Nihon's new drug candidate NPO-15 for the treatment of Myasthenia Gravis has been adopted by AMED's Drug Discovery Support Program for Orphan drug prior to the Designation

Tokyo, Japan, May 13, 2019 – Nihon Pharmaceutical Co., Ltd. (Nihon Pharm, Head offices in Chuo-ku, Tokyo, President and CEO Hiroyuki Tsujiyama, Ph.D.), announced its new drug candidate NPO-15 designed by Nihon Pharm for the treatment of Myasthenia Gravis (MG) has been adopted by Japan Agency for Medical Research and Development (AMED)'s drug discovery support program of fiscal 2019, "Drug Discovery Support Program for Orphan Drug Prior to the Designation." A part of the R&D expenses for this program will be supported by AMED from April 1, 2019 to March 31, 2022.

Project title	Affiliation
Development of a new treatment agent for Myasthenia Gravis (NPO-15)	Nihon Pharmaceutical Co., Ltd.

[Drug Discovery Support Program for Orphan Drug Prior to the Designation]

This program aims research-oriented pharmaceutical companies to obtain the approval as orphan drugs and its objective is to improve the R&D environment and enable the practical application of orphan drugs promptly and effectively.

[Myasthenia Gravis (MG)]

MG is registered in the Ministry of Health, Labor and Welfare designated Intractable Disease 11, and it is an autoimmune disease in which the receptor on the muscle side is destroyed by autoantibodies at the joints (neuromuscular junctions) of peripheral nerves and muscles. It may cause weakness in the entire body and fatigue, and it may not be possible to swallow properly. If it becomes severe, it may cause paralysis of respiratory muscles and may cause dyspnea.

(Information from the website of Japan Intractable Disease Center as of May 2019)

[NPO-15]

NPO-15 is a new biopharmaceutical candidate that is designed to have a dual mechanism of actions; Autoantibody neutralization activity and cytotoxicity to autoantibody-producing B cells (Neurotherapeutics. 2017 Jan; 14 (1): 191-198, Patent No. 4857396).

[Further information on AMED]

Please visit the following site for further information and decision of the adoption on AMED's "Drug Discovery Support Program for Orphan Drug Prior to the Designation."

https://www.amed.go.jp/en/program/list/06/03/001_03-01.html

https://www.amed.go.jp/koubo/06/01/0601C_00053.html

<Media Contacts> e-mail: partnering@nihon-pharm.co.jp

(Supplementary information)

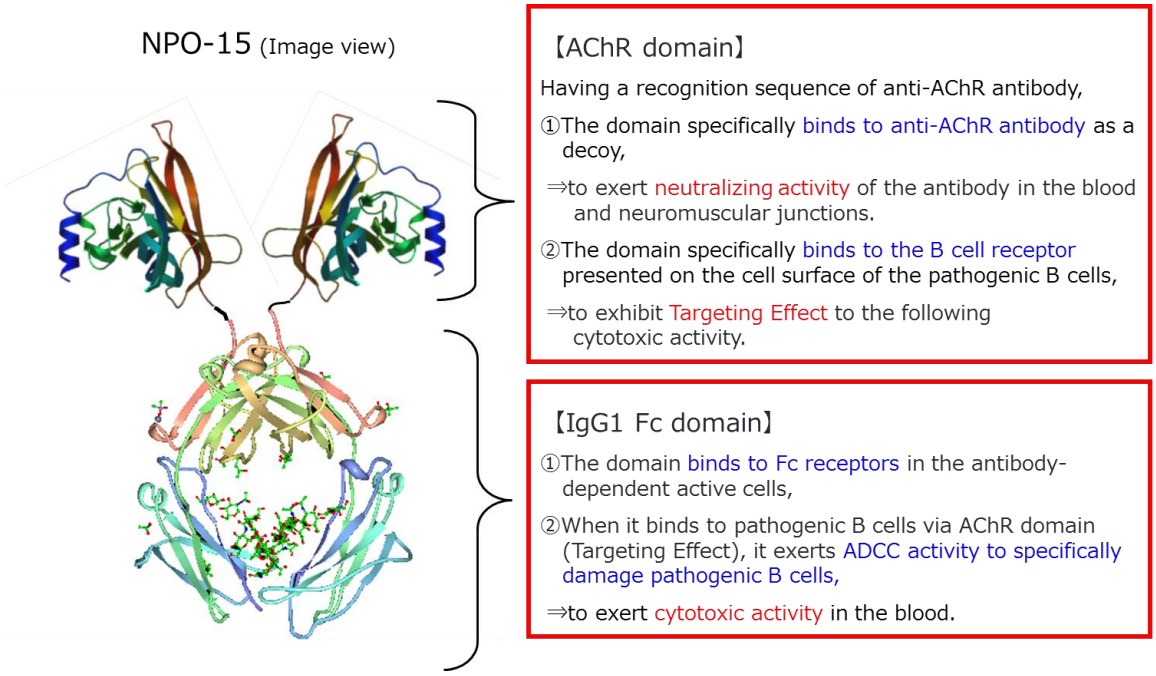
Expected dual action of NPO-15

Myasthenia Gravis (MG) is an autoimmune neurological disease which results from pathogenic autoantibodies that destroys nicotinic acetylcholine receptors on the side of postsynaptic membrane of the neuromuscular junction. This prevents nerve impulses from triggering muscle contractions to cause muscle weakness and fatigue. MGs are classified into systemic MG and ocular MG, and 80 to 85% of all MGs are positive for anti-acetylcholine receptor antibody (anti-AChR antibody).

NPO-15 is a recombinant Fc fusion protein consists of the human acetylcholine receptor α1 subunit extracellular domain (AChR domain) and human IgG1 Fc domain (IgG1 Fc domain). Thanks to this molecular design and mechanism of action, this targets anti-AChR antibody-positive patients.

In the AChR domain, there is a recognition sequence of anti-AChR antibody, a pathogenic autoantibody, which binds to the anti-AChR antibody by antigen-antibody reaction. This binding action acts as a decoy effect, and **autoantibody neutralizing activity** is exhibited in the patient's blood or in the neuromuscular junction.

The other IgG1 Fc domain has an Fc receptor binding site, which is a sequence deeply involved in antibody-dependent cellular cytotoxicity (ADCC). NPO-15 binds to autoantibody-producing B cells (pathogenic B cells), and then IgG1 Fc binds to Fc receptors so that it is exhibited to exert **ADCC activity** against the pathogenic B cells via effector cells such as natural killer cells.



NPO-15 has a unique molecule to be expected to have dual mechanisms of action, i.e., neutralizing activity against anti-AChR antibody and cytotoxic activity against pathogenic B cells.