BIOCYTOGEN PHARMACEUTICALS (BEIJING) CO., LTD.
百奧賽圖(北京)醫藥科技股份有限公司
(A joint stock company incorporated in the People's Republic of China with limited liability)
(Stock Code: 2315)

VOLUNTARY ANNOUNCEMENT

RENMICE® SERIES-FULLY HUMAN ANTIBODY AND TCR MOUSE MODELS-SHOWCASE BIOCYTOGEN'S CAPABILITIES TO INNOVATE THE DISCOVERY OF BIOLOGIC DRUGS

The board (the "**Board**") of directors (the "**Director(s)**") of Biocytogen Pharmaceuticals (Beijing) Co., Ltd. (the "**Company**" or "**Biocytogen**", together with its subsidiaries, the "**Group**") is pleased to officially announce to adopt its RenMice® series as the collection name for the Company's independently developed, fully human antibody mice and TCR mice with proprietary intellectual property. The term "Ren" is derived from the Chinese pinyin for "人" (rén), which integrates eastern cultural elements and represents the Company's commitment to developing innovative technologies that advance the discovery, development and delivery of novel therapeutics, ultimately safeguarding human health. The RenMice® series encompasses five strains of fully human antibody/TCR mice: RenMab®, RenLite®, RenNano®, RenTCR™, and RenTCR-mimic™. These mice provide support for the discovery of fully human monoclonal antibodies, bispecific antibodies, bispecific antibody-drug conjugates (**BsADCs**), nanobodies, fully human T-cell receptors (**TCRs**), and TCR-mimic antibodies. The Company is also generating more strains of fully human RenMice for major histocompatibility complex (MHC) cluster genes, natural killer cell (NK cell) cluster genes, and other gene clusters for diverse drug development purposes, which will be integrated into the RenMice® series upon successful development.

Since their successive release in 2019, RenMice® series has received global recognition in the biopharmaceutical field. As of June 30, 2023, the Company has entered into RenMice licensing agreements with 20 biopharmaceutical/biotechnology companies, including several partnerships with multinational pharmaceutical companies; 42 target-nominated antibody development projects have been initiated. After the initiation of Project Integrum, 50 antibodies, derived from RenMice mice, drug co-development/out-licensing/transfer agreements have been established. As Project Integrum has completed approximately 1,000 target-specific antibody discovery projects as a milestone in progress, the number of external therapeutic antibody co-development/out-licensing/transfer agreements are expected to increase significantly. In the future, the Company will continue to research and develop RenMice® series mice with different genetic backgrounds to meet the needs of drug development for different targets. Meanwhile, the development of fully human mice for MHC, NK cell and other gene clusters is in progress. The successful development of new technology platforms will further enhance the Company's technical capabilities in drug discovery and accelerate the development of new therapeutics in collaboration with global partners, benefiting human health.

This is a voluntary announcement made by the Company. Shareholders and potential investors of the Company are advised to exercise caution when dealing in the shares of the Company.

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By order of the Board
Biocytogen Pharmaceuticals (Beijing) Co., Ltd.
Shen Yuelei
*Chairman of the Board, Chief Executive Officer and Executive Director*

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Hong Kong, September 14, 2023

As at the date of this announcement, the Board comprises Dr. Shen Yuelei as chairman, chief executive officer and executive Director, Dr. Ni Jian and Dr. Zhang Haichao as executive Directors; Mr. Wei Yiliang, Dr. Zhou Kexiang and Ms. Zhang Leidi as non-executive Directors; Mr. Hua Fengmao, Dr. Yu Changyuan and Ms. Liang Xiaoyan as independent non-executive Directors.

Fully Human Antibody and TCR Mouse Models in RenMice® Series Showcase Biocytogen's Capabilities to Innovate the Discovery of Biologic Drugs

Beijing, China, September 14, 2023 – Biocytogen Pharmaceuticals (Beijing) Co., Ltd. ("**Biocytogen**" or the "**Company**") (Stock Code: 02315.HK) announces to adopt the RenMice® series as the collection name for the Company's independently developed, fully human antibody mice and TCR mice with proprietary intellectual property. The term "Ren" is derived from the Chinese pinyin for "人" (rén), which integrates eastern cultural elements and represents Biocytogen's commitment to developing innovative technologies that advance the discovery, development and delivery of novel therapeutics, ultimately safeguarding human health. The RenMice® series encompasses five strains of fully human antibody/TCR mice: RenMab®, RenLite®, RenNano®, RenTCR™, and RenTCR-mimic™. These mice provide support for the discovery of fully human monoclonal antibodies, bispecific antibodies, bispecific antibody-drug conjugates (**BsADCs**), nanobodies, fully human T-cell receptors (**TCRs**), and TCR-mimic antibodies. The Company is also generating more strains of fully human RenMice for major histocompatibility complex (MHC) cluster genes, natural killer cell (NK cell) cluster genes, and other gene clusters for diverse drug development purposes, which will be integrated into the RenMice® series upon successful development.

