Biocytogen Pharmaceuticals (2315 HK)

High-throughput antibody discovery platform empowers innovation

BUY

Target Price	**HK$43.85**
Up/Downside	**71.96%**
Current Price	**HK$25.50**

China Healthcare

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Stock Data

Mkt Cap (HK$ mn)	10,185
Avg 3 mths t/o (HK$ mn)	NA
52w High/Low (HK$)	28.8/23.5
Total Issued Shares (mn)	399.4

Source: FactSet

Shareholding Structure

Management	27.8%
SDIC Shanghai	10.6%

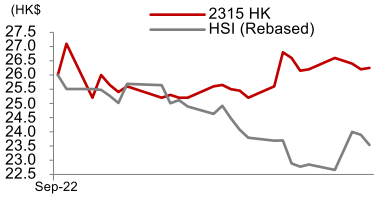
Source: HKEx

Share Performance

	Absolute	Relative
1-mth	-0.2%	12.2%
3-mth	NM	NM
6-mth	NM	NM

Source: FactSet

12-mth Price Performance



Source: FactSet

- **State-of-the-art platform to generate high-quality fully human antibodies.** Biocytogen has developed two transgenic RenMice platforms, which use RenMab mice and RenLite mice for generating mAb and BsAb, respectively. RenMab mice have full human heavy and light chain variable region, which enables the generation of fully human antibodies with high affinity, low immunogenicity, and favorable developability. RenLite mice have heavy chain antibody gene variable region humanized in situ, which resolve the light chain and heavy chain mismatch issues. Combined with its novel evidence-based *in vivo* efficacy screening methodology, Biocytogen is able to conduct large-scale antibody discovery and screening with high throughput.
- **Project Integrum to discover potential first-/ best-in-class antibodies.** Leveraging unique antibody discovery platform and high-throughput *in vivo* discovery capability, Biocytogen aims to rapidly and concurrently screen 1,000+ potential antibody drug targets, among which only ~300 targets have clinical-stage candidates. Project Integrum could become a powerful engine of innovation for potential first-in-class/ best-in-class antibodies targeting novel and/or challenging drug targets.
- **Flexible and successful monetization approach.** Currently, Biocytogen's revenue was mainly generated from 1) gene editing, 2) pre-clinical pharmacology and efficacy evaluation, 3) animal models selling, and 4) antibody development business. Driven by continuous growth of its preclinical research services business and successful monetization of antibody development business, we expect Biocytogen's total revenue to grow 73%/ 43%/ 43% YoY to RMB613mn/ RMB879mn/ RMB1,253mn in FY22E / 23E/ 24E. Especially, we highlight the revenue of antibody development business may grow 151%/ 43%/ 45% YoY to RMB223mn/ RMB318mn/ RMB461mn in FY22E/ 23E/ 24E, respectively.
- **Initiate at BUY with TP of HK$43.85.** Biocytogen's future cash flows will mainly rely on fast growth of its pre-clinical research services and antibody development business. We expect its attributable net loss to gradually narrow to RMB460mn/ RMB287mn/ RMB96mn in FY22E/ 23E/ 24E. We derive our TP of HK$43.85 based on a 14-year DCF model (WACC: 11.8%, terminal growth rate: 2.0%). We expect Biocytogen to generate net profit from 2025E.
- **Risks:** Risks relating to the research and development of drug candidates; extensive government regulation; failure in protecting IP rights.

Earnings Summary

(YE 31 Dec)	FY20A	FY21A	FY22E	FY23E	FY24E
Revenue (RMB mn)	254	355	613	879	1,253
YoY growth (%)	49	39	73	43	43
Net profit (RMB mn)	(428)	(546)	(460)	(287)	(96)
EPS (RMB)	na	na	(1.15)	(0.72)	(0.24)
Consensus EPS (RMB)	na	na	(1.20)	(0.74)	(0.08)
ROE (%)	(33)	(44)	(37)	(29)	(11)
ROA (%)	(20)	(24)	(20)	(11)	(3)
R&D expenses (RMB)	(276)	(558)	(613)	(571)	(564)

Source: Company data, Bloomberg, CMBIGM estimates

Contents

Investment thesis

Established in 2009, Biocytogen Pharmaceuticals (Beijing) Co., Ltd. (百奥赛图(北京)医药科技股份有限公司) ("Biocytogen") is a clinical-stage biopharmaceutical and revenue-generating pre-clinical research services company. Biocytogen has launched Project Integrum, which adopts an evidence-based *in vivo* efficacy screening methodology, and has established a rich in-house pipeline of first- / best-in-class biological drug candidates.

High-throughput in vivo antibody discovery platforms as powerful tools for innovation

Biocytogen's antibody discovery platform is based on the antibody discovery technology of RenMice platform and its self-developed in vivo drug efficacy screening technology. Together with hybridoma technology and Beacon single-cell photoconduction screening, Biocytogen's antibody discovery platform can generate a large amount of potential antibodies and conduct large-scale in vivo drug efficacy evaluation to screen and obtain antibody molecules with the potential to become drug candidate. Biocytogen's antibody discovery platform can provide a one-stop solution from antibody preparation to IND filing.

Biocytogen has developed two transgenic RenMice platforms, RenMab and RenLite. RenMab platform uses transgenic RenMab mice with full human heavy chain variable region and kappa light chain variable region replacement in situ, which allows for the natural *in vivo* pairing of human heavy and light chains. The natural pairing not only minimizes the need for excessive rounds of late-stage antibody engineering, but also simplifies the development of fully human antibodies with high affinity, low immunogenicity, and favorable developability. Fully human antibodies produced by RenMab platform will be of potentially better safety and efficacy profile, and have a potentially higher success rate during clinical development. RenLite platform uses transgenic RenLite mice, which contains the fully human immunoglobulin heavy chain variable region and a fixed common light chain. The presence of single human common kappa light chain ensures light chain complementarity for the future discovery of BsAb, while resolving the mismatch issues, thereby streamlining the CMC development process.

Based on RenMice platform, self-developed *in vivo* drug efficacy screening technology, as well as Beacon single-cell photoconduction screening, Biocytogen's antibody discovery platform is able to generate a large amount of potential antibodies and conduct large-scale *in vivo* drug efficacy evaluation to screen and obtain antibody molecules with the potential to become drug candidate. By bringing together many advantages of gene editing platform, model animal platform, pre-clinical pharmacology and evaluation platform and other resources, Biocytogen's antibody discovery platform can provide a one-stop solution from antibody preparation to IND filing.

RenMice platforms are validated through external licenses. As of 1H22, Biocytogen has reached license and trial collaboration agreements with 16 well-known pharmaceuticals such as Innovent (信达生物) and Xencor. As of 1H22, the licensees have initiated 33 projects in total.

Launching Project Integrum to develop high-quality antibodies

There are 1,000+ potential antibody drug targets in the human body, of which only 144 mAbs against ~60 targets have been approved by the FDA and EMA since 1986, according to F&S (Frost & Sullivan). Biocytogen launched Project Integrum (千鼠万抗) in Mar 2020, which adopts an evidence-based *in vivo* efficacy screening methodology as a novel

approach, to concurrently generate and screen antibodies against over 1,000 potential antibody drug targets, most of which have not been explored in clinical trials yet.

In contrast to the traditional approach, Project Integrum significantly accelerates the drug development process which **reduces the time needed from pre-clinical discovery to PCC from an average of 5.5 years to 12-18 months**.

Biocytogen plans to complete the preparation of targets knockout RenMab mice by 2022. As of 13 Aug 2022, Biocytogen has completed more than 980 knock-out under Project Integrum, including more than 280 targets entering into antibody immune stage and more than 40 targets entering into the molecular screening stage. The Company would be able to complete the antibody molecule selection for 200 to 300 potential targets per year with its development capacity.

Upon antibodies generated from Project Integrum, Biocytogen has pursued flexible business strategies, including 1) general co-development, 2) joint development with IP collaboration, and 3) antibody discovery service under RenMice Licensing.

As of 1H22, Biocytogen has reached 28 co-development deals with biotechnology and pharmaceutical companies, including RemeGen, Mabworks Biotech, China Resources Biopharm, Shanghai Institute of Biological Products, North China Pharmaceutical, Dragon Boat Biopharmaceutical, GeneQuantum, Libero Thera Co., Ltd, and Merck Healthcare KGAA. The co-development collaborations not only bring the Company substantial short-term and long-term economic returns, but also allows the Company to leverage partners' clinical and commercial resources to advance the development of the substantial number of potential antibody drug candidates.

Novel and highly differentiated in-house developed assets

Biocytogen has a pipeline of in-house developed antibody drug candidates with novel targets that are challenging for traditional antibody development or with in vivo efficacy or safety demonstrated in pre-clinical and clinical studies.

As of 18 Sep 2022, Biocytogen had built an antibody drug pipeline of 12 drug assets (YH003 & YH001 as core product candidates), including five clinical assets and seven pre-clinical stage assets. Three assets have reached out-licensing arrangements, including YH005 (Claudin 18.2 antibody) out-licensed to RemeGen to develop YH005 ADC (RC118), PD-L1 antibody out-licensed to GeneQuantum to co-develop YH011 (a bifunctional molecule), and YH001 with four indications out-licensed to TRACON in certain overseas regions.

