

BIOLOGIC THERAPEUTIC DRUGS: TECHNOLOGIES AND GLOBAL MARKETS



BIO079B
January 2013

Jackson Highsmith
Project Analyst

ISBN: 0-89336-713-3

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
METHODOLOGY AND INFORMATION SOURCES	3
ANALYST'S CREDENTIALS	3
RELATED REPORTS	3
BCC ON-LINE SERVICES	3
DISCLAIMER	4
CHAPTER 2 EXECUTIVE SUMMARY	6
<i>SUMMARY TABLE GLOBAL BIOLOGICS MARKET FORECAST BY TYPE OF PRODUCT, THROUGH 2017 (\$ MILLIONS)</i>	6
<i>SUMMARY FIGURE GLOBAL BIOLOGICS MARKET FORECAST BY TYPE OF PRODUCT, 2009-2017 (\$ MILLIONS)</i>	6
CHAPTER 3 OVERVIEW	9
BIOLOGICS NEW PRODUCTS IN DISEASE TREATMENT	9
<i>TABLE 1 SUBCLASSES OF BIOLOGICS DRUGS</i>	10
MONOCLONAL ANTIBODIES	10
<i>FIGURE 1 DIAGRAM OF TYPICAL ANTIBODY STRUCTURE</i>	11
THERAPEUTIC PROTEINS	12
HEMOPOIETIC GROWTH FACTORS (HGFS)	12
Cytokines	13
Blood Factors	13
VACCINES	14
Traditional Vaccines	14
Novel Vaccine Technologies	14
MAJOR BIOLOGICS PRODUCT CLASSES	15
<i>TABLE 2 MONOCLONAL ANTIBODY AND THERAPEUTIC PROTEIN DRUGS SUBCLASSES</i>	15
<i>TABLE 3 GLOBAL BIOLOGICS MARKET REVENUE, THROUGH 2017 (\$ MILLIONS)</i>	15
CHALLENGES WITH RNAI	16
ORPHAN DRUG DESIGNATION	17
CHAPTER 4 BIOPHARMACEUTICAL INDUSTRY AND COMPETITIVE ANALYSIS	20
BIOPHARMACEUTICAL INDUSTRY STRUCTURE	20
THE ORIGINS OF BIOTECHNOLOGY	20
INVOLVEMENT OF LARGE PHARMACEUTICAL COMPANIES	21
CHAPTER 5 BIOLOGICS MARKET OVERVIEW	23
<i>TABLE 4 MAJOR BIOPHARMACEUTICAL PLAYERS BY REVENUE, 2011 (\$ MILLIONS)</i>	23
<i>TABLE 5 TOP 25 BIOPHARMACEUTICAL PRODUCTS BY REVENUE, 2011 (\$ MILLIONS)</i>	24
<i>TABLE 6 TOP 50 REVENUE GENERATING BIOPHARMACEUTICAL PRODUCTS, 2010 (\$ MILLIONS)</i>	25
MONOCLONAL ANTIBODIES	26

