

INCRETIN-BASED DRUGS: MARKETS FOR DIABETES THERAPIES AND DEVELOPING TREATMENTS



PHM162A
February 2015

Kim Lawson
Project Analyst

ISBN: 1-62296-047-5



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 THIS STUDY	2
SCOPE OF REPORT	2
INTENDED AUDIENCE	3
METHODOLOGY	3
INFORMATION SOURCES	3
ANALYST'S CREDENTIALS	3
RELATED BCC RESEARCH REPORTS	4
BCC RESEARCH WEBSITE	4
DISCLAIMER	4
CHAPTER 2 EXECUTIVE SUMMARY	6
INCRETINS FILL NEED FOR GLYCEMIC CONTROL	7
TRENDS IN DISPENSING AND SALES	8
<i>SUMMARY TABLE GLOBAL MARKET FOR INCRETIN-BASED THERAPEUTICS, THROUGH 2019 (\$ MILLIONS)</i>	9
<i>SUMMARY FIGURE GLOBAL MARKET FOR INCRETIN-BASED THERAPEUTICS, 2012-2019 (\$ MILLIONS)</i>	10
GEOGRAPHICAL SHIFTS	11
KEY DRIVERS	11
KEY CHALLENGES	12
KEY TRENDS	12
CHAPTER 3 OVERVIEW AND MARKET FORECAST	15
<i>FIGURE 1 THE INCRETIN EFFECT ILLUSTRATED</i>	16
<i>FIGURE 2 PERCENTAGE OF DISPENSED PRESCRIPTIONS FOR NON-INSULIN ANTIDIABETICS, 2012 (%)</i>	17
DATA ON WHERE INCRETINS FIT	17
<i>FIGURE 3 PERCENTAGE OF DISPENSED PRESCRIPTIONS FOR GLP-1 RECEPTOR AGONISTS, 2012 (%)</i>	18
<i>FIGURE 4 PERCENTAGE OF DISPENSED PRESCRIPTIONS FOR DPP-4 INHIBITORS, 2012 (%)</i>	19
FOR SOME, A GLP-1 FOCUS	19
<i>TABLE 1 DIFFERENCES BETWEEN THE INCRETIN THERAPIES</i>	20
STANDARD DIABETIC TREATMENTS	21
METFORMIN	22
SULFONYLUREAS (SU)	22
THIAZOLIDINEDIONE (TZD)	23
ALPHA-GLUCOSIDASE INHIBITORS	23
INSULIN TREATMENT	24
Long-acting Insulin	24
Intermediate-acting Insulin	24
Regular or Short-acting Insulin	25
Rapid-acting Insulin	25
<i>TABLE 2 ADVANTAGES TO ADDING INCRETIN THERAPY</i>	25

TOPIC	PAGE NO.
OTHER NEW TREATMENTS	26
DIABETES FURTHER EXPLAINED	28
TYPES OF DIABETES	29
Type 1	29
Type 2	29
Gestational Diabetes	30
Impaired Glucose Tolerance (IGT) and Impaired Fasting Glycemia (IFG)	30
CARE MODEL UPDATED WITH INCRETINS	30
CONDITIONS RELATED TO DIABETES	32
Obesity	32
<i>FIGURE 5 ADA'S STANDARD OF MEDICAL CARE IN DIABETES, 2014</i>	32
Cardiovascular Disease	33
Pancreatitis	34
Cancer	35
<i>TABLE 3 CURRENT THINKING ON DIABETES MEDICATIONS AND CANCER RISK</i>	36
Polycystic Ovary Syndrome	36
COMPLICATIONS AND COMORBIDITIES	36
<i>TABLE 4 COMPLICATIONS/COMORBID CONDITIONS FROM DIABETES</i>	37
INCRETIN THERAPIES	37
<i>TABLE 5 COMMERCIALIZED INCRETIN THERAPY</i>	38
GLP-1 RECEPTOR AGONISTS	38
COMMERCIALIZED GLP-1 RECEPTOR AGONISTS	40
Exenatide	40
Liraglutide	41
Dulaglutide	42
Albiglutide	43
Lixisenatide	44
COMMERCIALIZED DPP-4 INHIBITORS	44
Linagliptin	45
Sitagliptin	46
Vildagliptin	46
Saxagliptin	47
Alogliptin	47
Teneligliptin	49
Anagliptin	50
Gemigliptin	50
MARKET LANDSCAPE	51
<i>TABLE 6 NUMBER OF COMMERCIALIZED INCRETIN-BASED THERAPEUTICS, 2014 AND 2019 (UNITS)</i>	51
<i>FIGURE 6 NUMBER OF COMMERCIALIZED INCRETIN-BASED THERAPEUTICS, 2014 AND 2019 (UNITS)</i>	51
<i>FIGURE 7 MARKET SHARE OF INCRETIN-BASED THERAPEUTICS, BY THERAPEUTIC AREA, 2014 AND 2019 (% OF REVENUE BY THERAPEUTIC AREA)</i>	52
<i>FIGURE 8 MARKET SHARE OF COMMERCIALIZED INCRETIN-BASED THERAPEUTICS, BY INCRETIN TYPE, 2014 AND 2019 (% OF REVENUE BY INCRETIN TYPE)</i>	54
<i>FIGURE 9 MARKET SHARE OF COMMERCIALIZED GLP-1 RECEPTOR AGONISTS, BY DOSING FREQUENCY, 2014 AND 2019 (%)</i>	54
DEALS IN THE INCRETIN MARKET	55

