BioPharmica Ltd (ASX:BPH) Announce Encouraging Trial Results for Monitoring Brain Function

Perth, Dec 17, 2007 (ABN Newswire) - An Australian invention designed to decrease the likelihood of patients remembering parts of their surgery and improve their recovery from anaesthesia has just completed a further stage of clinical trials at Royal Melbourne Hospital. The positive results following the completion of this trial are a significant development for BioPharmica's investee Cortical Dynamics.

The Cortical Dynamics BAR Index measures electrical activity in the brain and is being developed by Cortical Dynamics at Swinburne University of Technology.

The purpose of this study was to establish whether this physiologically based method of analysing the brain's electrical activity (the electroencephalogram of EEG) developed by Associate Professor Liley was better able to monitor depth of anaesthesia in the presence of opioid drugs when compared with the current industry standard, the Bispectral Index (BIS) monitor.

The trial was conducted by Associate Professor Kate Lesley, Head of Research, Department of Anaesthesia and Pain Management, Royal Melbourne Hospital. This involved 45 elective surgery patients randomised to receive remifentanil, a commonly used intraoperative opioid whilst anaesthesia was induced using propofol.

During this anaesthetic induction the EEG was monitored using electrodes placed on the forehead and connected to a BIS monitor. BIS index values and raw EEG were recorded and downloaded for later analysis. Each patient's study concluded when they were fully unconscious meaning that they had no eyelash reflex and had no response to either verbal command or stimulation of the ulnar nerve.

The raw EEG was analysed offline using Cortical Dynamics proprietary algorithm, to produce two theoretically derived measures of brain function known as the cortical state (the BAR index) and the cortical input. The cortical state, cortical input and BIS index corresponding to the recorded levels of consciousness and loss of responses were extracted, with some data excluded due to artefact. The results were initially analysed blind to the remifentanil randomisation and then with respect to three treatment groups.

Preliminary cortical state (BAR index) and cortical input results show that the physiologically based algorithm is capable of detecting drug induced changes in human EEG. Both measures show clear trends with decreasing levels of consciousness.

The BAR Index was compared to the BIS index and both the BAR and BIS indices were found to decrease with a reduction in the assessed level of consciousness. The spread of BIS values at low levels of awareness was significantly greater than that of the corresponding BAR values. Initial analyses with respect to the remifentanil levels suggest that the variation in the BIS values is related to the level of remifentanil. In notable contrast the BAR index produced similar results across all target remifentanil brain concentrations.

These preliminary outcomes imply that the BAR index is more reliable in monitoring depth of anaesthesia in the presence of opioids.

About the Current Clinical Trial:

The purpose of this study was to establish whether a physiologically based method of analysing the brain's electrical activity (the electroencephalogram or EEG) developed by A/Prof Liley at Swinburne University of Technology, was better able to monitor depth of anaesthesia in the presence of opioid drugs when compared with the current industry standard, the Bispectral Index (BIS) monitor.

The study involved 45 elective surgery patients randomised to receive remifentanil, a commonly used intraoperative opioid, at three target brain concentrations of either 0, 2 or 4µg/ml whilst anaesthesia was induced using propofol. Four minutes following the beginning of the randomised target remifentanil infusion a propofol infusion was started at a brain concentration of 1.5µg/ml, and increased by 0.5µg/ml every four minutes until patients were fully unconscious which meant that they had no eyelash reflex and had no response to either verbal command or electrical stimulation of the ulnar nerve. Each patient's study concluded when all responses were lost.

During this anaesthetic induction the EEG was monitored using electrodes placed on the forehead and connected to a BIS monitor. BIS index values and raw EEG were recorded and downloaded for later analysis. Haemodynamic measurements and event markers corresponding to the assessed levels of consciousness were also recorded.

Electroencephalographic Equipment

Electroencephalographic/ EEG Equipment Measure the electrical activity of the brain by means of electrodes placed on the scalp of the person. The wires connected to the electrodes on the patient's scalp are similar to the antennae in recording the electric waves emanating from the brain.

EEG processors are used during surgical interventions to monitor the patient condition. The processor records patient's brain activity and offers valuable inputs regarding the patient's state of health during and after a surgery. Continuous monitoring greatly enhances patient's safety and also reduces the surgical costs. An EEG is widely considered as superior methodology for patient monitoring during surgical and

anaesthesia-based interventions when compared to heart or oxygen saturation level monitoring.

EEG Processor Market Growing Sharply

The market for EEG processors is projected to grow at a brisk pace in future, owing to a rapid increase in the number of surgical procedures being performed world over. Currently, more than 40 million surgical interventions are carried out each year in the United States alone. The number of such incidences is poised to multiply swiftly in future with a rapid increase in the aging population.

