INTRODUCTION xv
STUDY OBJECTIVES xv
SCOPE AND CONTENT xv
METHODOLOGY AND SOURCES xvi
AUDIENCE FOR THIS REPORT xvi
ANALYST CREDENTIALS xvii
RELATED BCC PUBLICATIONS xvii
BCC ONLINE SERVICES xvii
DISCLAIMER xviii

EXECUTIVE SUMMARY xix
SUMMARY TABLE WORLDWIDE MARKET FOR PROTEIN DRUGS, THROUGH 2011 ($ BILLION) ..... *xix*
SUMMARY FIGURE WORLDWIDE SALES FORECAST FOR PROTEIN DRUGS, 2006 AND 2011 ($ BILLIONS) ..... *xx*

OVERVIEW 1
THE MAKING OF A PROTEIN 1
ADVANTAGES OF PROTEIN-BASED DRUGS 1
DRAWBACKS TO PROTEIN-BASED DRUGS 2
DRUG DELIVERY 2
Aerosol 2
TABLE 1 COMPANIES INVOLVED IN DEVELOPMENT OF PULMONARY DELIVERY SYSTEMS *3*
Oral Administration 3
Implanted Drug Delivery 4
Smart Materials 4
Sustained Delivery 4
Injection/I.V. 5
DRUG DISCOVERY—DEVELOPMENT OF PROTEIN BASED DRUGS 5
PROTEIN IMMUNOGENICITY 6
PROTEOMICS 6
PROTEIN CHIPS 7
SYNTHETIC BIOLOGY 7
Directed Evolution 7
Directed Evolution (Continued) 8
SOURCES 9
RECOMBINANT PROTEIN THERAPEUTICS 9
TABLE 2 TOP TEN RECOMBINANT THERAPEUTIC PROTEINS AND THEIR GLOBAL SALES, 2001-2005 ($ MILLIONS) *9*
HARVESTED PROTEINS 10
Human 10
Animal 10

Plant 11
Microbial 12
TYPES OF PROTEIN BASED DRUGS 12
Replacement proteins 12
Antibodies 12
Peptides versus whole proteins 13

INDUSTRY BACKGROUND 14
THE PHARMACEUTICAL INDUSTRY 14
TABLE 3 GLOBAL PHARMACEUTICAL SALES, 1998–2005 ($ BILLIONS) *15*
TABLE 4 LEADING PRODUCTS BY GLOBAL PHARMACEUTICAL SALES, 2005 ($ BILLIONS) *15*
THE FDA 16
GENERICS MARKET 16
GENERICS MARKET (CONTINUED) 17
TABLE 5 TOP PROTEIN DRUGS TO GO OFF PATENT, 2006–2010 ..... *18*
TABLE 6 U.S. GENERIC DRUG MARKET SHARE (DISPENSED PRESCRIPTIONS) (%) *18*
TECHNOLOGICAL ADVANCES OF NOTE 19
REAL TIME MONITORING OF PROTEIN PRODUCTION 19
PROTEIN FOLDING 19
PROTEIN PHOSPHORYLATION 20
FDA APPROVAL PROCESS 20
TABLE 7 COSTS OF EACH STAGE OF FDA APPROVAL PROCESS ($ MILLIONS) *21*
DEPENDENT INDUSTRIES: RESEARCH TOOLS 21
AUTOMATION 21
Expression 22
CELL CULTURE 22
TABLE 8 COMPANIES INVOLVED IN PROVIDING CELL CULTURE REAGENTS, EQUIPMENT AND CELL LINES, 2003-2005 ($ MILLION) *23*
TABLE 9 PRIVATE COMPANIES SELLING CELL CULTURE REAGENTS AND EQUIPMENT *24*
PROTEIN ASSAY KITS AND EQUIPMENT 24
TABLE 10 MARKET SHARES OF COMPANIES SELLING PROTEIN ASSAY KITS AND EQUIPMENT (%) *25*
Protein Refolding 26
PROTEIN ARRAYS 27
TABLE 11 MARKET SHARE OF COMPANIES SELLING PROTEIN ARRAYS *28*
PROTEIN ARRAYS (CONTINUED) 29
MICROWELL PLATES 30