TOPIC	PAGE NO.
<i>TABLE 7 MAJOR AGREEMENTS FOR INCRETIN-BASED THERAPY DEVELOPMENT</i>	56
CHAPTER 4 THE DEVELOPMENT PIPELINE	61
REGULATORY ENVIRONMENT	61
PATENTS	62
DEVELOPMENT PIPELINE	63
<i>FIGURE 10 NUMBER OF INCRETINS IN DEVELOPMENT BY PHASE, 2014</i>	64
KEY GLP-1 RECEPTOR AGONISTS IN DEVELOPMENT	64
Exenatide Formulations (Including ICTA, VRS-859/Exenatide-extended Release, and Microsphere Formulation of Exenatide, DA-3091)	64
Liraglutide for Obesity (Sandexa) and for Type 1 Diabetes (NN9211)	65
Lixisenatide (Lyxumia and LixiLan [Combined Lixisenatide and Basal Insulin])	65
Semaglutide (NN9535)	66
CJC-1134-PC	67
<i>TABLE 8 GLP-1 RECEPTOR AGONISTS IN LATE-STAGE DEVELOPMENT</i>	68
<i>TABLE 9 GLP-1 RECEPTOR AGONISTS IN EARLY-STAGE DEVELOPMENT</i>	69
KEY DPP-4 INHIBITORS IN DEVELOPMENT	69
Saxagliptin (Onglyza)/Dapagliflozin Combination (Forxiga)	69
Trelagliptin	69
Omarigliptin	70
Gosogliptin (Satyor)	71
Gemigliptin	71
<i>TABLE 10 DPP-4 INHIBITORS IN LATE-STAGE DEVELOPMENT</i>	71
<i>TABLE 11 DPP-4 INHIBITORS IN EARLY-STAGE DEVELOPMENT</i>	72
DEVELOPMENT CASE STUDY: PHENOMIX	72
PROMISING PIPELINE CANDIDATES AND NOVEL RESEARCH	73
NOVEL ACTIVE DRUG CANDIDATES	73
Dual GLP-1/Glucagon Agonists	73
Glucagon Receptor Agonists	74
GLP-2	75
GPR119	75
TGR5	76
Glucokinase Activators	76
OTHER NOVEL RESEARCH	77
Department of Medicine, Imperial College London, U.K.	77
Origenesis' Conversion of Liver Cells	77
DEVELOPMENT LANDSCAPE: OVERALL PHARMA MARKET	77
<i>TABLE 12 TOP PHARMA COMPANIES BY REVENUE, 2013 (\$ BILLIONS)</i>	78
<i>FIGURE 11 GEOGRAPHIC DISTRIBUTION OF PHARMACEUTICAL DRUGS, 2012 AND 2017 (PERCENT OF GLOBAL SALES)</i>	79
DIABETES AS SALES TERRITORY	80
<i>FIGURE 12 DIABETES-FOCUSED GEOGRAPHIC TERRITORY: NOVO NORDISK SALES, 2013 (% OF SALES)</i>	80
BIOLOGICS AND GLP-1 RECEPTOR AGONIST PRODUCTION	81
Growth Factors	83
Gene Therapy	83

