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FOR IMMEDIATE RELEASE

Nobelpharma Co., Ltd.
Eisai Co., Ltd.

NOBELPHARMA AND EISAI ANNOUNCE JAPAN LAUNCH OF ANTINEOPLASTIC AGENT GLIADEL® 7.7 mg IMPLANT

Nobelpharma Co., Ltd. (Headquarters: Tokyo, President & CEO: Jin Shiomura, "Nobelpharma") and Eisai Co., Ltd. (Headquarters: Tokyo, President & CEO: Haruo Naito, "Eisai") announced today that the two companies will launch Gliadel® 7.7 mg Implant (carmustine), an antineoplastic agent, in Japan on January 9.

Based on an existing license agreement between the companies, Nobelpharma has been conducting clinical studies of the agent and in 2012 acquired manufacturing and marketing authorization for Gliadel 7.7 mg Implant in Japan on September 28 and National Health Insurance (NHI) Drug Price List registration on November 22. Gliadel 7.7 mg Implant will be marketed domestically by Eisai and co-promoted by both companies.

Gliadel is the only sustained-release formulation approved for intracranial implantation in Japan. Each wafer contains carmustine, a nitrosourea alkylating agent, distributed in a biodegradable polymer matrix. Implanting the wafer into the brain following surgical removal of malignant glioma allows direct delivery of chemotherapy to the tumor site. The agent can thus be used prior to initiating other standard therapies such as radiation and chemotherapy. In Phase III clinical studies conducted outside Japan, Gliadel was shown to significantly extend overall survival in patients with newly diagnosed malignant glioma versus placebo as well as significantly increase the overall survival rate after six months in patients with recurrent glioblastoma. Furthermore, clinical studies conducted in Japan have demonstrated that the agent possesses excellent antitumor efficacy and a favorable safety profile in patients with newly diagnosed malignant glioma and recurrent glioblastoma. Gliadel is currently approved in 30 countries worldwide, including the United States and in Europe and Southeast Asia.

Glioma is a tumor of the brain that accounts for approximately 30% of all primary brain tumors, of which malignant glioma prevalence in Japan is estimated to be about 2,000 to 2,500 cases per year. Gliadel was designated as being of high medical need by the Investigational Committee for Usage of Unapproved Drugs in Japan in September 2008 and designated as an orphan drug in June 2009.

Malignant glioma remains difficult to treat and the two companies expect Gliadel 7.7 mg Implant to become a new treatment option for patients with malignant glioma. In accordance with approval conditions, the two companies will work together to conduct a post-marketing use results survey (all-case surveillance) in patients who are administered Gliadel 7.7 mg Implant until the predetermined number of patients has been reached, in order to promote the effective and safe use of the drug.

[Please refer to the following notes for a product outline and photograph of Gliadel 7.7 mg Implant as well as further information on glioma and the clinical studies mentioned.]

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<Note to editors>

1. Product Outline

1)	Product Name:	Gliadel® 7.7 mg Implant	
2)	Generic Name:	carmustine	
3)	Indications and Usage:	Malignant glioma	
4)	Dosage and Administration:	The usual adult dose is eight wafers (61.6 mg of carmustine), placed in and covering the resection cavity if the size and shape of the cavity allows, or less than but as close to eight wafers as possible if the size and shape does not accommodate eight wafers.	
5)	Listed price:	Gliadel® 7.7 mg Implant	156,442.60 yen per 7.7 mg wafer
6)	Packaging:	Gliadel® 7.7 mg Implant	Eight wafers
7)	Manufacturer:	Nobelpharma Co., Ltd.	
8)	Distributor:	Eisai Co., Ltd.	

2. About Glioma

Glioma is the general term for primary brain tumors originating from the glial cells that exist in essential brain tissue. They are mostly malignant with poor prognosis. Gliomas account for approximately 30% of all primary brain tumors and in many cases characteristically spread and develop (infiltrate) in the brain or spinal cord without a distinct tumor boundary, with normal brain tissue and tumor cells being both present in surrounding areas making it difficult to remove the tumor completely. In these cases, the tumor has a poor survival prognosis of 25% or less within the first five years.

Surgical removal (craniotomy) of the tumor is usually performed as standard treatment for glioma and in the majority of cases radiation and/or chemotherapy is administered adjunctively post-surgery. However, the active ingredients in chemotherapeutic agents administered during systemic chemotherapy regimens are often unable to be sufficiently delivered to the tumor site at the required dose because of the blood-brain barrier and the actual dose required also cannot be sufficiently administered without systemic adverse events. These difficulties are another reason for poor prognosis in patients with malignant glioma.

3. About the Clinical Study Conducted in Japan (NPC-08-01)

NPC-08-01 was a multicenter, non-comparative, non-blind study conducted with the aim of evaluating the drug's efficacy and safety in 16 patients with newly diagnosed malignant glioma ("newly diagnosed patients") and 8 patients with recurrent glioblastoma ("recurrent patients"). A maximum of eight wafers were placed in the resection cavity at the time of surgical removal and, 14 days after implantation, the newly diagnosed patients were administered temozolomide and radiation as adjunctive therapies and the recurrent patients were administered appropriate therapies (mainly temozolomide). Survival rates and safety were evaluated at 6 and 12 months after implantation, respectively. The survival rate for newly diagnosed patients after 12 months was 100.0% (16/16 cases) and the survival rate for recurrent patients after 6 months was 87.5% (7/8 cases) and after 12 months 62.5% (5/ 8 cases).

Furthermore, the rate of adverse events occurring (including laboratory abnormalities) was 54.2% (13/24 cases), with the most common adverse events being: brain edema (25.0%, 6/24 cases), fever (12.5%, 3/24 cases), lymphocytopenia (12.5%, 3/24 cases), hemiplegia (including hemiparesis) (12.5%, 3/24 cases), nausea (8.3%, 2/24 cases), vomiting (8.3%, 2/24 cases), loss of appetite (8.3%, 2/24 cases), headache (8.3%, 2/24 cases), and increased ALT (GPT) (8.3%, 2/24 cases).

4. About the Phase III Clinical Studies Conducted Outside Japan (T-301 and 8802)

Study T-301 was a multicenter, randomized, double-blind, placebo-controlled study that compared the efficacy and safety of Gliadel versus placebo in 240 newly diagnosed patients. Results from the study recorded a median overall survival rate of 13.9 months for Gliadel and 11.6 months for placebo, with significant improvement for Gliadel (p=0.03). Adverse events occurred at a rate of 55.8% (67/120 cases) for Gliadel and 60.8% (73/120 cases) for placebo. Study 8802 was a multicenter, randomized, double-blind, placebo-controlled, comparative clinical study in 222 recurrent patients. Results of this study recorded a survival rate after six months of 60.0% for Gliadel and 47.3% for placebo (p=0.06), with a median overall survival rate of 7.24 months for Gliadel and 5.42 months for placebo (p=0.30). However, in an analysis of just the 145 patients diagnosed with glioblastoma, the survival rate after six months was 55.6% for Gliadel and 35.6% for placebo, with a significant difference favoring Gliadel (p=0.02), while the median overall survival rate was 6.4 months for Gliadel and 4.6 months for placebo. Adverse events occurred at a rate of 60.9% (67/110 cases) for Gliadel and 63.4% (71/112 cases) for placebo.

[Product Photograph]