Other than clinical stage candidates, Biocytogen also has a pipeline of preclinical drug candidates, including BsAb and ADCs, targeting diseases with unmet medical needs.

Comprehensive pre-clinical CRO services

Biocytogen provides comprehensive pre-IND CRO services, including gene editing services and pre-clinical pharmacology and efficacy evaluation services. From 2020 to 2021, the total number of customers Biocytogen served annually increased from 782 to 796, including nine of the top ten largest pharmaceutical companies globally, according to F&S.

Biocytogen has developed powerful gene editing platforms, including SUPCE, CRISPR/EGE and ESC/HR. Compared with other common gene editing technologies that can only edit gene fragments of less than 30,000 bases at a time using plasmid, Biocytogen's unparalleled in-house developed SUPCE technology allows megabase-scale

chromosomal editing, with high stability and reproducibility. Compared with traditional CRISPR/Cas9, EGE technology can use fertilized eggs for genetic modification, so it is no longer limited to embryonic stem cells, which greatly broadens the application range of gene editing.

Leveraging advanced gene editing technologies, Biocytogen has created one of the most comprehensive sets of antibody discovery and disease mouse models worldwide (2,500+ gene-edited mouse/cell line projects). The Company also established world-class model animal production centers, including three animal facilities encompassing a total of ~55,500 square meters' animal facilities, with annual supply capacity of 800,000 gene edited mice.

Utilizing the animal models, Biocytogen is capable of providing vivo pharmacology services including *in vivo* efficacy, pharmacokinetics (PK), pharmacodynamics (PD) and biomarker assessments, and pathology and toxicology studies. Biocytogen's pharmacology team, which is based in China and the US, has built significant expertise in testing novel therapeutics such as mAbs, CAR-Ts, gene therapy and other therapeutic modalities for immuno-oncology, immune and autoimmune diseases as well as metabolic diseases to support drug discovery and development worldwide.

Net profit to break even in 2025E

Biocytogen has generated revenue from services related to gene editing, preclinical pharmacology and efficacy evaluation, animal models selling and antibody development. We expect total revenue to grow 73%/ 43%/ 43% YoY to RMB613mn/ RMB879mn/ RMB1,253mn in FY22E/ 23E/ 24E, mainly driven by fast growth of its pre-clinical research services and antibody development business.

We expect pre-clinical pharmacology & efficacy evaluation, animal models selling and antibody development will contribute the majority of revenue during 2022-24E. Especially, we highlight the revenue growth of antibody development business may grow 151%/ 43%/ 45% YoY to RMB223mn/ RMB318mn/ RMB461mn in FY22E/ 23E/ 24E, respectively.

Biocytogen recorded attributable net losses of RMB428mn/ RMB546mn/ RMB272mn in 2020/ 2021/ 1H22. We expect its attributable net loss to gradually narrow to RMB460mn/ RMB287mn/ RMB96mn in FY22E/ 23E/ 24E and we expect the Company to generate net profit from FY25E.

Initiate at BUY with TP of HK$43.85

Given that Biocytogen's future cash flows will mainly rely on fast growth of its pre-clinical research services and antibody development business, we believe DCF would be a reasonable method to value the Company. We derive our target price of HK$43.85 based on a 14-year DCF model (WACC: 11.8%, terminal growth rate: 2.0%).

Investment risks

1) Risks relating to the research and development of drug candidates;

2) Risks relating to extensive government regulation;

3) Failure in protecting intellectual property rights.

Revenue-generating company with technology advantages

Founded in 2009, Biocytogen is a biopharmaceutical and revenue-generating pre-clinical research services company. In Sep 2020, upon completion of restructuring, Eucure (Beijing) became a wholly-owned subsidiary of Biocytogen. To date, Biocytogen has established fully integrated research and development capabilities from early target validation, antibody generation, to clinical development.

Adopting a unique business model, Biocytogen has two distinctive business segments, including pre-clinical research services and drug development business. Biocytogen's drug development businesses include 1) research and development of oncology and autoimmune disease therapeutics, and 2) antibody development business. The Company utilizes its own antibody discovery platforms to identify antibodies which have the potential to become drug candidates and out-license or collaborate with partners for potential therapeutic antibody molecules. Biocytogen's pre-clinical research services include 1) gene editing, 2) pre-clinical pharmacology and efficacy evaluation, and 3) animal models selling.

Figure 1: Major milestones of Biocytogen

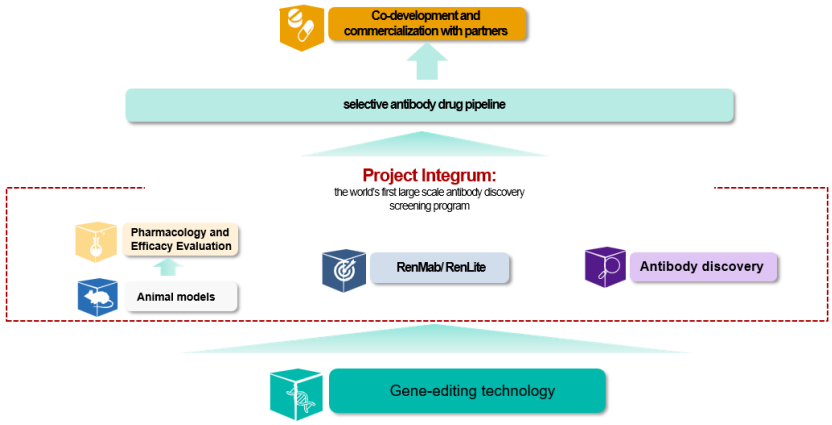
Time	Event
2009	Biocytogen was established in Beijing, as a headquarter to commence research and development of biotechnology in China.
2011	Developed ESC/HR-based gene editing technology platform and delivered gene editing services to first customer.
2013	Completed the series A round financing and raised an aggregate amount of approximately RMB35mn.
2014	Developed CRISPR/EGE-based gene editing technology, which enables simultaneous gene knock-in of two genes in rats. Developed the severe immunodeficient B-NDG mice and developed a series of immune checkpoint humanized mice based on the genetic background of C57BL/6.
2015	Established a comprehensive pharmacology service platform, covering cell-based functional assays, pharmacokinetic assays and drug metabolism assays. Completed the series B round financing and raised an aggregate amount of approximately RMB40mn.
2016	Haimen Animal Center began operations and earned the full-qualification AAALAC accreditation, building an international high-standard animal center. Established an evidence-based *in vivo* antibody discovery platform. Eucure (Beijing) was established to engage in pre-clinical and clinical development of drug candidates that are derived from Biocytogen's antibody discovery platform, including YH001 and YH003. Completed the series B+ round financing in the form of convertible loans of an aggregate amount of approximately RMB21.7mn, which was subsequently converted into equity in Feb 2018.
2018	BIOCYTOGEN BOSTON CORP was incorporated through which Biocytogen expanded its operations in the US. Completed the series C round financing and raised an aggregate amount of approximately RMB260mn.
2019	Developed technology for megabase-scale chromosomal editing and released RenMab Mice, a fully human antibody mouse model. Obtained approval for commencing Ph I trials of YH001 in patients with advanced solid tumors in the US in Oct. Completed the series D round financing and raised an aggregate amount of approximately RMB500mn.
2020	Completed first patient screening for Ph I studies of YH001 in May, YH002in Jun, and YH003 in Jun in Australia. Launched Project Integrum in Mar, a large-scale *in vivo* antibody discovery program. Completed the series D+ round financing and raised an aggregate amount of approximately RMB850mn.
2021	Completed first patient screening for Ph I trial of YH001 in Jan; obtained approval to initiate Ph I trial of YH003 in China in May. Entered Ph II clinical study of YH003 in Australia in August, and obtained approvals to commence Ph II clinical trials for YH001 in Jun and YH003 in Jun in the US and Ph I trial of YH004 in Jun in Australia. Completed Ph I trial of YH003, entered Ph II clinical study of YH003 in Australia in Aug, and obtained approvals to commence Ph II trials for YH001 in Jun and YH003 in Jul in the US and Ph I trial of YH004 in Jun in Australia. Completed the cross-over round financing and raised an aggregate amount of approximately RMB311.0mn. Entered into the Tracon Agreement with TRACON in relation to the development and commercialization of YH001 in the US in Oct. Obtained Taiwan FDA approval in Oct for and entered the Ph II clinical trial of YH001+Toripalimab. Obtained IND approval from the FDA of YH004 in Oct. Obtained IND approval from the NMPA to initiate and enter Ph II trail of YH003+Toripalimab in China in Oct.

Source: Company data, CMBIGM

Biocytogen has developed powerful gene editing platforms, including SUPCE, CRISPR/EGE and ESC/HR. The proven gene editing technology platforms have served as the foundation of Biocytogen's antibody discovery mouse models and disease animal models. Biocytogen's in-house developed SUPCE technology allows megabase-scale chromosomal editing, which is well validated by the RenMice platform. The EGE system is

developed based on the CRISPR/Cas9 gene targeting platform, and is ~20-fold more efficient at knocking in DNA fragments. Leveraging on its high efficiency, CRISPR/EGE is ideal for generating various types of genetically engineered models. With ESC/HR technology, edited genetic information is allowed to inherit reproductively. To date, Biocytogen has completed ~3,500 customized gene editing projects for its clients.

