Blood-Brain Barrier: Bridging Options for Drug Discovery and Development

By Allan B. Haberman, PhD

• Strategies to develop small- and large-molecule CNS drugs capable of crossing the blood-brain barrier (BBB)

• Interviews with leading researchers who are aggressively tackling the BBB challenge in CNS drug discovery and development

• Analysis of results from a Blood-Brain Barrier Survey, responded to by a range of companies involved in CNS research and drug discovery/development

Continued on next page
CNS diseases are a major focus of the pharmaceutical industry, with CNS drugs representing some of its most successful products. These include Pfizer’s Zoloft (sertraline, for treatment of depression and certain types of anxiety disorders), Lilly’s Cymbalta (duloxetine, for treatment of depression) and Bristol-Myers Squibb’s/Otsuka’s Abilify (aripiprazole, for treatment of bipolar disorder and schizophrenia). However, drug discovery and development researchers experience difficulty developing CNS drugs that complete clinical trials and win regulatory approval—especially drugs which meet major unmet needs in the CNS area, such as Alzheimer’s disease. The vast majority of drugs fail to cross the BBB, which is causing a major bottleneck in successful development of CNS drug candidates.

This report reviews the discovery, design and development of small- and large-molecule drugs that can efficiently cross the BBB. This includes more traditional, medicinal chemistry-based methods, as well as approaches that exploit carrier-mediated transport (CMT) and receptor-mediated transport (RMT). Also covered in the report is use of nanoparticle technology to enable BBB penetration. Further, the report presents in vitro and in vivo assays as well as imaging methods to ascertain a drug’s ability to cross the BBB and reach its target.

**Blood Brain Barrier: Bridging Options for Drug Discovery and Development** includes results of a survey of researchers and executives—from corporate and academic organizations—who are active in the CNS drug development area. The survey explores their involvement in BBB-related technologies and programs. The survey results are discussed in terms of what they reveal about the current state of BBB research and the future potential for developing drugs that are able to cross it.

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Please classify your organization under what functional role do your responsibilities fall?

What is your title?

Please indicate the product area/areas that your organization is pursuing for CNS drugs.

Has your involvement in CNS drugs changed over the past 4 years?

If your involvement has increased, in what aspect(s)?

If your involvement has increased, in which therapeutic areas?

How many CNS drugs do you expect to launch in 2008 or 2009?

How many CNS drugs do you have in the preclinical to preregistration pipeline?

Which indications do your pipeline drugs attempt to address?

What do you see as the biggest bottleneck in successful development of your CNS drugs?
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Pieter J. Gaillard, PhD, Founder & Chief Executive Officer, to-BBB, Leiden, The Netherlands
William M. Pardridge, MD, Chairman & Chief Scientific Officer, ArmaGen Technologies, Santa Monica, CA
Christopher L. Shaffer, PhD, Senior Principal Scientist, Neuroscience; Pharmacokinetics, Pharmacodynamics and Metabolism, Pfizer, Groton, CT
Noa Zerangue, PhD, Research Director, XenoPort, Santa Clara, CA

Chapter 7: Selected Company Profiles
Amgen
Cellial Technologies
GlaxoSmithKline
Merck & Co.
MethylGene
Pfizer
Wyeth
XenoPort

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Company Index with Web Addresses
Potential Breakthroughs in Neurotherapeutics: Alzheimer's Disease, Parkinson's Disease, Depression, Bipolar Disorder, and Schizophrenia

This report provides a comprehensive assessment of truly innovative, early-stage research that we feel will translate into significant advances in neurotherapy. Specifically, it:

- Surveys current basic research relevant to drug or target discovery
- Highlights projects that show promise of future commercial potential
- Examines conditions in the technology transfer milieu relevant to these emerging opportunities
- Assesses the commercial potential for these emerging opportunities using a proprietary rating system
- Probes the views of authorities in industry and academia with insight into neurotherapeutic R&D

It begins with an analysis of the technology transfer process which bridges university research and the commercial world—its triumphs, but also its difficulties operating in the current risk-averse commercial environment.

For each of the 6 diseases, this report reviews consensus thinking about the pathophysiological mechanisms, targets, and the state-of-the-art in drug therapy. Then it launches into a review of significant research findings in each disease—the compounds and their targets already in discovery or early development with potential therapeutic value. It contains interviews with 8 thought leaders in neurotherapeutics from industry and academia, plus profiles of 20 companies at the forefront of CNS R&D.

To view a table of contents and executive summary, please visit www.InsightPharmaReports.com

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