Neuroprotection - Drugs, Markets and Companies

Description: This report describes the role of neuroprotection in acute disorders such as stroke and injuries of the nervous system as well as in chronic diseases such as neurodegenerative disorders because many of the underlying mechanisms of damage to neural tissues are similar in all these conditions and several products are used in more than one disorder. Over 500 products have been investigated for neuroprotective effects including those from the categories of free radical scavengers, anti-excitotoxic agents, apoptosis (programmed cell death) inhibitors, anti-inflammatory agents, neurotrophic factors, metal ion chelators, ion channel modulators and gene therapy. Some of the agents are old established pharmaceuticals whereas others are new biotechnology products.

Pathomechanisms of diseases are described with steps at which neuroprotective therapies are directed. Diseases covered include cerebrovascular disorders, traumatic brain injury, spinal cord injury, Alzheimer’s disease, Parkinson’s disease, Huntington’s disease, amyotrophic lateral sclerosis, multiple sclerosis, epilepsy and ischemic optic neuropathy as well as retinal degeneration. Although anesthetics such as propofol are neuroprotective as well, neuroprotection during surgery and anesthesia is discussed with the aim of preventing and treating complications that result in CNS damage.

The report contains profiles of 142 companies that have a neuroprotective product or products along with 120 collaborations. Some of the products in development at academic institutions that do not have a commercial sponsor are also included. Although an up-to-date search of the literature was performed and selected 1,100 references are included. Clinical trials of various neuroprotective agents are described and failures of trials are analyzed with suggestions for improving the selection of drugs and design of trials. The report is supplemented with 77 tables and 16 figures.

Market analysis of currently used products that have a neuroprotective effect are analyzed for the year 2015. Some of these products are approved for other indications but are known to have a neuroprotective effect. With the approval of new products and takeover of markets for obsolete symptomatic therapies, the neuroprotection market value will rise by the year 2020 when it will constitute a major and important component of the CNS market. Forecasts are made until 2025. By that time neuroprotection will be an established part of the neurological practice and measures will be available to achieve this effectively.

Contents:

Part I: Drugs & Markets

0. Executive Summary

1. Introduction
   Definitions
   Historical development of neuroprotection
   Intrinsic neuroprotective factors
   Neuroprotective gene expression
   Upregulation of GADD34
   Induction of N4R4A proteins by CREB in neurons
   Elevation PGC-1a for neuroprotection in PD
   Neurotrophic factors
   Intrinsic nonenzymatic antioxidants
   Activation of transcription factor Nrf2
   Intrinsic neuroprotective proteins
   aB-crystallin
   Excitatory amino acid transporters
   Extracellular serine protease thrombin
   Galanin
   Neuroglobin
   Nuclear factor I-A
   Prion protein
   Rai adaptor protein
Stem cell factor
Role of the immune system in neuroprotection
Role of astrocytes in neuroprotection
Role of lymphatic system in neuroprotection
Role of sleep in neuroprotection
Role of cerebral metabolism in neuroprotection
Role of circadian genes in neuroprotection
Role of blood-brain barrier in neuroprotection
Role of the gut microbiota in development of integrity of the BBB
Induction of DNA repair enzymes for neuroprotection
Microtubule-based neuroprotective response to axonal injury
Pathomechanisms of CNS injury as basis for neuroprotection
Biomarkers of neurological disorders and neuroprotection
CNS biomarker identification using proteomics
Brain imaging for detection of biomarkers
Role of neuroprotection in various neurological disorders
Neuroprotection and neuroregeneration
Acute versus chronic neuroprotection
Discovery and evaluation of neuroprotective agents
Neuroprotective drug discovery
Discovery of CNS drugs that penetrate the blood-brain barrier
In vitro assays for the evaluation of neuroprotective agents
Oxidative injury model to test neuroprotective drugs
Apoptosis model for designing neuroprotective drugs
Transgenic mouse models of neurological disorders
Evaluating effects of neuroprotective drugs on living brain slices
Role of brain imaging in neuroprotective drug discovery and development
Positron emission tomography
Role of single photon emission computed tomography
Functional CT scanning to evaluate cerebrovascular protection
Magnetic resonance imaging for the evaluation of neuroprotectives
Application of nanotechnology to neuroprotection
Nanoparticles as neuroprotective antioxidants
Cadmium telluride nanoparticles prevent Aβ fibril formation
Evaluation criteria for potential neuroprotective agents

