Positive Phase II clinical data for Clavis Pharma’s Elacytarabine presented at ASH Annual Meeting

Elacytarabine demonstrated threefold survival benefit in patients with acute myeloid leukaemia

Oslo, Norway, December 7, 2009.

Clavis Pharma ASA (OSE: CLAVIS) announces that positive clinical data from its Phase II study with its lead cancer product candidate elacytarabine in patients with late-stage acute myeloid leukaemia (AML) was presented at the 51st American Society of Hematology (ASH) Annual Meeting in New Orleans, LA, USA. Elacytarabine is a novel, patented, lipid-conjugated form of the anti-cancer drug cytarabine (Ara-C) that has the potential to improve treatment outcomes in patients with AML and other haematological malignancies (leukaemias). Elacytarabine has Orphan Drug Designation in the USA and Europe for the treatment of AML.

The poster entitled “A Phase II Multicenter Study with Elacytarabine as Second Salvage Therapy in Patients with AML” was presented by Susan O’Brien, M.D. of the University of Texas MD Anderson Cancer Center, Houston, TX, in collaboration with researchers at other leading cancer centres and Clavis Pharma. This is the first time clinical results of this trial for all 61 patients have been presented at a leading cancer congress.

The poster can be downloaded from http://www.clavispharma.com/Products/Scientific+posters.

The data and analyses from the multicentre open-label trial showed elacytarabine to have a significantly superior survival benefit compared to published clinical outcome data for 594 late-stage AML patients receiving investigators choice of treatment¹. The results confirm the positive findings from the trial announced in June 2009.

Key results for elacytarabine compared to published clinical data are

- Median survival three times longer (5.3 months vs. 1.5 months)
- Remission rate significantly increased (14.8% vs 2.5%, p<0.0001)
- Well tolerated - short-term mortality substantially lower (13% vs. 25%)

Based on the encouraging results of this trial, Clavis Pharma is about to begin a 350-patient Phase III randomised, controlled registration study in the USA and Europe designed to demonstrate its superiority over the investigator's choice of the best alternative therapy in late-stage AML patients.

Clavis Pharma has also received approval to enrol patients in a Phase II study of elacytarabine in combination with idarubicin in AML patients who have failed their first course of treatment.

In addition to evaluating survival in all patients, the studies will analyze patients’ expression levels of the hENT1 tumour protein. The hENT1 (human equilibrative nucleoside transporter 1) cell membrane transporter is believed to be critical for cytarabine entry into tumour cells, whereas elacytarabine enters and kills tumour cells in a hENT1-independent manner. The goal is to demonstrate that the efficacy of elacytarabine is independent of the patient’s hENT1 status.

Geir Christian Melen, CEO of Clavis Pharma, commented: “These positive clinical results give us great confidence that elacytarabine could improve the treatment of late-stage AML patients, a group for which there are few effective therapeutic options. We look forward to starting a randomised, controlled Phase III trial to further demonstrate the benefit that we have already seen with elacytarabine in treating these patients.

Mr Melen added, “The results represent an important proof of concept for our approach to developing improved cancer drugs based on our Lipid Vector Technology. This approach was recently validated in our $380 million deal with Clovis Oncology for CP-4126 to treat pancreatic and other solid tumours.

¹ Giles, F et al, Outcome of patients with acute myelogenous leukemia after second salvage therapy. Cancer (2005)104: 547-554
Both elacytarabine and CP-4126 are designed using LVT to bypass the hENT1 transporter mechanism that limits the efficacy of cytarabine and gemcitabine, respectively. We are excited about the potential of both these drugs and also that, as a result of the deal with Clovis, sufficient resources are available to drive the clinical programmes forward."

Extended survival, improved remissions

In the Phase II study, 61 patients (41 male and 20 female) with late stage AML who failed to respond or relapsed after two separate rounds of treatments received third-line therapy (also called second salvage) with intravenous elacytarabine. A dose of 2000 mg/m²/day was given as continuous infusion for five days. The response to treatment was compared with a detailed historical outcome analysis of 594 similar second salvage AML patients, who were treated at the MD Anderson Cancer Center (Houston, TX, USA) (published by Giles et al, Cancer 2005;104:547-54). Median overall survival in the elacytarabine study was an impressive three times that of the historical control patients (5.3 months vs. 1.5 months). The 6 month survival rate was 44%.

