	61
Polymer Carriers/Nanoparticles	62
<i>TABLE 12 POLYMER CARRIERS/NANOPARTICLES FOR RNAI DELIVERY</i>	63
Liposomes and Lipoplexes	64
<i>TABLE 13 LIPOSOMES/LIOPLEXES AND RNAI DELIVERY</i>	65
Case Study-siRNA in Mammalian Cells	65
Gene Silencing (RNAi) in Neuronal Cells	65
Concerns about RNAi Delivery	65
KEY COMPANIES	66
siRNA Transfection	66
<i>TABLE 14 COMPANIES INVOLVED IN DRUG DELIVERY TECHNOLOGIES FOR SIRNA</i>	67
Delivery as Particles or Complexes	67
Delivery with Modifications	68
SUMMARY	68
CHAPTER 5 RNAI-BASED THERAPEUTICS	71
RNAI-BASED THERAPEUTICS: THE EMERGING INDUSTRY LANDSCAPE	71
DELIVERING RNAI THERAPEUTICS	72
RNAi and Cancer Therapeutics	74
REGULATORY CONCERNS	74
RNAI IN CLINICAL TRIALS	75
Clinical Trials: RNAi	75
<i>TABLE 15 THE GLOBAL RNA INTERFERENCE THERAPEUTIC PIPELINE</i>	76
Other Candidates in Clinic	78
Terminated Programs	79
Other Programs	80
THERAPEUTIC RNAI DEVELOPMENTS	80
ALN-VSP02	80
Alnylam's ALN-RSV: Respiratory Syncytial Virus	82
ALN-RSV01 Treatment of Respiratory Syncytial Virus Infection in Lung Transplant Patients	83
<i>TABLE 16 RECENT UPDATES: RNAI CLINICAL TRIALS</i>	84
<i>TABLE 17 CLINICAL TRIALS: RNAI-SYSTEMIC DELIVERY</i>	85
CHALLENGES: RNAI-BASED THERAPIES	87
CHAPTER 6 RNAI LANDSCAPE	90
FUTURE TRENDS	90
WHAT IS RNA INTERFERENCE?	90
Locked Nucleic Acid	91
RNAI AS A RESEARCH TOOL	91
THE IMPORTANCE OF RNAI DESIGN	91
FACTS AND TIMELINES	92

TOPIC	PAGE NO.
MARKET GROWTH	92
GLOBAL MARKET FOR RNAI	93
<i>TABLE 18 GLOBAL RNAI RESEARCH SALES AND FORECAST, THROUGH 2018 (\$ MILLIONS)</i>	93
<i>FIGURE 1 GLOBAL RNAI RESEARCH SALES, 2010-2018 (\$ MILLIONS)</i>	93
<i>TABLE 19 GLOBAL TOOLS, REAGENTS AND THERAPEUTIC MARKET FOR RNAI, THROUGH 2018 (\$ MILLIONS)</i>	94
<i>FIGURE 2 GLOBAL TOTAL MARKET FOR RNAI, 2012-2018 (\$ MILLIONS)</i>	94
RNAI TECHNOLOGIES/PRODUCTS IN RESEARCH APPLICATIONS	95
RNAi Screening for Drug Discovery	96
Individual versus Pooled siRNAs	97
Necessary Controls	97
High-throughput siRNA Delivery	97
RNAI TOOL AND REAGENT MARKET	99
Transfection Products	100
Key Companies	100
<i>TABLE 20 RNAI COMPANIES WITH TRANSFECTION REAGENTS</i>	100
RNAi Reagents	101
Lipid Transfection	102
In Vivo Reagents and Therapeutics	102
RNAi Experiments in Animals	103
RNAI AND THERAPEUTICS	104
<i>TABLE 21 IN VIVO DELIVERY</i>	104
Viral-based Transfections	105
<i>TABLE 22 VIRAL BASED DELIVERY TECHNOLOGIES</i>	106
Other Methods	106
RNAi Reagents and Kits	107
<i>TABLE 23 RNAI TOOL/REAGENT COMPANIES</i>	108
KEY COMPANIES	109
Inc.Lonza	110
THE FUTURE OF RNAI THERAPEUTICS	110
CHAPTER 7 RNAI DRUG DELIVERY-MARKET DATA	112
MARKET TRENDS	112
MARKET SIZE AND GROWTH	112
RNAI DRUGS	113
GLOBAL PHARMACEUTICAL MARKET	113
<i>TABLE 24 GLOBAL PHARMACEUTICAL SALES AND FORECAST THROUGH 2018 (\$ BILLIONS)</i>	114
<i>FIGURE 3 GLOBAL PHARMACEUTICAL SALES AND FORECAST, 2011-2018 (\$ BILLIONS)</i>	114
Pharmaceutical Growth Rates	114
Emerging Markets	115
<i>TABLE 25 TOTAL UNAUDITED AND AUDITED GLOBAL PHARMACEUTICAL MARKET BY REGION, THROUGH 2017 (\$ BILLIONS)</i>	116
U.S. Pharmaceutical Industry	116
Global Pharmaceutical Companies	116
<i>TABLE 26 TOP 25 PHARMACEUTICAL COMPANIES, GLOBAL SALES, 2012 AND 2013 (\$ MILLIONS)</i>	117

TOPIC	PAGE NO.
