November, 2015

Anticancer drug "*Elplat®*"
Approval for the Supplemental New Drug Application for Postoperative Adjuvant Chemotherapy in Gastric Cancer

Tokyo, Japan, November 20, 2015 - Yakult Honsha Co., Ltd. (hereafter, Yakult) (President & COO: Takashige Negishi) announced today that it obtained approval for a supplemental new drug application relating to an additional indication for postoperative adjuvant chemotherapy in gastric cancer, with respect to its products, *Elplat® (50mg, 100mg and 200mg)*. This supplemental new drug application resulted in constitution of a new indication "gastric cancer", integrating "unresectable advanced of recurrent gastric cancer" approved in March 2015 and this approval for postoperative adjuvant chemotherapy in gastric cancer.

This supplemental new drug application was approved mainly based on the results of two clinical studies; a Phase III study which was conducted in overseas to verify the benefits of the combination therapy with *Elplat®* and an anticancer drug, capecitabine (CLASSIC study), and a Phase II study which was jointly conducted by Yakult and Chugai Pharmaceutical Co., Ltd. (hereafter, Chugai) (Chairman & CEO: Osamu Nagayama) in Japan.

Gastric cancer is the most common cancer in Japan and the number of newly diagnosed gastric cancer patients during 2011 is estimated at 132,033*[1].

Yakult will sincerely work for promoting proper use of *Elplat®*, and continuously attempt to provide cancer patients and medical staffs with new treatment options.

*1 Cancer Registry and Statistics. Cancer Information Service, National Cancer Center, Japan

1. *Elplat®*

Elplat® is an anticancer platinum drug, for which Yakult acquired development and commercialization rights in Japan from its licensor Debiopharm International SA (Switzerland) in 1997. *Elplat®* was approved for the indication for the treatment of "curatively unresectable advanced/recurrent colorectal cancer" in March 2005, and launched on the market in April of the same year. In August 2009, *Elplat®* became indicated for "postoperative adjuvant chemotherapy for colon cancer".
An additional dosage and administration for "curatively unresectable advanced/recurrent colorectal cancer" was approved in September 2009, and an additional dosage and administration for "postoperative adjuvant chemotherapy for colon cancer" was approved in November 2011. Subsequently, *Elplat®* was approved for the indication for the treatment of "curatively unresectable pancreatic carcinoma" in December 2013 and "unresectable advanced or recurrent gastric cancer" in March 2015.

2. Capecitabine

Capecitabine was developed by Nippon Roche K.K. (currently Chugai) and approved in 1998 for the first time in the US, Switzerland and Canada, in 2001 in the EU and has been approved in more than 100 countries worldwide (brand name: *Xeloda®*).

In Japan, *Xeloda®* was approved for the indication for the treatment of "inoperable or recurrent breast cancer" in 2003, "postoperative adjuvant chemotherapy for colon cancer" in 2007, "curatively unresectable advanced/recurrent colorectal cancer" in 2009 and "curatively unresectable advanced/recurrent gastric cancer" in 2011.

3. CLASSIC study*2

CLASSIC study is a randomized, controlled, open label Phase III study which was conducted in South Korea, China and Taiwan to verify the benefits of the combination therapy with *Elplat®* and capecitabine in postoperative adjuvant chemotherapy for gastric cancer.

The 3 year disease-free survival, which was the primary endpoint of the CLASSIC study, was 74% in the combination therapy group versus 59% in the surgery only group. Estimated 5 year overall survival was 78% in the combination therapy group versus 69% in the surgery only group.

These results showed a significant improvement in 3 year disease-free survival and estimated 5 year overall survival for the combination therapy vs surgery only.

*2 Lancet 2012; 379: 315-21, Lancet Oncology 2014; 15: 1389 -96

4. Phase II study in Japan*3

The purpose of this phase II study was to evaluate the dose intensity (the actual cumulative dose of each drug as a proportion of the planned cumulative dose of the drug that would have been administered if eight cycles had been completed without any suspension or dose reduction) of the combination therapy with *Elplat®* and capecitabine as the primary endpoint. As a result, the mean dose intensity was 73.4% for *Elplat®* and 67.2% for capecitabine. These were higher than the predefined threshold values and therefore the feasibility of the combination therapy with *Elplat®* and capecitabine in Japanese patients was confirmed.

*3 The 87th Annual Meeting of Japanese Gastric Cancer Association, W1-3