TOPIC	PAGE NO.
Recombinant Proteins	83
Monoclonal Antibodies	83
BIOLOGIC LANDSCAPE	84
<i>TABLE 13 BIOLOGICS IN DEVELOPMENT IN THE U.S. BY THERAPEUTIC CATEGORY, 2013</i>	84
PIPELINE FOR DIABETES AND DIABETES-RELATED MEDICATIONS	85
<i>TABLE 14 GLOBAL PIPELINE FOR PHASE II AND III STAGE DIABETES MEDICATIONS, THROUGH 2019</i>	85
<i>TABLE 15 GLOBAL PIPELINE FOR PHASE I STAGE DIABETES MEDICATIONS, THROUGH 2019</i>	87
<i>TABLE 16 GLOBAL PIPELINE FOR DIABETES-RELATED DISORDERS, THROUGH 2019</i>	88
OBESITY AS THERAPEUTIC CATEGORY	90
<i>TABLE 17 GLOBAL PIPELINE FOR OBESITY, THROUGH 2019</i>	91
<i>TABLE 18 DIABETES AND DRUG DEVELOPMENT RESOURCES</i>	92
CHAPTER 5 COMPANY PROFILES	95
ACTIVX BIOSCIENCES INC. (KYORIN PHARMACEUTICAL CO. LTD.)	95
AERPIO THERAPEUTICS INC.	95
AMPIO PHARMACEUTICALS INC.	96
AMUNIX	96
ARAIM PHARMACEUTICALS INC.	97
ARISAPH	98
ASTRAZENECA	99
BECTON, DICKINSON AND COMPANY	99
BOEHRINGER INGELHEIM GMBH	100
BRISTOL-MYERS SQUIBB	101
CEBIX INC.	102
CHEMOCENTRYX INC.	102
CODA THERAPEUTICS INC.	103
CONCERT PHARMACEUTICALS	104
CONJUCHEM	105
DIPEXIUM PHARMACEUTICALS INC.	105
DONG-A SOCIO HOLDINGS	106
ELI LILLY AND COMPANY	106
EMISPHERE TECHNOLOGIES INC.	107
EVOKE PHARMA INC.	109
FURIEX PHARMACEUTICALS INC.	109
GENKYOTEX S.A.	110
GLAXOSMITHKLINE PLC	111
GLYCADIA PHARMACEUTICALS	112
HANMI PHARMACEUTICAL CO. LTD.	112
ICO THERAPEUTICS INC.	113
INTARCIA THERAPEUTICS INC.	114
JOHNSON & JOHNSON	115
KOWA CO. LTD.	115
KYORIN PHARMACEUTICAL CO. LTD.	116
KYOWA HAKKO KIRIN CO. LTD.	116
LIGAND PHARMACEUTICALS INC.	117

TOPIC	PAGE NO.
LG LIFE SCIENCES LTD.	118
MANKIND CORP.	118
MERCK	119
MERRION PHARMACEUTICALS LTD.	120
mitsubishi tanabe pharma corp.	121
NEPHROGENEX INC.	122
NOVARTIS INTERNATIONAL AG	123
NOVO NORDISK A/S	124
ONO PHARMACEUTICALS	126
ORAMED PHARMACEUTICALS	127
OTSUKA PHARMACEUTICAL CO. LTD.	127
PFIZER	128
PHASEBIO PHARMACEUTICALS INC.	129
QUARK PHARMACEUTICALS INC.	130
ROCHE	130
ROYER BIOMEDICAL INC.	131
SANOFI	131
SANWA KAGAKU KENKYUSHO CO. LTD.	133
SATRX LLC	134
SIHUAN PHARMACEUTICAL HOLDINGS GROUP CO. LTD.	134
TAKEDA PHARMACEUTICAL CO. LTD.	135
TRANSITION THERAPEUTICS INC.	136
TRANSTECH PHARMA LLC	137
VIKING THERAPEUTICS INC.	138
ZEALAND PHARMA A/S	138
ZOSANO PHARMA CORP.	140