<i>TABLE 27 TWELVE LARGEST PHARMACEUTICAL COMPANIES 2010 (\$ MILLIONS)</i>	118
DRUG DELIVERY TECHNOLOGY LANDSCAPE	118
DRUG DELIVERY MARKET	119
Drug Delivery Technologies and Global Market	119
<i>TABLE 28 TOTAL GLOBAL DRUG DELIVERY TECHNOLOGIES MARKET, THROUGH 2018 (\$ MILLIONS)</i>	120
<i>FIGURE 4 TOTAL GLOBAL DRUG DELIVERY TECHNOLOGIES MARKET, 2011-2018 (\$ MILLIONS)</i>	120
<i>TABLE 29 KEY PLAYERS: DRUG DELIVERY TECHNOLOGIES MARKET</i>	122
European Drug Delivery Market	122
<i>TABLE 30 GLOBAL DRUG DELIVERY TECHNOLOGIES MARKET, THROUGH 2018 (\$ MILLIONS)</i>	123
<i>FIGURE 5 GLOBAL DRUG DELIVERY TECHNOLOGIES MARKET, 2011-2018 (\$ MILLIONS)</i>	123
Oral Drug Delivery	124
<i>TABLE 31 GLOBAL ORAL DRUG DELIVERY TECHNOLOGIES MARKET, THROUGH 2018 (\$ MILLIONS)</i>	124
<i>FIGURE 6 GLOBAL ORAL DRUG DELIVERY TECHNOLOGIES MARKET, 2010-2018 (\$ MILLIONS)</i>	124
Implantable and Injectable Drug Delivery	125
<i>TABLE 32 GLOBAL IMPLANTABLE/INJECTABLE DRUG DELIVERY MARKET, THROUGH 2018 (\$ MILLIONS)</i>	125
<i>FIGURE 7 GLOBAL IMPLANTABLE/INJECTABLE DRUG DELIVERY MARKET, 2011-2018 (\$ MILLIONS)</i>	125
Transdermal Drug Delivery	127
<i>TABLE 33 GLOBAL TRANSDERMAL DRUG DELIVERY TECHNOLOGIES MARKET, THROUGH 2018 (\$ MILLIONS)</i>	127
<i>FIGURE 8 GLOBAL TRANSDERMAL DRUG DELIVERY TECHNOLOGIES MARKET, 2011-2018 (\$ MILLIONS)</i>	127
Drug Delivery Market in the U.S.	128
<i>TABLE 34 U.S. DRUG DELIVERY TECHNOLOGIES MARKET AND FORECAST THROUGH 2018 (\$ MILLIONS)</i>	128
<i>FIGURE 9 U.S. DRUG DELIVERY TECHNOLOGIES MARKET, 2011-2018 (\$ MILLIONS)</i>	128
PULMONARY DRUG DELIVERY	129
<i>TABLE 35 TOP ASTHMA AND COPD DRUGS</i>	129
<i>TABLE 36 GLOBAL PULMONARY DELIVERY TECHNOLOGIES MARKET, THROUGH 2018 (\$ MILLIONS)</i>	130
<i>FIGURE 10 GLOBAL PULMONARY DELIVERY TECHNOLOGIES MARKET, 2011-2018 (\$ MILLIONS)</i>	130
RNAI MARKET ANALYSIS	130
LEADING PLAYERS	131
Rxi Pharmaceuticals	131
Tekmira Pharmaceuticals	132
Arrowhead Research Corp.	132
RNAI MARKET DYNAMICS	133
RNAI NUCLEIC ACID DRUG DELIVERY	134
<i>TABLE 37 GLOBAL NUCLEIC ACID DELIVERY TECHNOLOGIES MARKET, THROUGH 2018 (\$ MILLIONS)</i>	134
<i>FIGURE 11 GLOBAL NUCLEIC ACID DELIVERY TECHNOLOGIES MARKET, 2010-2018 (\$ MILLIONS)</i>	134

TOPIC	PAGE NO.
