Drug Delivery in Cancer - Technologies, Markets and Companies

Description:

Drug delivery remains a challenge in management of cancer. Approximately 12.5 million new cases of cancer are being diagnosed worldwide each year and considerable research is in progress for drug discovery for cancer. Cancer drug delivery is no longer simply wrapping up cancer drugs in a new formulations for different routes of delivery. The focus is on targeted cancer therapy. The newer approaches to cancer treatment not only supplement the conventional chemotherapy and radiotherapy but also prevent damage to normal tissues and prevent drug resistance.

Innovative cancer therapies are based on current concepts of molecular biology of cancer. These include antiangiogenic agents, immunotherapy, bacterial agents, viral oncolysis, targeting of cyclic-dependent kinases and tyrosine kinase receptors, antisense approaches, gene therapy and combination of various methods. Important methods of immunotherapy in cancer involve use of cytokines, monoclonal antibodies, cancer vaccines and immunogene therapy.

Several innovative methods of drug delivery are used in cancer. These include use of microparticles as carriers of anticancer agents. These may be injected into the arterial circulation and guided to the tumor by magnetic field for targeted drug delivery. Polyethylene glycol (PEG) technology has been used to overcome some of the barriers to anticancer drug delivery. Encapsulating anticancer drugs in liposomes enables targeted drug delivery to tumor tissues and prevents damage to the normal surrounding tissues. Monoclonal antibodies can be used for the delivery of anticancer payloads such as radionucleotides, toxins and chemotherapeutic agents to the tumors.

Antisense oligonucleotides have been in clinical trials for cancer for some time now. RNAi has also been applied in oncology. Small interfering RNAs (siRNAs) can be targeted to tumors and one example is suppression of H-ras gene expression indicating the potential for application in therapy of ovarian cancer. Cancer gene therapy is a sophisticated form of drug delivery for cancer. Various technologies and companies developing them are described. Nucleic acid-based cancer vaccines are also described.

Drug delivery strategies vary according to the type and location of cancer. Role of drug delivery in the management of cancers of the brain, the bladder, the breast, the ovaries and the prostate are used as examples to illustrate different approaches both experimental and clinical. Biodegradable implants of carmustine are already used in the treatment of malignant brain tumors.

The market value of drug delivery technologies and the anticancer drugs are difficult to separate. Cancer market estimates from 2015-2025 are given according to organs involved and the types of cancer as well as according to technologies. Distribution of the into major regions is also described.

Profiles of 230 companies involved in developing innovative cancer therapies and methods of delivery are presented along with their 269 collaborations. The bibliography contains over 650 publications that are cited in the report. The report is supplemented with 66 tables and 12 figures.

Contents:

0. Executive Summary

1. Basics of Drug Delivery to the Central Nervous System
   Introduction
   Historical evolution of drug delivery for CNS disorders
   Neuroanatomical and neurophysiological basis of drug delivery
   The cerebrospinal fluid
   The lymphatic drainage system of the brain
   The extracellular space in the brain
   Neurotransmitters
   Extracellular vesicles as drug delivery vehicles
   Neuropharmacology relevant to drug delivery
   Introduction to neuropharmacology
   Pharmacokinetics
Absorption and distribution of drugs
Drug metabolism and elimination
Pharmacodynamics
Receptors
Sites of drug action in the CNS
Receptors coupled to guanine nucleotide binding proteins
Acetylcholine receptor channels
Dopamine receptors
GABA receptor channels
Glutamate receptor channels
Non-competitive NMDA antagonists
Serotonin receptors
G-protein coupled receptors
In vivo study of drug action in the CNS in human patients
Electroencephalography
Brain imaging
Chronopharmacology as applied to the CNS
Role of drug delivery in personalized therapy of CNS disorders

