

NUCLEIC ACID APTAMERS FOR DIAGNOSTICS AND THERAPEUTICS: GLOBAL MARKETS



BIO071B
October 2012

George W. Jackson
Project Analyst

ISBN: 0-89336-163-1

bcc | Research
Market Forecasting

BCC Research
49 Walnut Park, Building 2
Wellesley, MA 02481
866-285-7215, 781-489-7301
www.bccresearch.com
Custom Reports: carol.laverty@bccresearch.com

TABLE OF CONTENTS

TOPIC	PAGE NO.
CHAPTER 1 INTRODUCTION	1
STUDY GOALS AND OBJECTIVES	1
REASONS FOR DOING THE STUDY	1
SCOPE OF REPORT	1
INTENDED AUDIENCE	2
INFORMATION SOURCES	2
ANALYST CREDENTIALS	2
RELATED BCC REPORTS	2
BCC ONLINE SERVICES	3
DISCLAIMER	3
CHAPTER 2 SUMMARY	5
SUMMARY TABLE A GLOBAL MARKETS FOR APTAMERS, THROUGH 2017 (\$ MILLIONS)*	5
SUMMARY FIGURE GLOBAL MARKETS FOR APTAMERS, 2011-2017 (\$ MILLIONS)*	5
SUMMARY TABLE B POTENTIAL MARKETS FOR APTAMER THERAPEUTICS, THROUGH 2017 (\$ MILLIONS)	6
SUMMARY TABLE C HISTORICAL U.S. SALES FOR MACUGEN, THE FIRST FDA-APPROVED APTAMER DRUG, 2005-2011 (\$ MILLIONS)	7
SUMMARY TABLE D POTENTIAL MARKETS FOR APTAMER-BASED IN-VITRO DIAGNOSTICS, THROUGH 2017 (\$ MILLIONS)	8
CHAPTER 3 OVERVIEW	10
INTRODUCTION: APTAMERS AS AFFINITY REAGENTS	10
FIGURE 1 SIMPLIFIED SCHEMATIC OF SELEX PROCESS FOR IN-VITRO SELECTION OF (DNA) APTAMERS	10
APTAMERS AS AFFINITY REAGENTS	11
TABLE 1 APTAMERS AND ANTIBODIES: KEY DIFFERENCES	12
INDUSTRY DEFINITION AND HISTORICAL DEVELOPMENT	12
ECONOMIC IMPORTANCE	13
PRODUCT LIFE CYCLE	13
INTELLECTUAL PROPERTY AND REGULATORY ISSUES	13
POTENTIAL FUTURE DEVELOPMENTS	14
CHAPTER 4 MARKETS BY TECHNOLOGY TYPE	16
INTRODUCTION	16
ENABLING TECHNOLOGY	16
OLIGONUCLEOTIDE SYNTHESIS	16
MODIFIED OLIGONUCLEOTIDES	17
Aptamer Modifications for Diagnostic Purposes	18
Nuclease Stability of Aptamers in the Body and ADME Properties	19
TABLE 2 MODIFICATIONS EMPLOYED TO ENHANCE APTAMERS	20
NANOPARTICLES AND QUANTUM DOT LABELS	20
NEXT-GENERATION SEQUENCING	20
TABLE 3 CURRENT PRICE PER MEGABASE FOR 'NEXT GENERATION' DNA SEQUENCING (\$/MEGAPHASE)	21
SURFACE PLASMON RESONANCE AND BIOLAYER INTERFEROMETRY	21