2. Neuroprotective Agents
Classification of neuroprotective agents
a1 adrenoreceptor agonists
Dexmedetomidine
Activated protein C
Activity-dependent neuroprotective protein
Davunetide
Adenosine analogs
Propentofylline
Antidepressants
Antidepressant-induced neurogenesis
Neurogenesis induced by electroconvulsive therapy
Neuroprotective effect of selective serotonin reuptake inhibitors
Antiepileptic drugs as neuroprotectives
Phenytoin
Valproic acid
Levetiracetam
Antiinflammatory agents
Aspirin
Interleukin-1 antagonists
COX-2 inhibitors
Nimesulide
Gold microparticles as anti-neuroinflammatory agents
Minocycline
Prostaglandin receptor antagonists
Anti-apoptosis agents
Activated protein C
Calpain inhibitors
Caspase inhibitors
DNA binding drugs
Lithium
Melatonin
Olesoxime
Omega-3 fatty acids
Docosahexaenoic acid
Poly(ADP-ribose) polymerase inhibitors
Prevention of apoptosis by binding of proNGF to sortilin
Antioxidants/free radical scavengers
Free radical generation
Natural defenses against oxidative stress
Effects of oxidative damage
Oxidative damage and aging
Neuronal damage by free radicals
Oxidative damage and neurodegenerative disorders
Measures to control oxidative stress
Categories of therapeutic antioxidants
Alpha-phenyl-tert-butylnitrone
Coenzyme Q10
Dihydroergocryptine
Flavonoids
Mitochondria-targeted antioxidants
Neuroleptics as antioxidants
Nitrones
NRF2 for augmenting neuroprotection against oxidative stress
Translation of antioxidant neuroprotection from preclinical to clinical
Carbon monoxide and heme oxygenase
Cell transplants
Cells secreting neuroprotective substances
Stem cells
Stem cell activation for neuroprotection/regeneration by glucocorticoids
Use of neural stem cells to construct the blood brain barrier
Cytokines
Erythropoietin
Non-erythropoietic EPO variants and mimics
Granulocyte colony-stimulating factor
Delta-opioid receptor agonists
Delta opioid peptide-induced hibernation for neuroprotection
FK960
Gene therapy
Glucagon-like peptide
Glatiramer acetate
Glutamate antagonists
Neuroprotection by scavenging blood glutamate
N-acylethanolamines for protection against glutamatergic excitotoxicity
Glutamate transporters
Glutamate transporter-mediated neuroprotective effect of drugs
Neuroprotection by targeting KAI subunit of kainate receptor
Glycine-proline-glutamate analogs
Hydrogen sulfide
Hibernation induced by hydrogen sulfide
NMDA receptor ion channel complex
NMDA receptor antagonists
NMDA NR2B subunit receptor antagonists
Ifenprodil
Memantine as a neuroprotective agent
NAALADase inhibitors
Gacyclidine
N-alkylglycines
AMPA receptor modulators
Metabotropic glutamate receptor modulators
Cannabinoids
Dexanabinol
Glutathione
Heat shock proteins
Histone deacetylase inhibitors for neuroprotection
Hormones
Estrogen and neuroprotection
Neuroprotective effect of estrogen receptor ligands
Selective estrogen receptor modulators
Mitochondrial mechanisms of estrogen neuroprotection
Insulin
Ion Channel modulators
Calcium channel blockers.
Na+Ziconotide channel blockers.
Neuroprotective potassium channel inhibitors
Kynurenic acid inhibitors
Leukocyte adhesion inhibitors
Modafinil
Neural regeneration protein
Neurite outgrowth-promoting prostaglandin compounds
Neuroimmunophilins
Cyclosporin-A
FK506
Rapamycin
Neurotrophic factors
Activity-dependent neurotrophic factor
Bone morphogenetic proteins
Brain-derived neurotrophic factor
Ciliary neurotrophic factor
Fibroblast growth factors
Glial cell line-derived neurotrophic factor
Insulin-like growth factor
Nerve growth factor
Neurotrophins
Osteogenic protein-1
Pigment epithelium-derived factor
Transforming growth factor-β1
Vascular endothelial growth factor
Neurotrophic factor-related neuroprotective agents
Amitriptyline as a TrkA and TrkB receptor agonist
Colivelin
Gamboic amide
Inosine
Meteorin
Oxygen-regulated protein 150 kDa
Prosaptide
Siagoside
Small molecule activators of the Trk receptors
Nicotine and nicotinic receptor agonists
Neuroprotective effect of galantamine mediated via a7nAChRs
Galantamine-induced Aβ clearance via a7nAChRs
Nitric oxide-based neuroprotection
Nitric oxide synthase inhibitors
Nitric oxide mimetics
Nitric oxide donating derivatives
Nootropics
Piracetam
Nutraceuticals and naturally-derived compounds
Cinnamon
Coffee
Creatine
Curcumin/curry
Mechanism of neuroprotective effect of curcumin
Flavonoids
Glyceryltriacetate
Green tea
Herbal preparations
Flavonoid wogonin
Ginseng
Nicotinamide
Punicalagin from pomegranate
Resveratrol
Osmotic diuretics
Mannitol
Osteopontin
Oxygen therapeutics
Oxygen carriers
Hemoglobin-based oxygen carriers
Perfluorocarbons as oxygen carriers
Hyperbaric oxygen therapy
P7C3 compounds
Peptides
C3-derived peptide for neuroprotection and neuroregeneration
Corticotropin-releasing hormone
Thyrotropin-releasing hormone
Vasoactive intestinal peptide
Pharmacological preconditioning
PPARs as drug targets for neuroprotection
Protein kinase C activators
Riluzole
Role of RNA interference in neuroprotection
Role of miRNA in neuroprotection
Sigma receptor agonists as neuroprotective agents
SIRT group of proteins
Statins
Steroids
Dehydroepiandrosterone
HF0220
Sulforaphane
Tauroursodeoxycholic acid
Tetanus toxin as a neuroprotective agent
Thrombolytic agents as neuroprotective agents
Uncoupling protein 2
Vaccines as neuroprotectives
Vitamins as neuroprotective agents
Vitamin B12
Vitamin D
Non-pharmacological approaches to neuroprotection
Caloric restriction
Electrical fields for improvement of cerebral function in neurodegeneration
Environmental enrichment
Hypothermia
Limitations of hypothermia
Hypothermic neuroprotection in hypoxia-ischemia
Ketogenic diet
Mental training
Mediterranean diet
Nonpharmacological preconditioning for neuroprotection
Physical exercise
Suspended animation and neuroprotection
Transcranial magnetic stimulation

