CeNeS Announces Further Positive Results of its Phase II Clinical Trials of Morphine-6-glucuronide (M6G)

Cambridge, UK, 15 November 2002 - CeNeS Pharmaceuticals plc (LSE: CEN) today announced additional positive results from its recent Phase II trial comparing the analgesic efficacy of morphine-6-glucuronide (M6G) with morphine. The study showed that patients undergoing hip replacement surgery obtained equivalent post-operative pain relief with M6G as with a standard regime of morphine. The study was carried out under the CeNeS/Elan Corporation, plc (NYSE:ELN) ("Elan") joint venture that was initiated in June 2001. M6G is now ready to enter its Phase III trial programme in Europe subject to regulatory approval.

M6G is a metabolite of morphine that exerts analgesic effects with a reduction in the nausea and vomiting associated with morphine therapy. The Phase II trial just completed was to establish that M6G was genuinely as effective in pain relief as equivalent doses of morphine. The 68 patients undergoing hip replacement surgery were divided into three groups: one group received M6G at induction of anaesthesia, the second group received M6G after surgery and the third group received morphine after surgery. Following these treatments, morphine was available to all patients for further pain management. The degree of analgesia conferred by the initial treatments was measured in two ways: using a pain rating scale and also by measuring the patient administered levels of morphine post-surgery. All three groups scored equivalent degrees of pain relief with no statistical differences, thus confirming that M6G was as effective as morphine in pain relief when administered both pre- and post-operatively. After either initial M6G treatment, but particularly following treatment with the higher dose of M6G, morphine consumption, nausea and retching/vomiting were lower than that following the initial treatment with morphine.

"We are very pleased with the positive results of M6G. The study proves that M6G is just as effective an analgesic agent as morphine in the treatment of post-operative pain. We remain positive on the potential market application for M6G as an analgesic with a better side effect profile than morphine" said Neil Clark, Chief Operating Officer and Financial Director of CeNeS.

M6G has undergone several Phase II clinical trials with more than 450 patients receiving M6G. The most recent Phase II trials were designed to establish the analgesic effects of different doses of M6G administered at different times compared to a standard morphine treatment regime. Phase III efficacy studies are currently being planned: a pivotal, dose-ranging placebo controlled study is scheduled to commence as a multi-centre study in

Europe in early 2003 in patients undergoing knee replacement surgery with spinal anaesthesia. This will be followed by a second Phase III trial in Europe comparing M6G and morphine treatment in patients with postoperative pain following gastrointestinal and gynaecological surgery. Side-effect profiles of M6G will be investigated in both studies. If these trials are successful then M6G will be on target to be launched in Europe in 2005. M6G is currently partnered with Elan under a joint venture arrangement. This arrangement has worked well to date and facilitated the further development of M6G. As previously announced, CeNeS has started discussions with its partner Elan to simplify the current joint venture. It is therefore expected that these later trials will be managed and funded outside of the joint venture. Further details will be announced in due course as the particulars of the new arrangements are finalised.

CeNeS is a biopharmaceutical company specialising in the development and commercialisation of drugs for pain control and CNS disorders The company currently markets four products, and has research and development assets targeting pain and CNS disorders. The company is based in Cambridge, England. For further information visit www.cenes.co.uk.

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Notes to Editors:

M6G
M6G, a natural metabolite of morphine, is in development by CeNeS for the treatment of moderate to severe pain. Morphine is a highly effective analgesic that has been used for many years despite the unpleasant side-effects of nausea and vomiting and the potential dangers of respiratory depression.

Details of Study
The treatment groups received a single intravenous dose of M6G, either 20mg/70kg at induction of general anaesthesia (n=24) or 30mg/70kg at the end of surgery (n=20), or morphine 10mg/70kg at the end of surgery (n=24). Results showed that both M6G treatments were as effective as the morphine treatment in controlling post-operative pain. Assessing the pain scores over a 24-hour period, there was no statistical difference

between any of the treatment groups. The mean values for the total dose of morphine received by the patients who were treated initially with either M6G 20mg/70kg or 30mg/70kg were lower than that administered by patients initially treated with morphine 10mg/70kg.

Side effects
The incidence of nausea and vomiting appeared related to the consumption of morphine over the 24-hour period and not to M6G administration. There was no increased reporting of respiratory depression in the M6G treated groups compared to morphine. This study, however, was not powered to show statistical significance for these events.

Opiate Analgesia
Analgesia is the process of pain-relief and any pain-relieving drug is called an analgesic. The most potent known class of analgesics are the opiates, derived from the opium poppy, which confer a high degree of pain-relief for severe pain. Opiates, like morphine and codeine, act centrally in the brain in an area called the periaqueductal grey area where they mimic the actions of neuromodulators called endogenous opiates and 'switch off' the sensation of pain centrally.

The markets for M6G
M6G has potential as an analgesic for two types of pain, post –operative pain and chronic pain, both of which are currently treated with morphine.

For post-operative pain morphine is often used as the first line analgesic in many of the 95 million operations performed in the USA and Europe each year. Estimated annual sales of morphine in this market are £400m (source: IMS and Front Line Pain Management Report, 2001). However, the undesirable side effects of morphine include nausea, vomiting, respiratory depression and sedation. M6G is likely to offer significant clinical benefits to morphine in the treatment of post-operative pain due to the reduced incidence and severity of some of these side effects, whist offering equal analgesic efficacy.

Morphine is also used frequently to treat many of the 2.7 million patients who develop cancer each year in the USA and Europe. M6G could compete in this £600m morphine market because M6G could potentially lead to a reduced incidence and severity of nausea and vomiting compared with morphine and so could improve patient well being and quality of life.

CeNeS is initially developing M6G is for the treatment of post-operative pain, with phase III studies planned for early 2003. CeNeS plans to also develop M6G for the treatment of chronic pain such as cancer pain.