Figure 2: Biocytogen's fully integrated research and development capability

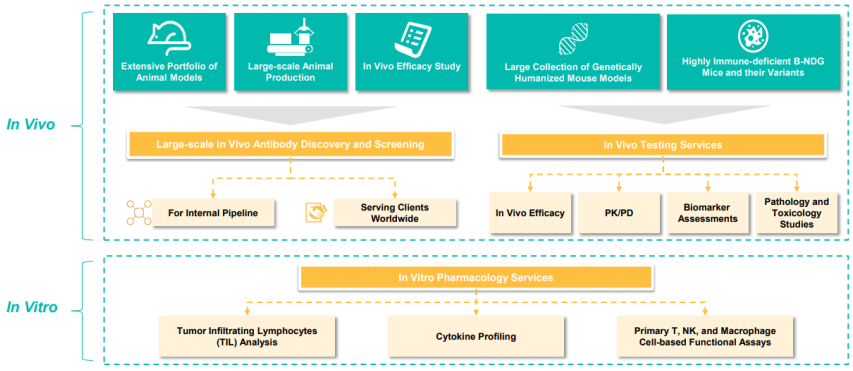


Source: Company data, CMBIGM

Empowered by CRISPR/EGE technology, Biocytogen has created a comprehensive set of antibody discovery and disease mouse models worldwide, including 2,500+ gene-edited animal/cell line models. Moreover, Biocytogen has also established large-scale animal production capability, including three animal facilities encompassing a total of ~55,500 sq.m., with annual supply capacity of 800,000 genetically edited mice. Utilizing large collection of self-produced genetically humanized mouse models, Biocytogen is capable of providing vivo pharmacology services including in vivo efficacy, PK/PD, biomarker assessments, and pathology and toxicology studies. Meanwhile, the Company is also capable of providing in vitro pharmacology services, including immune cell profiling such as TIL analysis, cytokine profiling, primary T, NK, and macrophage cell-based functional assays.

Biocytogen has also built a dedicated and experienced cross-country pharmacology team in Beijing, Haimen and Boston of 300+ researchers to support internal and client service projects. The team has succeeded in evaluating the efficacy of multiple therapeutic modalities, including monoclonal antibodies, bi-specific antibodies, ADCs, small molecules, CAR-T cell therapy, and oncolytic viruses, and has completed 500+ drug evaluation projects for 200+ partners globally.

Figure 3: Biocytogen's *in vivo*/*in vitro* testing services



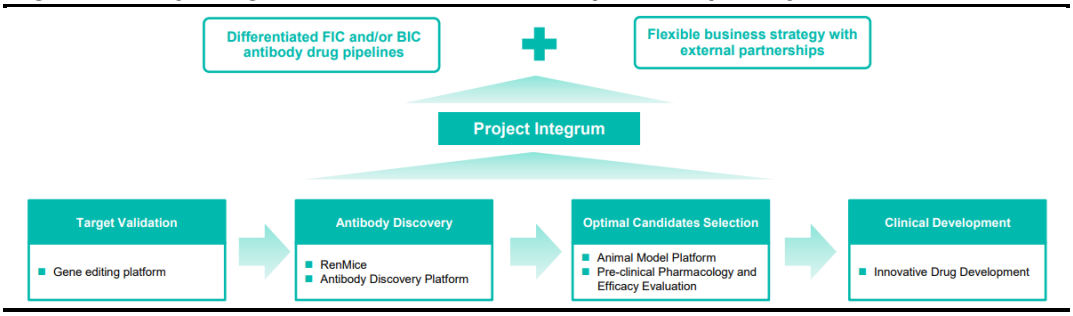
Source: Company data, CMBIGM

Leveraging the SUPCE technology, Biocytogen has developed RenMice platforms, including RenMab and RenLite. RenMab mice are transgenic mice with full human heavy chain/ kappa light chain variable region replacement in situ. Using RenMab rice, RenMab platform may discover and generate fully human mAbs. According to F&S, RenMab platform is one of the three fully human transgenic mice antibody generation platforms globally generated by in situ replacement technology. RenLite mice have their heavy chain antibody gene variable region replaced with full human heavy chain variable region in situ, and can produce diverse bsAbs and to generate bi-specific ADCs. Since the kappa chain variable domain of RenLite has been replaced by a single fixed human common kappa light chain, it ensures light chain complementarity for the future discovery of bsAbs.

RenMice platforms are validated through external licenses. As of 1H22, Biocytogen has reached license and trial collaboration agreements with 16 well-known multinational pharmaceuticals such as Innovent (信达生物) and Xencor. As of 1H22, the licensees have initiated 33 projects in total.

Empowered by its state-of-art RenMice platforms, as well as its self-developed in vivo drug efficacy screening (based on genetically humanized mouse models), Biocytogen launched Project Integrum (千鼠万抗) in Mar 2020. Project Integrum is the world's first large scale antibody discovery screening program, which simplifies the complex drug development process by following the principle of "beginning with the end". Project Integrum reduces the time needed from pre-clinical discovery to PCC (pre-clinical candidate compound) from an average of 5.5 years to 12-18 months, according to F&S. Biocytogen would be able to simultaneously complete the antibody molecule selection for 200 to 300 potential targets per year. As of 13 Aug, Biocytogen has completed 980+ knock-out, including 280+ targets entering into antibody immune stage and 40+ targets entering into molecular screening stage.

Figure 4: Fully integrated research and development capability



Source: Company data, CMBIGM

As of 1H22, Biocytogen has reached 28 co-development deals with pharmaceutical and biotechnology companies in China, Germany and Japan under Project Integrum, including RemeGen (9995 HK, NR), Mabworks Biotech, China Resources Biopharm, Shanghai Institute of Biological Products, North China Pharmaceutical, Dragon Boat Biopharmaceutical, GeneQuantum, Libero Thera Co., Ltd and Merck Healthcare KGAA. As of 13 Aug, Biocytogen has three collaboration models with partners for Project Integrum, namely general co-development, joint development with IP collaboration, and antibody discovery service under RenMice licensing.

Besides external partnerships, the unique evidence-based *in vivo* antibody discovery and screening methodology have also been validated in Biocytogen's in-house drug pipelines. As of 18 Sep 2022, Biocytogen had strategically built an antibody drug pipeline of 12 drug assets (YH003 & YH001 as core product candidates), including five clinical assets and

seven pre-clinical stage assets. Three assets have reached out-licensing arrangements, including YH005 (Claudin 18.2 mAb) out-licensed to RemeGen to develop YH005 ADC (RC118), PD-L1 antibody out-licensed to GeneQuantum to co-develop YH011 (a bifunctional molecule), and YH001 with four indications out-licensed to TRACON in certain overseas regions.

Figure 5: Antibody drug pipeline with first-/best-in-class potential

Source: Company data, CMBIGM

Notes:

1) Biocytogen co-develops YH001 with Tracon for selected indications in the North American regions (the US, Canada and Mexico) and is entitled to collect double-digit percentage royalties on net sales in North America once commercialized, at the same time, Biocytogen remains development/ commercialization rights in regions other than the North American regions.

2) Biocytogen is entitled to collect licensing fee from RemeGen for the out-license of YH005.

3) Biocytogen is entitled to collect licensing fee from GeneQuantum for PD-L1 antibody and co-own the intellectual property rights.

Strong revenue growth driven by a clear strategy in monetization

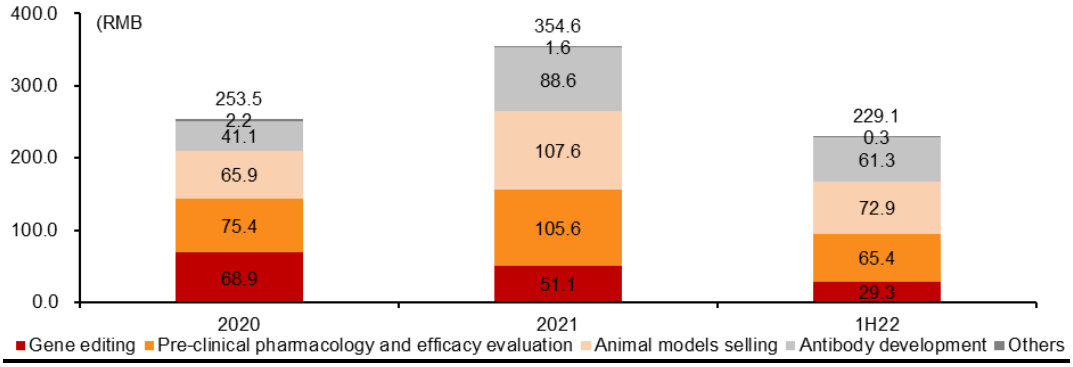
Adopting a unique business model, Biocytogen has two distinctive business segments, including pre-clinical research services and drug development business. Biocytogen's drug development businesses include 1) research and development of oncology and autoimmune disease therapeutics, and 2) antibody development business. The Company utilizes its own antibody discovery platforms to identify antibodies which have the potential to become drug candidates and out-license or collaborate with partners for potential antibody molecules. Biocytogen's pre-clinical research services include 1) gene editing, 2) pre-clinical pharmacology and efficacy evaluation, and 3) animal models selling.