<i>TABLE 38 GLOBAL APTAMERS THERAPEUTIC MARKET, THROUGH 2018 (\$ MILLIONS)</i>	136
<i>FIGURE 12 GLOBAL APTAMERS THERAPEUTIC MARKET, THROUGH 2018 (\$ MILLIONS)</i>	137
NUCLEIC ACID APTAMER-BASED NANOPARTICLES	137
TARGETED DELIVERY	138
THE TOTAL NANOPARTICLE MARKET	138
<i>TABLE 39 GLOBAL NANOPARTICLE DRUG DELIVERY TECHNOLOGIES MARKET, THROUGH 2018 (\$ MILLIONS)</i>	138
<i>FIGURE 13 GLOBAL NANOPARTICLE DRUG DELIVERY TECHNOLOGIES MARKET, 2012-2018 (\$ MILLIONS)</i>	139
DELIVERY OF THERAPEUTICS TO THE TARGET TISSUES	139
<i>TABLE 40 GLOBAL TARGETED DRUG DELIVERY TECHNOLOGIES MARKET, THROUGH 2018 (\$ MILLIONS)</i>	139
<i>FIGURE 14 GLOBAL TARGETED DRUG DELIVERY TECHNOLOGIES, MARKET, 2012-2018 (\$ MILLIONS)</i>	139
RNAI DELIVERY APPROACHES AND CURRENT DEVELOPMENTS	140
DEVELOPMENT OF RNAI-BASED THERAPEUTICS	141
NANOPARTICLE-BASED DELIVERY	142
RNAi Drugs under Investigation	143
<i>TABLE 41 NON-VIRAL SIRNAS</i>	143
LIPOSOME AND NANOPARTICLES	145
POLYMERS	146
CALANDO PHARMACEUTICALS	147
INTRADIGM	147
MESOPOROUS SILICA NANOPARTICLES	147
PROTEIN OR PEPTIDE-BASED NANOPARTICLES	148
BACTERIOPHAGE BASED NANOPARTICLES	149
SOLSTICE BIOLOGICS	150
GENZYME	150
<i>TABLE 42 KEY RNAI COMPANIES</i>	150
QUARK PHARMACEUTICALS	151
Marina Biotech	152
Lipid and Polymer-Based Systems	152
<i>TABLE 43 LIPID-BASED TECHNOLOGIES-COMPANIES</i>	152
<i>TABLE 44 POLYMER-BASED AND LIPOSOMAL RNAi DELIVERY SYSTEMS (%)</i>	153
RNAI INTO THE PATIENTS	154
ROCHE	154
Polyconjugate Technologies	154
Polymer-Based Systems-Limitations	155
RXi	156
<i>TABLE 45 NANOPARTICLES TECHNOLOGIES-COMPANIES</i>	156
Single siRNA Delivery	157
<i>TABLE 46 SINGLE RNAi DELIVERY TECHNOLOGIES, COMPANIES</i>	157
DICERNA PHARMACEUTICALS	158
CONCLUSIONS	159
CHAPTER 8 RNAI DRUG DELIVERY STRATEGIES AND CURRENT MARKET DYNAMICS	161
SYSTEMIC DELIVERY STRATEGIES	161

TOPIC	PAGE NO.