TABLE 12 COMPANIES INVOLVED IN PRODUCTION OF MICROWELL PLATES *30*
IMAGING 31
Fluorescence 31
TABLE 13 SALES OF COMPANIES OFFERING BIOLOGICAL STAINS, DYES AND OTHER IMAGING REAGENTS, 2003-2006 ($ MILLION) *31*
ION CHANNELS 32
Ion Channels (Continued) 33
TABLE 14 COMPANIES INVOLVED IN ION CHANNELS AND PATCH CLAMPING SYSTEMS *34*
Designer Cells 34
X-ray Crystallography 35
Spectroscopy 35
PURIFICATION/SEPARATION 36
Separation 36
Spectroscopy 36
Flow Cytometry 37
TABLE 15 COMPANIES INVOLVED IN FLOW CYTOMETRY TECHNOLOGY *37*
Western Blots 37
BIOINFORMATICS 38
PROTEIN DATABASES 39
EFFECT OF PATENTING/TRADE SECRETS OF RESEARCH TOOLS 39

PROTEIN DRUGS 40
TABLE 16 TOP SELLING PROTEIN DRUGS WORLDWIDE, 2002–2005 ($ MILLION) *40*
TABLE 17 GLOBAL MARKET FORECAST FOR TYPES OF PROTEIN DRUGS, THROUGH 2011 ($ MILLIONS) *41*
FIGURE 1 GLOBAL MARKET FORECAST FOR TYPES OF PROTEIN DRUGS 2006 AND 2011 ($ MILLIONS) *41*
PROTEIN DRUGS (CONTINUED) 42
REPLACEMENT PROTEINS 43
TABLE 18 GLOBAL MARKET FORECAST OF REPLACEMENT PROTEINS, THROUGH 2011 ($ MILLION) *43*
FIGURE 2 GLOBAL MARKET FORECAST OF REPLACEMENT PROTEINS, 2006 AND 2011 ($ MILLION) *44*
HORMONE REPLACEMENT 44
GROWTH HORMONE 45
OTHER RECOMBINANT REPLACEMENT PROTEINS 45
THERAPEUTIC ENZYMES 45
TABLE 19 WORLDWIDE SALES OF THERAPEUTIC ENZYMES, 2003-2011 ($ MILLION) *46*
RECOMBINANT PROTEIN DRUGS 46

TABLE 20 WORLDWIDE SALES OF RECOMBINANT/BIOENGINEERED PROTEIN DRUGS, 2003-2005 ($ MILLION) *47*
GROWTH FACTORS 47
TABLE 21 GLOBAL MARKET SALES GROWTH FACTORS, 2003-2011 ($ MILLION) *48*
FIGURE 3 GLOBAL MARKET SALES GROWTH FACTORS, BY MANUFACTURER, 2006 AND 2011 ($ MILLION) *48*
TABLE 22 WORLDWIDE SALES GROWTH FACTOR INHIBITORS, 2003-2005 ($ MILLIONS) *49*
PEPTIDE DRUGS 49
CURRENTLY MARKETED PEPTIDE DRUGS 49
Fuzeon 49
Integrilin 50
Cubicin 50
Prialt 50
NON-NATURAL AMINO ACIDS 50
PEPTIDE DRUGS IN DEVELOPMENT 51
Oxytocin Analogs 51
Icatibant 51
Neurovax 52
HURDLES TO PEPTIDE DRUG DEVELOPMENT 52
COAGULANTS 53
TABLE 23 WORLDWIDE SALES OF COAGULANTS, THROUGH 2011 ($ MILLION) *54*
HORMONES 54
TABLE 24 WORLDWIDE SALES OF HORMONES, THROUGH 2011 ($ MILLION) *55*
ESTROGEN ANALOGS 55
Raloxifene 56
Premarin 56
Gonal-F 56
GONADAL STEROIDS 57
Tibolone 57
HORMONE REPLACEMENT THERAPY (HRT) 57
THYROID AND PARATHYROID DERIVED HORMONES 58
Parathyroid Hormone (Teriparatide) 59
MONOCLONAL ANTIBODIES 59
TABLE 25 CURRENTLY APPROVED THERAPEUTIC MONOCLONAL ANTIBODIES, UNITED STATES *60*
TABLE 26 WORLDWIDE SALES OF MONOCLONAL ANTIBODIES USED AS THERAPEUTICS, 2003-2005 ($ MILLION) *61*
DENOSUMAB 62
MORPHOTEK 62