Figure 6: Overview of Biocytogen's business and platforms

Source: Company data, CMBIGM

Currently, Biocytogen's revenue was mainly generated from 1) gene editing, 2) pre-clinical pharmacology and efficacy evaluation, 3) animal models selling, and 4) antibody development business. As of 18 Sep 2022, Biocytogen had built an antibody drug pipeline of 12 drug assets, including five clinical assets and seven pre-clinical stage assets, while three assets have reached out-licensing arrangements. We expect the in-house drug pipelines to generate significant future income.

Figure 7: Breakdown of Biocytogen's revenue, 2020-1H22



Source: Company data, CMBIGM

According to F&S, for Biocytogen's pre-clinical research services, gene editing services had a global market share of 0.3% and China market share of 1.3% in 2020, respectively; pre-clinical pharmacology and efficacy evaluation services had a global market share of 0.2% and China market share of 0.8% in 2020, respectively; animal model selling services had a market share of 0.1% globally and 1.8% in China in 2020, respectively. Most of Biocytogen's customers are pharmaceutical and biotechnology companies, including Chinese and global leading pharmaceutical companies and small-to-medium-sized

biotechnology companies. From 2020 to 2021, the total number of customers Biocytogen served annually increased from 782 to 796, including nine of the top ten largest pharmaceutical companies globally, according to F&S.

Since pre-clinical CRO services help guide strategic decisions, which help to improve success rate and reduce costs, the pharmaceutical pre-IND CRO market is growing steadily. According to F&S, in 2020, gene editing services had an estimated global market size of US$3.5bn, and an estimated China market size of RMB3.0bn; pre-clinical pharmacology and efficacy evaluation services had a global market size of US$5.8bn, and a China market size of RMB4.9bn; animal model selling services had an estimated global market size of US$8.1bn, and an estimated China market size of RMB3.0bn.

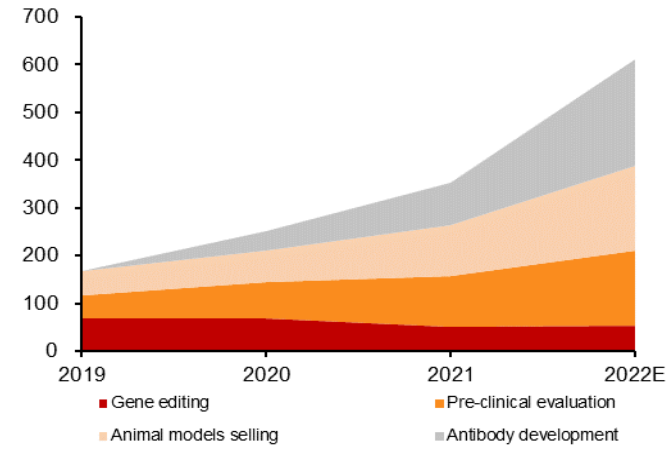
As Biocytogen has strategically shifted its gene editing capacity towards internal research and development, the total number of gene-editing customized projects delivered was decreasing, which was approximately 750/ 600 in FY20/ FY21, respectively. The gross profit margin for gene editing remained stable at 47.3%/ 46.9%/ 43.7% in FY20/ FY21/ 1H22, respectively. However, leveraging its proven gene editing capability, Biocytogen has been attracting existing customers to its growing pre-clinical pharmacology and efficacy evaluation and animal models selling and related services.

With increasaing demand from customers in pre-clinical pharmacology and efficacy evaluation service, the total number of contracts Biocytogen completed was approximately 460/ 580 in FY20/ FY21, respectively. The gross profit margin of pre-clinical pharmacology and efficacy evaluation service remained stable at 64.6%/ 65.3%/ 68.7% in FY20/ FY21/ 1H22, respectively. In FY20/ FY21, the number of sales of humanized mice sold was approximately 69,000/ 109,000 heads, respectively. The humanized mice have a higher unit market price than other animal models, and the gross profit margin of Biocytogen's animal model selling was at 72.2%/ 76.6%/ 75.2% in FY20/ FY21/ 1H22, respectively.

Leveraging the state-of-the-art fully humanized antibody development platforms, Biocytogen has implemented Project Integrum. As of 1H22, Biocytogen has signed 28 co-development deals with pharmaceutical and biotechnology companies in China, Germany and Japan under Project Integrum.

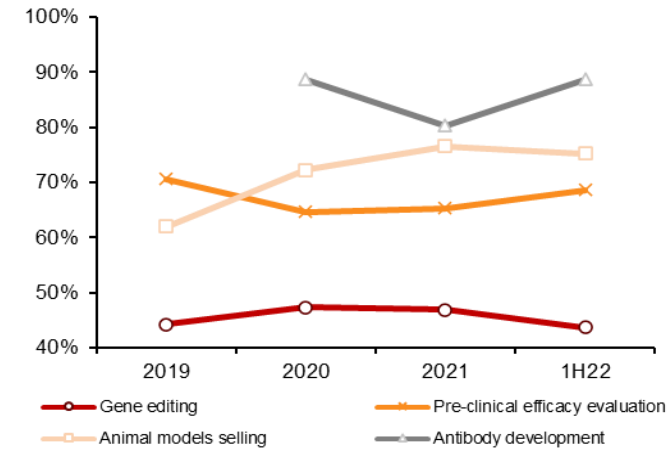
Driven by continuous growth of its preclinical research services business and monetization of antibody development business, Biocytogen's total revenue has grown 49%/ 40%/ 75% YoY to RMB254mn/ RMB355mn/ RMB229mn in FY20/ FY21/ 1H22, respectively, and we expect the total revenue to grow 73% YoY to RMB613mn in 2022E.

Figure 8: Biocytogen's by segment revenue, 2019-22E



Source: Company data, CMBIGM estimates

Figure 9: Biocytogen's by segment GPM, 2019-1H22



Source: Company data, CMBIGM

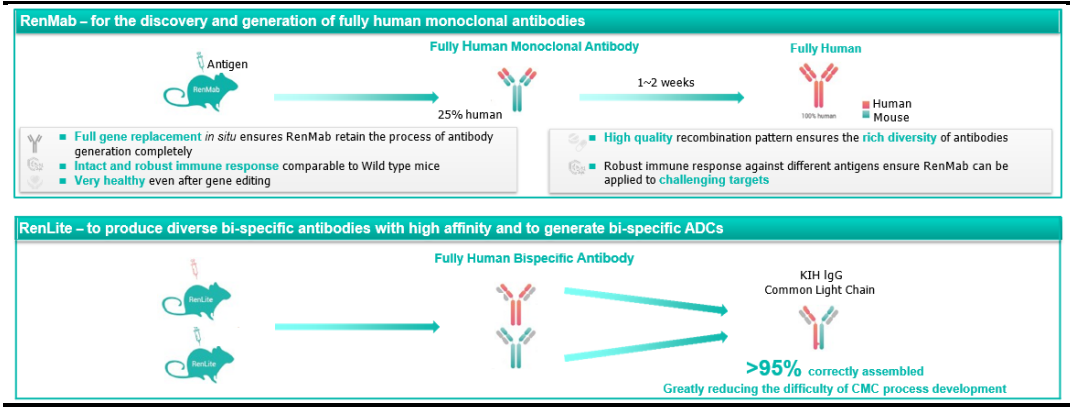
State-of-the-art fully humanized RenMice platform as a key technology advantage

Empowered by its proprietary gene editing technology, Biocytogen has developed transgenic RenMice platforms and gene edited animal models. RenMice platforms are for antibody discovery, which consist of two fully human transgenic mice lines, RenMab and RenLite.

RenMab platform uses Biocytogen's in-house developed RenMab mice for the discovery and generation of fully human monoclonal antibodies. With full human heavy chain variable region and kappa light chain variable region replacement in situ, RenMab mice carry the full human immunoglobulin variable region repertoire, and have an intact immune system and are healthy even after gene editing. According to F&S, Biocytogen's RenMab platform is one of the top three fully human transgenic mice antibody generation platforms globally, together with VelocImmune from Regeneron and Kymouse from Kymab/Sanofi.

RenLite platform is used for producing diverse bi-specific antibodies with high affinity, and to further generate bi-specific ADCs. The heavy chain antibody gene variable region of RenLite mice is replaced with full human heavy chain variable region in situ, which ensures the diversity and affinity of immune responses. The kappa chain variable domain has been replaced by a single fixed human common kappa light chain, which ensures light chain complementarity for the future discovery of bi-specific antibodies. Leveraging upper design, RenLite mice are able to seamlessly resolve the light chain and heavy chain mismatch issues, thereby greatly reducing the difficulty of CMC process development.

Figure 10: RenMice platforms for generating fully human antibodies



Source: Company data, CMBIGM

Biocytogen's RenMice platforms are validated through external licenses. As of 1H22, Biocytogen has reached license and trial collaboration agreements with 16 well-known pharmaceuticals such as Innovent (信达生物) and Xencor. As of 1H22, the licensees have initiated 33 projects in total.

