Aprea presents preclinical data at AACR - Strong synergistic effect with APR-246 and cisplatin

STOCKHOLM – April 9, 2013. Aprea AB today presented preclinical data at the American Association for Cancer Research (AACR) meeting in Washington, DC, USA. The results from these studies show that Aprea’s lead candidate APR-246, a compound that reactivates mutant p53, acts synergistically with platinum compounds. Aprea, which is part of the Karolinska Development portfolio, is now preparing a Phase II study with APR-246 in platinum resistant ovarian cancer.

The title of Aprea’s poster presentation at AACR was “Strong synergistic effects with cisplatin and APR-246, a novel compound reactivating mutant p53, in ovarian cancer cell lines and primary cells from patients”. In the studies presented today, the anticancer effect of APR-246 alone, and in combination with platinum compounds, on ovarian cancer cells were investigated. The results show that APR-246 acts synergistically with platinum compounds and reverses the cisplatin-sensitivity to cisplatin-resistant p53 mutant ovarian cancer cells.

Aberrations in p53 are common in many cancer forms and are associated with increased resistance to standard chemotherapy resulting in a poor prognosis for the patient. About 60% of ovarian cancer patients have p53 mutations.

Mikael von Euler, CMO of Aprea, commented; “We are very pleased with this comprehensive set of preclinical data supporting our planned Phase II study in platinum-resistant Epithelial Ovarian Cancer (EOC) patients who are candidates for further platinum-based chemotherapy. APR-246 has the potential to be an important new treatment for these patients with high unmet medical need”. The full abstract (Abstract # 3448), is available on www.aacr.org.

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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. The other main owners are Östersjöstiftelsen, Praktikerinvest and KCIF 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 II Proof of Concept study in ovarian cancer patients carrying mutant p53 is currently being prepared.

About the AACR data
In a p53 mutant ovarian cancer cell line that was established from a patient resistant to clinically relevant concentrations of cisplatin, doxorubicin and melphalan, and expressed a high level of p53 protein, a strong synergistic effect of APR-246 in combination with cisplatin was observed. In cisplatin-resistant ovarian cancer cell lines with p53 mutations expressing lower levels of p53, synergistic or strong synergistic effects were observed. These resistant cancer cell lines were developed from parental cisplatin-sensitive cell line by chronic exposure to cisplatin. The platinum drug carboplatin and the anthracycline drug doxorubicin showed cross-resistance in cisplatin-resistant cell lines, while the sensitivity to APR-246 did not change compared to the cisplatin-sensitive parental cell line.

Primary ovarian cancer cells obtained from patients were also investigated and strong synergistic effect of APR-246 in combination with cisplatin was found in all experiments. Also in an in vivo study using a p53 mutant cisplatin-resistant ovarian cancer cell line, a good combination effect of APR-246 and cisplatin was observed. The full abstract (Abstract # 3448) is available on www.aacr.org.

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