3. Neuroprotection in Cerebrovascular Disease
Introduction
Pathophysiology of cerebral ischemia
Calcium overload
Ion channel dysfunction in stroke
Role of oxygen free radicals in cerebral ischemia
Role of nitric oxide in cerebral ischemia
Glutamate as a biomarker of stroke
Cerebral edema in stroke
Gene expression in response to cerebral ischemia
Induction of heat shock proteins in stroke
Role of cytokines and adhesion molecules in stroke
Tumor necrosis factor-a
Interleukin-1 and IL-6
Adhesion molecules
DNA damage and repair in cerebral ischemia
Role of neurotrophic factors in stroke
Problems requiring investigation of the role of NTFs in stroke
Role of Poly(ADP-ribose) polymerase (PARP) gene
Role of protease-activated receptor 1
Reperfusion injury after cerebral ischemia
Neuroprotection according to zones in cerebral infarction
Zone of ischemic infarction
Penumbra
Current management of stroke
Neuroprotection in stenosis of intracranial arteries
Neuroprotection in stroke with intracerebral hemorrhage
Prevention of hemorrhage from cerebral cavernous malformation
Neuroprotection in transient ischemic attacks
Secondary prevention of stroke
Neuroprotective therapies for stroke
aB-crystallin as a neuroprotectant in stroke
Acid-sensing ion channel blockers
AMPA receptor antagonists as neuroprotectives for stroke
Zonampanel
Antiapoptotic neuroprotectives
NIM811
Creatine as neuroprotective in stroke
Lithium as a neuroprotective in stroke
TUDCA as a neuroprotective in stroke
Antiepileptic drugs as neuroprotectives in stroke
Tiagabine
Topiramate
Zonisamide
Anti-HMGB1 monoclonal antibody
Antioxidant approaches
Carnosine as a neuroprotective in stroke
Dehydroascorbic acid
Tocotrienols
Uric acid
Antiglutamate compounds
MRZ 2/576
L-Phenylalanine
Arimoclomol for stroke
Cardiac glycosides as neuroprotectives in stroke
Clenbuterol
Coagulation inhibitors as neuroprotectives
Heparin and enoxaparin
Warfarin vs dabigatran
Apixaban
Cox-2 inhibitors for ischemic stroke
Curcumin as a neuroprotectant in stroke
Docosahexaenoic acid for ischemic stroke
Ephrin-A5 blockers
Estrogen for stroke
Extendin-4
Flavones for neuroprotection in stroke
Epicatechin
Isorhamnetin
Granulocyte-macrophage colony-stimulating factor for cerebral ischemia
Hamartin induction by cerebral ischemia as a basis for neuroprotection
Histone deacetylase inhibitors for neuroprotection in stroke
Modulation of histamine H-receptors
Inosine for stroke
Insulin-like growth factor-I
Intravenous immunoglobulin as neuroprotective in stroke
Ischemic preconditioning for neuroprotection in stroke
Histone deacetylase inhibitors for neuroprotection in stroke
Ketone bodies for neuroprotection in stroke
Magnesium
Mineralocorticoid receptor blockade for neuroprotection
miR-223 and neuroprotection in stroke
Multifunctional neuroprotective agents
NA-1 as neuroprotective against ischemic stroke
Nasal delivery of neuroprotective agents in stroke
Neuroserpin as a neuroprotective in stroke
N-2-mercaptopropionyl glycine
NeuroAid
Neurotrophic factors as neuroprotectives for stroke
Brain-derived neurotrophic factor
Fibroblast growth factor
G-CSF
Glial cell line-derived neurotrophic factor
Insulin-like growth factor-1
Neuregulin-1
NO-based strategies for neuroprotection in cerebral ischemia
Omega-3 fatty acids for neuroprotection after cerebral ischemia-hypoxia
Pannexin channel blockers for neuroprotection in stroke
Perlecan domain V
Peroxisome proliferator-activated receptor-? agonists
PGE EP2 receptor activation
Pioglitazone for reduction of stroke risk
Progestosterone
Propofol as neuroprotective in stroke
Proteoglycan-degrading enzymes
Proteosome inhibitors
Statins for prevention and neuroprotection in stroke
Sildenafil
Src receptor blockade
Stroke vaccine
SUN N4057
Thrombosis inhibitors
Aspirin
Clopidogrel
Dipyridamole
Ticagrelor
Vitamin E for neuroprotection in stroke
Neuroprotection in ischemia-reperfusion injury
Aminoguanidine
Dexmedetomidine
Methylene blue for neuroprotection in ischemia-reperfusion injury
Miscellaneous agents for neuroprotection in reperfusion injury
Prevention of hemorrhage following ischemic stroke
Non-pharmacological neuroprotective therapies for stroke
Hypothermia for neuroprotection in acute stroke
Hyperbaric oxygen therapy for neuroprotection in acute stroke
Hypothermia combination with other neuroprotective strategies
Infrared laser therapy for ischemic stroke
Preconditioning for neuroprotection against cerebral ischemia
Neurosurgical procedures for stroke
Neurosurgical procedures for neuroprotection in acute stroke
Neurosurgical procedures for chronic cerebral ischemia
Neurostimulation of sphenopalatine ganglion
Stent versus surgery for asymptomatic carotid stenosis
Neurorehabilitation in relation to neuroprotection in stroke
Protective effect of physical activity on stroke in the elderly
Cell therapy for stroke
Stem cell transplant for stroke
Immortalized cell grafts for stroke
Stimulation of intrinsic stem cells for repair of brain in stroke
Neuroprotective vaccines for stroke
Gene therapy for neuroprotection in cerebrovascular disease
Regulation of microRNAs for neuroprotection in cerebral ischemia
RNAi-based therapy for neuroprotection in stroke
Neuroprotective therapies for cerebral ischemia: clinical trials
Albumin
Free radical scavengers
DP-b99
Mildronate
Minocycline for neuroprotection in stroke
Perindopril
Failed clinical trials of neuroprotection in stroke
Ancrod
Aptiganel
Cerovive
Citocline
Desmoteplase
Erythropoietin as a neuroprotective in stroke
SPD 502
Tirilazad mesylate
Selfotel
Lubeluzole
Nalmefene
Gavestinel
Nimodipine
Sipatrigine
Causes of failure of stroke trials
Measures for prevention of failures in stroke trials
Design of acute stroke trial to facilitate drug approval
The ideal neuroprotective agent for stroke
Future prospects for neuroprotection in stroke

4. Neuroprotection in Traumatic Brain Injury
Introduction
Cerebral hypoxia/ischemia as a complication of trauma
Epidemiology of TBI
TBI in the military
Pathophysiology of TBI
Immediate damage following TBI
Cerebral edema following TBI
Neurometabolic cascade after TBI
Delayed damage following TBI
Mechanism of axonal damage after TBI
Role of neuroinflammation in TBI
BBB damage after TBI
Molecular events following TBI
Chronic traumatic encephalopathy
Neurocognitive sequelae of TBI
Changes in neurotrophic factors following TBI
Changes in neurotransmitters following TBI
Proteomics of TBI
Genetic influences on outcome following TBI
Management of TBI
Management during acute phase of head injury
Control of intracranial pressure and cerebral edema
Corticosteroids
Neuroprotection in TBI
Amantadine
Antioxidants
Barbiturates
ß- and δ-secretase inhibitors
Beta blockers
Bradykinin B antagonists
Cell cycle inhibitors for TBI
COX-2 inhibitors for neuroprotection in TBI
Cyclosporin for neuroprotection in TBI
Dexanabinol for TBI
Erythropoietin for neuroprotection in TBI
Gold implants for neuroprotection in focal TBI
Histone deacetylase inhibitors for neuroprotection in TBI
KN 38-7271
Levosimendan
Magnesium sulfate
Minocycline for TBI
Multipotential neuroprotective agents for TBI
Nutritional approaches to neuroprotection in TBI
Branched chain amino acids to ameliorate cognitive impairment in TBI
Creatine for neuroprotection in TBI
Nicotinamide for neuroprotection in TBI
Omega 3 fatty acids as neuroprotectives in TBI
Neurotrophic factors for TBI
Neurosteroids as neuroprotective agents for TBI
NMDA receptor antagonists
NP-1
Nogo-A inhibitor
Oxygen carriers for TBI
Polyethylene glycol for neuroprotection in TBI
Propofol for neuroprotection in TBI
Rapamycin as neuroprotective in TBI
Simvastatin as neuroprotective in TBI
Thyrotropin-releasing hormone analogs
Traxoprodil
Biological approaches to neuroprotection in TBI
Antisense approaches to TBI
Cell therapy for TBI
Gene therapy for TBI
Vaccines for TBI
Non-pharmaceutical approaches to neuroprotection in TBI
Deep brain stimulation for TBI
Hyperbaric oxygen therapy for TBI
Hypothermia
Reduction of microglial migration after TBI
Vacuum for mechanical tissue resuscitation in TBI
Prophylactic neuroprotection against TBI
Role of helmets in protection against TBI
Role of physical exercise in protection against TBI
Neuroprotection against late sequelae of TBI
Antiepileptic drugs for prevention of seizures and neuroprotection
Neuroprotection during rehabilitation phase of TBI
Neuroregeneration following TBI
Intrinsic factors that influence regeneration following TBI
Causes of lack of regeneration following TBI
Approaches to regeneration of the brain following TBI
Clinical trials of neuroprotective agents in TBI
Ongoing clinical trials in TBI
Failed clinical trials in TBI
Differences between clinical trials and studies in animal models of TBI
Subgroup analysis
Improving the clinical trial design
Clinical trials combining multiple treatment strategies
Shortening the trial time
Conclusions and future prospects of neuroprotection in TBI

