PRESS RELEASE

# Oasmia's lead human oncology product Paclical shows a positive risk/benefit profile versus standard treatment in pivotal phase III clinical study

## *Submission for European marketing approval of Paclical in 2015*

UPPSALA, SWEDEN – October 21, 2014. Oasmia Pharmaceutical AB (publ) today announced that the full clinical trial report of Paclical, for the treatment of epithelial ovarian cancer, shows a positive risk/benefit profile. The data will serve as the basis of a Marketing Authorisation Application to the European Medicines Agency (EMA), which the company intends to submit in early 2015.

"Shorter infusion time and no need for pre-medication with corticosteroids or antihistamines give Paclical an advantage over paclitaxel (Taxol®)", said Professor Ignace Vergote, principal investigator of the study and Chairman of the Leuven Cancer Institute, University Hospitals Leuven, Leuven, Belgium

The primary objective of the Phase III clinical study, which included in total 789 patients, was to show non-inferiority of Paclical (250 mg/m$^2$) versus Taxol (175 mg/m$^2$), both in combination with carboplatin. Tumour response and progression was assessed using computed tomography (CT) evaluated centrally according to Response Evaluation Criteria in Solid Tumors (RECIST).

The initial data of the study, presented on June 16, 2014, showed that Paclical, which has orphan designation for epithelial ovarian cancer in the EU and in the US, met the pre-defined requirement of non-inferiority compared with Taxol.

Oasmia has now completed a full analysis of the study data, including a comprehensive risk/benefit evaluation, which shows a positive risk/benefit profile for Paclical.

"The conclusion after examining all data in the study is that the benefit with Paclical treatment exceeds the risks with the treatment. The data will serve as the basis of a Marketing Authorisation Application to the European Medicines Agency (EMA), which we intend to submit in the second quarter of 2015", commented Julian Aleksov, CEO of Oasmia.

The risk/benefit analysis is based on data from the study, including:

- The percentage of patients with a substantial decrease in tumour burden - including normalized levels of the biomarker used for this evaluation - is 86% for patients treated with Paclical and 85% for patients treated with paclitaxel (Taxol). The percentage of those with normalized biomarker levels (=complete response) is 62% for both treatments. This implies that Paclical is an effective treatment of ovarian cancer when used in combination with carboplatin.

- Time of progression free survival is 10.2 months compared to Taxol (10.0 months) and is in line with what has previously been published for patients after the first or second relapses. More frequent CTs (every 3 months) were done in a substantial subgroup of 243 patients. The median PFS time in this subgroup was 12.2 months for Paclical and 10.2 for paclitaxel (Taxol).

- The intended infusion time for Paclical is 1 hour, compared to Taxol's 3-hour infusion time, and only on rare occasions were there any prolongation of the infusion time.

- Corticosteroids and antihistamines are not indicated as pre-treatment before Paclical, which was confirmed in this study, as only a limited number of patients received such medication before treatment with Paclical.

- The overall safety profile of Paclical is in line with what was expected for paclitaxel. However, a dose-dependent increase in frequency and severity of adverse events was not seen, apart from those related to the white blood cells. This means that despite the higher dose compared to Taxol, adverse events related to paclitaxel are not more common with Paclical.

- Neuropathy (numbness of hands and feet) is an adverse event related to treatment with paclitaxel. Neuropathy is also seen with Paclical, but to a somewhat lesser degree than with Taxol, despite the higher Paclical dose.

- Despite the adverse events reported, including frequent blood cell related adverse events, the dose was reduced in only 18% of the patients. Dose-reduction below 200 mg/$m^2$ was rare. The investigators did thus not reduce the dose of Paclical to the level of Taxol (175 mg/$m^2$).

All data examined shows a consistent although not significant advantage of Paclical in all efficacy variables compared with Taxol. The safety profile was similar with an expected increase in frequency and severity of white blood cell related events and a non-expected decrease in neuropathy. Dose reduction to the level of Taxol (175 mg/$m^2$) was rare although allowed according to the protocol.

"The study shows that Paclical is at least as good as paclitaxel (Taxol) in providing time without progression in patients with ovarian cancer, and Paclical gives the patients the advantage of a shorter infusion time and allergic reactions are very rare compared to paclitaxel (Taxol). I am really happy with the results and to have participated in this study", commented Professor Vergote.

Oasmia now intends to submit a Marketing Authorisation Application to EMA in Q2 2015.

Overall survival data are expected in Q3 2015.

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**Notes to editors:**

**About Oasmia Pharmaceutical AB**
Oasmia Pharmaceutical AB develops new generations of drugs in the field of human and veterinary oncology. The company's product development aims to create and manufacture novel nanoparticle formulations and drug-delivery systems based on well-established cytostatics, which, in comparison with current alternatives, show improved properties, reduced side effects, and expanded applications. The company's product development is based on its proprietary in-house research and company patents. Oasmia is listed on NASDAQ OMX Stockholm (OASM) and the Frankfurt Stock Exchange (OMAX, ISIN SE0000722365). www.oasmia.com

**About the Phase III clinical study of Paclical**
The Phase III open, randomized, multi-centre study, which included in total 789 patients, was designed to compare the efficacy and safety between Paclical and Taxol, which is also a paclitaxel-based product. Both Paclical and Taxol were administered in combination with carboplatin.

Paclitaxel in combination with carboplatin, or any other platinum containing compound, has emerged as a standard in a first line setting in patients with epithelial ovarian cancer, and is used also as second line treatment, providing the patient had a response time of at least 6 months. These patients are defined as platinum sensitive.

