



cerenseSM

CerenseSM is the world's first integrated solution to release the value of your CNS portfolio by unlocking the blood-brain barrier and measuring brain penetration. This is achieved through the combination of Genzyme Pharmaceuticals' patented CNS drug delivery technology and the unique expertise of Pharmidex to determine neuro-pharmacokinetics.

Two major obstacles are recognised to inhibit the successful development of CNS medicines:

- 1 Difficulties in getting compounds across the blood-brain barrier (BBB).**
- 2 Difficulties in successfully measuring BBB penetration and neuro-pharmacokinetics.**

The challenges encountered in overcoming these twin obstacles contribute to a significantly lower probability of development success for CNS drug candidates compared with compounds targeting other therapeutic areas.

CNS drug candidates often fail to demonstrate efficacy in the clinic due to poor transport from the blood into brain extracellular fluid (ECF). Traditional approaches to delivering compounds into the brain are crude and include the direct injection of therapeutic agents into the brain via neurosurgery. This is both costly as well as invasive.

Equally, in assessing efficacy, it is not sufficient to rely just on a PK profile in blood, when the true need is to assess the PK profile in the ECF of the brain region relevant to the disorder under investigation. Actual measurement of the free concentration of drug candidates in brain ECF has often been overlooked.

Thus there is a clear need for a safe, reliable and consistent method of delivering compounds across the BBB, and assessing their neuro-pharmacokinetics in brain ECF.

CerenseSM provides the vital key by overcoming the twin obstacles that block the creation of successful CNS therapeutics. It can be used to

- 1 substantially improve BBB penetration of potential CNS drugs whose utility is constrained by poor BBB penetration,
- 2 reduce the likelihood of safety issues associated with off-target pharmacological interactions outside the CNS,
- 3 extend and enhance the patent life of existing CNS drugs.

About CerenseSM

CerenseSM is a unique integrated solution designed to substantially improve the development success of potential CNS medicines that normally exhibit poor permeation of the BBB. By bringing together the strengths of Genzyme Pharmaceuticals and Pharmidex, CerenseSM overcomes the challenges of CNS drug delivery and assessment.

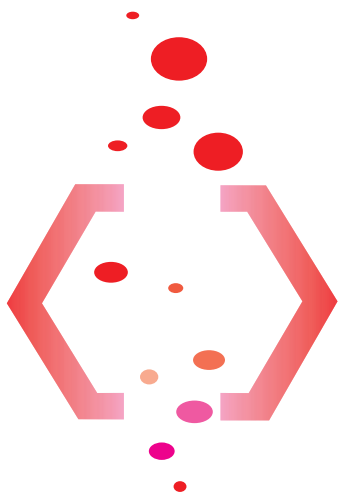
Genzyme Pharmaceuticals' patented formulation technology opens the BBB and delivers unmodified drug compounds into the brain, avoiding the disadvantages of direct application of poorly brain penetrant compounds into the brain. This overcomes the first major obstacle.

Pharmidex is the only company offering direct assessment of brain penetrability and free concentration of compounds in ECF using microdialysis. This is underpinned by the integration of neuroscience, DMPK and CNS drug discovery expertise. The knowledge delivered by their studies overcomes the second major obstacle.

CNS drug delivery studies, conducted in state-of-the-art facilities by the Pharmidex team, provides a comprehensive assessment of the concentration and duration of the test compound in brain ECF. The design of in-life experiments, coupled with clear and consistent data, will facilitate sound decision making for CNS drug discovery projects. Drug candidates can subsequently be developed and administered using Genzyme's novel and patented CNS delivery technology.

CerenseSM, thus, provides a unique product development platform designed to unlock the potential of compounds constrained by poor BBB penetration, as well as opens new avenues for the creation of CNS medicines. Companies that overcome the twin obstacles, and develop CNS medicines with a good therapeutic ratio, stand to dominate this fastest growing sector of the pharmaceuticals market.

The blood-brain barrier is open for business.
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CerenseSM has substantial potential to facilitate the development of many new drug products to treat CNS disorders including Alzheimer's disease, Parkinson's disease, multiple sclerosis, stroke, brain tumors and infections, traumatic brain injury, anxiety, depression and schizophrenia.

CerenseSM is available exclusively through a partnership between Genzyme Pharmaceuticals and Pharmidex Pharmaceutical Services. The product development platform can be confidentially reviewed at your company and a customised programme of study tailored to your specific drug therapy needs. Drug compounds are assessed under a Product Collaboration Agreement that is exclusive for the duration of your study.



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Open the blood-brain barrier. Reveal the potential.

The blood-brain barrier (BBB)

Unlike nearly all other organs of the body where there is a free exchange between blood and extracellular fluid (ECF), the capillaries in the brain have tight junctions which constrain the movement of molecules and cells between blood and brain.

This important characteristic provides a natural defence against toxic or infective agents circulating in the blood, and is conferred by cell adhesion molecules allowing endothelial cells to form tight junctions.

While fulfilling a protective role, the BBB severely limits the movement of medicines and potential medicines into the brain. Thus most molecules have to take a trans-cellular route into the brain, and so the overwhelming majority of small molecules, proteins (eg. antibodies), nucleotids (eg. RNAi) and peptides do not cross the BBB.

A safe, reliable and consistent method to deliver compounds across the BBB and assess their neuro-pharmacokinetics would therefore open new vistas for CNS pharmacotherapy.

Genzyme Pharmaceuticals

One of the world's foremost biotechnology companies, Genzyme is dedicated to making a major positive impact on the lives of people with serious diseases. Founded in Boston in 1981, Genzyme has grown from a small start-up to a diversified enterprise with annual revenues exceeding \$3.2 billion and more than 9,000 employees in locations spanning the globe. Genzyme Pharmaceuticals, a business unit of Genzyme Corporation, develops and manufactures drug delivery technologies for delivery of drugs across the BBB, and specialty pharmaceutical materials such as lipids, peptides, and amino acid derivatives at its cGMP manufacturing facility.

Pharmidex Pharmaceutical Services

Headquartered within the UK's Golden Biotech Triangle of Cambridge-Oxford-London, Pharmidex focuses on the prediction and assessment of the ability of potential new medicines to cross the blood-brain barrier (BBB). This adds value by accelerating time to market and improving the probability of success of potential CNS medicines. Pharmidex serves clients worldwide, and in 2005 was awarded the prestigious 'Service Company of the Year' by UK's Department of Trade and Investment.