LIST OF TABLES

TABLE HEADING	PAGE NO.
SUMMARY TABLE GLOBAL MARKET FOR INCRETIN-BASED THERAPEUTICS, THROUGH 2019 (\$ MILLIONS)	9
TABLE 1 DIFFERENCES BETWEEN THE INCRETIN THERAPIES	20
TABLE 2 ADVANTAGES TO ADDING INCRETIN THERAPY	25
TABLE 3 CURRENT THINKING ON DIABETES MEDICATIONS AND CANCER RISK	36
TABLE 4 COMPLICATIONS/COMORBID CONDITIONS FROM DIABETES	37
TABLE 5 COMMERCIALIZED INCRETIN THERAPY	38
TABLE 6 NUMBER OF COMMERCIALIZED INCRETIN-BASED THERAPEUTICS, 2014 AND 2019 (UNITS)	51
TABLE 7 MAJOR AGREEMENTS FOR INCRETIN-BASED THERAPY DEVELOPMENT	56
TABLE 8 GLP-1 RECEPTOR AGONISTS IN LATE-STAGE DEVELOPMENT	68
TABLE 9 GLP-1 RECEPTOR AGONISTS IN EARLY-STAGE DEVELOPMENT	69
TABLE 10 DPP-4 INHIBITORS IN LATE-STAGE DEVELOPMENT	71
TABLE 11 DPP-4 INHIBITORS IN EARLY-STAGE DEVELOPMENT	72
TABLE 12 TOP PHARMA COMPANIES BY REVENUE, 2013 (\$ BILLIONS)	78
TABLE 13 BIOLOGICS IN DEVELOPMENT IN THE U.S. BY THERAPEUTIC CATEGORY, 2013	84
TABLE 14 GLOBAL PIPELINE FOR PHASE II AND III STAGE DIABETES MEDICATIONS, THROUGH 2019	85
TABLE 15 GLOBAL PIPELINE FOR PHASE I STAGE DIABETES MEDICATIONS, THROUGH 2019	87
TABLE 16 GLOBAL PIPELINE FOR DIABETES-RELATED DISORDERS, THROUGH 2019	88
TABLE 17 GLOBAL PIPELINE FOR OBESITY, THROUGH 2019	91
TABLE 18 DIABETES AND DRUG DEVELOPMENT RESOURCES	92

LIST OF FIGURES

FIGURE TITLE	PAGE NO.
SUMMARY FIGURE GLOBAL MARKET FOR INCRETIN-BASED THERAPEUTICS, 2012-2019 (\$ MILLIONS)	10
FIGURE 1 THE INCRETIN EFFECT ILLUSTRATED	16
FIGURE 2 PERCENTAGE OF DISPENSED PRESCRIPTIONS FOR NON-INSULIN ANTIDIABETICS, 2012 (%)	17
FIGURE 3 PERCENTAGE OF DISPENSED PRESCRIPTIONS FOR GLP-1 RECEPTOR AGONISTS, 2012 (%)	18
FIGURE 4 PERCENTAGE OF DISPENSED PRESCRIPTIONS FOR DPP-4 INHIBITORS, 2012 (%)	19
FIGURE 5 ADA'S STANDARD OF MEDICAL CARE IN DIABETES, 2014	32
FIGURE 6 NUMBER OF COMMERCIALIZED INCRETIN-BASED THERAPEUTICS, 2014 AND 2019 (UNITS)	51
FIGURE 7 MARKET SHARE OF INCRETIN-BASED THERAPEUTICS, BY THERAPEUTIC AREA, 2014 AND 2019 (% OF REVENUE BY THERAPEUTIC AREA)	52
FIGURE 8 MARKET SHARE OF COMMERCIALIZED INCRETIN-BASED THERAPEUTICS, BY INCRETIN TYPE, 2014 AND 2019 (% OF REVENUE BY INCRETIN TYPE)	54
FIGURE 9 MARKET SHARE OF COMMERCIALIZED GLP-1 RECEPTOR AGONISTS, BY DOSING FREQUENCY, 2014 AND 2019 (%)	54
FIGURE 10 NUMBER OF INCRETINS IN DEVELOPMENT BY PHASE, 2014	64
FIGURE 11 GEOGRAPHIC DISTRIBUTION OF PHARMACEUTICAL DRUGS, 2012 AND 2017 (PERCENT OF GLOBAL SALES)	79
FIGURE 12 DIABETES-FOCUSED GEOGRAPHIC TERRITORY: NOVO NORDISK SALES, 2013 (% OF SALES)	80