2. Blood Brain Barrier
Introduction
Features of the blood-brain barrier relevant to CNS drug delivery
The neurovascular unit
Functions of the BBB
BBB as an anatomical as well as physiological barrier
BBB as a biochemical barrier
Role of shear stress on development of BBB
Genomics of BBB
Proteomics of BBB
Other neural barriers
Blood-cerebrospinal fluid barrier
Blood nerve barrier
Blood-retinal barrier
Blood-labyrinth barrier
Passage of substances across the blood-brain barrier
Transporters localized in the BBB
Glucose transporter
Amino acid transporters
Ionic transporter
Efflux transport systems
BBB-specific enzymes
Receptor-mediated transcytosis
Lysophosphatidic acid-mediated increase in BBB permeability
Folate transport system
Transferrin receptor
Molecular biology of the BBB
Transport of peptides and proteins across the BBB
Passage of leptin across the BBB
Passage of cytokines across the BBB
Passage of hormones across the BBB
Passage of enzymes across the BBB
Passage of omega-3 fatty acids across the BBB
Drugs that cross the BBB by binding to plasma proteins
Current concepts of the permeability of the BBB
Factors that increase the permeability of the BBB
BBB disruption as an adverse effect of pharmaceuticals
BBB disruption as adverse effect of vaccines for CNS disorders
CNS disorders and BBB
Autoimmune disorders
Brain tumors
Primary brain tumors
Cerebral metastases
Central nervous system injuries
Cerebrovascular disease
Cerebral ischemia
Intracerebral hemorrhage
Epilepsy
Infections
Mitochondrial encephalopathies
Multiple sclerosis
Neurodegenerative disorders
BBB in Alzheimer disease
BBB in Parkinson disease
BBB in amyotrophic lateral sclerosis
West Nile virus infection
Testing permeability of the BBB
In vitro models of BBB
In vivo study of BBB
Brain imaging
In silico prediction of BBB
Relevance of the BBB penetration to pharmacological action
BBB penetration and CNS drug screening
CERENSE SM
In vivo brain distribution of P-glycoprotein
Transthyretin monomer as a marker of blood-CSF barrier disruption
Evaluation of BBB permeability by brain imaging
Biomarkers of disruption of blood-brain barrier
Future directions for research on the BBB
Use of neural stem cells to construct the blood brain barrier
Strategies to cross the BBB

3. Methods of Drug Delivery to the CNS
Introduction
Routes of drug delivery to the brain
Drug deliveries to the brain via the nasal route
Devices for nasal administration of drugs for CNS
Nasal mucosal patch to facilitate drug delivery across the BBB
Passage of viruses to the brain via the nasal route
Potential and limitations of nasal drug delivery to the brain
Drugs that can be delivered to the brain via the nasal route
Erythropoietin
Hypocretin
IFN beta-1b
Lysosomal enzymes
Midazolam
Neurotrophic factors
Thyrotropin-releasing hormone
Neuroprotective drugs for stroke
Transdermal drug delivery for neurological disorders
Drug delivery to the brain via inner ear
Drug delivery for disorders of the spinal cord
Intrathecal drug delivery
Anatomical & physiological aspects of intrathecal drug delivery
Advantages of intrathecal drug delivery
Drugs that can be delivered by intrathecal route
Pharmacokinetics of intrathecal drug delivery
Retrograde delivery to the brain via the epidural venous system
Devices for drug delivery to the CNS
Catheters for drug delivery to the CNS
Reservoirs and pumps for drug delivery to the CNS
Invasive neurosurgical approaches
Intraarterial drug delivery to the brain
Direct injection into the CNS substance or CNS lesions
Targeted delivery of biologicals to the spinal cord by microinjection
Intraventricular injection of drugs
Strategies for drug delivery to the CNS across the BBB
Increasing the permeability (opening) of the BBB
Osmotic opening of the BBB
Focal disruption of BBB by ultrasound
Chemical opening of the BBB
Cerebral vasodilatation to open the BBB
Modulation of vascular permeability by laser irradiation
Neurostimulation for opening BBB
Use of nitric oxide donors to open the BBB
Manipulation of the sphingosine 1-phosphate receptor system
Pharmacological strategies to facilitate transport across the BBB
2B-Trans™ technology
ABC afflux transporters and penetration of the BBB
Carrier-mediated drug delivery across the BBB
Fusion of receptor-binding peptide from apoE with therapeutic protein
G-Technology®
Glycosylation Independent Lysosomal Targeting
Inhibition of P-glycoprotein to enhance drug delivery across the BBB
LipoBridge? technology
Modification of the drug to enhance its lipid solubility
Monoclonal antibody fusion proteins
Neuroimmunophilins
Peptide-mediated transport across the BBB
Prodrug bioconversion strategies and their CNS selectivity
Transport of small molecules across the BBB
Transport across the BBB by short chain oligoglycerolipids
Transvascular delivery across the BBB
Trojan horse approach
Role of the transferrin-receptor system in CNS drug delivery
Use of receptor-mediated transcytosis to cross the BBB
Cell-based drug delivery to the CNS
Activated T lymphocytes
Microglial cells
Neural stem cells
Drug delivery to the CNS by using novel formulations
Crystalline formulations
Liposomes
Monoclonal antibodies
Microspheres
Microbeads
Brain-targeted chemical delivery systems
Nanotechnology-based drug delivery to CNS
Nanoparticles for drug delivery across the BBB
NanoDel? technology for crossing the BBB
Masking BBB-limiting characteristics by nanotechnology
Nanovesicles for transport across BBB
Peptide-nanoparticle conjugates for crossing the BBB
Penetration of BBB by nanoparticles coated with polysorbate 80
Transcytosis of transferrin-containing nanoparticles across the BBB
Nanotechnology-based devices and implants for CNS
Biochip implants for drug delivery to the CNS
Controlled-release microchip
Retinal implant chip
Convection-enhanced delivery to the CNS
Systemic administration of drugs for CNS effects
Sustained and controlled release drug delivery to the CNS
Fast dissolving oral selegiline
Choice of the route of systemic delivery for effect on the CNS disorders
Methods of delivery of biopharmaceuticals to the CNS
Delivery of biopharmaceuticals across the BBB
Methods of delivery of peptides for CNS disorders
Alteration of properties of the BBB for delivery of peptides
Challenges for delivery of peptides across the BBB
CNS delivery of peptides via conjugation to biological carriers
Delivery of conopeptides to the brain
Direct delivery of neuropeptides into the brain
Molecular manipulations of peptides to facilitate transport into CNS
Transport to spinal cord motor neurons after peripheral injection
Transnasal administration of neuropeptides
Delivery of neurotrophic factors to the nervous system
Systemic administration of NTFs
Delivery systems to facilitate crossing of the BBB by NTFs
Direct application of NTFs to the CNS
Intracerebroventricular injection
Intrathecal administration
Implants for delivery of neurotrophic factors
Use of neurotrophic factor mimics
Use of microspheres for delivery of neurotrophic factors
Use of nanobiotechnology for delivery of neurotrophic factors
Use of microorganisms for therapeutic entry into the brain
Bacteriophages as CNS therapeutics
Intracellular drug delivery in the brain
Local factors in the brain affecting drug action
Methods for testing drug delivery to the CNS
Animal models for testing drug delivery
Screening for drug-P-gp interaction at BBB

