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# Dosing initiated in Phase I/II clinical trial of APR-246 in ovarian cancer

**STOCKHOLM – April 16, 2014. Aprea AB announced today that dosing has begun in the Phase I/II proof-of-concept clinical trial of APR-246 in combination with chemotherapy in patients with relapsed platinum sensitive high grade serous ovarian cancer. Aprea is a Karolinska Development AB portfolio company.**

Cancers develop and spread due to the malfunction of the cells' normal growth control mechanisms. One of the best-known cancer genes is p53 that can trigger the cellular suicide program to eliminate cancer cells. In about half of all tumors, p53 is mutated and no longer functions normally. This allows cancer cell survival and rapid tumor growth. Aprea has successfully developed substances that can restore normal function to the p53 protein and thereby induce efficient cancer cell death and overcome resistance to antitumoral therapy. To the company's knowledge, APR-246 is the only compound with this mechanism of action in clinical development.

"Ovarian cancer has a poor prognosis, as the disease is often fairly advanced by the time these patients experience their first symptoms. Present therapies for recurrent ovarian cancer have little impact on survival, and we are eager to evaluate whether APR-246 can extend the efficacy of second line therapy", said John A Green, Principal Investigator of the clinical trial.

"The synergistic effects of APR-246 and carboplatin have resulted in very potent antitumor activity in preclinical models. We now look forward to evaluate the compound's safety profile and clinical activity in combination treatment of ovarian cancer patients", said Ulf Björklund, CEO at Aprea.

APR-246 has previously been tested in a clinical Phase I/II trial in 32 patients with refractory hematological malignancies or prostate carcinoma. Promising data from this trial has been presented in Journal of Clinical Oncology.

"We are excited about this trial and will follow it with great interest. About 60% of all ovarian cancer patients have mutated p53 and ovarian cancer patients with p53 mutations are less responsive to platinum than patients with wild type p53. Thus, it is an indication where Aprea's APR-246 could make a difference for these patients with a great need for better treatment", said Torbjörn Bjerke, CEO of Karolinska Development.

**About the PiSARRO trial**
The Phase I/II trial is designed to evaluate the safety, efficacy, pharmacokinetics and pharmacodynamics of APR-246 in combination with carboplatin (AUC 5) and pegylated doxorubicin (30 mg/$m^2$), a second line standard of care chemotherapy for relapsed platinum sensitive high grade serous ovarian cancer. The Phase I/II trial is a two-part study that will enroll approximately 180 patients. Part A is an open-label, multiple ascending dose study. The primary objectives of Part A are to evaluate the safety and tolerability of APR-246 in combination with carboplatin and pegylated doxorubicin, and to confirm the dose of APR-246. Pending successful completion of this phase, Aprea expects to initiate Part B of the trial, which will be a randomized, controlled study investigating the safety and antitumor activity of APR-246 administered in combination with carboplatin and pegylated doxorubicin, compared with carboplatin and pegylated doxorubicin alone. Primary end point of part B will be Progression Free Survival (PFS). For details on the PiSARRO trial please visit: www.ClinicalTrials.gov.

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**TO THE EDITORS**

**About Aprea**
Aprea AB is a Swedish biotech company focusing on discovery and development of novel anticancer compounds targeting the tumor suppressor protein p53. The main owner of Aprea is KDev Investments AB, part of Karolinska Development AB (publ). The other main owners are Östersjöstiftelsen, Praktikerinvest and KD Co-Investment Fund KB. For more information, please visit www.aprea.com

**About APR-246**
APR-246 has been developed based on results from researchers at Karolinska Institutet, and has been shown to reactivate the non-functional tumor suppressor protein p53 and induce programmed cell death in many human cancer cells. In preclinical studies APR-246 has demonstrated unique pharmacological properties as compared to conventional chemotherapy, by being effective also in cancer cells with p53 mutations and by preferentially targeting tumor cells over normal cells. A clinical phase I/II study on hematological malignancies and prostate cancer with APR-246 has been completed with promising results. It had a good safety profile and both biological and clinical responses were observed**.** A Phase I/II proof-of-concept study in ovarian cancer patients carrying mutant p53 is currently ongoing.

**About Karolinska Development AB**
Karolinska Development aims to create value for patients, researchers, investors and society by developing innovations from world class science into differentiated products that can be partnered. The business model is to: SELECT the most commercially attractive medical innovations that can potentially satisfy unmet medical needs; DEVELOP innovations to the stage where the greatest return on investment can be achieved; and COMMERCIALIZE the innovations through the sale of companies or out-licensing of products. An exclusive deal flow agreement with Karolinska Institutet Innovations AB, along with other cooperation agreements with leading universities, delivers a continuous flow of innovations. Today, the portfolio consists of 34 projects, of which 17 are in clinical development. For more information, please visit www.karolinskadevelopment.com.

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