TABLE 27 GLOBAL MARKET SALES OF MONOCLONAL ANTIBODIES USED AS THERAPEUTICS, 2003-2011 ($ MILLION) *63*
FIGURE 4 GLOBAL MARKET SALES OF MONOCLONAL ANTIBODIES USED AS THERAPEUTICS, 2006 AND 2011 ($ MILLION) *63*
VACCINES 64
ROTAVIRUS 64
HEAT SHOCK PROTEINS 64
Heat Shock Proteins (Continued) 64

DISEASES 65
DIABETES 65
INSULIN DELIVERY SYSTEMS 65
Inhaled—Exubera 65
Inhaler—Nektar Therapeutic 66
Alternatives to insulin 66
Byetta (Eli Lilly/Amylin) 66
Glucophage 67
DIABETIC RETINOPATHY 67
HEMOPHILIA 68
ANTI-COAGULANTS 69
HEART DISEASE 70
APOA-1 70
LIPITOR 71
RAISING HDL 71
VEGF AS A TREATMENT 72
TABLE 28 WORLDWIDE SALES OF PROTEIN DRUGS USED FOR TREATMENT OF CARDIOVASCULAR DISEASE, 2003-2005 ($ MILLION) *72*
NEURODEGENERATIVE DISEASE 73
TABLE 29 POSITION IN THE PIPELINE OF BIOTECHNOLOGY THERAPIES TARGETING ALZHEIMER'S DISEASE *73*
TABLE 29 (CONTINUED) *74*
RESPIRATORY DISEASES 74
CYSTIC FIBROSIS 75
EMPHYSEMA 75
PULMONARY FIBROSIS 76
INFECTIOUS DISEASE 76
ANTIBIOTIC RESISTANCE 76
FUNGAL DISEASES 77
TWEAK 78
SKIN DISEASES/INJURIES 78
PSORIASIS 78
Psoriasis (Continued) 79
LESIONS 80

WOUND TREATMENT 80
ARTHRITIS 81
RHEUMATOID ARTHRITIS 81
TABLE 30 WORLDWIDE SALES OF PROTEIN DRUGS FOR ARTHRITIS, 2003-2005 ($ MILLION) *82*
PSORIATIC ARTHRITIS 82
OSTEOARTHRITIS 82
CONGENITAL DISEASE 83
ORPHAN DRUG ACT 83
CANCER 83
TABLE 31 WORLDWIDE SALES BY TYPE OF CANCER DRUGS, THROUGH 2011 ($ MILLION) *84*
INTERFERONS 84
Interferon -2a (Roferon-A) 84
Interferon -2b (Intron A) 85
Interferon -n3 (Alferon N) 85
Interferon con-1 (Infergen) 85
Interferon -1a (Avonex) 85
Interferon -1b (Betaseron) 86
Interferon -1b (Actimmune) 86
COMBINATION THERAPY 86
PEGYLATED INTERFERONS 86
TABLE 32 GLOBAL MARKET FORECAST OF INTERFERON, THROUGH 2011 ($ MILLION) *87*
FIGURE 5 GLOBAL MARKET FORECAST OF INTERFERON, 2006 AND 2011 ($ MILLION) *87*
Cytokines 87
CANCER VACCINES 88
Cancer Vaccines (Continued) 89
TABLE 33 COMPANIES INVOLVED IN DEVELOPMENT OF CANCER VACCINES BASED ON PROTEIN THERAPEUTICS *90*
COLORECTAL CANCER 91
TABLE 34 PROTEIN THERAPEUTICS FOR THE TREATMENT OF COLORECTAL CANCER *91*
ANGIOGENESIS INHIBITORS 92
FIGURE 6 CHEMOTHERAPY DRUG TARGETS THAT MAY HAVE ANTIANGIOGENIC EFFECTS *93*
Angiogenesis Inhibitors (Continued) 94
Angiogenesis Inhibitors (Continued) 95
TABLE 35 STRATEGIES TARGETING ENDOTHELIAL AND NON-ENDOTHELIAL CELLS TO INHIBIT TUMOR ANGIOGENESIS *96*
TABLE 36 SELECTED BREAST CANCER BIOTECH COMPANIES AND DRUG CANDIDATES IN THE CLINIC ($ MILLION) *97*
NON-SMALL-CELL LUNG CARCINOMA 98