4. Delivery of Cell, Gene and Antisense Therapies to the CNS
Introduction
Cell therapy of neurological disorders
Methods for delivering cell therapies in CNS disorders
Cerebrospinal fluid-stem cell interactions for therapy of CNS disorders
Engineered stem cells for drug delivery to the brain
Encapsulated cells
Intrathecal delivery of stem cells
Intraparenchymal delivery of stem cells to the spinal cord
Intravascular administration
Neural stem cells as therapeutic delivery vehicles
Gene therapy techniques for the nervous system
Introduction
Methods of gene transfer to the nervous system
AAV vector mediated gene therapy for neurogenetic disorders
Ideal vector for gene therapy of neurological disorders
Promoters of gene transfer
Routes of delivery of genes to the nervous system
Direct injection into CNS
Introduction of the genes into cerebral circulation
Introduction of genes into cerebrospinal fluid
Intravenous administration of vectors
Delivery of gene therapy to the peripheral nervous system
Cell-mediated gene therapy of neurological disorders
Neuronal cells
Neural stem cells and progenitor cells
Astrocytes
Cerebral endothelial cells
Implantation of genetically modified encapsulated cells into the brain
Genetically modified bone marrow cells
Nanoparticles as non-viral vectors for CNS gene therapy
Applications of gene therapy for neurological disorders
Companies involved in cell/gene therapy of neurological disorders
Antisense therapy of CNS disorders
Delivery of antisense oligonucleotides to the CNS
Delivery of oligonucleotides cross the BBB
Cellular delivery systems for oligonucleotides
High-flow microinfusion into the brain parenchyma
Systemic administration of peptide nucleic acids
Introduction of antisense compounds into the CSF Pathways
Intrathecal administration of antisense compounds
Intracerebroventricular administration of antisense oligonucleotides
Nanoparticle-based delivery of antisense therapy to the CNS
Methods of delivery of ribozymes
Delivery aspects of RNAi therapy of CNS disorders
Delivery of siRNA to the CNS
Future drug delivery strategies applicable to the CNS