5. Neuroprotection in Spinal Cord Injury
Introduction
Pathophysiology of SCI
Secondary mechanisms of SCI
Neurotrophic factor changes in SCI
Management of SCI
Pharmacological neuroprotective agents for SCI
4-aminopyridine
Antibodies as neurite growth inhibitors in SCI
Antie excitotoxic agents
Gacyclidine
GM-1 ganglioside
Bacterial enzyme chondroitinase ABC
Docosahexaenoic acid as neuroprotective in SCI
Erythropoietin as a neuroprotective in SCI
Free radical scavengers for neuroprotection in SCI
GYKI 52466
Immunosuppressants as neuroprotectants in SCI
Interleukin-10 for neuroprotection in SCI
Matrix metalloproteinase inhibitors for SCI
Methylprednisolone
Minocycline as neuroprotective in SCI
Modulation of macrophage responses for neuroprotection after SCI
Neurotrophic factors for neuroprotection after SCI
Promotion of regeneration of neurons in SCI
Rho pathway and Rho antagonists in SCI
Selenium as a neuroprotective for SCI
Sialidase for enhancing recovery after SCI
Targeting the inflammatory response for neuroprotection in SCI
Uric acid as neuroprotective in SCI
Non-pharmacological approaches to SCI
Hyperbaric oxygen therapy
Hypothermia for SCI
Cell therapy for SCI
Autoimmune T cells against CNS myelin-associated peptide
Fetal neural grafts for SCI
Olfactory-ensheathing cells for SCI
Oligodendrocyte precursor cells for treatment of SCI
Schwann cell transplants for SCI
Transplantation of glial cells for SCI
Stem cells for SCI
Bone marrow stem cells for SCI
Embryonic stem cells for SCI
Transplantation of induced pluripotent stem cells in SCI
Transplantation of MSCs for SCI
Transplantation of NSCs for SCI
Transdifferentiation of stem cells into cholinergic neurons for SCI
Gene therapy for SCI
Combined approaches to spinal cord injury
Discovery of new targets for neuroprotective therapies in SCI
Clinical trials in SCI

6. Neuroprotection in Neurodegenerative Disorders
Introduction
Pathomechanism of neurodegeneration
Aging and neurodegeneration
Dual role of a-synuclein in neuroprotection and neurodegeneration
Dysregulation of cyclin-dependent kinase 5
Role of exosomes in the CNS and neurodegeneration
Lack of neurotrophic factors
Neuroinflammation in neurodegenerative disorders
Neurodegeneration associated with protein misfolding
Modulation of neurodegeneration by molecular chaperones
Intrabodies targeting protein misfolding in neurodegeneration
Targeting proteins aggregation to prevent amyloid formation
Tau and neurodegeneration
Role of apoptosis in neurodegenerative disorders
Role of glia in neurodegeneration
Role of metals in neurodegeneration
Spread of neurodegeneration
TDP-43 proteinopathy and neurodegenerative diseases
Viral infections and neurodegeneration
AIDS and the nervous system
Avian influenza as cause of neurodegeneration
Neurodegenerative disorders with dementia
Dementia with Lewy bodies
Pick disease
Progressive supranuclear palsy
Genetic disorders with neurodegeneration
Batten disease
Friedrich ataxia
Pathomechanism of FA
Neuroprotection in FA
Niemann-Pick type C disease
Creutzfeldt-Jakob disease
Neuroprotection in Creutzfeldt-Jakob disease
Pharmacological neuroprotectants against CJD
Innovative approaches to neuroprotection in CJD and future prospects
Approaches to neuroprotection in neurodegenerative disorders
Glutamate-based therapies for neurodegenerative disorders
Histone deacetylase inhibitors for neurodegenerative disorders
Iron chelation for neuroprotection
Mitochondria permeability transition pore complex and neuroprotection
Genomics-based research in neurodegenerative diseases

