Press Release

Shionogi and HanaVax Enter into a License Agreement for *Streptcoccus Pneumoniae* Vaccine Candidate

Osaka and Tokyo, Japan, September, 30, 2020 – Shionogi & Co., Ltd. (Head Office: Osaka, Japan; President & CEO: Isao Teshirogi, Ph.D.; hereafter "Shionogi") and HanaVax Inc. (Head Office: Tokyo, Japan; President & CEO: Pohsing Ng.; hereafter "HanaVax"), a drug-discovery venture company originating from the University of Tokyo, today announced they have entered into a license agreement for research, development, manufacturing, distribution, and commercialization of HanaVax's *Streptococcus pneumoniae* (hereafter "*S. pneumoniae*") nasal vaccine candidate. Shionogi will make an upfront payment to HanaVax in return for exclusive worldwide rights to this vaccine candidate. HanaVax will be eligible to receive additional development milestones and royalties based on sales of the vaccine.

The vaccine aims to prevent people from acquiring pneumococcal disease. Pneumonia is the fifth leading cause of death in Japan. *S. pneumoniae* is one of the most important pneumonia pathogens and the leading bacterial cause of pneumonia deaths worldwide. Infants and the elderly are especially vulnerable to *S. pneumoniae*, which can cause severe pneumonia, sepsis and meningitis, referred to collectively as "invasive pneumococcal diseases (IPD)". Although *S. pneumoniae* is known to have more than 90 different serotypes, marketed vaccines are only able to cover a limited number of them. Therefore, unmet medical need remains for more comprehensive protection from IPD caused by serotypes not covered by the marketed vaccines.

The vaccine is comprised of PspA antigens, which are expected to provide broader protection than current vaccine antigens, carried in HanaVax's proprietary cationic nanogel delivery system[1]. In the nonclinical studies, the vaccine effectively induced systemic and respiratory mucosal immunity[2,3], and provided protection from *S. pneumoniae* infection[3], when applied nasally. The vaccine will also avoid the pain associated with injections.

Shionogi and HanaVax will accelerate research and development of an innovative, next generation nasal vaccine to protect people from *S. pneumoniae* related diseases, by merging Shionogi's expertise in infectious diseases with HanaVax's pioneering research and technology related to mucosal immunity.

About PspA

Pneumococcal Surface Protein A (PspA) is known as a virulence factor found on the surface of all pathogenic *S. pneumoniae* bacteria. PspA is believed to help the bacteria avoid immune surveillance. It is expected to induce protection against a broader range of *S. pneumoniae* serotypes compared to current vaccines.

About HanaVax's cationic nanogel delivery system

Mucosal immunity is of great importance for the prevention of respiratory system infections, because the respiratory mucosa is the first line of defense against pathogens. HanaVax's proprietary cationic nanogel delivery formulation provides a protective carrier for antigens and consists of a polysaccharide pullulan molecule modified with cholesterol and cationic amines. The nanogel helps PspA antigens increase their retention on the mucosal surface and their gradual uptake by the immune cells. This effectively initiates the induction of both mucosal and systemic immunity.

About Shionogi

Shionogi is committed to "Protect people worldwide from the threat of infectious diseases" as our key focus. We are not limiting ourselves to the research and development of therapeutic medications, but are also focused on the total care of infectious disease, through awareness building, prevention, diagnosis, and treating exacerbations, as well as the infection itself. For more information, please visit https://www.shionogi.com/global/en/.

About HanaVax

HanaVax is a drug discovery biotechnology startup founded with the mission of "Developing nasal vaccines for a healthier society". The proprietary nasal vaccine that is the subject of this license was developed on the basis of ten years of collaborative research between two pioneers of mucosal immunity and chemical engineering in the service of improved drug and vaccine delivery, Distinguished Prof. Dr. Hiroshi Kiyono (The University of Tokyo and Chiba University) and Prof. Dr. Kazunari Akiyoshi (Kyoto University). For more information, please visit https://www.hanavax.co.jp/en/.

Reference

1, Nochi T. et.al., "Nanogel antigenic protein delivery system for adjuvant-free intranasal vaccines" *Nature Materials*, **2010**, 9, 572-578. https://www.nature.com/articles/nmat2784

2, Fukuyama Y. et al., "Nanogel-Based pneumococcal surface protein A nasal vaccine induces microRNA-associated Th17 cell responses with neutralizing antibodies against *Streptococcus pneumoniae* in macaques" *Mucosal Immunology,* **2015**, *8*, 1144-1153. https://www.nature.com/articles/mi20155

3, Kong H. Gyu et al., "Nanogel-Based PspA Intranasal Vaccine Prevents Invasive Disease and Nasal Colonization by *Streptococcus pneumoniae*" *Infection and Immunity,* **2013**, *81*, 1625-1634.

https://iai.asm.org/content/81/5/1625.long

Forward-Looking Statements

This announcement contains forward-looking statements. These statements are based on expectations in light of the information currently available, assumptions that are subject to risks and uncertainties which could cause actual results to differ materially from these statements. Risks and uncertainties include general domestic and international economic conditions such as general industry and market conditions, and changes of interest rate and currency exchange rate. These risks and uncertainties particularly apply with respect to product-related forward-looking statements. Product risks and uncertainties include, but are not limited to, completion and discontinuation of clinical trials; obtaining regulatory approvals; claims and concerns about product safety and efficacy; technological advances; adverse outcome of important litigation; domestic and foreign healthcare reforms and changes of laws and regulations. Also, for existing products, there are manufacturing and marketing risks, which include, but are not limited to, inability to build production capacity to meet demand, unavailability of raw materials and entry of competitive products. The company disclaims any intention or obligation to update or revise any forward-looking statements whether as a result of new information, future events or otherwise.

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