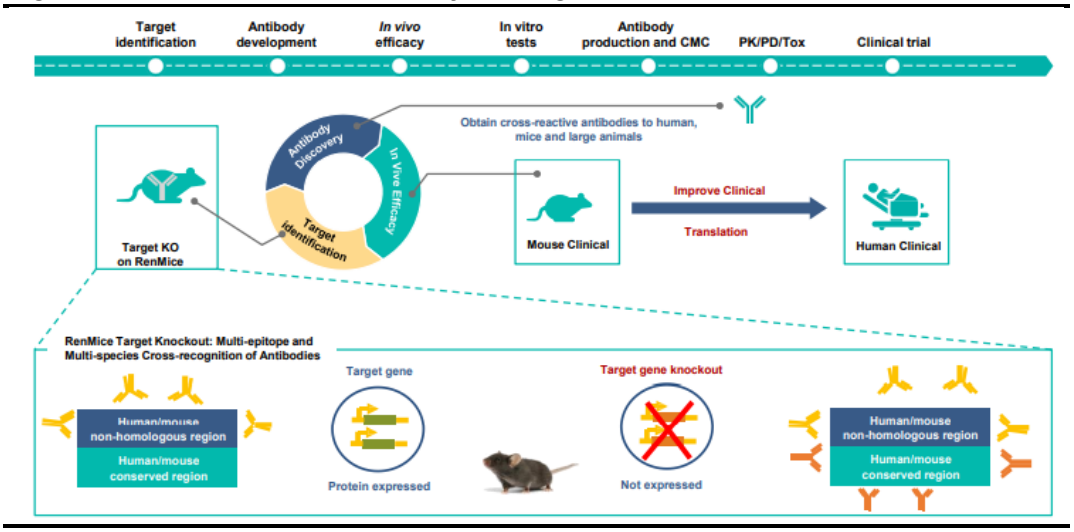
Project Integrum to generate high-quality antibodies with high throughput

Project Integrum adopts a unique evidence-based *in vivo* efficacy screening methodology as a novel approach. This method has significantly accelerated the drug development process, and has the potential to develop antibodies with better efficacy and safety for clinical application, compared to the traditional approach.

Integrating its self-developed platforms and animal models, Biocytogen has created a seamlessly-designed workflow, which simplifies drug development process. Aiming to

generate and screen antibodies against 1,000+ potential antibody drug targets (only ~300 of which have clinical-stage products in the market), the major processes of Project Integrum include: 1) knocking out targets genes one-by-one to create 1000+ target knock-out mouse lines, 2) for each type of knock-out RenMab Mice, generating 400~600 antibodies, 3) for each target, screening 100~200 molecules that cross-recognize human and mouse targets using Beacon optofluidic systems, 4) finding 10~20 molecules with the best potency against each target using *in vivo* screening, 5) validating 1~2 molecules in larger animals with spontaneous diseases and entering human clinical trials.

Figure 11: Process overview of Project Integrum



Source: Company data, CMBIGM

As such, Project Integrum has advantages of high throughput and cost efficiency. **Project Integrum reduces the time needed from pre-clinical discovery to PCC from an average of 5.5 years to 12-18 months, according to F&S.** Project Integrum enables the Company to rapidly determine the druggability of a target and discover antibodies for novel and/or challenging drug targets with desirable safety and efficacy profiles, thus ensuring a higher success rate during clinical development.

Biocytogen plans to complete the preparation of targets knockout RenMab mice by 2022. The Company aims to complete antibody discovery for over 1,000 potential targets, among which it expects to find PCC antibody molecules for hundreds of targets, within the next three to five years.

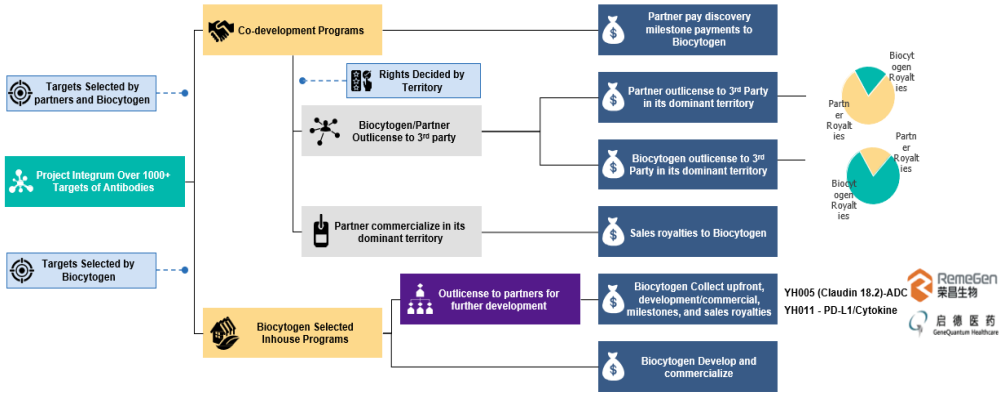
As of 13 Aug 2022, the Company has finished with 980+ target gene knocked out, among which 280+ targets have entered into antibody immune stage, and 40+ targets entering into molecular screening stage. Biocytogen would be able to complete the drug research and development for 200 to 300 potential targets per year with its development capacity. Biocytogen also intends to promote the IND filing and clinical development of the potentially first-in-class and/or best-in-class antibodies identified in Project Integrum through internal research and development and external partnerships.

Upon antibodies generated from Project Integrum, Biocytogen has pursued flexible business strategies, including 1) general co-development, 2) joint development with IP collaboration, and 3) antibody discovery service under RenMice Licensing.

As of 1H22, Biocytogen has signed 28 co-development agreements with biotechnology and pharmaceutical companies, including RemeGen, Mabworks Biotech, China Resources

Biopharm, Shanghai Institute of Biological Products, North China Pharmaceutical, Dragon Boat Biopharmaceutical, GeneQuantum, Libero Thera Co., Ltd, and Merck Healthcare KGAA. The co-development collaborations not only bring the Company substantial short-term and long-term economic returns, but also allow the Company to leverage partners' clinical and commercial resources to advance the development of the substantial number of potential antibody drug candidates.

Figure 12: Monetization of Project Integrum



Source: Company data, CMBIGM

Unique business model provides lucrative long-term return

Antibody development business leverating RenMice platforms

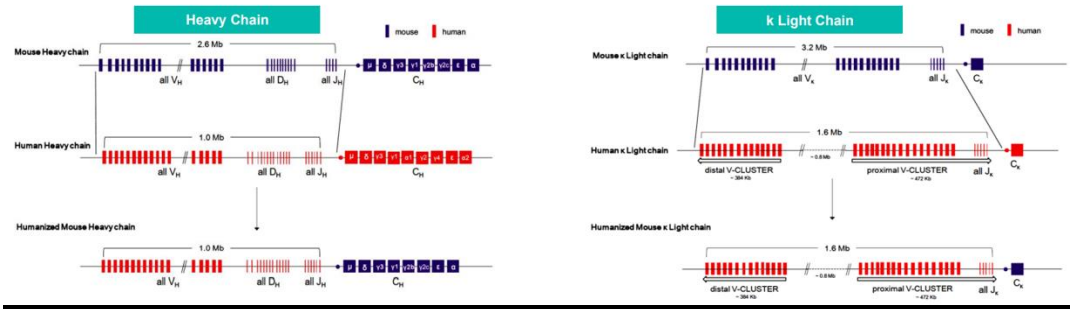
Biocytogen's antibody development is based on the antibody discovery technology of RenMice platform and its self-developed in vivo drug efficacy screening technology. Together with hybridoma technology and Beacon single-cell photoconduction screening, Biocytogen generates a large amount of potential antibodies and conducts large-scale in vivo drug efficacy evaluation to screen and obtain antibody molecules with the potential to become drug candidates.

Biocytogen adopts an evidence-based in vivo screening methodology as a disruptive approach, which enables the Company to rapidly and concurrently screen over 1,000 potential antibody drug targets, most of which have not been explored in clinical trials yet, thus significantly facilitating the discovery and development process of novel therapeutic antibody drug candidates. As of 1H22, Biocytogen reached 28 co-development deals with pharmaceutical and biotechnology companies in China, Germany and Japan under Project Integrum.

State-of-the-art RenMice platforms

RenMab platform: Generated by Size-unlimited and Precise Chromosome Engineering System (SUPCE) technology, the RenMab mice have full human variable region, which allow the natural in vivo pairing of human heavy and light chains. Adapting transgenic RenMab mice, Biocytogen's RenMab platform can generate fully human antibodies, with high affinity, low immunogenicity, and favorable developability. RenMab platform can also minimize the need for excessive rounds of late-stage antibody engineering and validation that is necessary when using in vitro discovery methods.

