



Embargo date: 6 February 2004

**DEPOCYTE<sup>®</sup>: NEW ADVANCE IN TREATMENT OF LYMPHOMATOUS  
MENINGITIS LAUNCHED IN EUROPE BY  
MUNDIPHARMA/NAPP/NORPHARMA**

Cambridge, 6<sup>th</sup> February 2004: Mundipharma/Napp/Norpharma independent associated companies, together with their partner SkyePharma PLC (Nasdaq: SKYE; LSE: SKP), today announce the European launch of DepoCyt<sup>®</sup>, a major advance in the treatment of lymphomatous meningitis, a serious late-stage complication of lymphoma, a form of cancer affecting the lymphatic system.

In its pivotal clinical trial DepoCyt<sup>®</sup> (cytarabine delivered through a novel sustained-release technology) provided a significant increase in the number of patients achieving a total response to the metastases within the neuraxis when compared with the current standard of care, immediate-release cytarabine (72% of patients receiving DepoCyt<sup>®</sup> achieved total response versus 18% of patients who received immediate-release cytarabine).

Dr Mark Hill, Director of Medical Affairs, Napp Pharmaceuticals, Cambridge, UK said: "In managing lymphomatous meningitis one of the key areas that needed to improve was in the delivery of an effective agent – two to three injections every week is too great a burden for the patient. By being able to deliver cytarabine once every two weeks, DepoCyt<sup>®</sup> represents a real advance in the management of lymphomatous meningitis."

Lymphomatous meningitis is a devastating complication of cancer that is often under-diagnosed and under-treated, however, it is comparatively uncommon condition with approximately 10,000 cases reported worldwide each year. It occurs when secondary tumours (metastases) form in the meninges, the membrane that surrounds the brain and spinal cord, causing severe neurological effects, such as blindness and deafness, often at a time when cancer patients, and their families, are already struggling to come to terms with the end-stages of their illness.

DepoCyt<sup>®</sup> (known as DepoCyt<sup>®</sup> in the USA) is a sustained release injectable formulation of cytarabine, a well-known cytotoxic agent used in the treatment of lymphomatous meningitis. It is the first product to utilise the innovative DepoFoam<sup>™</sup> Sustained Release System pioneered by SkyePharma. DepoCyt<sup>®</sup> is approved in both the USA and Europe for the treatment of lymphomatous meningitis.

Cytarabine is rapidly metabolised and so patients require spinal (intrathecal) injections every two to three days – these are uncomfortable and inconvenient for the patient and carry significant risks including the introduction of infection. DepoCyt<sup>®</sup> is a major advance on cytarabine and the key to this improvement is the DepoFoam<sup>™</sup> delivery technology. Through the DepoFoam<sup>™</sup> technology, cytarabine dissolved in water is encapsulated within minute particles of lipid that, after injection, gradually degrade, prolonging the release of the drug and extending the period required between injections to two weeks. This brings much less disruption to the life of the patient, reduces the associated risks accompanying frequent injections and also brings savings in hospital costs with the reduced admission rate. But perhaps most importantly, the ability of DepoCyt<sup>®</sup> to maintain high levels of cytarabine in the cerebrospinal fluid for a prolonged period, may also delay the progression of the disease.

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## **Notes for editors:**

### **Key advantages of DepoCyte®:**

- Fewer intrathecal injections = reduced patient discomfort, reduced risk and reduced admissions
- DepoCyte® provides an even distribution of active drug throughout the neuraxis i.e. it spreads to all areas that the metastases might be
- DepoCyte® holds back the spread of the cancer within the cerebrospinal fluid (CSF)
- 400% increase in the number of total responders – 72% of patients had total clearance of metastases from the meninges with DepoCyte® compared with 18% of patients on immediate-release cytarabine.

### **About Lymphomatous meningitis**

Lymphomatous meningitis, for which DepoCyte® is licensed, is where secondary tumours (metastases) form in the meninges, the membrane that surrounds the brain and spinal cord. The symptoms are pain and progressive neurological deterioration and few patients survive more than a few months, either from neurological dysfunction or from the primary tumour. The goal of therapy is palliation, not cure. The principal treatments are normally radiotherapy and chemotherapy to clear the cerebrospinal fluid of malignant cells and to prevent or slow recurrence. Most cytotoxic drugs do not cross the blood-brain barrier so the main chemotherapy treatments are methotrexate or cytarabine, injected intrathecally. These drugs reduce pain and slow neurological degradation but are rapidly cleared from the circulation and so require frequent injections.

### **About DepoFoam™**

DepoFoam™, SkyePharma's proprietary sustained release injectable delivery technology, consists of tiny lipid-based particles that contain discrete water-filled chambers dispersed through the lipid matrix. The particles are 10-30 microns in diameter and are suspended in saline. The suspension resembles skimmed milk and can be injected through a fine needle. The water-filled chambers containing active drug account for most of the weight of the particles. The lipids are naturally occurring substances (or close analogues) such as lecithin and triglycerides. The small amount of lipid is cleared rapidly in the body as the particles deliver their drug payload over a period that can be modified from 1 to 30 days. For example in DepoCyte® the circulating half-life of the drug cytarabine is increased from 3.4 hours to 141 hours.

### **About Mundipharma / Napp / Norpharma**

The Mundipharma / Napp / Norpharma independent associated companies; are privately owned companies and joint ventures that cover the world's pharmaceutical markets. The companies have particular expertise in bringing to patients the benefits of novel drug delivery systems such as those used to enhance medicines for the relief of severe pain. For further information, visit [www.mundipharma.co.uk](http://www.mundipharma.co.uk).

### **About SkyePharma**

SkyePharma PLC develops pharmaceutical products benefiting from world-leading drug delivery technologies that provide easier-to-use and more effective drug formulations. There are now nine approved products incorporating three of SkyePharma's five technologies in the areas of oral, injectable, inhaled and topical delivery, supported by advanced solubilisation capabilities. For more information, visit [www.skyepharma.com](http://www.skyepharma.com).