TOPIC	PAGE NO.
BIOINFORMATICS	22
TRENDS IN ENABLING TECHNOLOGIES	23
APTAMERS AS DIAGNOSTIC SENSORS	23
SELF-REPORTING SENSORS	23
SENSOR PLATFORM TECHNOLOGIES	25
Homogeneous Solution Assays in Microplate Readers	25
Quartz Crystal Microbalance	25
Nano- and Microcantilever Sensors Using Aptamers	26
Surface Plasmon Resonance (SPR) and SPR Arrays	27
Biolayer Interferometry (BLI)	28
TRENDS IN APTAMERS AS DIAGNOSTICS	28
APTAMERS AS THERAPEUTICS	28
APTAMERS AS TARGETING AGENTS	30
APTAMERS AND INFECTIOUS DISEASE	30
APTAMER MODIFICATIONS	30
APTAMERS AS IMAGING LABELS	31
APPLICATION OF APTAMERS AS MODIFIERS OF SURGICAL IMPLANTS	31
WHOLE CELL SELEX	31
'CAPTAMERS'	32
VEGF APTAMERS	32
<i>TABLE 4 MEDICALLY RELEVANT APTAMER TARGETS</i>	33
MACUGEN'S PATH TO FDA APPROVAL	33
CLINICAL TRIALS INVOLVING APTAMERS	34
PRE-CLINICAL TRIAL STAGE	34
PHASE I TRIALS	35
PHASE II TRIALS	36
<i>TABLE 5 APTAMER CLINICAL TRIALS (C: COMPLETED, R: RECRUITING, A: ACTIVE, NOT RECRUITING, T: TERMINATED, W: WITHDRAWN, P: PENDING)</i>	37
APTAMER DELIVERY	43
APTAMERS AND AGE-RELATED MACULAR DEGENERATION (AMD)	43
Valeant Pharmaceuticals International, Inc. (Valeant)	43
Ophthotech	44
APTAMERS IN CANCER	45
Antisoma/Archemix	45
Aptamers to Biomarkers-Tenascin-C	45
Enzon Pharmaceuticals, Inc.	46
Archemix/Merck KGaA	46
Aptamer-Drug Conjugates	46
Aptagen	47
APTAMERS AS ANTICOAGULANTS	47
APTAMERS IN OTHER INDICATIONS	48
TRENDS IN APTAMERS AS THERAPEUTICS	48
<i>TABLE 6 EMERGING APPLICATIONS FOR APTAMERS IN THERAPEUTICS</i>	49
APTAMERS IN BIOSEPARATION	49
APTAMERS AS RESEARCH TOOLS	50
<i>TABLE 7 NUMBER OF NIH FUNDED GRANTS EMPLOYING APTAMERS, 2005-2011</i>	51
<i>TABLE 8 NIH FUNDING FOR DISEASES CONSIDERED AS POSSIBLE APPLICATIONS FOR APTAMERS, 2008-2013 (\$ MILLIONS)</i>	51

TOPIC	PAGE NO.
<i>TABLE 9 NIH FUNDING FOR TECHNOLOGIES CONSIDERED AS POSSIBLE APPLICATIONS FOR APTAMERS, 2008-2013 (\$ MILLIONS)</i>	51
<i>TABLE 10 TOTAL NIH FUNDING, 2005-2011 (\$ MILLIONS)</i>	52
<i>TABLE 11 NUMBER OF PUBLICATIONS IN ISI WEB OF KNOWLEDGE UNDER THE TOPIC "APTAMER," 2005-2012</i>	52
MARKET LEADERS (U.S.)	52
ARCHEMIX	52
Collaborations	53
OSI PHARMACEUTICALS	54
REGADO	54
OPHTHOTECH	55
MARKET LEADERS (INTERNATIONAL)	56
NOXXON	56
CHAPTER 5 MARKETS BY APPLICATIONS	60
INTRODUCTION	60
APPLICATION OF APTAMERS AS DIAGNOSTICS	60
APPLICATION OF APTAMERS IN HUMAN CLINICAL DIAGNOSTIC ASSAYS	60
Somalogic Somascan	61
APPLICATION OF APTAMERS IN ENVIRONMENTAL MONITORING AND FOOD AND WATER SAFETY	62
Application Example #1-Veterinary Residue Testing	62
<i>TABLE 12 EXAMPLE OF VETERINARY RESIDUE TESTS (ELISAS) OFFERED BY A LEADING U.S. VENDOR (ABRAXIS KITS, LLC)</i>	63
<i>TABLE 13 OTHER ENVIRONMENTAL ELISAS OFFERED BY ABRAXIS KITS, LLC1</i>	65
Application Example #2-Algal Toxin Sensing	66
APPLICATION OF APTAMERS IN VETERINARY DIAGNOSTICS	66
<i>TABLE 14 NUMBERS OF RESEARCH GRANTS FROM THE USDA ON ZOO NOTIC DISEASES</i>	67
<i>TABLE 15 USDA-SPONSORED RESEARCH GRANTS ON "APTAMERS"</i>	68
Application Example #3-Foot and Mouth Disease (FMD) Virus	69
Application Example #4-Leptospira Detection	71
OVERALL MARKET POTENTIAL OF APTAMERS IN DIAGNOSTICS AND ENVIRONMENTAL TESTING	71
<i>TABLE 16 U.S. DIAGNOSTICS AND TESTING MARKETS IN WHICH APTAMERS COULD PLAY A SIGNIFICANT ROLE, THROUGH 2017 (\$ MILLIONS)</i>	72
APPLICATION OF APTAMERS AS THERAPEUTICS	73
APTAMER DRUGS CURRENTLY ON THE MARKET	73
Pegaptanib	73
<i>TABLE 17 MARKET COMPARISON (MACUGEN, LUCENTIS, AND AVASTIN), 2004-2011</i>	73
PROJECTED TO REACH THE MARKET WITHIN FIVE YEARS	73
E10030	73
Nox-A-12	74
Nox-E-36	74
NU-172	74
REG1	74
CONDITIONS TARGETED BY APTAMERS	75
Stem Cell Technology	75
Acute Coronary Syndrome	75
AMD	75