CHALLENGES WITH RNAI DRUG DELIVERY	162
RNAI THERAPEUTIC MARKET	162
<i>TABLE 47 SELECTED RNAI-BASED DRUGS IN DEVELOPMENT</i>	163
COMMERCIAL POTENTIAL OF RNAI	163
<i>TABLE 48 COMMERCIAL POTENTIAL OF RNAI</i>	163
RNAI'S THERAPEUTIC POTENTIAL	164
HOW DOES RNAI WORK?	165
RNAIS AND PRECLINICAL AND CLINICAL STUDIES	165
CEQ508 in Clinic	166
RNAi as a Therapy	167
GLOBAL MARKET OF THERAPEUTIC RNAI	167
RNAi Therapeutic Market to Play a Key Role by 2020	167
<i>TABLE 49 GLOBAL MARKET FOR THERAPEUTIC RNAi, THROUGH 2018 (\$ MILLIONS)</i>	168
<i>FIGURE 15 GLOBAL MARKET FOR THERAPEUTIC RNAi, 2013 AND 2018 (\$ MILLIONS)</i>	168
<i>TABLE 50 RNAi THERAPEUTIC COMPANIES</i>	169
Benitec's Clinical Program	170
<i>TABLE 51 ONGOING RNAi CLINICAL TRIALS: NANOPARTICLE DRUG DELIVERY</i>	171
MicroRNA and Market	171
MIRNA MARKET	172
<i>TABLE 52 TOTAL MIRNA MARKET AND FORECAST, THROUGH 2018 (\$ MILLIONS)</i>	173
<i>FIGURE 16 TOTAL MIRNA MARKET AND FORECAST, 2013 AND 2018 (\$ MILLIONS)</i>	173
<i>TABLE 53 TOTAL MIRNA MARKET SALES, 2008 (%)</i>	174
RECENT DEVELOPMENTS	174
RNAI LICENSING DEALS	175
<i>TABLE 54 MAJOR RNAI LICENSING DEALS, 2005-2010</i>	177
TARGETED DELIVERY	179
<i>TABLE 55 SYSTEMIC DELIVERY TECHNOLOGIES, COMPANIES</i>	180
KEY THERAPEUTIC COMPANIES AND HISTORICAL DEVELOPMENTS	181
ALNYLAM	181
Takeda Alliance	182
Other Discovery and Development Alliances	182
Isis Collaboration	182
Novartis Broad Alliance	183
Product Alliances	184
Kyowa Hakko Kirin Alliance	184
Cubist Alliance	184
Government Funding	185
NIH Contract	185
<i>TABLE 56 ALNYLAM: PIPELINE</i>	186
TEKMIRA	187
Funding	188
Tekmira's LNP Technology	188
TKM-ApoB	189
TKM-PLK1	190
PHASE I/II TKM-PLK1 CLINICAL TRIAL	190
TKM-Ebola	191
Roche	192

TOPIC	PAGE NO.
Merck	192
Bristol-Myers Squibb	192
<i>TABLE 57 TEKIRA'S PIPELINE 17</i>	192
HUMAN CLINICAL TRIAL OF TKM-EBOLA	193
RXI PHARMACEUTICALS	194
Pipeline	194
<i>TABLE 58 RXi PHARMACEUTICALS' DEVELOPMENT PIPELINE</i>	194
RXi 109	195
CONNECTIVE TISSUE GROWTH FACTOR (CTGF) AND SCARRING	196
Clinical Program	196
Phase 2	196
RXi Agreements	197
Philips	197
Other Collaborative Agreements	197
Scientific Achievements	198
NIH Grant	198
MARINA BIOTECH	198
Pipeline	199
<i>TABLE 59 MARINA BIOTECH'S DEVELOPMENT PIPELINE</i>	199
Revenue	199
Ongoing Collaborations	199
Beth Israel Deaconess Medical Center-Boston, Mass.	199
Institut Pasteur	200
University of British Columbia (UBC)/Vancouver Prostate Centre (VPC)	200
University of Helsinki	200
<i>TABLE 60 MARINA BIOTECH SELECTED COLLABORATIONS</i>	200
CALANDO PHARMACEUTICALS	201
CALAA-01	201
ISIS PHARMACEUTICALS	202
Pipeline	202
<i>TABLE 61 ISIS PHARMACEUTICALS DRUG DEVELOPMENT PIPELINE</i>	202
Strategic Alliances	203
Pharmaceutical Partners	204
SILENCE THERAPEUTICS	204
Proprietary Delivery Technologies	204
Pipeline	205
<i>TABLE 62 SILENCE THERAPEUTICS, DEVELOPMENT PIPELINE</i>	205
Collaborations	206
Quark Pharmaceuticals	207
Clinical Studies	207
<i>TABLE 63 QUARK PHARMACEUTICALS CURRENT CLINICAL TRIALS</i>	208
Pipeline	208
<i>TABLE 64 QUARK PHARMACEUTICALS-DEVELOPMENT PIPELINE, 2010</i>	208
QPI-1002	209
ROCHE	209
MERCK	210
SIRNAOMICS	210

TOPIC	PAGE NO.