TOPIC	PAGE NO.
TABLE 7 GLOBAL MARKET FORECAST FOR MABS, THROUGH 2017 (\$ MILLIONS)	27
TABLE 8 LEADING MONOCLONAL ANTIBODY PRODUCTS, 2011 (\$ MILLIONS)	27
TABLE 9 VOLUME OF MAMMALIAN CELL CULTURE PRODUCED MABS, 2012 AND 2017	28
CONJUGATED ANTIBODIES	29
ANTIBODY FRAGMENTS	30
LARGE PHARMACEUTICAL COMPANIES AND BIOPHARMA	30
LARGE PHARMACEUTICAL COMPANY CONSORTIUM FORMED	31
THERAPEUTIC PROTEINS	31
TABLE 10 REVENUE FOR THERAPEUTIC PROTEINS SEGMENT OF BIOLOGICS MARKET, THROUGH 2017 (\$ MILLIONS)	32
HEMOPOIETIC GROWTH FACTORS	32
TABLE 11 LEADING HEMOPOIETIC GROWTH FACTOR BIOLOGIC PRODUCTS (\$ MILLIONS)	33
Hemopoietic Growth Factor Clinical Trials	34
TABLE 12 CLINICAL TRIALS ON G-CSF RECEPTORS IN 2012	34
CYTOKINES	35
TABLE 13 CLINICAL TRIALS ON CYTOKINES UNDERWAY IN 2012	36
ANTIHEMOPHILIA PRODUCTS	37
TABLE 14 TOP 30 REVENUE-GENERATING THERAPEUTIC PROTEIN PRODUCTS, 2011 (\$ MILLIONS)	37
VACCINES	39
VACCINE MARKET REVENUES	39
TABLE 15 VACCINE REVENUES, THROUGH 2017 (\$ MILLIONS)	40
TABLE 16 CLINICAL TRIALS ON VACCINES, 2012	40
CHAPTER 6 IMPACT OF BIOSIMILAR DRUGS ON BIOLOGICS MARKET	43
TABLE 17 PATENT AND MARKETING EXCLUSIVITY EXPIRATION FOR TOP SELLING BIOLOGICS	44
TABLE 18 NUMBER OF BIOSIMILARS PREDICTED TO BE LAUNCHED DURING PERIOD 2012-2019	44
TABLE 19 TOP 10 BIOLOGICS DRUGS IN (2011 REVENUES) WITH GREATEST LEVEL OF BIOSIMILAR COMPETITION (\$ MILLIONS)	45
RATIONALE FOR BIOSIMILAR DEVELOPMENT	45
ERYTHROPOIETIN	45
GRANULOCYTE-COLONY STIMULATING FACTOR	46
INTERFERONS	46
HUMAN GROWTH HORMONE	46
OPPORTUNITY AND THREAT FROM BIOSIMILARS	46
MARKET TRENDS: GROWTH DRIVERS AND RESISTORS	47
BIOSIMILARS: REGULATORY UPDATE	48
U.S. FDA	48
EUROPEAN BIOSIMILAR REGULATORY GUIDANCE	48
CHAPTER 7 MAJOR PLAYERS IN BIOLOGIC AND BIOSIMILARS DRUG MARKET	51
MONOCLONAL ANTIBODIES	51
TABLE 20 TOP 10 SELLING MABS IN 2011	51
TABLE 21 MAJOR PLAYERS (BY REVENUE) IN MAB MARKET IN 2011 (\$ MILLIONS)	52
THERAPEUTIC PROTEINS	52
TABLE 22 TOP 10 THERAPEUTIC PROTEIN PRODUCTS, 2011 (\$ MILLIONS)	53

TOPIC	PAGE NO.
<i>TABLE 23 MAJOR PLAYERS (BY REVENUE) IN THE THERAPEUTIC PROTEINS MARKET, 2011 (\$ MILLIONS)</i>	53
VACCINES	54
<i>TABLE 24 TOP 10 VACCINES BY REVENUE, 2011 (\$ MILLIONS)</i>	55
CHAPTER 8 GEOGRAPHIC DISTRIBUTION OF BIOLOGICS MARKET	57
GEOGRAPHIC MARKET ANALYSIS	57
<i>TABLE 25 GEOGRAPHIC DISTRIBUTION OF TOTAL BIOLOGICS MARKET, THROUGH 2017 (\$ MILLIONS, % OF TOTAL)</i>	58
CHAPTER 9 PIPELINE ANALYSIS	60
<i>TABLE 26 BIOLOGIC DRUGS OBTAINING FDA APPROVAL FROM 2010 TO 2012</i>	60
BIOLOGICS IN COMPANY PIPELINES 2012	61
AMGEN	61
<i>TABLE 27 AMGEN BIOLOGICS PIPELINE, 2012</i>	61
ROCHE	62
<i>TABLE 28 ROCHE/GENENTECH/CHUGAI BIOLOGICS PIPELINE, 2012</i>	62
BAYER	63
<i>TABLE 29 BAYER BIOLOGICS PIPELINE, 2012</i>	63
NOVO NORDISK	64
<i>TABLE 30 NOVO NORDISK BIOLOGICS PIPELINE, 2012</i>	64
MERCK	65
<i>TABLE 31 MERCK BIOLOGICS PIPELINE, 2012</i>	65
PFIZER	65
<i>TABLE 32 PFIZER BIOLOGICS PIPELINE, 2012</i>	66
BIOGEN IDEC	66
<i>TABLE 33 BIOGEN IDEC BIOLOGICS PIPELINE, 2012</i>	67
SANOFI	67
<i>TABLE 34 SANOFI BIOLOGICS PIPELINE, 2012</i>	68
CHAPTER 10 BIOLOGICS CLINICAL TRIALS	70
<i>TABLE 35 DESCRIPTION OF PHASES OF CLINICAL TRIALS REQUIRED FOR NEW DRUG APPROVAL</i>	70
CANCER BIOLOGIC DRUGS	71
<i>TABLE 36 LIST (PARTIAL) OF BIOLOGIC DRUGS IN CLINICAL TRIAL FOR CANCER TREATMENT, 2012</i>	71
GASTROINTESTINAL AND RELATED DISEASES	74
<i>TABLE 37 LIST (PARTIAL) OF BIOLOGIC DRUGS IN CLINICAL TRIAL FOR GI AND RELATED DISEASE TREATMENT, 2012</i>	74
HEART DISEASE	75
<i>TABLE 38 LIST (PARTIAL) OF BIOLOGIC DRUGS IN CLINICAL TRIAL FOR HEART AND RELATED DISEASE TREATMENT, 2012</i>	76
CHAPTER 11 MERGER AND ACQUISITIONS IN BIOLOGICS AREA	78
<i>TABLE 39 LICENSING, DEVELOPMENT AGREEMENTS, ACQUISITIONS AND PARTNERSHIPS IN BIOLOGICS</i>	78
<i>TABLE 40 LICENSING, DEVELOPMENT AGREEMENTS, ACQUISITIONS AND PARTNERSHIPS IN BIOLOGICS (CONTINUED)</i>	82

