



LiberoThera and Biocytogen Achieve Milestone Progress in Co-Development of Fully Human GPCR Antibody Drugs

Tokyo, Japan, and Beijing, China, July 21, 2022 - February 1st 2021, LiberoThera Co., Ltd ("LiberoThera") entered a strategic collaboration with Biocytogen Pharmaceuticals (Beijing) Co., Ltd. ("Biocytogen") to co-develop fully human GPCR antibodies using LiberoThera's outstanding membrane antigen preparation technology combined with Biocytogen's advanced antibody discovery platform based on fully human antibody RenMab[™] mice. In around a year since the collaboration was established, the two parties have screened out a number of fully human therapeutic antibody clones with excellent anti-tumor activity *in vitro* and *in vivo* against the first mutually selected GPCR target, CCR8, which has the potential to become a best-in-class product. These antibody clones exhibit high affinity binding to human CCR8 with species cross-reactivity and good manufacturability. Mechanistically, these clones can deplete Tregs from the tumor micro-environment through enhanced ADCC activity, and can also inhibit the activities of Tregs in the tumor micro-environment by inhibiting CCR8 signaling mediated by its ligand CCL1, thereby enhancing the anti-tumor immune response. In the future, the collaborations between two parties will also be extended to other GPCR targets.

GPCRs are seven-transmembrane proteins with short extracellular domains and high homology among them which make it difficult to find antibodies against them with high specificity and desired functions. However, both the success rate and the speed of GPCR antibody discovery have greatly increased by combining Biocytogen's target knocked-out fully human antibody mice RenMab KO, various immunization and antibody discovery technologies, high-throughput *in vitro* and *in vivo* screening platform and LiberoThera's deep understanding of GPCR target structures plus membrane antigen preparation technologies.

"Many GPCRs are important drug targets for a variety of indications. However, due to the special structure of such targets, the development of antibody drugs against them has always been challenging," said Dr. Toru Kanke, CEO of LiberoThera. "The structural GPCR antigens prepared with LiberoThera's proprietary cell-free membrane synthesis technologies together with non-natural amino acid incorporation methods can provide a solution for generating quality antibodies against the challenging targets. Biocytogen's streamlined fully human antibody development platform greatly accelerates the translation of GPCR research. We are very happy to see the rapid progress and discovery of the best-in-class therapeutic antibodies against CCR8 under the collaboration of both parties. We also look forward to the collaborations in the future with Biocytogen to work on more GPCR targets so that to benefit more patients around the world."

"We are very pleased that with the joint efforts of us and LiberoThera, the drug development of CCR8, a potential target for tumor immunotherapy, is progressing smoothly," said Dr. Yuelei Shen, Founder, Chairman and CEO of Biocytogen. "This undoubtedly validates that LiberoThera's advanced antigen preparation technology synergizes with our RenMice KO platform to generate



diverse fully human antibodies. Furthermore, our high-throughput *in vivo* and *in vitro* screening capabilities ensured that antibodies against GPCRs can be efficiently obtained. We look forward to advancing our CCR8 antibodies into the clinic soon and we also look forward to continue working with LiberoThera to tackle more GPCR targets.”

About LiberoThera

LiberoThera is a drug discovery company targeting membrane proteins including GPCRs. Founded on the revolutionary research by Prof. Shigeyuki Yokoyama, Emeritus Professor at The University of Tokyo and Distinguished Senior Scientist at RIKEN, LiberoThera utilizes its cutting-edge cell-free protein expression system and non-natural amino acid technology which enable complexed membrane proteins to be prepared in natural forms with structural and functional integrity. LiberoThera is developing novel therapeutic candidates targeting physiologically important membrane proteins, such as GPCRs, in collaboration with multiple partners. For more information, visit <https://www.liberothera.com/>.

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About Biocytogen

Biocytogen Pharmaceuticals (Beijing) Co., Ltd. is a global biotechnology company that drives the research and development of novel antibody-based drugs with innovative technologies. Using its proprietary RenMab™ /RenLite® mice platforms for fully human monoclonal and bispecific antibody development, Biocytogen has integrated its *in vivo* drug efficacy screening platforms and strong clinical development expertise to streamline the entire drug development process. Biocytogen is undertaking a large-scale project to develop antibody drugs for more than 1000 targets, known as Project Integrum, and has entered ongoing collaborations with dozens of partners worldwide to produce a variety of first-in-class and/or best-in-class antibody drugs. At present, many GPCR projects from Project Integrum are under development that are important for treating cancer, metabolic diseases and beyond. In the future, Project Integrum will continue producing more fully human antibodies against GPCRs and other difficult targets. Biocytogen wishes to collaborate with partners around the world to discover, develop and deliver new medicines through innovative technologies that benefit human health. The company's pipeline includes 12 core products, among which two products are in phase II multi-regional clinical trials and two products are in phase I. Headquartered in Beijing, Biocytogen has branches in Haimen Jiangsu, Shanghai, Boston, USA and Heidelberg, Germany. For more information, please visit <http://en.biocytogen.com.cn/>.

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