Figure 13: How humanized RenMab mice are generated by SUPCE

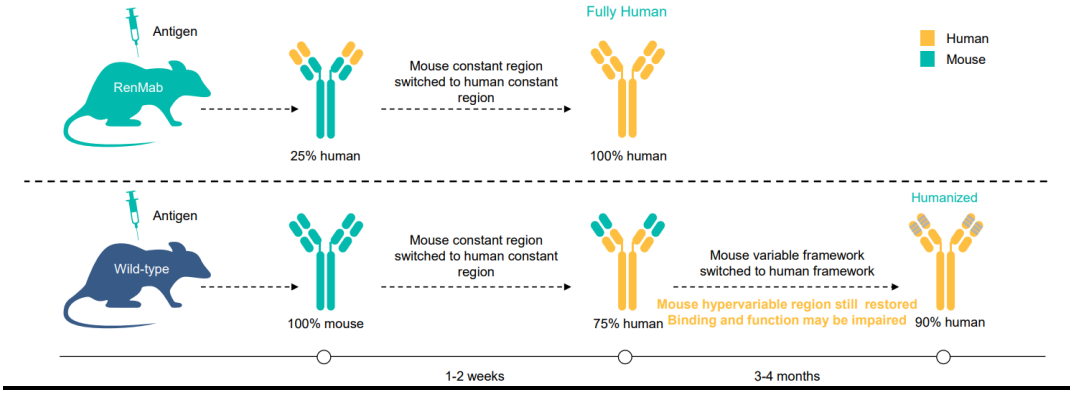


Source: Company data, CMBIGM

The Company's proprietary, Mb-scale editing technology enabled the efficient replacement of the entire murine immunoglobulin heavy chain and kappa light chain variable regions (including distal Vk) with the corresponding human immunoglobulin variable regions in situ. The use of SUPCE technology means that the entire human variable region, including the noncoding regions inside the VDJ loci, remains intact in the RenMab mice. Moreover, the murine constant region in the RenMab mice also remains intact, in ensuring robust immune cell responses and proper B cell development. The constant domain is then easily swapped with the human constant domain in later stages.

RenMab mice generate a highly diverse B cell repertoire for the maximum of successful antibody hits with high affinity. Producing fully human antibodies using RenMab platform ensures that the antibody candidates will be of potentially better safety and efficacy profile and have a potentially higher success rate during clinical development.

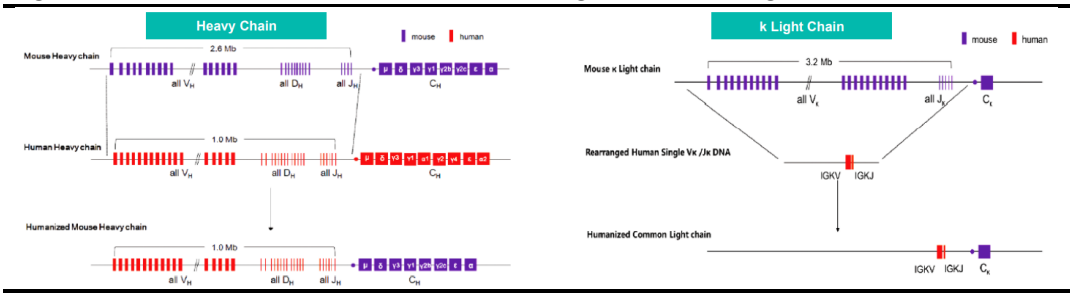
Figure 14: Advantages of RenMab platform when producing fully human antibodies



Source: Company data, CMBIGM

RenLite platform: Biocytogen's RenLite platform uses transgenic RenLite mice containing the fully human immunoglobulin heavy chain variable region and a fixed common light chain, which are used to develop bi-specific antibodies and bi-specific ADCs. In the RenLite mice, the mouse heavy chain antibody gene variable region has been replaced with a fully human heavy chain variable in situ, which results in diversified heavy chain repertoire similar to that of human's. Moreover, Biocytogen's RenLite mice have also been genetically altered with a single human common kappa light chain.

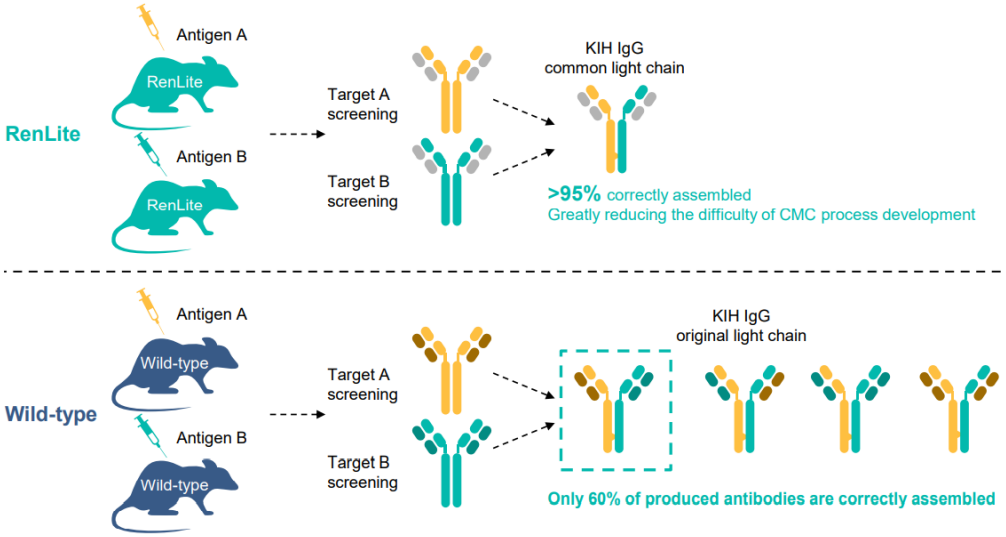
Figure 15: How humanized RenLite mice are generated using SUPCE



Source: Company data, CMBIGM

The presence of such single human common kappa light chain ensures light chain complementarity for the future discovery of bi-specific antibodies, while at the same time resolving the mismatch issues of the light chain and the heavy chain, thereby streamlining the CMC development process. This simple bi-specific antibody structural design also allows Biocytogen to explore on a large scale whether different targets can be combined to generate bi-specific antibodies.

Figure 16: Advantages of RenLite platform when producing fully human antibodies



Source: Company data, CMBIGM

Global customer base of RenMice Platforms:

Biocytogen's RenMice platforms have a global and diversified customer base, consisting of well-known multinational pharmaceutical companies and leading local pharmaceutical and biotechnology companies. As of 1H22, Biocytogen has reached license and trial collaboration agreements with 16 well-known pharmaceuticals such as Innovent (信达生物) and Xencor.

Biocytogen out-licenses its RenMice platforms using two methods, including: 1) Without specific target limitations, under which scenario the licensee only needs to provide target codes and Biocytogen is entitled to collect upfront payment, milestone payments and royalties; 2) With specific target limitations, under which scenario Biocytogen will negotiate customized fees with licensees considering the extent of services requested and the targets the customer selected.

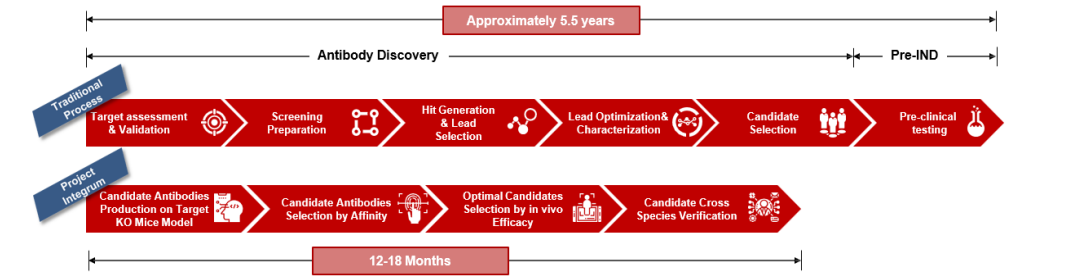
In both types of licensing, Biocytogen holds exclusive intellectual property rights of RenMice. The licensees are entitled to the intellectual property rights of the products developed with RenMice, and Biocytogen is not entitled to utilize the licensees' results for its antibody development. As of 1H22, the licensees have initiated 33 projects in total.

Project Integrum to become a strong revenue driver

The traditional innovative drug development starts from MOA and needs to go through the whole procedure of target identification, discovery and optimization of lead antibodies, in vivo pharmacological and pharmacodynamic studies, CMC, safety rating and clinical trials. According to F&S, there are 1,000+ drug targets in the human body, most of which are still to be further explored. So far, the FDA and the EMA have approved 144 mAbs against ~60 targets.

Project Integrum empowers Biocytogen with the capability to identify PCC antibody for potential targets circumventing traditional methods. Biocytogen adopts an evidence-based in vivo screening methodology, which uniquely enables rapid and concurrent screening of 1,000+ potential antibody drug targets, thus significantly facilitating the discovery and development process of novel therapeutic antibody drug candidates.