5. Drug Delivery for Treatment of Neurological Disorders
Introduction
Parkinson's disease
Drug delivery systems for Parkinson's disease
Methods of delivery of levodopa in PD
Duodenal levodopa infusion
Sublingual apomorphine
Transdermal drug delivery for PD
Transdermal dopamine agonists for PD
Transdermal administration of other drugs for PD
Intracerebral administration of GDNF
Cell therapy for PD
Human dopaminergic neurons for PD
Graft survival-enhancing drugs
Xenografting porcine fetal neurons
Encapsulated cells for PD
Stem cells for PD
Engineered stem cells for drug delivery to the brain in PD
Human retinal pigment epithelium cells for PD
Delivery of cells for PD
Gene therapy for Parkinson disease
Rationale
Techniques of gene therapy for PD
Prospects of gene therapy for PD
Companies developing gene therapy for PD
RNAi therapy of Parkinson's disease
Alzheimer disease
Drug delivery for Alzheimer disease
Blood-brain partitioning of an AMPA receptor modulator
Clearing amyloid through the BBB
Delivery of the passive antibody directly to the brain
Delivery of thyrotropin-releasing hormone analogs by molecular packaging
Nanoparticle-based drug delivery for Alzheimer's disease
Perispinal etanercept
Slow release implant of an AChE inhibitor
Intranasal insulin in Alzheimer disease
Transdermal drug delivery in Alzheimer's disease
Trojan-horse approach to prevent build-up of Aß aggregates
Cell and gene therapy for Alzheimer disease
NGF gene therapy
Neprilysin gene therapy
RNAi therapy of Alzheimer's disease
Huntington's disease
Treatment of HD
Gene therapy of HD
Encapsulated genetically engineered cellular implants
Viral vector mediated administration of neurotrophic factors
RNAi therapeutics for the treatment of HD
Amyotrophic lateral sclerosis
Treatment of ALS
Drug delivery in ALS
Delivery of stem cell therapy for ALS
Gene and antisense therapy of ALS
Neurotrophic factor gene therapies of ALS
Antisense therapy of ALS
RNAi therapy of amyotrophic lateral sclerosis
Cerebrovascular disease
Treatment of stroke
Drug delivery in stroke
Intraarterial administration of tissue plasminogen activator in stroke
Drug delivery for prevention of restenosis of carotid arteries
In-stent restenosis
Targeted local anti-restenotic drug delivery
Catheter-based drug delivery for restenosis
Stents for prevention of restenosis
Drug-eluting stents
Antisense approach to prevent restenosis
Drug-eluting stents for the treatment of intracranial atherosclerosis
Tissues transplants for stroke
Transplant of encapsulated tissue secreting neurotrophic factors
Methods for delivery of neurotrophic factors in stroke
Cell therapy for stroke
Stem cell transplant into the brain
Immortalized cell grafts for stroke
Intravenous infusion of marrow stromal cells
Intravenous infusion of umbilical cord blood stem cells
Future of cell therapy for stroke
Gene therapy of cerebrovascular diseases
Gene transfer to cerebral blood vessels
NOS gene therapy for restenosis
Gene therapy for cerebral ischemia
Gene therapy of strokes with a genetic component
Drug delivery to intracranial aneurysms
Drug delivery for vasospasm following subarachnoid hemorrhage
Intrathecal tissue plasminogen activator
Gene therapy for vasospasm
Drug delivery in multiple sclerosis
An electronic device for self injection of interferon beta-1a
Oral therapies for MS
Drug delivery for MS across the BBB
Delivery of methylprednisolone across the BBB
Monoclonal antibodies for MS and the BBB
Antisense and RNAi approaches to MS
Cell therapy for multiple sclerosis
Hematopoietic stem cell transplantation for multiple sclerosis
Embryonic stem cells and neural precursor cells for MS
Gene therapy for multiple sclerosis
Drug delivery in epilepsy
Routes of administration of antiepileptic drugs
Controlled-release preparations of carbamazepine
Intravenous carbamazepine
Various routes of administration of benzodiazepines
Methods of delivery of novel antiepileptic therapies
Regulated activation of prodrugs
Use of neuronal membrane transporter
Delivery of the antiepileptic conopeptides to the brain
Nasal administration of AEDs
Intracerebral administration of AEDs
The role of drug delivery in status epilepticus
Cell therapy of epilepsy
Gene therapy for epilepsy
Gene therapy for neuroprotection in epilepsy
Concluding remarks on drug delivery in epilepsy
Drug delivery for pain
Intranasal delivery of analgesics
Intranasal administration of morphine
Intranasal morphine derivatives
Intranasal fentanyl
Intranasal buprenorphine
Intranasal ketamine
Intranasal ketorolac
Delivery of analgesics by inhalation
Delivery of analgesics to peripheral nerves
Spinal delivery of analgesics
Epidural dexamethasone
Epidural morphine
Relief of pain by intrathecal ziconotide
Intrathecal neostigmine
Intrathecal prostaglandin antagonists
Intrathecal fadolmidine
Intrathecal siRNA for relief of neuropathic pain
Concluding remarks on intrathecal delivery of analgesic agents
Intracerebroventricular drug delivery for pain
Delivery of analgesics to the CNS across the BBB
Drug delivery for migraine
Management of migraine
Novel drug delivery methods for migraine
Nasal formulations for migraine
Sublingual spray for migraine
Needle-free drug delivery for migraine
Drug delivery for traumatic brain injury
Cell therapy of traumatic brain injury
Gene therapy for traumatic brain injury
Drug delivery for spinal cord injury
Administration of neurotrophic factors for spinal cord injury
Cell therapy for spinal cord injury
Transplantation of glial cells for SCI
Fetal neural grafts for SCI
Embryonic stem cells for SCI
Schwann cell transplants for SCI
Olfactory glial cells for SCI
Marrow stromal cells for SCI
Intravenous injection of stem cells for spinal cord repair
Combinatorial approach for regeneration in SCI
Cell therapy of syringomyelia
Gene therapy of spinal cord injury
Drug delivery in CNS infections
Drug delivery in neuroAIDS
Drug delivery for miscellaneous neurological disorders
Drug delivery for CNS involvement in Hunter syndrome
Intrathecal antisense delivery for spinal muscular atrophy
Genetically modified stem cells for metachromatic leukodystrophy
Relief of spasticity by intrathecal baclofen
Drug delivery for retinal disorders
Age-related macular degeneration
Squalamine
Combretastatin A4P for myopic macular degeneration
Gene therapy for AMD
Anti-VEGF approach to AMD
Delivery of pegaptanib for treatment of AMD
Stem cell therapy for retinitis pigmentosa
Proliferative retinopathies
Drug delivery for inner ear disorders
Delivery of stem cells for hearing loss
Auditory hair cell replacement by gene therapy
Future prospects of drug delivery to the inner ear
Drug delivery in psychiatric disorders
Delivery of antidepressants
Transdermal delivery of antidepressants
Nasal delivery of antidepressants
Delivery methods and formulations of antipsychotics
Long-acting injectable antipsychotics
Transdermal haloperidol
Transdermal risperidone for treatment of schizophrenia
Transdermal blonanserin for treatment of schizophrenia
Transdermal lithium for bipolar disorder