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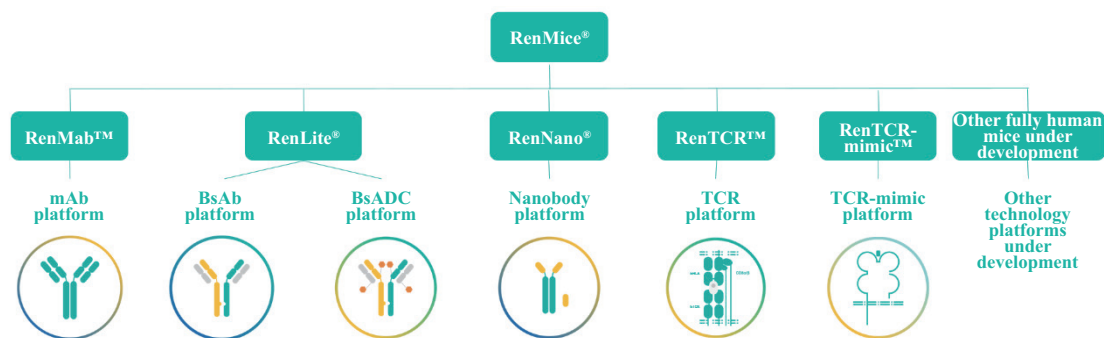
RenMice® series mice and the fully human antibody/TCR technology platform constructed with them

RenMab Mice: Platform for Fully Human Monoclonal Antibody

Biocytogen developed RenMab mice using its proprietary Size-Unlimited Precise Chromosome Engineering (**SUPCE**) technology, which allowed for replacement of the murine antibody heavy and light chain variable region genes with the corresponding human counterparts *in situ*. RenMab is a world leading mouse model self-developed by Biocytogen that completely replace human antibody heavy chain and light chain variable region genes. The RenMab mouse model retains the full diversity of human antibody sequences. Following immunization, RenMab mice generate diverse fully human monoclonal antibody sequences targeting various epitopes with affinity similar to wild-type mice. These antibodies possess excellent specificity and physicochemical properties and do not require additional *in vitro* humanization, leading to substantial time and cost savings in downstream development, and an elevated likelihood of successful clinical translation. As a fully human antibody mouse model developed independently in China, RenMab received Chinese patent authorization in 2023.

RenLite Mice: Platform for Fully Human Bispecific Antibodies and Bispecific ADCs

Similar to RenMab mice, RenLite mice feature the complete *in situ* replacement of human antibody heavy chain variable region genes. Unlike RenMab mice, RenLite mice possess a single human antibody light chain variable region gene. Antibodies generated by RenLite mice share a common light chain, effectively reducing heavy and light chain mismatching when assembled into bispecific antibodies (**BsAbs**). By incorporating Knobs-into-Holes (**KIH**) technology, and further aviod the mismatch of heavy-heavy chain, resulting in an assembly success rate of over 95%, significantly reducing the complexity of the CMC process. BsAbs assembled from RenLite-derived antibodies resemble monoclonal antibodies and exhibit favorable physicochemical properties. Apart from the discovery of bispecific antibodies, Biocytogen uses the RenLite mice scaleablely developed bispecific ADCs.

RenNano Mice: Platform for Fully Human Nanobodies

RenNano mice were developed via genetic modification of the antibody constant region in RenMab mice. Following immunization, RenNano mice produce fully human heavy-chain-only antibodies (**HCAbs**) that can bind to antigens without a light chain. RenNano-derived HCAbs possess diverse CDR3 sequences and can recognize a variety of epitopes with excellent specificity and affinity. HCAbs derived from RenNano mice demonstrate robust biological function both *in vitro* and *in vivo*, making them suitable for various drug modalities, including bispecific antibodies, multispecific antibodies, and cell therapies. Using RenNano mice, Biocytogen initiated the "Nano 100 Project" in early 2023 to discover fully human therapeutic nanobodies against over 100 targets scaleablely.