7. Neuroprotection in Parkinson Disease
Introduction
Epidemiology of Parkinson's disease
Pathophysiology of Parkinson's disease
Alteration of dopamine homeostasis
Apoptosis
Asynchronous neuronal activity
Disruption of iron homeostasis
Excitotoxicity
Genetic factors in PD
Oxidative stress
Role of neurotrophic factors
Role of misfolding proteins
Neuroprotective strategies for PD based on pathomechanism
A genetic animal model of PD for testing neuroprotective strategies
Aldehyde dehydrogenase 1 protects nigrostriatal dopaminergic neurons
RNAi screening to identify neuroprotective genes in a PD model
Management of Parkinson's disease
Limitation of conventionally administered dopamine therapy
Neuroprotective therapy in PD
Neuroprotective effect of currently used drugs for PD
Pramipexole
Rasagiline mesylate
Ropinirole
Rivastigmine for treatment of dementia and falls associated with PD
Selegiline
Non-pharmacological strategies for neuroprotection in PD
Deep brain stimulation for PD
Effect of exercise and environmental enrichment on PD
Low-calorie diet in PD
Development of neuroprotective therapies for PD
2B3-201 for targeted delivery of methylprednisolone
9-methyl-β-carboline
Adenosine A
A receptor antagonists
Antiapoptotic strategies for PD
ATP13A2 activation
Augmenting CNS glucocerebrosidase activity
Calcium channel blockers for PD
Cell therapies for PD
Stem cells for PD
Activation of endogenous stem cells and neural precursors
Cogane
Creatine and minocycline
Conserved dopamine neurotrophic factor for PD
Free radical scavengers for neuroprotection in Parkinson's disease
Antioxidants
Diapocynin
Tea extracts as neuroprotectives
Gene therapy for PD
Implantation of genetically engineered cells
Gene therapy using GDNF and neurturin
Glutamic acid decarboxylase gene therapy
Parkin gene therapy
Concluding remarks about gene therapy for PD
Heat shock protein 70
Liver X receptor β agonists
Melatonin as a neuroprotectant in PD
Nicotine as a neuroprotective in PD
Nilotinib for PD
Neuroprotective effect of leucine-rich repeat kinase-2 inhibitors
Neuroprotective effect of DJ-1 protein
Neurotrophic factors
Basic fibroblast growth factor for PD
BDNF for PD
GDNF for PD
MANF for PD
Neurturin for PD
Platelet derived growth factor
Clinical trials with NTFs
Nrf2-mediated neuroprotection in PD
Omega-3 polyunsaturated fatty acids
RAB3B overexpression
RNAi therapy for PD
Safinamide
Sirtuin 2 inhibitors for neuroprotection in PD
Statins and PD
Targeting Bax
Vitamin D for neuroprotection in PD
Vaccine for PD
Clinical trials of neuroprotection in Parkinson's disease
Evaluation of neuroprotective therapies for PD
Current status and future challenges for neuroprotection in PD

8. Neuroprotection in Alzheimer Disease
Introduction
Pathomechanism of Alzheimer's disease
Role of glutamate transport dysfunction in AD
Role of neurotrophic factors in the pathomechanism of AD
Management of Alzheimer's disease
Neuroprotection in Alzheimer's disease
Inhibition of Aβ formation and aggregation
AN-1792
Clioquolin
Colostrinin
FKBPS2 for neuroprotection from Cu toxicity in AD
Monoclonal antibody m266
Phenerine
Secretase inhibitors
Inhibition of neuroinflammation
Etanercept
Neurotrophic factors for neuroprotection in AD
AL-108
NGF gene therapy
Small molecule compounds binding to neurotrophin receptor p75NTR
Targeting plasminogen activator inhibitor type-1 gene
Estrogen and AD
Antioxidants
NSAIDS
Melatonin for AD
Memantine
Dimebon
Cerebrolysin
Curcumin as a neuroprotectant in Alzheimer disease
Ginko biloba
Tetrahydrocannabinol for neuroprotection in AD
Ladostigil tartrate
Phosphodiesterase inhibitors as neuroprotectives
PPAR-? agonists
Role of statins in reducing the risk of AD
Combined therapeutic approaches to AD
Clinical trials in AD
Future prospects of neuroprotection in AD
Mild cognitive impairment
Relation of MCI to AD
Neuroprotection in MCI

9. Neuroprotection in Huntington Disease
Introduction
Pathophysiology of HD
Management of Huntington's disease
Neuroprotection in Huntington's disease
Antipsychotic D and 5-HT1A antagonists
Caspase inhibitors
Clioquinol for HD
Creatine for stabilizing bioenergetic defects
Cysteamine
Drugs that block inappropriate calcium release from neurons
Enhancing protease activity for clearance of mHtt
Eicosapentaenoic acid
Free radical scavengers
Histone deacetylase inhibitors
Inhibitors of polyglutamine aggregation HD
Metal-protein attenuating compounds
Pridopidine
RRAS signaling pathway inhibition
Simvastatin as a neuroprotective in HD
Single chain Fv antibodies
SIRT1 activators for neuroprotection in HD
SIRT2 inhibitors for neuroprotection in HD
Synaptic activation of NMDA receptors
Targeting mutant huntingtin protein
Tetrabenazine
Combinatorial therapy and targeting multiple pathways in HD
Cell transplants
Neurotrophic factors and gene therapy
RNAi and antisense therapies for Huntington's disease

10. Neuroprotection in Amyotrophic Lateral Sclerosis

Introduction
Pathophysiology of ALS
Neuroprotective therapies for ALS
Activated protein C
AEOL 10150
AIMSPRO
Anakinra
Antisense therapy
Arimoclomol for ALS
Ceftriaxone for ALS
Coenzyme Q10 for ALS
COX-2 inhibitors for ALS
Creatine for ALS
Dexmipexole
Diallyl trisulfide
Erythropoietin for ALS
Gene therapy for ALS
Glatiramer acetate
GM602
Insulin-like growth factor
Ketogenic diet for neuroprotection in ALS
Lenalidomide
Lithium for neuroprotection in ALS
Masitinib
Melatonin for ALS
Methylcobalamin
Minocycline for ALS
Olesoxime as neuroprotective for ALS
ONO-2506 for ALS
Riluzole
RNAi-based therapy for ALS
Sodium phenylbutyrate
Stem cell therapy
Clinical applications
Stem cell-based drug discovery for ALS
Suppressors of mTDP-43 toxicity
Talampanel
Tamoxifen
Vaccination for ALS caused by SOD1 mutations
Vascular endothelial growth factor for ALS
Vitamin E for ALS
Clinical trials of neuroprotective therapies for ALS
Concluding remarks and future prospects