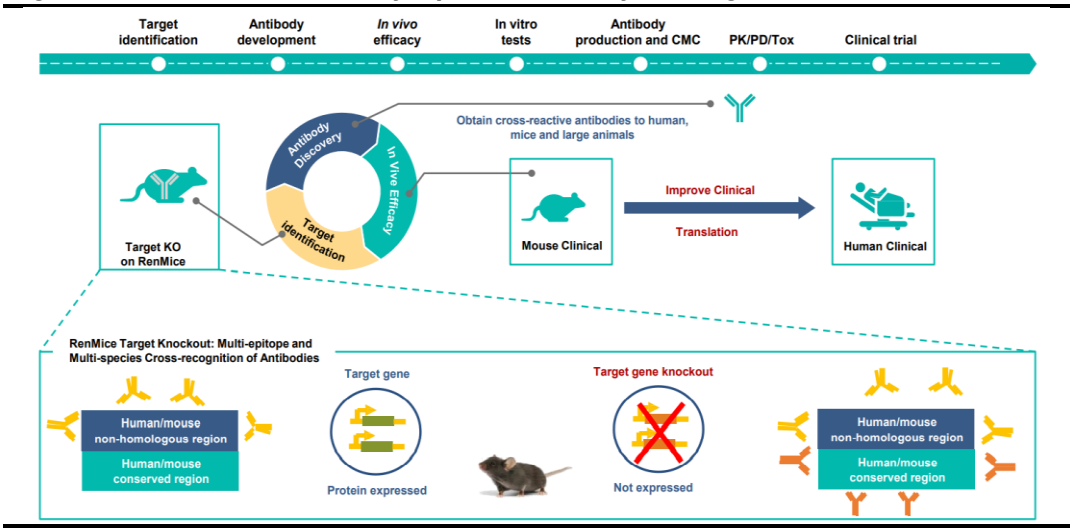
Figure 17: Traditional pre-clinical process vs Biocytogen's evidence-based *in vivo* screening



Source: Company data, CMBIGM

As of 13 Aug 2022, Biocytogen had completed 980+ knock-out under Project Integrum, including 280+ targets entering into antibody immune stage and 40+ targets entering into the molecular screening stage. The Company would be able to complete the antibody molecule selection for 200~300 potential targets per year. The chart below illustrates the major process of Project Integrum.

Figure 18: Flowchart of the major process of Project Integrum



Source: Company data, CMBIGM

1) Non-lethally knock out target genes to obtain ~1,000 Target KO RenMice. By knocking out these targets, Biocytogen disrupts the immune tolerance in mice and significantly expands the variety of antibody molecules. As of 13 Aug 2022, Biocytogen has knocked out 980+ target genes, among which ~300 targets have clinical-stage products in the market. With Target KO RenMice, Biocytgen may develop best-in-class or first-in-class antibody molecules. The Company has also initiated approximately 250 RenLite knockout projects with its bi-specific antibody developing platform.

2) Conduct large-scale and high-throughput screening of antibodies by cross-immunization with multi-species antigens. Biocytogen adopts the Beacon optofluidic system to improve antibody screening throughput. Currently, the Company has three Beacon optofluidic systems to support antibody screening of three targets every day. Usually, Biocytogen first prepares antibodies against 1,000+ targets using Target KO RenMice and for each target, selects 400~600 antibody clones, and then screens out 100-200 antibody molecules per target that cross-recognize human and mouse targets to perform subsequent in vivo efficacy evaluation and ranking.

3) Find approximately 10-20 antibody molecules with the best potency against each target using in vivo screening. For the screened antibodies that recognize human and mouse targets, Biocytogen measures the size of tumor after injection of the antibodies into diseased mice to identify the antibody with the best efficacy. For the antibody with the best in vivo efficacy, the Company will conduct further in vitro drug ability analysis.

4) Conduct further validation in larger animals. For the effective targets and antibody molecules in mice, Biocytogen conducts further validation in larger animals with spontaneous diseases, with approximately one to two antibody molecules available for each target. Currently, the Company's larger animal oncology medical translation center is under construction.

5) File antibody IND application. For antibody drug candidates that are effective in larger animals, the Company will further file antibody IND application.

Wide collaborations under Project Integrum:

Biocytogen generates revenue from out-licensing or collaborations with its partners on a target exclusive basis for potential therapeutic antibody molecules discovered by Project Integrum. The targets for codevelopment program are usually co-decided by Biocytogen and its partners. The rights of the codevelopment product will be divided by territory or by specific field between Biocytogen and its partner. Biocytogen is generally entitled to receive milestone payments from its partners.

As of 1H22, Biocytogen reached 28 co-development deals with pharmaceutical and biotechnology companies. Biocytogen's partners include RemeGen, Mabworks (北京天广实), China Resources Biopharm (华润医药), Shanghai Institute of Biological Products (上海生物制品研究所), North China Pharmaceutical (华北制药), Dragon Boat Biopharma (宝船生物), GeneQuantum, and LiberoThera. Biocytogen has three collaboration models with partners for Project Integrum, including 1) general co-development, 2) joint development with IP collaboration, and 3) antibody discovery service under RenMice licensing.

Under the first collaboration model, Biocytogen co-owns the IP rights of the co-developed products with its partners. As most of Biocytogen's partners are located in China and focus on China business, they are typically granted China rights and are required to pay Biocytogen royalties for profits generated from China. While Biocytogen enjoys the overseas rights of the co-developed products and would need to pay royalties to its partners for profits generated outside of China.

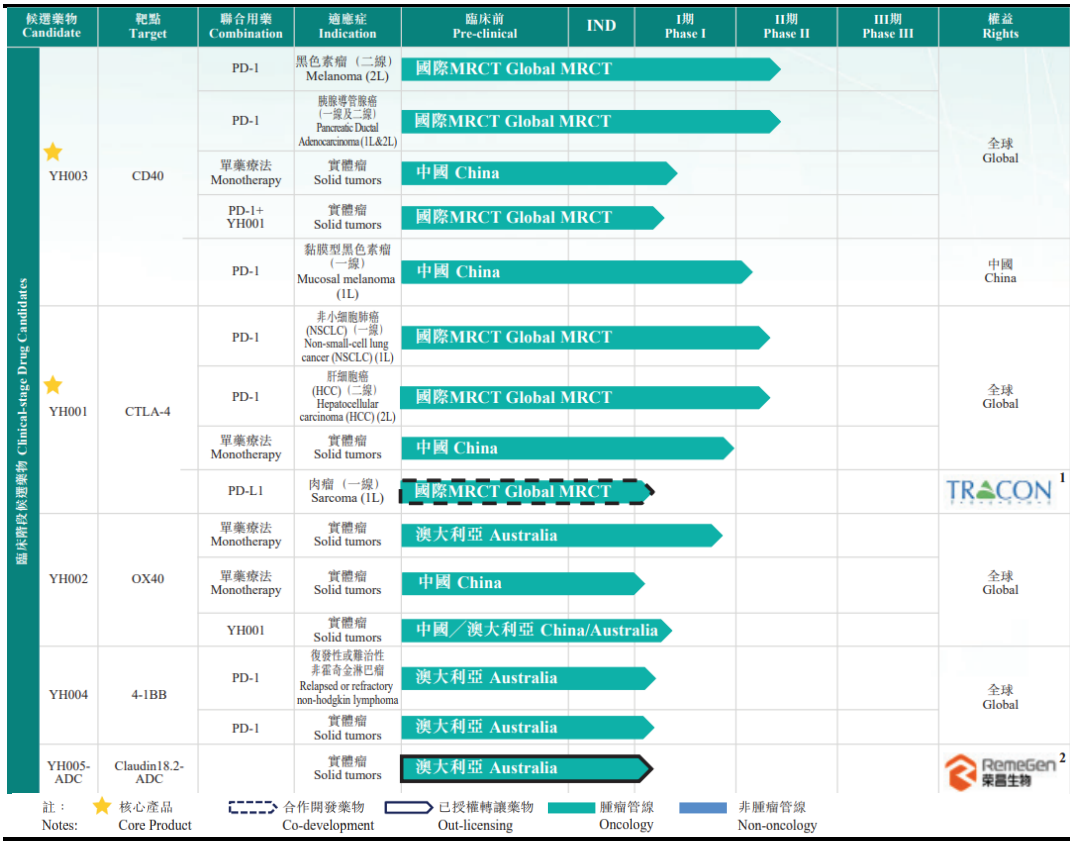
Under the second collaboration model, Biocytogen and its partners will allocate product rights in proportion to their contribution. The material terms of co-development are set by project, and the two parties will generally bear the R&D investments of respective responsibilities.

Under the third collaboration model, Biocytogen will license RenMice for partner's development of an antibody drug with a specific target. Biocytogen will also carry out antibody discovery and related PD in vitro and in vivo pharmacology studies. Partners generally pay for licensing fee for RenMice and service fees for antibody discovery and PD in vitro and in vivo pharmacology studies. Partners own the intellectual properties of the co-developed antibody drugs.

In-house developed pipeline drugs with large out-license potential

As of 18 Sep 2022, Biocytogen established an antibody drug pipeline of 12 drug candidates, including five clinical assets and seven pre-clinical stage assets. Currently, Biocytogen has four ongoing clinical trials and eight clinical trials planned for initiation. Three of the pipeline drug candidates have out-licensing arrangements, including CTLA-4 antibody YH001, Claudin 18.2 antibody YH005 and PD-L1 antibody YH011. YH001 has under co-development with Tracon for selected indications in the North American regions, and YH005 was out-licensed to RemeGen to develop a YH005 ADC (RC118), which has obtained TGA approval for clinical trials in Australia.

Figure 19: Biocytogen's clinical stage drug candidates



Source: Company data, CMBIGM
Notes:
1) Biocytogen co-develops YH001 with Tracon for selected indications in the North American regions (the US, Canada and Mexico) and is entitled to collect double-digit percentage royalties on net sales in North America once commercialized. The Company remains development/ commercialization rights in regions other than the North American regions.
2) Biocytogen is entitled to collect licensing fee from RemeGen for the out-license of YH005.