RenTCR Mice: Platform for Fully Human TCR

Developed using SUPCE technology, RenTCR mice can directly produce fully human TCR sequences after immunization to develop TCR-T and cellular connectors, etc.. These mice lack tolerance to foreign antigens, such as those from humans or viruses, enabling the generation of high-affinity TCRs targeting human TAAs and viral antigens. These TCRs use human genes to avoid immunogenicity concerns. Furthermore, they do not require further mutagenesis to improve binding affinity, reducing the risk of introducing off-target toxicity. Using RenTCR mice for human TCR discovery does not require patient samples, unlike traditional tumor-infiltrating lymphocyte (**TIL**) therapy, and can generate a more diverse range of TCR sequences than TILs. The successful launch of RenTCR mice will accelerate collaborations with research institutions focused on therapeutic TCR molecules, including TCR-T cell therapy companies.

RenTCR-mimic Mice: Platform for Fully Human TCR-mimic Antibodies

RenTCR-mimic mice are RenMab/HLA or RenLite/HLA mice and are developed via humanization of class I MHC molecules in RenMab and RenLite mice. Immunization of RenTCR-mimic mice with pHLA complexes yields TCR-mimic antibodies that specifically target pHLA without recognizing human HLA molecules. Unlike traditional antibodies that can only recognize cell surface or extracellular antigens, antibodies generated by RenTCR-mimic mice can target intracellular antigens by recognizing pMHC complex on the cell surface, significantly expanding the range of druggable targets. Combined with its high-throughput antibody screening platform, the Company can rapidly identify highly specific and high-affinity TCR-mimic antibodies, overcoming limitations associated with low affinity and tumor immune escape caused by endogenous TCRs. Fully human TCR-mimic antibody sequences can be used in the development of T-cell engagers and CAR-T. Currently, TCR-mimic antibodies against over 10 intracellular TAAs, CTAs, mutated antigens, and viral antigens have been developed.

RenMice KO Mice and Project Integrum

Due to the presence of immune tolerance, it is difficult to use conventional mouse immunization methods to generate antibodies targeting antigens with high homology between human and mouse. Knocking out the target gene in RenMice can reduce immune tolerance to the antigen, making it possible to obtain high-affinity, highly specific fully human antibodies against both homologous and heterologous regions following immunization, increasing the divesity of antibodies insignificantly. This strategy can increase antibody diversity against challenging targets like GPCRs and highly homologous targets, thereby improving screening success rates. It also increases the chances of obtaining species cross-reactive antibodies, facilitating downstream multi-species in vivo efficacy and safety evaluation. Over the past three years, Biocytogen's Project Integrum has been utilizing RenMice KO mice to develop fully human antibody drugs against over 1,000 different targets. This initiative has yielded numerous fully human antibodies capable of cross-species recognition and established an antibody library consisting of 400,000 to 500,000 antibody sequences, which can ultimately help partners significantly improve project predictability, reduce development time and cost, and increase the success rate of drug development.

About Biocytogen

Biocytogen (Stock Code: 02315.HK) is a global biotechnology company that drives the research and development of novel antibody-based drugs with innovative technologies. Biocytogen is committed to becoming the global birthplace of new drugs, with the mission of focusing on technological innovation, continuous new drug output and guarding human health. Using its independently self-developed RenMice® platform (including RenMab®, RenLite®, RenNano® mice) with fully independent intellectual property rights, Biocytogen has organicly integrated monoclonal antibody, bispecific/multispecific antibody and nanobody development platforms, its in vivo drug efficacy screening platforms and strong clinical development expertise to form a unique new drug research and development capability covering the whole process of drug research and development. Biocytogen is undertaking a large-scale project to develop first-in-class and/or best-in-class antibody drugs for more than 1,000 targets, known as Project Integrum. As of June 30, 2023, 50 therapeutic antibody co-development/out-licensing/transfer agreements and 42 target-nominated RenMice licensing projects have been established worldwide, including several partnerships with multinational pharmaceutical companies (MNCs). Biocytogen's pipeline is comprised of 10 core assets, with partnerships established for multiple clinical assets. In the future, Biocytogen will continue to work with global partners to produce many antibody drugs to better benefit patients. Headquartered in Beijing, Biocytogen has branches in China (Haimen Jiangsu, Shanghai), USA (Boston, San Francisco), and Germany (Heidelberg).

For more information, please visit our website at **http://en.biocytogen.com.cn.**

Forward-Looking Statements

The forward-looking statements made in this announcement relate only to the events or information as of the date on which the statements are made in this announcement. Except as required by law, we undertake no obligation to update or revise publicly any forward-looking statements, whether as a result of new information, future events or otherwise, after the date on which the statements are made or to reflect the occurrence of unanticipated events. You should read this announcement completely and with the understanding that our actual future results or performance may be materially different from what we expect. In this announcement, statements of, or references to, our intentions or those of any of our directors or our Company are made as of the date of this announcement. Any of these intentions may alter in light of future development.