

July 6, 2021

Veneno Technologies Co., Ltd.

NAGASE & CO., LTD.

Veneno Technologies Co., Ltd. and NAGASE & CO., LTD. Sign Agreement on Distribution and Capital Alliance for DRP Drug Discovery Business

In May 2021, Veneno Technologies Co., Ltd. (Tsukuba; CEO and President: Kazunori Yoshikawa) and NAGASE & CO., LTD. (Chuo-ku, Tokyo; Representative Director and President: Kenji Asakura) entered into a distribution and capital alliance contract for drug discovery using DRP functional peptides.

In order to ensure healthy lifestyles and cope with various diseases, drug discovery innovation is urgently needed for the development of more effective drugs. In the pharmaceuticals market, antibody drugs have been growing their share compared to small molecule drugs. However, with drug discovery for small molecule drugs seeming to have hit a dead end recently, and issues such as exhausting targets and economic rationality for antibody drugs, there has been increased attention on downsizing antibody drugs (large molecule drugs) and on new drug discovery in the area of medium-size molecules such as miniproteins and peptide drugs.

Veneno focused on the high bioactivity of disulfide-rich peptides (DRP)*¹, and developed the unique drug discovery technologies of the Veneno Suite™*² as a new solution to accelerate DRP drug discovery. With this platform's technologies, they are engaged in the drug discovery business and biochemicals business for membrane proteins such as ion channels and transporters, and GPCRs*³, where until now drug discovery was difficult.

Utilizing the NAGASE Group's peptide and protein production technology in its pharmaceutical materials and intermediates manufacturing and supply businesses, and its powerful presence and business development capabilities for a wide range of materials and business fields, NAGASE & CO., LTD., as a domestic and international distributor for Veneno, will support the global expansion of the DRP drug discovery business and the acceleration of pharmaceutical development in fields where drug discovery was difficult with existing methods.

[Comment from Veneno Technologies Co., Ltd. CEO and President Kazunori Yoshikawa]

"I am very excited about this distribution and capital alliance agreement with NAGASE & CO., LTD. This alliance is an important partnership for our goal of accelerating DRP drug discovery and building a new paradigm of next-generation peptides to succeed antibody drugs. I am hopeful this will be a major step towards realizing our goals."

[Comment from NAGASE & CO., LTD. Representative Director and President Kenji Asakura]

"I am extremely happy to be able to work together with Veneno on developing and supplying DRP drugs, which have significant potential as next-generation drugs. Open innovation through

collaborations with companies engaged in next-generation businesses is necessary as a driving force to maintain sustainable growth. By utilizing the strengths of NAGASE as a whole to support the development of revolutionary medicines, we will contribute to a sustainable world where people live with peace of mind.”

■ **About Veneno Technologies Co., Ltd.**

Veneno Technologies Co., Ltd. was established with the goal of contributing to society and to advanced, sustainable medicine by accelerating the research and development of DRP functional peptides. By combining revolutionary DRP discovery technology researched for many years at the National Institute of Advanced Industrial Science and Technology (AIST) with DRP production technology currently being developed, Veneno Technologies is leading the research and development of DRP drug discovery in areas such as new medicines, research reagents, agricultural chemicals, and biostimulants. Veneno Technologies has entered into a patent licensing agreement with AIST as part of its technology transfer program, and has been recognized as an AIST Start-Up.

(1) Company Name	Veneno Technologies Co., Ltd.
(2) Head Office	Tsukuba Startup Park, 2-5-1 Azuma Tsukuba, Ibaraki, Japan
(3) Representative	Kazunori Yoshikawa
(4) Established	July 9, 2020
(5) Business Overview	Through the Veneno Suite™ DRP drug discovery technologies, operating pharmaceutical and biochemical businesses with DRP discovery, research, and development for membrane proteins such as ion channels and transporters, and GPCRs
(6) URL	https://veneno.co.jp/

■ **About NAGASE & CO., LTD.**

As a trading company with distribution rights allowing it to import and sell quality overseas products in Japan, NAGASE & CO., LTD. has acquired technology, information, and an overseas network and worked to strengthen its manufacturing, processing, and R&D functions while shifting its business structure. In 2032, the 200th anniversary of the founding of the company, and beyond, NAGASE & CO., LTD. will design new businesses as a business designer which has grown beyond being a chemicals trading company.

(1) Company Name	NAGASE & CO., LTD.
(2) Head Office	Chuo-ku, Tokyo
(3) Representative	Representative Director and President: Kenji Asakura
(4) Established	1832

(5) Business Overview	Import/export and domestic sales of chemicals, plastics, electronics materials, cosmetics and health foods
(6) URL	https://www.nagase.co.jp/

[Notes]

*1: Disulfide-rich peptide (DRP)—Peptides with three or more disulfide bonds and a unique structure, consisting of around 20 to 60 amino acids. DRPs are potent bioactive peptides widely found in nature, from bacteria to humans, often in the venom of animals, and they are a frequent subject of research. As animals use DRPs as a primary component of venom, DRPs have evolved to have a powerful effect even in small quantities, and DRPs are a natural modulator with high activity and high selectivity for ion channels and receptors. As they have a rigid molecular structure due to the multiple disulfide bonds in the molecule, DRPs also have improved heat, pH, and proteolytic enzyme stability compared to linear peptides. The unique properties of DRPs have led to growing attention in recent years as a new potential base for drug discovery.

The molecular properties of the current main pharmaceutical molecules, small molecule compounds and antibodies, make it difficult to design pharmaceutical molecules for ion channels and GPCRs, and the side effects of some small molecule drugs on the market have become problematic. In contrast, as an excellent natural modulator for ion channels and GPCRs, attempts have been made to use DRPs in medicinal drugs and diagnostic pharmaceuticals, but the complex molecular structure of DRPs makes chemical synthesis difficult and there are limited effective drug screening methods when targeting membrane proteins. Therefore, despite their potential as effective functional components, progress towards their practical use failed to materialize.

*2: Veneno Suite™—Focusing on the usefulness of DRPs as functional peptides, Veneno Suite is a DRP drug discovery system combining a DRP discovery method targeting membrane proteins which was researched at the National Institute of Advanced Industrial Science and Technology with a simple and inexpensive synthesis method. Veneno Suite™ consists of three core technologies:

- (1) DRP Space™: Technology to build large-scale DRP-focused libraries
- (2) PERISS™: High-speed screening technology using the periplasmic display method
- (3) Super Secrete™: Production technology using *E. coli* secretion

*3: Membrane proteins such as ion channels and transporters, and GPCRs—For cells to carry out their vital functions, environments inside and outside the cell must remain stable, and it is necessary to allow through molecules which cannot permeate through the cell membrane (the lipid bilayer membrane), such as inorganic ions and many water-soluble organic materials involved in metabolism. The special “devices” allowing this function are ion channels and transporters, made from membrane proteins. G protein-coupled receptors (GPCRs) receive neurotransmitters and hormones outside the cell and communicate these signals to inside the cell, contributing to maintaining homeostasis inside and outside the cell. There are

numerous kinds of ion channels and transporters, and GPCRs, and they are involved in many diseases, so they are an important target for drug discovery.

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