TOPIC	PAGE NO.
CHAPTER 12 PATENTS FOR BIOLOGIC DRUGS	90
MONOCLONAL ANTIBODY PATENTS	90
<i>TABLE 41 U.S. PATENTS FOR MONOCLONAL ANTIBODIES</i>	90
THERAPEUTIC PROTEIN PATENTS	93
<i>TABLE 42 PATENTS ISSUED FOR THERAPEUTIC PROTEINS</i>	93
VACCINE PATENTS	96
<i>TABLE 43 PATENTS ISSUED FOR VACCINES (OR VACCINE RELATED PRODUCTS) ASSOCIATED WITH BIOLOGICALS</i>	96
CHAPTER 13 BIOLOGICS MANUFACTURING	100
BIOPHARMACEUTICAL MANUFACTURING PROCESS	100
THE PREPARATION PROCESS	101
Cell Banking and Seed Culture	101
Production	101
Cell Culture Formats	101
Batch and Continuous Processing	102
Perfusion and Fed-Batch Mode	102
<i>TABLE 44 BIOLOGICS PRODUCTS USING PERFUSION METHOD</i>	103
Perfusion Methods	103
Fed-Batch Methods	103
<i>TABLE 45 BIOLOGICS THERAPEUTIC PRODUCTS USING FED-BATCH METHOD</i>	104
Harvest and Concentration	104
THE FINISHING PROCESS	104
PURIFICATION OF BIOPHARMACEUTICALS	105
AUTOMATED PROCESSING SYSTEMS-SKIDS	106
FORMULATION	107
LYOPHILIZATION	107
CRYOGRANULATION	107
SPRAY DRYING	107
UNDERCOOLING	108
PROCESS INTEGRATION: THE CRITICAL ACTIVITY	108
EXPRESSION SYSTEMS FOR THERAPEUTIC PROTEIN PRODUCTION	108
MICROBIAL THERAPEUTIC PROTEIN PRODUCTION	109
E.COLI ADVANTAGES FOR MICROBIAL PRODUCTION	109
Fast Accumulation	109
Safety Advantage	109
Growth on Inexpensive Carbon Sources	109
Propensity for High-Cell-Density Fermentations	109
Simple Process Scale-Up	110
<i>TABLE 46 MARKETED BIOPHARMACEUTICALS USING E.COLI EXPRESSION SYSTEM</i>	110
MAMMALIAN CELL THERAPEUTIC PROTEIN PRODUCTION	110
<i>TABLE 47 MARKETED BIOPHARMACEUTICALS USING ANIMAL CELL LINE EXPRESSION SYSTEM</i>	111
EMERGING PRODUCTION SYSTEMS	112
<i>PICHIA</i> AND FILAMENTOUS FUNGI	112
TRANSGENIC PROTEIN PRODUCTION SYSTEMS	113
TRANSGENIC PLANTS	113