In addition, 9 patients responded to elacytarabine with a complete remission (CR) or complete remission without full recovery of platelet counts (CRp) as assessed by the investigator, representing an overall remission rate of 14.8 per cent. By contrast, the expected remission rate for similar group of patients, matched for prognostic factors as described by Giles et al. was only 2.5 per cent. Using a pre-defined statistical analysis method, the improvement in outcome was statistically highly significant (corresponding to p<0.0001). In addition to the 9 patients with a complete remission, 5 patients responded to elacytarabine with a partial response.

Elacytarabine was relatively well tolerated, also by elderly patients, and 30 day all cause mortality following treatment was substantially lower than published data for existing therapies (13 per cent vs. 25 per cent). Out of the 61 patients treated with elacytarabine, 10 were referred for stem cell transplantation following treatment, including some patients in complete remission and others with a more modest level of clinical benefit. Stem cell transplantation represents a potential cure for life for these patients.

For further information, please contact:
Geir Christian Melen
Chief Executive Officer
Office : +47 24 11 09 50
Mobile : +47 91 30 29 65
E-mail : geir.christian.melen@clavispharma.com

Gunnar Manum
Chief Financial Officer
Office : +47 24 11 09 71
Mobile : +47 95 17 91 90
E-mail : gunnar.manum@clavispharma.com

For international press enquiries:
Mark Swallow / Nina Enegren / David Dible
Citigate Dewe Rogerson
Office : +44 207 282 2948
E-mail : clavispharma@citigatedr.co.uk

NOTES FOR EDITORS

About Leukaemia
Approximately 300,000 new cases of leukaemia are diagnosed globally each year, resulting in around 220,000 deaths. Leukaemia represents a market with high unmet medical needs, which may open for accelerated approval processes to expedite market access for new drugs. It is a segmented market covering a broad variety of disorders. A major clinical concern is the high rate of disease recurrence.
The five-year survival for the most common acute leukaemia type, acute myeloid leukaemia (AML), is in the range of 5-10% for treated elderly patients, and approximately 30% for treated younger adults. The AML market is estimated to be a multi-hundred USD market and is expected to grow significantly over the coming years.

About Clavis Pharma

Clavis Pharma ASA is a clinical stage oncology focused pharmaceutical company based in Oslo, Norway with a portfolio of novel anti-cancer drugs in development. These potential breakthrough products are New Chemical Entities (NCEs) made using Clavis Pharma’s Lipid Vector Technology (LVT) chemistry to introduce new properties to already established, commercially successful drugs. Data generated suggests the resulting patentable NCEs offer improved efficacy and reduced side effects through enhanced pharmacokinetic properties, greater tissue penetration, altered metabolism and, in certain cases, additional modes of action.

Clavis Pharma’s has several drug candidates in formal development studies:
- Elacytarabine, an improved form of Ara-C, a leukaemia drug – about to commence a Phase III randomized, controlled registration study in late-stage acute myeloid leukaemia;
- Intravenous CP-4126, an improved version of gemcitabine – currently in a Phase II comparative study with gemcitabine for the treatment of pancreatic cancer;
- Oral CP-4126 – currently being evaluated in an escalating dose Phase I study in solid tumours; and
- CP-4200, an azacitidine derivative – in preclinical development for myelodysplastic syndrome (MDS), often a precursor to myeloma or leukaemia.

Clavis Pharma intends to commercialise its products through strategic alliances and partnerships with experienced oncology businesses and, where and when commercially appropriate, by establishing its own sales and marketing capabilities. CP-4126 is licensed to Clovis Oncology in Americas and Europe. Clavis Pharma has retained rights in other territories and an option to co-promote CP-4126 in Europe.

The shares of Clavis Pharma ASA are listed on the Oslo Stock Exchange (ticker: CLAVIS).

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