6. Drug delivery for brain tumors
Introduction
Methods for evaluation of anticancer drug penetration into brain tumor
Innovative methods of drug delivery for glioblastoma multiforme
Delivery of anticancer drugs across the blood-brain barrier
Anticancer agents with increased penetration of BBB
BBB disruption
Nanoparticle-based targeted delivery of chemotherapy across the BBB
Tyrosine kinase inhibitor increases topotecan penetration into CNS
Bypassing the BBB by alternative methods of drug delivery
Intranasal perillyl alcohol
Intraarterial chemotherapy
Enhancing tumor permeability to chemotherapy
PDE5 inhibitors for increasing BTB permeability
Local delivery of therapeutic agents into the brain
Biodegradable microspheres containing 5-FU
Carmustine biodegradable polymer implants
Fibrin glue implants containing anticancer drugs.
Interstitial delivery of dexamethasone for reduction of peritumor edema
Magnetically controlled microspheres
Convection-enhanced delivery
CED for receptor-directed cytotoxin therapy
CED of topotecan
CED of a modified diphtheria toxin conjugated to transferrin
CED of nanoliposomal CPT-11
CED for delivery
I-chTNT-1/B MAb
Anticancer drug formulations for targeted delivery to brain tumors
Intravenous delivery of anticancer agents bearing transferrin
Liposomes for drug delivery to brain tumors
MAbs targeted to brain tumors
Targeted delivery of drug-peptide conjugates to GBM
Multiple targeted drugs for brain tumors
Nanoparticles for targeted drug delivery in glioblastoma multiforme
Targeted antiangiogenic/apoptotic/cytotoxic therapies
Introduction of the chemotherapeutic agent into the CSF pathways
Intraventricular chemotherapy for meningeal cancer
Intrathecal chemotherapy
Photodynamic therapy for chemosensitization of brain tumors
Nanoparticles for photodynamic therapy of brain tumors
Innovative delivery of radiotherapy to brain tumors
GliaSite Radiation Therapy System
Boron neutron capture therapy for brain tumors
Cell therapy for glioblastoma multiforme
Mesenchymal stem cells to deliver treatment for gliomas
Gene therapy for glioblastoma multiforme.
Antiangiogenic gene therapy
Anticancer drug delivery by genetically engineered MSCs
Intravenous gene delivery with nanoparticles into brain tumors
Ligand-directed delivery of dsRNA molecules targeted to EGFR
Neural stem cells for drug/gene delivery to brain tumors
Peptides targeted to glial tumor cells
RNAi gene therapy of brain cancer
Single-chain antibody-targeted adenoviral vectors
Targeting normal brain cells with an AAV vector encoding interferon-?
Treatment of medulloblastoma by suppressing genes in Shh pathway
Virus-mediated oncolytic therapy of brain cancer
HIV-mediated Oncolysis
Autophagy by conditionally replicating adenoviruses
Reovirus-mediated Oncolysis
Measles virus-mediated oncolysis
Oncolytic virus targeted to brain tumor stem cells
Oncolysis with vesicular stomatitis virus
Future prospects of viral-mediated oncolysis
Vaccination for glioblastoma multiforme