TABLE 65 SIRNA THERAPEUTIC PROGRAM	210
STP702 (FluQuit): siRNA Therapeutics against Influenza Infection (Pandemic Flu)	211
STP601 (Acurita) siRNA Therapeutics for AMD and Retinopathy	211
STP705 (Cutasil) siRNA Therapeutics for Skin Scarless Wound Healing (SSWH)	211
STP503 (Trisilensa) siRNA Therapeutics for Breast Cancer	212
ACCESS PHARMACEUTICALS	212
KEY MIRNA THERAPEUTIC COMPANIES	212
MIRNA THERAPEUTICS	212
Pipeline	213
TABLE 66 MIRNA, DEVELOPMENT PIPELINE	213
MRX34	214
REGULUS	214
Pipeline	214
TABLE 67 MIRNA PROGRAMS	215
LOCAL THERAPY	215
DRUG DELIVERY IN CANCER	216
RNAI MARKETPLACE CHALLENGES	217
RNAI'S GROWTH AND FUTURE	217
CONCLUSIONS	218
CHAPTER 9 COMPANY PROFILES	220
RNAI-DISCOVERY AND GROWTH	220
COMPANY PROFILES	221
ACCESS PHARMACEUTICALS	221
ALNYLAM PHARMACEUTICALS	221
AMBION	222
APARNABIO	223
ARMAGEN TECHNOLOGIES	223
ARROWHEAD RESEARCH	224
ASURAGEN	224
B-BRIDGE INTERNATIONAL	224
BIO-RAD LABORATORIES	225
CALANDO PHARMACEUTICALS	225
CLONTECH LABORATORIES	225
CYNTELLECT	226
DHARMACON	226
DICERNA PHARMACEUTICALS	227
GENECOPOEIA	227
GENETHERA	228
GENLANTIS	228
GENOSENSOR	228
GENERAL RESEARCH LABORATORY	229
IMGENEX	229
INTEGRATED DNA TECHNOLOGIES (IDT)	230
INVITROGEN	230
INVIVOGEN	230

TOPIC	PAGE NO.
ISIS PHARMACEUTICALS	231
MARINA BIOTECH	231
MERCK	232
MIRAGEN THERAPEUTICS	232
MIRNA THERAPEUTICS INC.	232
NEW ENGLAND BIOLABS	233
OPEN BIOSYSTEMS	233
ORIGENE TECHNOLOGIES	233
PANOMICS	234
PHASERX	234
PROMEGA CORP.	235
PRONAI THERAPEUTICS	235
QUARK PHARMACEUTICALS	235
REGULUS THERAPEUTICS	236
RXI PHARMACEUTICALS	236
SIGMA-ALDRICH	237
SILENCE THERAPEUTICS	237
SIRNAOMICS	238
SOLSTICE BIOLOGICS	239
SOMAGENICS	239
SYSTEM BIOSCIENCES	240
TACERE THERAPEUTICS	240
TEKMIRA PHARMACEUTICALS CORP.	241
COMPANY PROFILES-EUROPE	241
ACTIGENICS	241
AMAXA	242
CENIX BIOSCIENCE	242
EXIQON	242
GENOVIS	243
PROSENSA HOLDING	243
QIAGEN	243
RNAX	243
SANTARIS PHARMA	244
COMPANY PROFILES-ASIA-PACIFIC	244
ALPHAGEN	244
BENITEC	245
BIONEER	245
U.S.	245
CYTOPATHFINDER INC. INC.	245
GENESIS RESEARCH & DEVELOPMENT CORP.	246
KOKEN CO. LTD.	246
ONCOLYS BIOPHARMA INC. INC.	246
SHANGHAI GENE PHARMA CO. LTD.	247
SHANGHAI GENOMICS	247
TRANSGENE BIOTEK	247
CHAPTER 10 MARKET SHIFTS IN RNAI SPACE	249

TOPIC	PAGE NO.
