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ASKA Pharmaceutical Co., Ltd.  
Yakult Honsha Co., Ltd.

**ASKA Pharmaceutical Co., Ltd. and Yakult Honsha Co., Ltd. Announce  
Conclusion of Agreement on License of Anticancer Agent Soblidotin**

ASKA Pharmaceutical Co., Ltd. (President: Takashi Yamaguchi), (“ASKA”) and Yakult Honsha Co., Ltd. (President: Sumiya Hori, “Yakult”) concluded the agreement on the license of Soblidotin (ASKA’s Code No.: TZT-1027), which is under development by ASKA as an anticancer drug. Under this agreement, Yakult has received the exclusive rights to develop and market Soblidotin (Yakult’s Code No.: YHI-501) worldwide (including Japan).

Soblidotin is a peptide discovered by ASKA and shows strong anti-tumor action. The origin of the compound is Dolastatins extracted from Sea Hare (*Dolabella Auricularia*). The compound is considered to exert cytotoxic action by binding to tubulin and inhibiting polymerization of microtubule proteins. Furthermore, in non-clinical studies the compound showed selective inhibition of blood flow in the tumor vessels, causing inhibition of the supply of nutrients to tumor tissues. The above actions reveal that the compound is a potent anticancer agent which can induce the tumor necrosis in wide area. Phase I studies have been conducted in Japan, and Early Phase II studies have been conducted overseas. Efficacy responses were seen in some patients in these clinical studies.

ASKA expects Yakult’s accumulated experience in the clinical development in cancer field and has licensed Yakult an exclusive rights of the compound worldwide (including Japan).

Yakult will develop Soblidotin by contributing the maximum of their potential making the best use of the experience of the development of its anti-cancer drugs, including Irinotecan HCL (Product Name: Campto) and Oxaliplatin (Product Name: Elplat), and tries to expand the pipeline of the products in cancer field, which is one of its important business areas.

## 【Reference】

{ Generic Name }

Soblidotin

{ Chemical Name }

$N^2$ -(*N,N*-dimethyl-L-valyl)- $N^1$ -[(1*S*,2*R*)-2-methoxy-4-[(2*S*)-2-[(1*R*,2*R*)-1-methoxy-2-methyl-3-oxo-3-[(2-phenylethyl)amino]propyl]-1-pyrrolidinyl]-1-[(1*S*)-1-methylpropyl]-4-oxobutyl]- $N^1$ -methyl-L-valinamide

{ Origin & Characteristics }

Dolastatin 10 with potent antitumor activity has been isolated from *Dolabella Auricularia*. Soblidotin is a derivative of Dolastatin 10 whose dolaphenine moiety is substituted for phenethylamine. Soblidotin shows a broad antitumor spectrum on human and murine tumors. The mode of cytotoxicity of Soblidotin has been ascribed to the inhibition of microtubule assembly through the binding to tubulins. Soblidotin showed antitumor activity against human tumors (stomach, colon, breast and lung) and tumors which are resistant to vincristine (having the same mode of activity as this compound). In addition to potent cytotoxicity against cancer cells, Soblidotin showed selective inhibition of blood flow in the tumor vessels by an antivascular effect, causing inhibition of the supply of nutrients to tumor tissues followed by the induction of the tumor necrosis in wide area.