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Press Release

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Decision to Grant a Patent Related to Antigenic Peptides Derived  
from the T790M Point Mutation of Epidermal Growth Factor Receptor

GreenPeptide Co., Ltd. announces that a patent application for the cancer peptide vaccine GRN-1301, a product developed by the company, has received a decision to grant a patent\*<sup>1</sup> in Japan, following an equivalent grant in the United States of America (USA), as described below.

1. Overview of the patent

Title of the invention	Antigen peptide originated from T790M point-mutated* <sup>2</sup> sequence of epidermal growth factor receptor (EGFR)* <sup>3</sup>
Patent application number	Japanese Patent Application No. 2014-529551
Patent holder	GreenPeptide Co., Ltd.

Of patients with non-small-cell lung cancer, which accounts for 80% of all lung cancer types, those with epidermal growth factor receptor (EGFR) mutations are typically prescribed with tyrosine kinase inhibitors (TKIs) as first-line therapy. However, with prolongation of their TKI treatments, approximately 60% of patients experience the T790M point mutation, which induces TKI resistance in the EGFR. The peptide vaccine GRN-1301, derived from the T790M point mutation, is designed to target the neoantigen\*<sup>4</sup> and exert longer-term treatment effects by suppressing the emergence of TKI-resistant cancer cells associated with the mutation mentioned above. We have been engaged in the research and development of this drug jointly with the Kanagawa Prefectural Hospital Organization.

The peptide derived from this invention integrates the T790M point mutation, a “driver mutation” directly involved in the malignant transformation of cancer, so that it is recognized as a non-self in the patient’s immune system, thereby holding great expectations for high immunogenicity. This peptide also has other characteristics, such

as a low likelihood of an escape from immunological surveillance occurring due to a loss of cancer vaccine antigens in the cancer cell.

From the viewpoint of intellectual property rights, this decision to grant a patent will protect the GRN-1301 cancer immunotherapeutic under development in a highly secure manner. This patent has already been registered in the USA.

## 2. Impact on projections for financial results

This decision to grant a patent will not have any impact on the company's financial results for the fiscal year ending March 31, 2018.

### [Explanation of terms]

- \*1: Decision to grant a patent: Results of an examination by each country's patent office to be notified when it has been determined that "the invention described in the application deserves being entitled a patent." Payment of the patent fee upon receipt of such decision will have the patent registered and its right established in relevant countries.
- \*2: T790M point mutation: The mutation of the 790th amino acid of the EGFR, from threonine to methionine. This mutation is considered to eventually acquire drug resistance to the first- and second-generation tyrosine kinase inhibitors extensively used as first-line therapy, such as Tarceva and Iressa.
- \*3: Epidermal growth factor receptor (EGFR): The receptor that binds to the epidermal growth factor, which regulates cell proliferation and growth, thereby mediating signal transmission. The activation of this receptor will lead to cell differentiation and proliferation. The EGFR is found in many cells, and its mutation can trigger canceration, infiltration, and metastasis in the cells.
- \*4: Neoantigen: An antigen that involves gene mutations (amino acid mutations) and develops with gene abnormalities unique to cancer cells. This cancer-specific antigen manifests only through gene mutations unique to cancer cells of individual patients and does not exist in normal cells. It is expected that targeting a neoantigen, which is recognized as a "non-self" by the immune system, will efficiently induce cancer cell-killing immunity.

#### About GreenPeptide Co., Ltd.

GreenPeptide is a drug discovery venture company engaged in the development of innovative “cancer immunotherapy” as the fourth cancer treatment following surgery, radiotherapy, and chemotherapy. Clinical trials of the company’s cancer peptide vaccines are being conducted in Japan and the USA. In addition, the company recently started the development of a new T-cell therapy using the induced pluripotent stem cell regeneration of antigen-specific T cells, as well as the development of new drugs based on neoantigens (gene mutation antigens), a highly innovative approach the world over.