INTELLECTUAL PROPERTY AND PATENT ASPECTS	249
<i>TABLE 68 MAJOR RNAI COMPANIES IN THE U.S.- PATENT DISTRIBUTION</i>	249
FUTURE DEVELOPMENTS	250
SOME SELECTED PATENTS	250
RNAI PLATFORMS	251
SIRNA LITIGATIONS	252
RECENT PATENT NEWS	253
<i>TABLE 69 PATENTS</i>	255
LICENSES FOR RNAI PATENTS	257
KEY COMPANIES AND PATENTS	258
ALNYLAM	258
RXI	258
ISIS	259
QUARK	259
BENITEC	259
PARTNERSHIPS, ALLIANCES, MERGERS AND ACQUISITIONS	260
ALNYLAM COLLABORATORS: SIGNIFICANT NEW ADVANCES IN RNAI DELIVERY	261
ALNYLAM, MEDTRONIC, AND CHDI FOUNDATION	262
ALNYLAM AND TEKIRA	263
CONCLUSIONS	264
CHAPTER 11 BIBLIOGRAPHY	266

LIST OF TABLES

TABLE HEADING	PAGE NO.
SUMMARY TABLE GLOBAL MARKET FOR RNAI DRUG DELIVERY TECHNOLOGIES, THROUGH 2018 (\$ MILLIONS)	7
TABLE 1 VARIOUS TECHNOLOGIES FOR GENE SUPPRESSION	13
TABLE 2 THERAPEUTICALLY TARGETED APTAMERS	24
TABLE 3 REQUIRED STEPS FOR DEVELOPING EFFECTIVE RNAI DRUG	30
TABLE 4 ROLE OF DRUG DELIVERY	38
TABLE 5 DIFFERENT RNAI DELIVERY APPROACHES	41
TABLE 6 COMPANIES WITH PLASMID RNAI VECTORS	43
TABLE 7 RNAI VIRAL VECTOR DELIVERY METHODS	43
TABLE 8 LENTIVIRAL DELIVERY PRODUCTS AND COMPANIES	44
TABLE 9 THERAPEUTIC STRATEGIES	52
TABLE 10 SIMPLE EXCIEPIENTS FOR RNAI DELIVERY	60
TABLE 11 CONJUGATES, PEPTIDES, AND PROTEINS, OTHERS	61
TABLE 12 POLYMER CARRIERS/NANOPARTICLES FOR RNAI DELIVERY	63
TABLE 13 LIPOSOMES/LIPOPLEXES AND RNAI DELIVERY	65
TABLE 14 COMPANIES INVOLVED IN DRUG DELIVERY TECHNOLOGIES FOR SIRNA	67
TABLE 15 THE GLOBAL RNA INTERFERENCE THERAPEUTIC PIPELINE	76
TABLE 16 RECENT UPDATES: RNAI CLINICAL TRIALS	84
TABLE 17 CLINICAL TRIALS: RNAI-SYSTEMIC DELIVERY	85
TABLE 18 GLOBAL RNAI RESEARCH SALES AND FORECAST, THROUGH 2018 (\$ MILLIONS)	93
TABLE 19 GLOBAL TOOLS, REAGENTS AND THERAPEUTIC MARKET FOR RNAI, THROUGH 2018 (\$ MILLIONS)	94
TABLE 20 RNAI COMPANIES WITH TRANSFECTION REAGENTS	100
TABLE 21 IN VIVO DELIVERY	104
TABLE 22 VIRAL BASED DELIVERY TECHNOLOGIES	106
TABLE 23 RNAI TOOL/REAGENT COMPANIES	108
TABLE 24 GLOBAL PHARMACEUTICAL SALES AND FORECAST THROUGH 2018 (\$ BILLIONS)	114
TABLE 25 TOTAL UNAUDITED AND AUDITED GLOBAL PHARMACEUTICAL MARKET BY REGION, THROUGH 2017 (\$ BILLIONS)	116