TOPIC	PAGE NO.
<i>TABLE 48 PLANT-BASED TRANSGENIC COMPANIES AND THEIR PIPELINES OF RECOMBINANT PROTEINS</i>	114
TRANSGENIC ANIMALS	115
<i>TABLE 49 THERAPEUTIC PROTEINS PRODUCED IN TRANSGENIC ANIMALS</i>	115
<i>TABLE 50 MARKETED BIOPHARMACEUTICALS USING MURINE (MOUSE) HYBRIDOMA EXPRESSION SYSTEM</i>	117
CHAPTER 14 COMPANY PROFILES	119
ABBOTT LABORATORIES	119
BIOLOGICAL PRODUCTS	119
ADVAXIS INC.	119
BIOLOGICAL PRODUCTS	120
AGENNIX AG	120
AKEBIA THERAPEUTICS INC.	121
AMGEN INC.	121
BIOLOGICAL PRODUCTS	121
APOGENIX GMBH	122
BAXTER BIOSCIENCE INC.	122
BIOLOGICAL PRODUCTS	123
BAYER SCHERING PHARMA AG	123
BIOLOGICAL PRODUCTS	123
BIOGEN IDEC INC.	124
BIOLOGICAL PRODUCTS	124
BIOINVENT INTERNATIONAL AB	124
BIOLOGICAL PRODUCTS	125
BIOVITRUM AB	125
CELLDEX THERAPEUTICS INC.	125
BIOLOGICAL PRODUCTS	126
CHUGAI PHARMACEUTICALS	126
BIOLOGICAL PRODUCTS	126
CSL BEHRING	126
BIOLOGICAL PRODUCTS	127
CYTHERIS SA	127
DEBIOPHARM GROUP	127
DENDREON CORPORATION	128
DYAX CORP.	128
BIOLOGICAL PRODUCTS	129
ELI LILLY & CO.	129
BIOLOGICAL PRODUCTS	129
ERYTECH PHARMA	130
BIOLOGICAL PRODUCTS	130
GENENTECH INC.	130
BIOLOGICAL PRODUCTS	131
GENMAB A/S	131
BIOLOGICAL PRODUCTS	131
GENZYME CORPORATION	132
BIOLOGICAL PRODUCTS	132
GLAXOSMITHKLINE PLC	132

TOPIC	PAGE NO.
BIOLOGICAL PRODUCTS	133
GLYCOTOPE GMBH	133
BIOLOGICAL PRODUCTS	134
H. LUNDBECK A/S	134
CURRENT PRODUCTS	134
HAWAII BIOTECH INC.	135
HELIX BIOPHARMA CORPORATION	135
HUMAN GENOME SCIENCES INC.	135
BIOLOGICAL PRODUCTS	136
IMCLONE SYSTEMS INC.	136
BIOLOGICAL PRODUCTS	137
IMMUNOGEN INC.	137
BIOLOGICAL PRODUCTS	137
IMMUNOVACCINE TECHNOLOGIES INC.	138
BIOLOGICAL PRODUCTS	138
IMMUTEP S.A.	138
BIOLOGICAL PRODUCTS	139
INNATE PHARMA	139
BIOLOGICAL PRODUCTS	139
INTERCELL AG	140
BIOLOGICAL PRODUCTS	140
IPSEN	140
BIOLOGICAL PRODUCTS	141
MEDAREX INC.	141
BIOLOGICAL PRODUCTS	141
MERCK & CO. INC. USA	142
BIOLOGICAL PRODUCTS	142
MERCK SERONO S.A.	142
BIOLOGICAL PRODUCTS	142
NOVARTIS AG	143
BIOLOGICAL PRODUCTS	143
NOVO NORDISK A/S	143
BIOLOGICAL PRODUCTS	144
OCTAPHARMA AG	144
BIOLOGICAL PRODUCTS	144
PFIZER INC.	145
BIOLOGICAL PRODUCTS	145
PHOSPHAGENICS LIMITED	145
PROTEON THERAPEUTICS INC.	146
ROCHE LTD.	146
BIOLOGICAL PRODUCTS	146
SANOFI-AVENTIS	147
BIOLOGICAL PRODUCTS	147
SEATTLE GENETICS INC.	147
BIOLOGICAL PRODUCTS	148
SHIRE PLC	148
BIOLOGICAL PRODUCTS	149