7. Markets for Drug Delivery in CNS Disorders
Introduction
Methods of calculation of CNS drug delivery markets
Markets for CNS drug delivery technologies
Drug delivery share in selected CNS markets
CNS share of drug delivery technologies
Geographical distribution of CNS drug delivery markets
Impact of improved drug delivery on CNS drug markets
Neurodegenerative disorders
Alzheimer disease
Parkinson disease
Huntington disease
Amyotrophic lateral sclerosis
Epilepsy
Migraine and other headaches
Stroke
Central nervous system trauma
Multiple sclerosis
Brain tumors
Limitations of the current drug delivery technologies for CNS
Unmet needs in CNS drug delivery technologies
Future strategies for expanding CNS drug delivery markets
Education of neurologists
Demonstration of the advantages of the newer methods of delivery
Rescue of old products by novel drug delivery methods
Facilitation of the approval process of new drugs

8. Companies
Introduction
Profiles of companies
4s3 Bioscience Inc
AbbVie Inc
Alexza Pharmaceuticals
Alkermes
Alnylam Pharmaceuticals Inc
Alseres Pharmaceuticals Inc
ALZA
Amgen Inc
AngioChem Inc
Archimedes Pharma
Ariston Pharmaceuticals Inc
Argolyx Bioscience Inc
ArmaGen Technologies Inc
AstraZeneca
AVI Biopharma Inc
Avigen Inc
Bayer Pharma AG
BBB Therapeutics BV
Biogen Idec
BiOasis Technologies Inc
Biovail Corporation
BrainsGate Ltd
Cell Cure Neurosciences Ltd
Celtic Pharma Management LP
CepTor Corporation
Codman
Cynapsus Therapeutics Inc
Direct Therapeutics Inc
D-Pharm
DURECT Corporation
Elan Corporation plc
Endovasc Ltd
Ethyrpharm SA
Garnet BioTherapeutics Inc
GenVec Inc
Genzyme Corporation
ImaRx Therapeutics Inc
Intra-Cellular Therapies Inc
IVAX Corporation
Living Cell Technologies Ltd
Medtronic Inc
MGi Pharma Inc
MRI Interventions
NanoDel Technologies GmbH
NanoMed Pharmaceuticals Inc
Neurologix Inc
NeuroNova AB
Neurorecovery Inc
Neurotech SA
NsGene
NuPathe Inc
Oxford Biomedica plc
Pharmidex
Pherin Pharmaceuticals Inc
Raptor Pharmaceuticals Corporation
ReNeuron (UK) Ltd
Sagetis Biotech
Sangamo BioSciences Inc
Sanofi
Schwarz Pharma
Shire Plc
Spherics Inc
StemCells Inc
Sumitomo Dainippon Pharma Co Ltd
Synt:em
Tapestry Pharmaceuticals Inc
Theradigm Inc
Therataxis LLC
Titan Pharmaceuticals Inc
Upsher-Smith Laboratories Inc
Valeant Pharmaceuticals International
Vasogen Inc
VECT-HORUS SAS
Voyager Pharmaceutical Corporation
XenoPort Inc
Collaborations