The period from randomization to relapse or death (PFS) becomes shorter with the number of relapses, and hence treatment periods, that the patient goes through. A study comparing the period of the first PFS with the second showed a difference of 7 months, 17.8 compared to 10.8 months.

The study showed a PFS period of 10.3 months for Paclical + carboplatin compared to 10.1 months for Taxol + carboplatin. The result corresponds well with literature data from studies in platinum sensitive patients in second line treatment, e.g. 10.8 months (ref 1) and 9.4 months.

The study was designed to achieve the following primary objective:

> *PFS: to show non-inferiority of Paclical (250 mg/m2) vs Taxol (175 mg/m2, using computed tomography (CT) scans according to Response Evaluation Criteria in Solid Tumors (RECIST), as assessed by central review.*

Inclusion criteria included patients who relapsed at least six months after end of first line or second line treatment including platinum based therapy. Paclical was administered as a one-hour intravenous infusion at its recommended dose of 250 mg/m2. Taxol was administered as a three-hour intravenous infusion at its recommended dose of 175 mg/m2. Both drugs were dosed in six three-week cycles.

Patients treated with Taxol received systemic pre-treatment with corticosteroids, antihistamines and H2 receptor antagonists. Patients treated with Paclical did not receive such treatment to the same extent Carboplatin was given as an intravenous infusion starting 30 minutes after the end of the paclitaxel infusion. The carboplatin dose is based on kidney function measured as creatinine clearance ("5-6 AUC") that means that the variation in dose between patients is large, with a mean of approximately 625 mg/cycle, but it can be twice that much for an individual patient. After completing the treatment cycles, patients were followed until progression.

**About Paclical**
Paclical is a water-soluble formulation of the well-known cytostatic paclitaxel combined with Oasmia's excipient technology XR-17. Paclitaxel is one of the most widely used anticancer substances and is included in the standard treatment of a variety of cancers such as lung cancer, breast cancer and ovarian cancer. Paclical consists of a freeze-dried powder dissolved in conventional solution for infusion. It has orphan drug designation in the EU and the US.

**About the Paclical market**
The two leading paclitaxel-based products on the market are Taxol and Abraxane, two widely used cancer drugs. Taxol generated $1.6 billion in sales in 2000 alone, prior to losing its patent protection in 2001. In 2013, Taxol generated $92 million in post-patent sales. Abraxane, which received FDA approval in 2005 for metastatic breast cancer, followed by approvals for lung (in 2012) and pancreatic cancer (in 2013), generated $427 million in worldwide annual sales in 2012 and generated $649 million in 2013.

In order to deliver paclitaxel, Taxol contains the solvent Cremophor EL. The toxicity of Cremophor EL limits the dose of Taxol that can be administered during a reasonable time, potentially limiting the efficacy of the drug. In addition, patients receiving Taxol require premedication with steroids and antihistamines to prevent the toxic side effects associated with the combination of paclitaxel and Cremophor EL.

Abraxane was developed as a Cremophor-free product containing paclitaxel suspended in human albumin. Because Abraxane contains no Cremophor EL solvent, Abraxane's recommended dosing enables the delivery of 50% more paclitaxel while maintaining a similar safety profile, and requires no routine pre-medication to prevent hypersensitivity reactions or the immediate allergic effects that often prevent or limit treatment. Like Abraxane, Paclical is free of Cremophor EL, but unlike Abraxane, Paclical does not contain human albumin.

**About XR-17**
XR-17 is Oasmia's proprietary excipient and is based on Vitamin A. It forms micelles that are between 20 and 60 nanometres in size. One property that makes XR-17 special is that it can also form micelles with water-soluble substances. This increases its potential uses significantly. Once XR-17 has delivered the encapsulated molecule or molecules to the target, the excipient is metabolized naturally. XR-17 facilitates the ease of administration and allows for higher doses than some of the other existing pharmaceutical products on the market, including cytostatics such as paclitaxel.

**About epithelial ovarian cancer**
Epithelial ovarian cancers account for about 85% to 90% of ovarian cancers, and are the most aggressive and dangerous sub-type. According to the National Cancer Institute, in 2011, the most recent year in which data is available, there were over 185,000 women living with ovarian cancer in the U.S. The five-year survival rate for ovarian cancer from 2004 to 2010 was 44.6%, and it is estimated that 21,980 women will develop and 14,270 women will die from ovarian cancer in 2014.

In the EU, the five-year survival rate for ovarian cancer was 37.6% from 2000-2007 according to a study published in The Lancet. In 2012, there were 44,149 diagnosed cases of ovarian cancer in the EU, according to the European Cancer Observatory/International Agency for Research on Cancer, while 29,758 women died of ovarian cancer. In the U.S., 51% of women with ovarian cancer are diagnosed with stage III cancer, characterized by microscopically confirmed peritoneal metastasis outside the pelvis and/or regional lymph node metastasis. Common chemotherapy drugs used for the treatment for ovarian cancer include cisplatin or carboplatin, and paclitaxel or docetaxel, which are most often given in combination.

**About Risk/Benefit analysis**
When you do a risk/benefit analysis, you put together all the factors that can be negative to the patient (risk), for instance side effects, if a certain medicine is needed before the treatment, and negative effects of quality of life, with factors that affect the patient in a positive way (benefit), such as disease free period, shorter infusion time and positive effects on quality of life, thereby getting a full overview where the benefit has to be greater than the risk.

Information is also available at www.oasmia.com www.nasdaqomxnordic.com www.boerse-frankfurt.de twitter.com/oasmia

*"Oasmia is required under the Financial Instruments Trading Act to make the information in this press release public. The information was submitted for publication at 08.30, CET on October 21, 2014."*