11. Neuroprotection in Miscellaneous Neurological Disorders

Introduction
Neuroprotection in dementia
Age-related dementia
Aging brain and oxidative stress
Enhancing endogenous neurotrophic support of the aging brain
Hsp70 and age-related neurodegeneration
Pharmacological approaches for treatment of age-related dementia
Physical exercise to prevent decline of mental function with aging
Vascular dementia
Prediction of dementia in persons with vascular risk factors
Management of subcortical vascular dementia
Dementia with Lewy bodies
Neuroprotection in AIDS dementia
Multiple system atrophy
Epilepsy
Mechanisms of neuronal damage in epilepsy
Strategies for neuroprotection in epilepsy
Control of seizures by AEDs and neuroprotection
Prevention of seizures by ketogenic diet
Hyalurona-based preservation of brain ECS volume for seizure control
Cell therapy for neuroprotection in epilepsy
Cell therapy of posttraumatic epilepsy
Cell therapy for temporal lobe epilepsy
Cell therapy for pharmacoresistant epilepsies
Gene therapy for neuroprotection in epilepsy
Neurogenetic disorders
Leigh syndrome
Spinal and bulbar muscular atrophy
Spinal muscular atrophy
Multiple sclerosis
Introduction
Epidemiology of multiple sclerosis
Pathophysiology
Current management of multiple sclerosis
Specific therapies for MS based on pathomechanism
Neuroprotection in multiple sclerosis
Clinical trials of neuroprotective therapies for MS
Neuroprotection by control of progressive forms of multiple sclerosis
Neuroprotection by controlling autoimmune inflammation in the brain
Neuroprotection by sealing the BBB with imatinib
TRPM4 cation channel blockers
Remyelination for neuroprotection in multiple sclerosis
Agents for neuroprotection in multiple sclerosis
Angiotensin-II inhibitors
Antiglutamate agents
Antioxidants for neuroprotection in MS
Antisense and RNAi approaches to MS
B cell depletion therapy
Cell therapy for multiple sclerosis
Cannabinoids for neuroprotection in MS
Cladribine
Curcumin as a neuroprotectant in multiple sclerosis
Cytokine-directed therapies in MS
Dalfampridine in MS
Dimethyl fumarate
DNA vaccine for MS
Erythropoetin as a neuroprotective in MS
Fingolimod
Fusokine composed of GM-CSF and IL-15 for immune suppression
Gene therapy for MS
Ibudilast for MS
Iron chelators
IVIG for MS
Kinase inhibitors
Laquinimod
Melatonin for MS
Monoclonal antibodies for MS
Natalizumab
Natural human antibodies for repair of myelin
Neurotrophic factors for multiple sclerosis
Oral immunomodulatory agents for MS
Protein kinase Cβ as a therapeutic target for stabilizing BBB in MS
Recombinant T-cell ligands
Statins for MS
Teriflunomide
Tolerance-directed immunotherapy for MS
Concluding remarks and future prospects for neuroprotection in MS
Neuroprotection in transverse myelitis
Neuroprotection in decompression sickness
Neuroprotection in victims of drowning
Neuroprotection in CSF circulatory disorders
Neuroprotection in hydrocephalus
Neuroprotection in normal pressure hydrocephalus
Neuroprotection in infections of the CNS
Neuroprotection in bacterial meningitis
Mechanism of neural injury in bacterial meningitis
Strategies for neuroprotection
Neuroprotection in cryptococcal meningitis
Neuroprotective approach to rabies
Neuroprotection in cerebral malaria
Neuroprotection in complications of systemic disorders
Neurological complications of cardiovascular disorders
Neuroprotection after myocardial infarction
Neuroprotection in hypertensive encephalopathy
Management of hypertension to prevent dementia
Neuroprotection in complications of diabetes
Neuroprotection in hypoglycemic coma
Neuroprotection in diabetic retinopathy
Neurological complications of liver disorders
Hepatic encephalopathy
Bilirubin encephalopathy
Neuroprotection in neurological complications of renal disease.
Neuroprotection in toxic encephalopathies
Encephalopathy due to organophosphorus poisoning
Neuroprotection against chemotherapy-induced brain damage
Neuroprotection against alcohol
Alcoholic neurologic disorders
Fetal alcohol syndrome
Pathogenesis of alcohol-induced damage to the nervous system
Neuroprotection against neurotoxicity of alcohol
Neuroprotection against exposure to therapeutic radiation
Neuroprotection against radiation encephalopathy
Role of SOD in protection again radiation-induced hippocampal dysfunction
Catalase reduces mitochondrial ROS for neuroprotection from proton irradiation
Neuroprotection in hypoxia-ischemia
Neuroprotection in neonatal hypoxic-ischemic brain injury
Pathomechanism of neonatal hypoxic-ischemic brain injury
Management of neonatal hypoxia-ischemia
Approaches to neuroprotection in neonatal hypoxia-ischemia
Hyperbaric oxygen for neonatal hypoxia-ischemia
Hypothermia for neonatal hypoxia-ischemia
Melatonin for neonatal hypoxia-ischemia
Minocycline for neonatal hypoxia-ischemia
Nicotinamide mononucleotide adenylyl transferase 1
Nitric oxide inhalation for neonatal hypoxia-ischemia
Plasminogen activator inhibitor-1 for neonatal hypoxia-ischemia
Recombinant erythropoietin for neonatal hypoxia-ischemia
Neuroprotection in carbon monoxide poisoning
Pathomechanism of CO poisoning as a basis for neuroprotection
Management of CO poisoning
Syndrome of delayed post-hypoxic leukoencephalopathy
Neuroprotection of the fetus
Neuroprotection in sleep apnea
Neuroprotection in mitochondrial dysfunction
Mitochondrial permeability transition
Mitochondrial approaches for neuroprotection
Methylene blue
Role of nanolasers in evaluation of mitochondrial neuroprotectants
Neuroprotection in mitochondrial encephalopathies
Neuroprotection in psychiatric disorders
Cognitive impairment in schizophrenia
Electroconvulsive therapy and neuroprotection
Neuroprotection in schizophrenia
Neuroplasticity and neuroprotection in stress-induced psychiatric disorders
Neuroprotection in hearing loss
Causes of hearing loss
Pathomechanism of hearing loss
Prevention and treatment of hearing loss
Hyperbaric oxygen for hearing loss
Stem cell therapy for hearing loss
Auditory hair cell replacement by gene therapy
Pharmaceutical approaches to hearing loss
Neuroprotection of peripheral nerves
Neuroprotective agents for peripheral nerves
Acetyl-L-carnitine for peripheral nerve injuries
Atorvastatin for peripheral nerve injuries
Erythropoietin for neuroprotection in peripheral nerve injuries
Neuroprotection in peripheral nerve injuries
Role of hyperbaric oxygen in peripheral nerve injuries
Role of neurotrophic factors in peripheral nerve injuries
Pharmacological approaches to Schwann cells
Role of gene therapy in neuroprotection of injured peripheral nerves
Schwann cell transplantation for peripheral nerve injury
Targeting Wallerian degeneration slow protein for neuroprotection
Peripheral neuropathy
Neuroprotection in diabetic neuropathy
Cell therapy for neuroprotection in diabetic neuropathy
Gene therapy with zinc finger DNA-binding proteins
Neuroprotection in chemotherapy-induced neuropathy
Chronic inflammatory demyelinating polyradiculoneuropathy
Neuroprotection in CIDP