TABLE 26 TOP 25 PHARMACEUTICAL COMPANIES, GLOBAL SALES, 2012 AND 2013 (\$ MILLIONS)	117
TABLE 27 TWELVE LARGEST PHARMACEUTICAL COMPANIES 2010 (\$ MILLIONS)	118
TABLE 28 TOTAL GLOBAL DRUG DELIVERY TECHNOLOGIES MARKET, THROUGH 2018 (\$ MILLIONS)	120
TABLE 29 KEY PLAYERS: DRUG DELIVERY TECHNOLOGIES MARKET	122
TABLE 30 GLOBAL DRUG DELIVERY TECHNOLOGIES MARKET, THROUGH 2018 (\$ MILLIONS)	123
TABLE 31 GLOBAL ORAL DRUG DELIVERY TECHNOLOGIES MARKET, THROUGH 2018 (\$ MILLIONS)	124
TABLE 32 GLOBAL IMPLANTABLE/INJECTABLE DRUG DELIVERY MARKET, THROUGH 2018 (\$ MILLIONS)	125
TABLE 33 GLOBAL TRANSDERMAL DRUG DELIVERY TECHNOLOGIES MARKET, THROUGH 2018 (\$ MILLIONS)	127
TABLE 34 U.S. DRUG DELIVERY TECHNOLOGIES MARKET AND FORECAST THROUGH 2018 (\$ MILLIONS)	128
TABLE 35 TOP ASTHMA AND COPD DRUGS	129

TABLE HEADING	PAGE NO.
TABLE 36 GLOBAL PULMONARY DELIVERY TECHNOLOGIES MARKET, THROUGH 2018 (\$ MILLIONS)	130
TABLE 37 GLOBAL NUCLEIC ACID DELIVERY TECHNOLOGIES MARKET, THROUGH 2018 (\$ MILLIONS)	134
TABLE 38 GLOBAL APTAMERS THERAPEUTIC MARKET, THROUGH 2018 (\$ MILLIONS)	136
TABLE 39 GLOBAL NANOPARTICLE DRUG DELIVERY TECHNOLOGIES MARKET, THROUGH 2018 (\$ MILLIONS)	138
TABLE 40 GLOBAL TARGETED DRUG DELIVERY TECHNOLOGIES MARKET, THROUGH 2018 (\$ MILLIONS)	139
TABLE 41 NON-VIRAL SIRNAS	143
TABLE 42 KEY RNAI COMPANIES	150
TABLE 43 LIPID-BASED TECHNOLOGIES-COMPANIES	152
TABLE 44 POLYMER-BASED AND LIPOSOMAL RNAI DELIVERY SYSTEMS (%)	153
TABLE 45 NANOPARTICLES TECHNOLOGIES-COMPANIES	156
TABLE 46 SINGLE RNAI DELIVERY TECHNOLOGIES, COMPANIES	157
TABLE 47 SELECTED RNAI-BASED DRUGS IN DEVELOPMENT	163
TABLE 48 COMMERCIAL POTENTIAL OF RNAI	163
TABLE 49 GLOBAL MARKET FOR THERAPEUTIC RNAI, THROUGH 2018 (\$ MILLIONS)	168
TABLE 50 RNAI THERAPEUTIC COMPANIES	169
TABLE 51 ONGOING RNAI CLINICAL TRIALS: NANOPARTICLE DRUG DELIVERY	171
TABLE 52 TOTAL MIRNA MARKET AND FORECAST, THROUGH 2018 (\$ MILLIONS)	173
TABLE 53 TOTAL MIRNA MARKET SALES, 2008 (%)	174
TABLE 54 MAJOR RNAI LICENSING DEALS, 2005-2010	177
TABLE 55 SYSTEMIC DELIVERY TECHNOLOGIES, COMPANIES	180
