

October 12, 2021

Epsilon Molecular Engineering, Inc.

EME Announces Collaboration Agreement on Development of VHH Antibody

Saitama, Japan – October 12, 2021 – Epsilon Molecular Engineering, Inc. (HQ: Saitama, Japan; President & CEO: Naoto Nemoto; “EME”) announces that it entered into VHH-based drug discovery and development collaboration with Maruho Co., Ltd. (HQ: Osaka, Japan; President & CEO: Atsushi Sugita; “Maruho”) for a target molecule.

EME will conduct antigen preparation, VHH(*1) identification with its unique humanized VHH screening platform (Screening technology that combines “*PharmaLogical*® Library”(*2) with cDNA display(*3)), and optimize VHH candidates from screening. Maruho will have the right to develop VHH candidates optimized by EME.

Under the term of this agreement, EME will receive an undisclosed upfront payment within this year and milestone payment depending on the following phase in research. Besides EME will receive milestone payments in pre-clinical, clinical development, and sales royalties with a future contract.

* 1 VHH: Variable Domain of Heavy Chain of Heavy Chain Antibody found in camelids. Superior stability and easily molecularly designed than conventional IgG

* 2 *PharmaLogical*® Library: Original Humanized Artificial VHH Library with Structure based Design that contributes to the paratope formation on VHHs

* 3 cDNA display: A Stable and Simple Genotype-Phenotype Coupling Using a Cell-Free Translation System, enabling 10^{13-14} repertoires of VHHs to be screened at once

【Features of *PharmaLogical*® Library】

- **Design based on crystal structure analysis data of VHH antibody**

A humanized VHH library designed based on the structural characteristics resulting from the crystal structure analysis data of the human sequence and VHH that have already been clinically applied to the antibody framework part (FR). The three CDRs (Complementarity Determining Regions) that form the antigen recognition site are designed based on the structural property information obtained from the alpaca-derived VHH, and are known to contribute most to antigen binding. By randomizing the CDR3s, large diversity is demonstrated.

- **Design to minimize the frequency on occurrence of amino acids that cause heterogeneity in formulation**

Amino acids that are susceptible to modification and that can cause major structural changes, such as cysteine and proline residues, cause heterogeneity in the formulation process. By designing a CDR that minimizes the frequency of appearance of these amino acids, it can be expected to minimize the problems that arise in the drug discovery process.

- **Innovative VHH screening method by combining *PharmaLogical*® Library with cDNA display**

The combination of *PharmaLogical*® Library which has a diverse library size of 10^{13-14} (10 trillion to 100 trillion), and a screening system based on the cDNA display technology enables an innovative VHH screening.

【About Epsilon Molecular Engineering】

EME is a biopharmaceutical startup that has been developing innovative modality and drugs based on evolutionary molecular engineering since 2016. Taking advantage of our unique screening technology and molecular design method, we are engaged in research and development of diagnostic agents and reagents for regenerative medicine as well as drug development. With the corporate mission of "creating future biomolecules," we aim to contribute to a wide range of society and people's lives.

Website: <https://www.epsilon-mol.co.jp/eng/>

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