TOPIC	PAGE NO.
SOLIGENIX INC.	149
TEVA PHARMACEUTICAL INDUSTRIES LTD.	149
BIOLOGICAL PRODUCTS	150
THROMBOGENICS NV	150
BIOLOGICAL PRODUCTS	151
TOLERX INC.	151
TRIPEP AB	151
TRUBION PHARMACEUTICALS INC.	152
UCB S. A.	152
BIOLOGICAL PRODUCTS	153
VICAL INC.	153
BIOLOGICAL PRODUCTS	154
WILEX AG	154
XCELLEREX INC.	154
ZYMOGENETICS INC.	155
BIOLOGICAL PRODUCTS	155

LIST OF TABLES

TABLE HEADING	PAGE NO.
SUMMARY TABLE GLOBAL BIOLOGICS MARKET FORECAST BY TYPE OF PRODUCT, THROUGH 2017 (\$ MILLIONS)	6
TABLE 1 SUBCLASSES OF BIOLOGICS DRUGS	10
TABLE 2 MONOCLONAL ANTIBODY AND THERAPEUTIC PROTEIN DRUGS SUBCLASSES	15
TABLE 3 GLOBAL BIOLOGICS MARKET REVENUE, THROUGH 2017 (\$ MILLIONS)	15
TABLE 4 MAJOR BIOPHARMACEUTICAL PLAYERS BY REVENUE, 2011 (\$ MILLIONS)	23
TABLE 5 TOP 25 BIOPHARMACEUTICAL PRODUCTS BY REVENUE, 2011 (\$ MILLIONS)	24
TABLE 6 TOP 50 REVENUE GENERATING BIOPHARMACEUTICAL PRODUCTS, 2010 (\$ MILLIONS)	25
TABLE 7 GLOBAL MARKET FORECAST FOR MABS, THROUGH 2017 (\$ MILLIONS)	27
TABLE 8 LEADING MONOCLONAL ANTIBODY PRODUCTS, 2011 (\$ MILLIONS)	27
TABLE 9 VOLUME OF MAMMALIAN CELL CULTURE PRODUCED MABS, 2012 AND 2017	28
TABLE 10 REVENUE FOR THERAPEUTIC PROTEINS SEGMENT OF BIOLOGICS MARKET, THROUGH 2017 (\$ MILLIONS)	32
TABLE 11 LEADING HEMOPOIETIC GROWTH FACTOR BIOLOGIC PRODUCTS (\$ MILLIONS)	33
TABLE 12 CLINICAL TRIALS ON G-CSF RECEPTORS IN 2012	34
TABLE 13 CLINICAL TRIALS ON CYTOKINES UNDERWAY IN 2012	36
TABLE 14 TOP 30 REVENUE-GENERATING THERAPEUTIC PROTEIN PRODUCTS, 2011 (\$ MILLIONS)	37
TABLE 15 VACCINE REVENUES, THROUGH 2017 (\$ MILLIONS)	40
TABLE 16 CLINICAL TRIALS ON VACCINES, 2012	40
TABLE 17 PATENT AND MARKETING EXCLUSIVITY EXPIRATION FOR TOP SELLING BIOLOGICS	44
TABLE 18 NUMBER OF BIOSIMILARS PREDICTED TO BE LAUNCHED DURING PERIOD 2012-2019	44
TABLE 19 TOP 10 BIOLOGICS DRUGS IN (2011 REVENUES) WITH GREATEST LEVEL OF BIOSIMILAR COMPETITION (\$ MILLIONS)	45
TABLE 20 TOP 10 SELLING MABS IN 2011	51
TABLE 21 MAJOR PLAYERS (BY REVENUE) IN MAB MARKET IN 2011 (\$ MILLIONS)	52
TABLE 22 TOP 10 THERAPEUTIC PROTEIN PRODUCTS, 2011 (\$ MILLIONS)	53
TABLE 23 MAJOR PLAYERS (BY REVENUE) IN THE THERAPEUTIC PROTEINS MARKET, 2011 (\$ MILLIONS)	53
TABLE 24 TOP 10 VACCINES BY REVENUE, 2011 (\$ MILLIONS)	55
TABLE 25 GEOGRAPHIC DISTRIBUTION OF TOTAL BIOLOGICS MARKET, THROUGH 2017 (\$ MILLIONS, % OF TOTAL)	58
TABLE 26 BIOLOGIC DRUGS OBTAINING FDA APPROVAL FROM 2010 TO 2012	60
TABLE 27 AMGEN BIOLOGICS PIPELINE, 2012	61
TABLE 28 ROCHE/GENENTECH/CHUGAI BIOLOGICS PIPELINE, 2012	62
TABLE 29 BAYER BIOLOGICS PIPELINE, 2012	63
TABLE 30 NOVO NORDISK BIOLOGICS PIPELINE, 2012	64
TABLE 31 MERCK BIOLOGICS PIPELINE, 2012	65
TABLE 32 PFIZER BIOLOGICS PIPELINE, 2012	66
TABLE 33 BIOGEN IDEC BIOLOGICS PIPELINE, 2012	67
TABLE 34 SANOFI BIOLOGICS PIPELINE, 2012	68
TABLE 35 DESCRIPTION OF PHASES OF CLINICAL TRIALS REQUIRED FOR NEW DRUG APPROVAL	70
TABLE 36 LIST (PARTIAL) OF BIOLOGIC DRUGS IN CLINICAL TRIAL FOR CANCER TREATMENT, 2012	71