TABLE 37 ONGOING FIRST-LINE TRIALS OF PROTEIN THERAPIES FOR NON-SMALL CELL LUNG CANCER *98*
AUTOIMMUNE DISORDERS 99
MULTIPLE SCLEROSIS 99
PAIN 99
AGING 100
Growth Hormones Used to Help the Elderly 100
AGE-RELATED MACULAR DEGENERATION 101
OBESITY 102

COMPANY PROFILES 103
MAJOR PLAYERS—GENERAL INFORMATION 103
TABLE 38 PROTEIN DRUG COMPANY PROFILES *103*
TABLE 38 (CONTINUED) *104*
TABLE 38 (CONTINUED) *105*
MERGERS/ACQUISITIONS 2000–2005 105
FOCUS ON INVITROGEN 105
2003 105
2005 106
2006 106
MERCK—SERONO 107
CORIXA—GLAXO SMITHKLINE 107
STRATEGIC ALLIANCES 2000–2006 107
MULTISPAN AND MOLECULAR DEVICES 107
SANOFI-AVENTIS/PFIZER/NEKTAR THERAPEUTICS 107
MILLIPORE AND JPT PEPTIDE TECHNOLOGIES 108
APO2L/TRAIL—GENENTECH AND AMGEN 108
JUVENILE DIABETES RESEARCH FOUNDATION AND IMMUNE TOLERANCE NETWORK 108
HELIX BIOPHARMA AND QSV BIOLOGICS 108
ARADIGM AND NOVO NORDISK 109
INCYTE GENOMICS AND LEXICON GENETICS 109
Incyte Co-Promotion of LexVision 110
Access to LexVision and Lifeseq Gold for Drug Discovery Research 110
FDA APPROVED DRUGS 110
TABLE 39 FDA APPROVED PROTEIN DRUGS, BY COMPANY, JAN 2000–MAY 2006 ..... *111*

PATENT LANDSCAPE 112
TYPES OF PATENTS/MAJOR PATENT PORTFOLIOS 112
TABLE 40 PATENT OWNERSHIP, 2000-2006 ..... *112*
TABLE 40 (CONTINUED) *113*
TABLE 40 (CONTINUED) *114*
TABLE 40 (CONTINUED) *115*

TABLE 40 (CONTINUED) *116*
TABLE 40 (CONTINUED) *117*
TABLE 40 (CONTINUED) *118*
TABLE 40 (CONTINUED) *119*
TABLE 40 (CONTINUED) *120*
TABLE 40 (CONTINUED) *121*
TABLE 40 (CONTINUED) *122*
TABLE 41 RECENT PATENTS AND PATENT APPLICATIONS FOR PROTEIN THERAPEUTICS, JANUARY 2000–JUNE 2006 ..... *123*
TABLE 41 (CONTINUED) *124*
FUTURE DRIVERS: PATENT EXPIRATIONS 124
TABLE 42 PROTEIN THERAPEUTICS LOSING PATENT PROTECTION *125*
FUTURE DRIVERS: RESEARCH INITIATIVES 126
PHARMASTART 126
SECRETED PROTEIN DISCOVERY INITIATIVE 127
LITIGATION 127
CAMBRIDGE ANTIBODY TECHNOLOGY V. ABBOTT 128
ELI LILLY V. ARIAD 128
ELI LILLY & CO V. MASSACHUSETTS INSTITUTE OF TECHNOLOGY AND HARVARD UNIVERSITY 129
NOVO NORDISK V. PFIZER 130
BRISTOL-MYERS SQUIBB V. APOTEX 130
DAIICHI PHARMACEUTICAL CO. V. APOTEX INC 130
FUTURE DRIVERS: FUNDING 130
BRISTOL-MYERS SQUIBB (BMS) 130
EUROPEAN SCIENCE FOUNDATION 131
NATIONAL CANCER INSTITUTE—PROTEOMICS 131
CLINICAL TRIAL TRENDS 132