September 6, 2019

EA Pharma Co., Ltd.
National Center of Neurology and Psychiatry

# National Center of Neurology and Psychiatry and EA Pharma Co., Ltd. Sign a Global License Agreement for OCH-NCNP1

EA Pharma Co., Ltd. (President, Yuji Matsue; Headquarters, Tokyo, Japan) (hereinafter "EA Pharma") and National Center of Neurology and Psychiatry (President, Hidehiro Mizusawa; Headquarters, Tokyo, Japan) (hereinafter "NCNP") have signed a worldwide exclusive license agreement for development, manufacture and marketing for all indications of OCH-NCNP1, which is under development by NCNP (hereinafter "OCH").

Under the above agreement, EA Pharma pays an initial fee, milestone fees and royalties to NCNP.

OCH was designed and synthesized by Dr. Takashi Yamamura (Director, Department of Immunology, National Institute of Neuroscience, NCNP) and his colleague by modifying the structure of glycolipid alpha-galactosylceramide (alpha-GalCer) produced by bacteria parasitizing marine sponge.[1)] In recent years, it was found that human enteric bacteria produce analogues of alpha-GalCer, similar to OCH. Such gut bacteria-derived glycolipids are thought to contribute to immune homeostasis by inducing Th1 and Th2 cytokines from natural killer T cells (NKT).[2), 3)] Although alpha-GalCer induces both Th1 and Th2 cytokines from NKT cells, OCH selectively induces production of Th2 cytokines. Therefore, OCH has the therapeutic potentials to suppress the activity of Th1 cytokines and to improve chronic inflammation caused by excessive actions of Th1 cytokines. NCNP has conducted an investigator-initiated PI trial for OCH with patients suffering from multiple sclerosis and now plans to proceed to PIIa. Keio University Hospital has been conducting jointly with NCNP an investigator-initiated PI/II clinical trial for OCH with patients with Crohn's disease since 2016.[4)]

The above agreement was realized through the opportunity of introduction of OCH to EA Pharma by Translational Research Center for Medical Innovation (TRI)* of Foundation for Biomedical Research and Innovation at Kobe, which supports development of research seeds in universities and other research institutes of Japan. EA Pharma and NCNP collaborate to promote development of OCH to contribute to treatment and increase of QOL of patients with intractable diseases.

End

1) Miyamoto K, Miyake S, Yamamura T., A synthetic glycolipid prevents autoimmune encephalomyelitis by inducing TH2 bias of natural killer T cells. *Nature*. 2001; 413: 531-534.
2) An D et al., Sphingolipids from a symbiotic microbe regulate homeostasis of host intestinal natural killer T cells. *Cell*. 2014; 156: 123-133.
3) Wieland Brown LC et al., Production of -α-galactosylceramide by a prominent member of the human gut microbiota. *PLoS Biol*. 2013; 11: e1001610.
4) Keio University and AMED initiate an investigator-initiated clinical trial to investigate the safety and efficacy of an investigational drug for treatment of intractable Crohn's disease (Press release in Japanese only) https://www.keio.ac.jp/ja/press-releases/2016/9/15/28-18435/
* Translational Research Center for Medical Innovation (TRI): https://advances.tri-kobe.org/

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・Ministry of Health, Labour and Welfare (Japan) Research Grants.
・Japan Agency for Medical Research and Development (AMED) Research Grants.


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More Information

## 1. About natural killer T (NKT) cells and Th1/2 cytokines

Natural killer T (NKT) cells are a unique lymphocyte population that recognize glycolipid antigen bound to CD1d. In response to antigen receptor stimulation, NKT cells immediately secrete a large amount of bioactive substances including cytokines and chemokines. The cytokines produced by NKT cells include Th1 cytokines (interferon gamma, TNF alpha, etc.) that strengthen cellular immunity and Th2 cytokines (interleukin-4, IL-5, IL-13, etc.) that strengthen humoral immunity. Th1 and Th2 cytokines mutually antagonize each other. NKT cells produce Th1 or Th2 cytokines as appropriate to maintain the lymphocyte balance and suppress excessive immunoreaction and inflammatory response. NKT cells can be a key in a wide range of disease areas including autoimmune diseases, allergic diseases, organ transplantation and immunology of infectious diseases.

## 2. About EA Pharma Co., Ltd. (EA Pharma）

EA Pharma Co., Ltd., a subsidiary of Eisai Co., Ltd. for gastrointestinal disease area, was established in April 2016 by integration of the gastrointestinal business unit with more than 60 year's history of the Eisai Group and the gastrointestinal business unit of the Ajinomoto Group having amino acid as its business core. EA Pharma is a gastrointestinal specialty pharma with a full value chain covering R&D, production & logistics and sales & marketing. EA Pharma has been actively engaged in academia-industry collaboration projects to transform the values created in Japanese academia into pharmaceutical products.
For more information on EA Pharma, please see http://www.eapharma.co.jp/en/

## 3. About National Center of Neurology and Psychiatry (NCNP)

In NCNP, our hospital and institutions work together in research and development to overcome mental disorders, neurological and muscular diseases, and developmental disorders with the mission to use our research results for providing advanced medical services and to spread our services across the country.
For more information on NCNP, please see https://www.ncnp.go.jp/english/