12. Neuroprotection of the Optic nerve and the Retina
Introduction
Optic neuropathy
Pathophysiology
Neuroprotection in optic neuritis
Evaluating efficacy of drugs for optic neuritis
Flupirtine
Sodium channel blockers
Resveratrol
Neuroprotection in optic nerve trauma
Potential regeneration of the optic nerve
Subthreshold transpupillary thermotherapy for protection of RGCs
Neuroprotection of optic nerve in glaucoma
Aminoguanidine as a neuroprotective in glaucoma
Antiglutamate agents for neuroprotection of optic nerve
Betaxolol
NGF eye drops
Targeting Aβ in glaucoma treatment
TNF-a blockers for neuroprotection in glaucoma
Concluding remarks about neuroprotection in glaucoma
Neuroprotection in retinal ischemia
Endogenous neuroprotection in the retina
β-adrenoceptor antagonists
Brimonidine as a neuroprotective is ischemic retinopathy
Thioredoxin as a neuroprotective agent in retinal ischemia
Erythropoietin for neuroprotection of retinal ischemia
Gene therapy for retinal neuroprotection
Hyperbaric oxygen for central retinal artery occlusion
Protection against oxygen-induced retinopathy
Neuroprotection in macular degeneration
Epidemiology
Pathomechanism of AMD
Current treatment of AMD
Novel neuroprotective strategies against retinal degeneration
Antiangiogenic agents
Humanized MAb against Aβ
LXR agonists
Neurotrophic factors for neuroprotection in AMD
CNTF for neuroprotection in AMD
N-acetylserotonin derivatives
Nutritional protection against AMD
Progestogenic hormones
Protection of retinal cells from oxidative-stress-induced apoptosis
Sulindac
Tandospirone
Cell therapy for macular degeneration
Retinal pigment epithelial cells
Stem cells
Neural progenitor cells
Gene therapy for retinal degeneration
RNAi-based treatments for AMD
Neuroprotection in proliferative diabetic retinopathy
RNAi-based approaches to diabetic retinopathy
Clinical trials for optic nerve and retinal neuroprotection

13. Neuroprotection during Anesthesia and Surgery
Introduction
Anesthetic agents as neuroprotectives
Barbiturates
Thiopental
Etomidate
Propofol
Ketamine
Gaseous anesthetics
Isoflurane
Xenon
Local anesthetics
Monitoring of CNS function during anesthesia and surgery
Monitoring of cerebral function
Monitoring of spinal cord function during spinal surgery
Perioperative neuroprotection
Neuroprotection during cardiovascular procedures
CNS complications of cardiac surgery
Neuroprotective strategies during cardiac surgery
Neuroprotection before anticipated or induced cardiac arrest
Neuroprotection during coronary artery bypass grafting
Preconditioning with hyperbaric oxygen
Spinal cord protection during cardiovascular surgery
Cerebral protection during organ transplantation surgery
Cerebral protection during neurosurgery
Cerebral angiography and endovascular surgery
Cerebral protection during surgery for arteriovenous malformations
Cerebral protection during surgery of intracranial aneurysms
Management of subarachnoid hemorrhage
Vasospasm associated with subarachnoid hemorrhage
Cerebral protection during carotid endarterectomy
Cerebral protection during surgery of brain tumors
Neuroprotective measures prior to surgery
HBO preconditioning for neuroprotection during surgery
Neuroprotection following surgery
14. Markets for Neuroprotective Therapies

Introduction
The financial burden of CNS damage
Markets for neuroprotective therapies
Markets according to therapeutic areas
Stroke
CNS injury
Alzheimer disease
Parkinson disease
Multiple sclerosis
Epilepsy
Values of neuroprotective therapies in major world markets
Unmet needs in neuroprotectives
Future prospects of neuroprotective therapies
Challenges in neuroprotective drug development
Promising areas of research in neuroprotection
Autoreactive antibodies
Biological therapies for neuroprotection
Multidisciplinary approaches to neuroprotection