9. References

Tables
Table 1-1: Landmarks in the development of drug delivery to the CNS
Table 2-1: Proteins expressed at the neurovascular unit
Table 2-2: Transporters that control penetration of molecules across the BBB
Table 2-3: Enzymes that control the penetration of molecules across the BBB
Table 2-4: Factors that increase the permeability of the BBB
Table 2-5: Diseases with associated disturbances of BBB
Table 3-1: Various methods of drug delivery to the central nervous system
Table 3-2: Drugs available for intrathecal administration
Table 3-3: Investigational drugs administered by intrathecal route
Table 3-4: Strategies for drug delivery to the CNS across the BBB
Table 3-5: Specific inhibitors of P-glycoprotein in clinical development
Table 3-6: Molecules attached to Trojan horses injected intravenously for CNS effect
Table 3-7: Examples of controlled and sustained release drug delivery for CNS disorders
Table 3-8: Novel methods of delivery of drugs for CNS disorders
Table 3-9: Indications for the clinical applications of NTFs in neurologic disorders
Table 3-10: Methods for delivery of neurotrophic factors to the CNS
Table 4-1: Methods for delivering cell therapies in CNS disorders
Table 4-2: Classification of methods of gene therapy
Table 4-3: Methods of gene transfer as applied to neurologic disorders
Table 4-4: Potential indications for gene therapy of neurologic disorders
Table 4-5: Companies developing cell/gene therapies for CNS disorders
Table 4-6: Methods of antisense delivery as applied to the CNS
Table 5-1: Strategies for the treatment of Parkinson's disease
Table 5-2: Drug delivery systems for Parkinson's disease
Table 5-3: Types of cell used for investigative treatment of Parkinson's disease
Table 5-4: Status of cell therapies in development for Parkinson's disease
Table 5-5: Gene therapy techniques applicable to Parkinson disease
Table 5-6: Companies developing gene therapy for Parkinson's disease
Table 5-7: Classification of pharmacotherapy for Alzheimer disease
Table 5-8: Novel drug delivery methods for Alzheimer disease therapies
Table 5-9: Classification of neuroprotective agents for amyotrophic lateral sclerosis
Table 5-10: Methods of delivery of therapies in development for ALS
Table 5-11: Classification of treatments for stroke
Table 5-12: Treatments of stroke involving innovative drug delivery methods
Table 5-13: Drug delivery for prevention of carotid artery restenosis after angioplasty
Table 5-14: Gene transfer in animal models of carotid artery restenosis
Table 5-15: Neuroprotective gene transfer strategies in models of cerebral ischemia
Table 5-16: Gene Therapy for reducing cerebral infarction in animal stroke models
Table 5-17: Pharmacological agents for treatment of cerebral vasospasm
Table 5-18: Gene therapy strategies for vasospasm
Table 5-19: A classification of drug delivery methods used in management of pain
Table 5-20: Spinal administration of drugs for pain
Table 5-21: Investigational drugs for pain administered by intrathecal route
Table 5-22: Current management of migraine
Table 5-23: Novel drug delivery methods for migraine
Table 6-1: Innovative methods of drug delivery for glioblastoma multiforme
Table 6-2: Strategies for gene therapy of malignant brain tumors
Table 7-1: Share of drug delivery technologies in selected CNS markets: 2015-2025
Table 7-2: CNS market share of drug delivery technologies 2015-2025
Table 7-3: Value of CNS drug delivery in the major world markets from 2015-2025
Table 7-4: Limitations of the current drug delivery technologies for CNS
Table 8-1: Collaborations of companies in CNS drug delivery