TOPIC	PAGE NO.
APPLICATION OF APTAMERS AS DRUG DELIVERY VEHICLES IN CANCER	76
<i>TABLE 18 GLOBAL THERAPEUTICS MARKETS ADDRESSABLE IN NEAR TERM BY APTAMERS, THROUGH 2017 (\$ MILLIONS)</i>	77
<i>TABLE 19 CANCER THERAPEUTICS MARKETS IN THE U.S. BY SUBINDICATION, THROUGH 2017 (\$ BILLIONS)</i>	78
APPLICATION OF APTAMERS AS MODIFIERS OF SURGICAL IMPLANTS	78
APPLICATION OF APTAMERS IN BIOSEPARATION PROCESSES	78
CHAPTER 6 INTELLECTUAL PROPERTY ANALYSIS	81
BRIEF HISTORY	81
<i>APTAMERS AND SELEX AS PATENTABLE SUBJECT MATTER</i>	81
ORIGINAL APTAMER AND SELEX PATENTS	83
VALIDITY, LEGAL ACTION, AND INFRINGEMENT	84
<i>TABLE 20 MAJOR HOLDERS OF APTAMER/SELEX IP</i>	85
<i>TABLE 21 STRATEGIC (KNOWN OR PUBLISHED) TECHNOLOGY AND R&D ALLIANCES</i>	86
<i>TABLE 22 SELECTED APTAMER PATENTS</i>	87
<i>TABLE 23 SELECTED U.S. PATENT APPLICATIONS FOR THERAPEUTIC APTAMERS</i>	96
CHAPTER 7 INDUSTRY STRUCTURE AND COMPETITIVE ANALYSIS	98
APTAMER TECHNOLOGY IN THE BIOSCIENCE INDUSTRY	98
<i>FIGURE 2 COMPARISON OF TRADITIONAL SMALL MOLECULE, PROTEIN, AND APTAMER-BASED MODALITIES</i>	98
THE EVOLVING APTAMER IP LANDSCAPE	99
APTAMERS AND THE BIOTECHNOLOGY ECOSYSTEM	100
THERAPEUTICS	100
DIAGNOSTICS	101
OTHER APPLICATIONS	101
SIGNIFICANT OBSTACLES TO THE APTAMER INDUSTRY	101
CURRENT APTAMER MARKET LEADERS	102
<i>FIGURE 3 APTAMER INDUSTRY STRUCTURE</i>	102
PORTER MODEL ANALYSIS OF THE APTAMER INDUSTRY	105
THREAT OF SUBSTITUTE PRODUCTS IS HIGH	105
THREAT OF NEW ENTRANTS IS LOW (BUT LIKELY TO INCREASE)	105
BARGAINING POWER OF SUPPLIERS IS LOW	105
BARGAINING POWER OF CUSTOMERS IS HIGH	105
INTRA-INDUSTRY COMPETITION IS LOW	105
<i>FIGURE 4 PORTER ANALYSIS OF THE APTAMER INDUSTRY</i>	105
CHAPTER 8 COMPANY PROFILES	108
ABRAXIS KITS, LLC	108
ALIMERA SCIENCES	108
ALNYLAM PHARMACEUTICALS	109
AM BIOTECHNOLOGIES, LLC	109
ANGIOGENIX	110
APTAGEN, LLC	110
APTAMER SCIENCES INC.	111
APTASOL (APTAMER SOLUTIONS) LTD	112
BASE PAIR BIOTECHNOLOGIES, INC.	112

TOPIC	PAGE NO.
CYNVENIO BIOSYSTEMS, INC.	113
CYTOGENIX, INC.	114
ENVIROLOGIX, INC.	114
ENZON PHARMACEUTICALS INC.	114
EYETECH	115
ISIS PHARMACEUTICALS	115
mitsui & co. (U.S.A.), INC.	115
NEOVENTURES	115
NOXXON	116
OPHTHOTECH CORPORATION	118
OSI PHARMACEUTICALS, INC.	118
REGADO BIOSCIENCES	119
RINA GMBH	119
QUEST DIAGNOSTICS	120
SAW INSTRUMENTS GMBH	121
SOMALOGIC, INC.	121
SUMITOMO BAKELITE-NORTH AMERICA, INC.	122
CHAPTER 9 REFERENCES	124
REFERENCES	124