Market

Worldwide market for EEG/EMG/Brain function monitoring totalled US$690 million in 2005, and is independently estimated at US$749 million for 2006. The market is further projected to grow at a compounded annual growth rate of around 7.7% to reach around US$1 billion by 2010. In volume terms, the worldwide market is estimated to gross unit sales of 34,208 units for 2006. The market is anticipated to witness an annual growth of 8.9% through 2001- 2010, to sales of 47,487 units by 2010.

Europe represents the largest market for EEG/EMG/Brain function monitoring worldwide, however, the US is the single largest global market with an estimated share of 37.3% for the same year.

Electroencephalograph (EEG) Equipment is the largest segment of the worldwide EEG/EMG/Brain function monitoring market. The segment is estimated to record sales of 28,999 units for 2006, valued at about US$656 million. By the year 2010, the segment is expected to record sales of 42,180 units worth US$908 million. EEG equipment is forecast to hold dominant position in the global EEG/EMG/Brain function monitoring, with its market share soaring to reach 91% by the end of 2010 in value terms.

Background

The Bar Index has been used to quantitatively characterise the functional state of the brain based on a detailed understanding of how millions of neurons coordinate their activity to produce the EEG.

The monitoring of opioid effects during anaesthesia is unreliable using existing monitoring approaches and thus new methods are required in order to ensure optimal standards of clinical care. The current market leader is used in approximately 70% of hospitals in the USA, in clinical monitoring during anaesthesia containing an opioid. The competitor's market capitalisation in 2006 was approximately USD 400M.

When patients have a general anaesthetic, an anaesthetist may administer a combination of drugs through the intravenous drip in the patients arm. These could include an anaesthetic drug to put the patient to sleep and a morphine-like drug as a pain-killer.

Once the patient is asleep, the anaesthetist keeps the patient in this state by using a drip of anaesthetic drug or by giving the patient an anaesthetic gas to breathe. Using these combinations of drugs, the patient should be completely anaesthetised and not feel any pain.

Anaesthetists can currently measure the effect of these anaesthetic drugs on brain waves (also known as the electroencephalogram or EEG) using a widely available, market leading competing device. The market leader is used on many patients having general anaesthesia at hospitals. The competing monitor records EEG through a sticky sensor attached to the forehead. The monitor then produces a single number between 0 and 100 that the anaesthetist can use to adjust the depth of your anaesthetic.

Studies have shown that the use of a monitor decreases the likelihood of patients remembering parts of their surgery and also improves their recovery from anaesthesia.

However, there is evidence to suggest that some monitors may not track the effects of a number of important anaesthetic agents. This may mean that the leading offering is less accurate when these agents are used. In particular, morphine-like drugs may interfere with the ability of the leading monitor to measure the depth of anaesthesia accurately, by indicating a patient is less asleep than they really are. This means that patients may be receiving more anaesthetic than necessary.

The BAR Index method of analysing the EEG may overcome this limitation and provide a more accurate index of depth of anaesthesia in the presence of morphine-like drugs. The EEG information is obtained the same way, with a sticky sensor on the patient's forehead, but the monitor uses a different, potentially more mathematical method to analyse it.

Opioid analgesics are increasingly being used as part of a drug combination in nearly all anaesthetic regimes, however current monitors of anaesthetic depth do not reflect the effect of opioids on anaesthetic depth well, possibly because opioids do not directly affect the cortical EEG.

Upon the completion of the review of the clinical trial involving opioids, BioPharmica and Cortical will be in a strong position to move towards commercialisation on development related to anaesthesia, as well as making a case for development of other areas involving drugs, brain state and function.

The BAR Index has performed well in previous studies during midazolam and propofol-nitrous oxide anaesthesia providing the first indication that the BAR index is superior in a number of aspects to current approaches to measure brain function. It was able to measure separately both brain input - whether the patient is capable of receiving external input - and brain state - whether the patient is in a state of consciousness, hypnosis or amnesia.

The BAR Index has additional potential applications for the Alzheimer's and sedation markets. BioPharmica and partner Cortical Dynamics are working to develop the Bar Index as a monitoring tool in a number of neurodiagnostic settings that include detecting the early onset of degenerative diseases like Alzheimer's or Parkinson's as well as being used in drug discovery and evaluation associated with these conditions.

About Biopharmica Limited

BioPharmica [ASX: BPH] is an Australian Stock Exchange listed company developing biomedical research with academic and hospital institutes. The Company provides early stage funding for a direct collaboration, a spin out company or to secure a license. BioPharmica provides assistance with product development, funding and commercial strategies, whilst the institutional partner provides a majority of the infrastructure and research expertise.

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