15. References

Tables:
Table 1-1: Historical landmarks in the development of neuroprotection
Table 1-2: Intrinsic neuroprotective factors
Table 1-3: Common features of pathophysiology of brain damage in diseases
Table 1-4: Place of neuroprotection in management of CNS disorders
Table 1-5: Indications for the use of neuroprotection
Table 1-6: Neuroprotective nanoparticles
Table 2-1: A classification of neuroprotective agents
Table 2-2: The neuroprotective effect of antiepileptic drugs
Table 2-3: Neuroprotective affect of minocycline in animal models
Table 2-4: Classification of antioxidants or free radical scavengers with neuroprotective potential
Table 2-5: Role of erythropoietin in the nervous system
Table 2-6: Iontropic glutamate receptors
Table 2-7: Classification of metabotropic glutamate receptors (mGluRs)
Table 2-8: Methods for neuroprotection based on nonpharmacological preconditioning
Table 3-1: Cerebrovascular diseases that are relevant to neuroprotection
Table 3-2: Neuroprotective strategies for stroke
Table 3-3: Selected effective combinations of hypothermia with other neuroprotective strategies for the treatment of ischemic stroke in experimental models
Table 3-4: Neuroprotective gene transfer in models of cerebral ischemia
Table 3-5: Neuroprotective gene therapy in animal stroke models
Table 3-6: Neuroprotective agents in clinical development for acute cerebrovascular disease
Table 3-7: Some failed trials for neuroprotective therapy for stroke
Table 3-8: Preclinical assessment of neuroprotective agents in acute stroke models
Table 4-1: Classification of closed TBI
Table 4-2: Current conventional management of traumatic brain injury
Table 4-3: Neuroprotective strategies for traumatic brain injury
Table 4-4: Intrinsic factors that influence regeneration in the central nervous system
Table 4-5: A classification of approaches to regeneration of the brain following injury
Table 4-6: Ongoing or completed clinical trials for neuroprotection in TBI
Table 4-7: Discontinued or failed clinical trials for neuroprotection in TBI
Table 5-1: Secondary mechanisms in spinal cord injury
Table 5-2: Neuroprotective and regenerative approaches for SCI
Table 5-3: Clinical trials for neuroprotection in SCI
Table 6-1: Neurodegenerative disorders with dementia
Table 6-2: Approaches to neuroprotection in CJD
Table 6-3: Glutamate-based therapies in clinical development for neurodegenerative disorders
Table 7-1: Prevalence of Parkinson's disease in major markets 2013-2023
Table 7-2: Factors in the etiology of Parkinson's disease
Table 7-3: Strategies for the treatment of Parkinson's disease
Table 7-4: Current clinical trials of neuroprotective therapies for Parkinson disease
Table 7-5: Failed clinical trials of neuroprotective therapies for Parkinson disease
Table 7-6: Evaluation of neuroprotective agents for PD
Table 8-1: Cholinergic approaches to the treatment of Alzheimer's disease
Table 8-2: Neuroprotective agents for Alzheimer's disease
Table 8-3: Clinical trials for neuroprotection in Alzheimer disease
Table 8-4: Discontinued, failed or inconclusive clinical trials of Alzheimer disease
Table 8-5: Strategies for discovery of neuroprotective therapies for AD
Table 9-1: Neuroprotective approaches in HD
Table 10-1: Hypotheses for the pathogenesis of amyotrophic lateral sclerosis
Table 10-2: Classification of neuroprotective agents for amyotrophic lateral sclerosis
Table 10-3: Clinical trials of neuroprotective therapies for ALS
Table 10-4: Failed or discontinued trials of neuroprotective therapies for ALS
Table 11-1: Therapeutic approaches to subcortical vascular dementia
Table 11-2: Pharmacological neuroprotection against the sequelae of seizures
Table 11-3: Neuroprotective effect of AEDs in animal models of status epilepticus (SE)
Table 11-4: Specific therapies for MS based on postulated pathomechanisms
Table 11-5: Approved neuroprotective therapies for multiple sclerosis
Table 11-6: Neuroprotective therapies for multiple sclerosis in clinical trials
Table 11-7: Failed or discontinued trials of neuroprotective therapies for ALS
Table 11-8: Measures to prevent acute bilirubin encephalopathy
Table 11-9: Approaches to neuroprotection in neonatal hypoxia-ischemia
Table 11-10: Drugs with neuroprotective effect at mitochondrial level
Table 11-11: Causes of sensorineural hearing impairment
Table 11-12: Strategies for prevention and treatment of sensorineural hearing loss
Table 11-13: Agents for neuroprotection of the peripheral nervous system
Table 12-1: Causes of optic neuropathy
Table 12-2: Clinical trials of neuroprotective therapies in optic neuritis
Table 12-3: Neuroprotection of the optic nerve in glaucoma
Table 12-4: Strategies for neuroprotection in retinal ischemia
Table 12-5: Novel neuroprotective strategies against retinal degeneration
Table 12-6: Clinical trials for retinal neuroprotection
Table 13-1: CNS complications associated with cardiac procedures
Table 13-2: Strategies for protection of the brain during cardiac surgery
Table 13-3: Medical and surgical methods of cerebral vasospasm management
Table 13-4: Neuroprotection by prevention of vasospasm
Table 14-1: Neuroprotective market values 2015-2025
Table 14-2: Values of neuroprotective therapies in major world markets from 2015-25

Figures:
Figure 2-1: Mechanism of neuroprotective effect of sigma-1 receptor agonists
Figure 2-2: NMDA receptor ion channel complex
Figure 2-3: Neuroprotective effect of galantamine
Figure 3-1: Some steps in the ischemic cascade and site of action of neuroprotectives
Figure 3-2: A roadmap for neuroprotection
Figure 4-1: Cascade of events following traumatic brain injury
Figure 4-2: Neurometabolic cascade of mild TBI
Figure 4-3: Secondary injury mechanisms after TBI
Figure 5-1: Pathomechanism of acute spinal cord injury
Figure 7-1: Neuroprotective strategies against death of dopamine-containing neurons in PD
Figure 9-1: Role of HTT protein in pathogenesis of HD and points of intervention
Figure 9-2: Antisense therapeutic approaches to HD for lowering huntingtin
Figure 11-1: Common mechanisms of neural damage in cerebral ischemia and seizures
Figure 11-2: Role of neuroprotection in epilepsy and its treatment
Figure 11-3: Mechanisms of neonatal hypoxia-ischemia and targets for neuroprotection
Figure 14-1: Unmet therapeutic needs in neuroprotective therapies

Part II: Companies

16. Companies Developing Neuroprotective Therapies
Introduction
Profiles of companies
Collaborations
Tables
Table 16-1: Neuroprotectives in development by AstraZeneca
Table 16-2: Collaborations of companies in the area of neuroprotection

Ordering:
Order Online - [http://www.researchandmarkets.com/reports/39073/](http://www.researchandmarkets.com/reports/39073/)

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/

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

- Product Name: Neuroprotection - Drugs, Markets and Companies
- Web Address: http://www.researchandmarkets.com/reports/39073/
- Office Code: SCHZLDS3

Product Formats
Please select the product formats and quantity you require:

<table>
<thead>
<tr>
<th>Format Description</th>
<th>Quantity</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Electronic - Single User</td>
<td>☐</td>
<td>USD 5000</td>
</tr>
<tr>
<td>Hard Copy</td>
<td>☐</td>
<td>USD 5500 + USD 58 Shipping/Handling</td>
</tr>
<tr>
<td>Electronic - Enterprisewide</td>
<td>☐</td>
<td>USD 15000</td>
</tr>
<tr>
<td>Electronic and Hard Copy (PDF) - Single User</td>
<td>☐</td>
<td>USD 6000 + USD 58 Shipping/Handling</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>Field</th>
<th>Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Title</td>
<td>Mr ☐ Mrs ☐ Dr ☐ Miss ☐ Ms ☐ Prof ☐</td>
</tr>
<tr>
<td>First Name</td>
<td></td>
</tr>
<tr>
<td>Last Name</td>
<td></td>
</tr>
<tr>
<td>Email Address *</td>
<td></td>
</tr>
<tr>
<td>Job Title</td>
<td></td>
</tr>
<tr>
<td>Organisation</td>
<td></td>
</tr>
<tr>
<td>Address</td>
<td></td>
</tr>
<tr>
<td>City</td>
<td></td>
</tr>
<tr>
<td>Postal / Zip Code</td>
<td></td>
</tr>
<tr>
<td>Country</td>
<td></td>
</tr>
<tr>
<td>Phone Number</td>
<td></td>
</tr>
<tr>
<td>Fax Number</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:

<table>
<thead>
<tr>
<th>Account number</th>
<th>833 130 83</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sort code</td>
<td>98-53-30</td>
</tr>
<tr>
<td>Swift code</td>
<td>ULSBIE2D</td>
</tr>
<tr>
<td>IBAN number</td>
<td>IE78ULSB98533083313083</td>
</tr>
</tbody>
</table>
| 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