LIST OF TABLES

TABLE HEADING	PAGE NO.
SUMMARY TABLE A GLOBAL MARKETS FOR APTAMERS, THROUGH 2017 (\$ MILLIONS)*	5
SUMMARY TABLE B POTENTIAL MARKETS FOR APTAMER THERAPEUTICS, THROUGH 2017 (\$ MILLIONS)	6
SUMMARY TABLE C HISTORICAL U.S. SALES FOR MACUGEN, THE FIRST FDA-APPROVED APTAMER DRUG, 2005-2011 (\$ MILLIONS)	7
SUMMARY TABLE D POTENTIAL MARKETS FOR APTAMER-BASED IN-VITRO DIAGNOSTICS, THROUGH 2017 (\$ MILLIONS)	8
TABLE 1 APTAMERS AND ANTIBODIES: KEY DIFFERENCES	12
TABLE 2 MODIFICATIONS EMPLOYED TO ENHANCE APTAMERS	20
TABLE 3 CURRENT PRICE PER MEGABASE FOR 'NEXT GENERATION' DNA SEQUENCING (\$/MEGAPHASE)	21
TABLE 4 MEDICALLY RELEVANT APTAMER TARGETS	33
TABLE 5 APTAMER CLINICAL TRIALS (C: COMPLETED, R: RECRUITING, A: ACTIVE, NOT RECRUITING, T: TERMINATED, W: WITHDRAWN, P: PENDING)	37
TABLE 6 EMERGING APPLICATIONS FOR APTAMERS IN THERAPEUTICS	49
TABLE 7 NUMBER OF NIH FUNDED GRANTS EMPLOYING APTAMERS, 2005-2011	51
TABLE 8 NIH FUNDING FOR DISEASES CONSIDERED AS POSSIBLE APPLICATIONS FOR APTAMERS, 2008-2013 (\$ MILLIONS)	51
TABLE 9 NIH FUNDING FOR TECHNOLOGIES CONSIDERED AS POSSIBLE APPLICATIONS FOR APTAMERS, 2008-2013 (\$ MILLIONS)	51
TABLE 10 TOTAL NIH FUNDING, 2005-2011 (\$ MILLIONS)	52
TABLE 11 NUMBER OF PUBLICATIONS IN ISI WEB OF KNOWLEDGE UNDER THE TOPIC "APTAMER," 2005-2012	52
TABLE 12 EXAMPLE OF VETERINARY RESIDUE TESTS (ELISAS) OFFERED BY A LEADING U.S. VENDOR (ABRAXIS KITS, LLC)	63
TABLE 13 OTHER ENVIRONMENTAL ELISAS OFFERED BY ABRAXIS KITS, LLC1	65
TABLE 14 NUMBERS OF RESEARCH GRANTS FROM THE USDA ON ZOO NOTIC DISEASES	67
TABLE 15 USDA-SPONSORED RESEARCH GRANTS ON "APTAMERS"	68
TABLE 16 U.S. DIAGNOSTICS AND TESTING MARKETS IN WHICH APTAMERS COULD PLAY A SIGNIFICANT ROLE, THROUGH 2017 (\$ MILLIONS)	72
TABLE 17 MARKET COMPARISON (MACUGEN, LUCENTIS, AND AVASTIN), 2004-2011	73
TABLE 18 GLOBAL THERAPEUTICS MARKETS ADDRESSABLE IN NEAR TERM BY APTAMERS, THROUGH 2017 (\$ MILLIONS)	77
TABLE 19 CANCER THERAPEUTICS MARKETS IN THE U.S. BY SUBINDICATION, THROUGH 2017 (\$ BILLIONS)	78
TABLE 20 MAJOR HOLDERS OF APTAMER/SELEX IP	85
TABLE 21 STRATEGIC (KNOWN OR PUBLISHED) TECHNOLOGY AND R&D ALLIANCES	86
TABLE 22 SELECTED APTAMER PATENTS	87
TABLE 23 SELECTED U.S. PATENT APPLICATIONS FOR THERAPEUTIC APTAMERS	96

LIST OF FIGURES

FIGURE TITLE	PAGE NO.
SUMMARY FIGURE GLOBAL MARKETS FOR APTAMERS, 2011-2017 (\$ MILLIONS)*	5
FIGURE 1 SIMPLIFIED SCHEMATIC OF SELEX PROCESS FOR IN-VITRO SELECTION OF (DNA) APTAMERS	10
FIGURE 2 COMPARISON OF TRADITIONAL SMALL MOLECULE, PROTEIN, AND APTAMER-BASED MODALITIES	98
FIGURE 3 APTAMER INDUSTRY STRUCTURE	102
FIGURE 4 PORTER ANALYSIS OF THE APTAMER INDUSTRY	105