Figures
Figure 1-1: Interaction of neurotransmitters with receptors
Figure 2-1: The neurovascular unit
Figure 2-2: Various forms of passage of substances across the blood brain barrier
Figure 3-1: Routes of drug delivery to the brain
Figure 3-2: Penetration of CSF into spinal cord
Figure 3-3: Disposition of opioids after intrathecal administration
Figure 3-4: Use of receptor-mediated transcytosis to cross the BBB
Figure 3-5: Nanotechnology-based strategies for delivery of BDNF to the CNS
Figure 5-1: Oral versus transdermal administration of a drug in Parkinson's disease
Figure 5-2: Effect of tyrosine hydroxylase gene delivery on dopamine levels
Figure 6-1: A concept of targeted drug delivery to GBM across the BBB
Figure 7-1: Unmet needs in the CNS drug delivery technologies

Part II: Companies

8. Companies involved in cancer drug delivery
Introduction
Profiles of companies
Collaborations

Tables
Table 8-1: Oncology pipeline of GlaxoSmithKline
Table 8-2: Roche pipeline of oncology products
Table 8-3: Collaborations of companies in cancer drug delivery

Ordering:
Order Online - http://www.researchandmarkets.com/reports/39080/

Order by Fax - using the form below

Order by Post - print the order form below and send to

Research and Markets,
Guinness Centre,
Taylors Lane,
Dublin 8,
Ireland.
**Fax Order Form**

To place an order via fax simply print this form, fill in the information below and fax the completed form to 646-607-1907 (from USA) or +353-1-481-1716 (from Rest of World). If you have any questions please visit [http://www.researchandmarkets.com/contact/](http://www.researchandmarkets.com/contact/)

**Order Information**

Please verify that the product information is correct and select the format(s) you require.

<table>
<thead>
<tr>
<th>Product Name:</th>
<th>Drug Delivery in Cancer - Technologies, Markets and Companies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Web Address:</td>
<td><a href="http://www.researchandmarkets.com/reports/39080/">http://www.researchandmarkets.com/reports/39080/</a></td>
</tr>
<tr>
<td>Office Code:</td>
<td>SCPL8L5W</td>
</tr>
</tbody>
</table>

**Product Formats**

Please select the product formats and quantity you require:

<table>
<thead>
<tr>
<th>Product Format</th>
<th>Quantity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Electronic (PDF) - Single User</td>
<td>USD 4000</td>
</tr>
<tr>
<td>Hard Copy</td>
<td>USD 4500 + USD 57 Shipping/Handling</td>
</tr>
<tr>
<td>Electronic and Hard Copy (PDF) - Single User</td>
<td>USD 5000 + USD 57 Shipping/Handling</td>
</tr>
<tr>
<td>Electronic (PDF) - Enterprisewide</td>
<td>USD 12000</td>
</tr>
</tbody>
</table>

* Shipping/Handling is only charged once per order.

**Contact Information**

Please enter all the information below in **BLOCK CAPITALS**

<table>
<thead>
<tr>
<th>Title:</th>
<th>Mr ☐</th>
<th>Mrs ☐</th>
<th>Dr ☐</th>
<th>Miss ☐</th>
<th>Ms ☐</th>
<th>Prof ☐</th>
</tr>
</thead>
<tbody>
<tr>
<td>First Name:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Email Address: *</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Job Title:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Organisation:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Address:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>City:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postal / Zip Code:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Country:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phone Number:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fax Number:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Please refrain from using free email accounts when ordering (e.g. Yahoo, Hotmail, AOL)
Payment Information

Please indicate the payment method you would like to use by selecting the appropriate box.

☐ Pay by credit card: You will receive an email with a link to a secure webpage to enter your credit card details.

☐ Pay by check: Please post the check, accompanied by this form, to:
Research and Markets,
Guinness Center,
Taylors Lane,
Dublin 8,
Ireland.

☐ Pay by wire transfer: Please transfer funds to:
Account number 833 130 83
Sort code 98-53-30
Swift code ULSBIE2D
IBAN number IE78ULSB98533083313083
Bank Address Ulster Bank,
27-35 Main Street,
Blackrock,
Co. Dublin,
Ireland.

If you have a Marketing Code please enter it below:

Marketing Code: __________________________

Please note that by ordering from Research and Markets you are agreeing to our Terms and Conditions at http://www.researchandmarkets.com/info/terms.asp

Please fax this form to:
(646) 607-1907 or (646) 964-6609 - From USA
+353-1-481-1716 or +353-1-653-1571 - From Rest of World