TABLE 56 ALNYLAM: PIPELINE	186
TABLE 57 TEKmira'S PIPELINE 17	192
TABLE 58 RXI PHARMACEUTICALS' DEVELOPMENT PIPELINE	194
TABLE 59 MARINA BIOTECH'S DEVELOPMENT PIPELINE	199
TABLE 60 MARINA BIOTECH SELECTED COLLABORATIONS	200
TABLE 61 ISIS PHARMACEUTICALS DRUG DEVELOPMENT PIPELINE	202
TABLE 62 SILENCE THERAPEUTICS, DEVELOPMENT PIPELINE	205
TABLE 63 QUARK PHARMACEUTICALS CURRENT CLINICAL TRIALS	208
TABLE 64 QUARK PHARMACEUTICALS-DEVELOPMENT PIPELINE, 2010	208
TABLE 65 SIRNA THERAPEUTIC PROGRAM	210
TABLE 66 MIRNA, DEVELOPMENT PIPELINE	213
TABLE 67 MIRNA PROGRAMS	215
TABLE 68 MAJOR RNAI COMPANIES IN THE U.S.- PATENT DISTRIBUTION	249
TABLE 69 PATENTS	255

LIST OF FIGURES

FIGURE TITLE	PAGE NO.
SUMMARY FIGURE GLOBAL MARKET FOR RNAI DRUG DELIVERY TECHNOLOGIES, 2013-2018 (\$ MILLIONS)	7
FIGURE 1 GLOBAL RNAI RESEARCH SALES, 2010-2018 (\$ MILLIONS)	93
FIGURE 2 GLOBAL TOTAL MARKET FOR RNAI, 2012-2018 (\$ MILLIONS)	94
FIGURE 3 GLOBAL PHARMACEUTICAL SALES AND FORECAST, 2011-2018 (\$ BILLIONS)	114
FIGURE 4 TOTAL GLOBAL DRUG DELIVERY TECHNOLOGIES MARKET, 2011-2018 (\$ MILLIONS)	120
FIGURE 5 GLOBAL DRUG DELIVERY TECHNOLOGIES MARKET, 2011-2018 (\$ MILLIONS)	123
FIGURE 6 GLOBAL ORAL DRUG DELIVERY TECHNOLOGIES MARKET, 2010-2018 (\$ MILLIONS)	124
FIGURE 7 GLOBAL IMPLANTABLE/INJECTABLE DRUG DELIVERY MARKET, 2011-2018 (\$ MILLIONS)	125
FIGURE 8 GLOBAL TRANSDERMAL DRUG DELIVERY TECHNOLOGIES MARKET, 2011-2018 (\$ MILLIONS)	127
FIGURE 9 U.S. DRUG DELIVERY TECHNOLOGIES MARKET, 2011-2018 (\$ MILLIONS)	128
FIGURE 10 GLOBAL PULMONARY DELIVERY TECHNOLOGIES MARKET, 2011-2018 (\$ MILLIONS)	130
FIGURE 11 GLOBAL NUCLEIC ACID DELIVERY TECHNOLOGIES MARKET, 2010-2018 (\$ MILLIONS)	134
FIGURE 12 GLOBAL APTAMERS THERAPEUTIC MARKET, THROUGH 2018 (\$ MILLIONS)	137
FIGURE 13 GLOBAL NANOPARTICLE DRUG DELIVERY TECHNOLOGIES MARKET, 2012-2018 (\$ MILLIONS)	139
FIGURE 14 GLOBAL TARGETED DRUG DELIVERY TECHNOLOGIES, MARKET, 2012-2018 (\$ MILLIONS)	139
FIGURE 15 GLOBAL MARKET FOR THERAPEUTIC RNAI, 2013 AND 2018 (\$ MILLIONS)	168
FIGURE 16 TOTAL MIRNA MARKET AND FORECAST, 2013 AND 2018 (\$ MILLIONS)	173