TABLE HEADING	PAGE NO.
TABLE 37 LIST (PARTIAL) OF BIOLOGIC DRUGS IN CLINICAL TRIAL FOR GI AND RELATED DISEASE TREATMENT, 2012	74
TABLE 38 LIST (PARTIAL) OF BIOLOGIC DRUGS IN CLINICAL TRIAL FOR HEART AND RELATED DISEASE TREATMENT, 2012	76
TABLE 39 LICENSING, DEVELOPMENT AGREEMENTS, ACQUISITIONS AND PARTNERSHIPS IN BIOLOGICS	78
TABLE 40 LICENSING, DEVELOPMENT AGREEMENTS, ACQUISITIONS AND PARTNERSHIPS IN BIOLOGICS (CONTINUED)	82
TABLE 41 U.S. PATENTS FOR MONOCLONAL ANTIBODIES	90
TABLE 42 PATENTS ISSUED FOR THERAPEUTIC PROTEINS	93
TABLE 43 PATENTS ISSUED FOR VACCINES (OR VACCINE RELATED PRODUCTS) ASSOCIATED WITH BIOLOGICALS	96
TABLE 44 BIOLOGICS PRODUCTS USING PERFUSION METHOD	103
TABLE 45 BIOLOGICS THERAPEUTIC PRODUCTS USING FED-BATCH METHOD	104
TABLE 46 MARKETED BIOPHARMACEUTICALS USING <i>E.COLI</i> EXPRESSION SYSTEM	110
TABLE 47 MARKETED BIOPHARMACEUTICALS USING ANIMAL CELL LINE EXPRESSION SYSTEM	111
TABLE 48 PLANT-BASED TRANSGENIC COMPANIES AND THEIR PIPELINES OF RECOMBINANT PROTEINS	114
TABLE 49 THERAPEUTIC PROTEINS PRODUCED IN TRANSGENIC ANIMALS	115
TABLE 50 MARKETED BIOPHARMACEUTICALS USING MURINE (MOUSE) HYBRIDOMA EXPRESSION SYSTEM	117

LIST OF FIGURES

FIGURE TITLE	PAGE NO.
SUMMARY FIGURE GLOBAL BIOLOGICS MARKET FORECAST BY TYPE OF PRODUCT, 2009-2017 (\$ MILLIONS)	6
FIGURE 1 DIAGRAM OF TYPICAL ANTIBODY STRUCTURE	11