YH003, a potentially best / first-in-class anti-CD40 antibody

YH003 is a core product of Biocytogen, which is a recombinant, humanized agonistic anti-CD40 IgG2 mAb. Biocytogen is conducting a Ph I trial in Australia of YH003 + Toripalimab in patients with advanced solid tumors, which reached the primary end-point with the RP2D identified (0.3mg/kg) in Apr 2021. Currently, Biocytogen is also conducting a Ph II MRCT in patients with PD-1 refractory unresectable/ metastatic melanoma as well as pancreatic ductal adenocarcinoma to further investigate safety and efficacy of YH003 + Toripalimab in China and Australia. Biocytogen has completed the dosing of the first patient in Australia in Dec 2021, has commenced the Ph II MRCT in China in Mar 2022, and also expects to commence FPI of the Ph II MRCT in the US by 2H22.

Competition landscape of anti-CD40 antibodies:

There is no approved or commercialized anti-CD40 antibody globally as of Apr 2022, and all the CD40 antibody candidates are currently in an early phase of development, according to F&S.

Figure 20: Global CD40 antibody candidates as monotherapy, as of Apr 2022

Company	Drug	Drug type	Indication	Highest phase	First post	Location
Apexigen	APX005M	mAb	Unresectable/ Metastatic Melanoma	Ph 2	Apr-2020	Global
			Melanoma, NSCLC, UC, MSI-H, Head and Neck Cancer	Ph 1	Jun-2015	US
			GBM, High-grade Astrocytoma NOS, CNS Primary Tumor, Nos, Ependymoma, NOS, DIPG, Medulloblastoma	Ph 1	Jan-2018	US
Seagen	SEA-CD40	mAb	Advanced Tumors	Ph 1	Mar-2015	US
Celldex	CDX-1140	mAb	Advanced Tumors	Ph 1	Nov-2017	US
Lyvgen	LVGN7409	mAb	Advanced/Metastatic Tumors	Ph 1	Nov-2020	US
					Oct-2021	China
Biocytogen/ Eucure	YH003	mAb	Late-Stage Solid Tumors	Ph 1	Jul-2021	China
AbbVie	ABBV-927	mAb	Advanced Solid Tumors	Ph 1	Dec-2016	Global
PsiOxus	NG-350A	Oncolytic adenoviral vector expressing anti-CD40 antibody	Advanced/Metastatic Epithelial Tumors	Ph 1	Feb-2019	US
Roche	RO7300490	BsAb	Advanced Solid Tumors	Ph 1	Apr-2021	Global

Source: ClinicalTrials, CDE, Company data, F&S, CMBIGM
Notes: Location marked as "Global" if the trial is conducted in multiple countries

CD40 agonists have been combined with a variety of immuno-oncology agents or agonists to enhance the therapeutic effect.

Figure 21: Global CD40 antibody candidates in combination with other therapies, as of Apr 2022

Company	Drug	Drug type	Indication	Highest phase	First post	Location	Combination
Biocytogen/ Eucure	YH003	mAb	Unresectable/metastatic melanoma, pancreatic ductal adenocarcinoma	Ph 2	Sep-2021	N/A	Toripalimab (PD-1)
			Advanced solid tumors	Ph 1/2	Jul-2020	Australia	Toripalimab (PD-1)
AbbVie	ABBV-927	mAb	Advanced solid tumors	Ph 1	Dec-2016	Global	Budigalimab (PD-1)
			Locally advanced or metastatic solid tumors	Ph 1	Mar-2019	Global	ABBV-368, Budigalimab and/or Chemo
			Metastatic pancreatic cancer	Ph 2	Mar-2021	Global	Modified FOLFIRINOX with/without Budigalimab
Seagen	SEA-CD40	mAb	Advanced tumors	Ph 1	March-2015	US	Pembrolizumab, gemcitabine and nabpaclitaxel
Apexigen	APX005M	mAb	Resectable esophageal and GEJ	Ph 2	May-2017	US	Chemoradiation
				Orphan Drug Designation	Oct-2020	US	
			Unresectable or metastatic melanoma	Ph 2	Apr-2020	Global	Radiation therapy
			Locally advanced rectal adenocarcinoma	Ph 2	Oct-2019	US	mFOLFOX and Radiation
			Soft tissue sarcoma	Ph 2	Oct-2018	US	Doxorubicin
				Orphan Drug Designation	Aug-2021	US	
			Melanoma	Ph 1/2	Mar-2016	US	Pembrolizumab
			Cancer, NSCLC metastatic,	Ph 1/2	Apr-2017	Global	Nivolumab

			melanoma,neoplasm of lung				
			Pancreatic cancer	Orphan Drug Designation	Oct-2020	US	
			Metastatic pancreatic adenocarcinoma	Ph 1/2	Jul-2017	US	Gemcitabine and nab-Paclitaxel with/without Nivolumab
			Advanced melanoma, NSCLC, RCC	Ph 1	Apr-2018	US	Nivolumab and cabiralizumab
			Metastatic melanoma	Ph 1	Jul-2018	US	NEO-PV-01 vaccine Ipilimumab, and nivolumab
			Advanced melanoma, RCC	Ph 1	Jul-2020	US	Nivolumab and Ipilimumab
Alligator	Mitazalimab (ADC-1013)	mAb	Metastatic pancreatic ductal adenocarcinoma	Ph 1b/2	May-2021	Global	Chemotherapy
Lyvgen	LVGN7409	mAb	Advanced tumors	Ph 1	Nov-2020	US	LVGN3616 (PD-1), LVGN6051 (CD137)
Celldex	CDX-1140	mAb	Advanced tumors	Ph 1	Nov-2017	US	CDX-301(FLT3L), Pembrolizumab
Roche	Selicrelumab (RG7876)	mAb	Advanced and/or metastatic solid tumors	Ph 1	Dec-2014	Global	Atezolizumab
			Advanced/metastatic solid tumors	Ph 1	Jan-2016	Global	Vanucizumab Bevacizumab
	RO7300490	BsAb	Advanced solid tumors	Ph 1	April-2021	Global	Atezolizumab
PsiOxus	NG-350A	Oncolytic adenoviral vector	Advanced/metastatic epithelial tumors	Ph 1	Feb-2019	US	A check point inhibitor

Source: ClinicalTrials, CDE, Company data, F&S, CMBIGM

In China, there are limited number of CD40 antibody candidates at clinical stage, while Biocytogen's YH003 is one of the first two molecules to have entered into Ph II evaluation.

Figure 22: CD40 antibody candidates at clinical stage in China, as of Apr 2022

Company	Drug	Drug type	Indication	Highest phase	First post	Therapy type
Biocytogen/ Eucure	YH003	mAb	Mucosal melanoma, Pancreatic ductal adenocarcinoma	Ph 2	Dec-2021	+Toripalimab
Novartis	CFZ533	mAb	Lupus nephritis	Ph 2	Jun-2019	Mono
Biocytogen/ Eucure	YH003	mAb	Solid tumors	Ph 1	Jul-2021	Mono
Chaitai Tianqing	TQB2916	mAb	Advanced solid tumors	Ph 1	Dec-2021	Mono
Mabworks	MIL97	mAb	Solid tumors	Ph 1	Jan-2022	Mono
Lyvgen	LVGN7409	mAb	Tumors	Ph 1	Oct-2021	Mono

Source: ClinicalTrials, CDE, Company data, CMBIGM

Summary of phase I clinical trial:

Trial design & status: Biocytogen received the TGA approval for the Ph I trial in Jul 2020 and commenced first subject in Jul 2020. A 3+3 dose escalation design was used to identify maximum tolerated dose (MTD) and recommended RP2D of YH003 in combination with Toripalimab. 26 patients with advanced solid tumors received YH003 by IV administration Q3W as monotherapy at 0.03 mg/kg (n=3), 0.1mg/kg (n=3), 0.3mg/kg (n=9), 1.0 mg/kg (n=8) and 3.0 mg/kg (n=3) for the first cycle (21 days), followed by a combination phase where patients received YH003 plus Toripalimab (240 mg Q3W). Patients received a median of 3 prior lines therapy (range 1-7). As of the data cut-off date of 6 Jun 2022, 11 of the 26 enrolled patients had received previous immunotherapy (anti-PD-1, anti-PD-L1 or anti-PD-1, anti-CTLA-4 bispecific antibody, anti-PD-1 and TGF-ßRII bispecific antibody).

Safety data: Among the 26 patients, two experienced Grade 3 drug related adverse events (TRAEs), eight had Grade 2 AEs related to YH003 and five patients had Grade 2 AEs related to Toripalimab, one Grade 2 hepatitis at 0.3 mg/kg dose level related to YH003 and Toripalimab and four infusion reactions at 1.0 mg/kg dose level related to YH003. One Grade 3 TEAE (Transaminitis) related to YH003 was reported at 1.0 mg/kg dose level which led to permanent treatment discontinuation and met protocol defined DLT criteria and one Grade 3 TEAE (lipase increase) was reported at 0.1 mg/kg dose level which was only related to Toripalimab. No drug related SAE and AE leading to death occurred.

Biocytogen is conducting a Ph I clinical trial of YH003 as a single agent in patients with advanced solid tumors in China. YH003 was well tolerated up to 3.0 mg/kg dose levels. YH003 in combination with toripalimab is expected to be applied as a last-line therapy for patients with melanoma, and would be as a first-line therapy for patients with pancreatic cancer.

Efficacy data: Among 21 patients assessable for response, one patient with pancreatic ductal adenocarcinoma who failed first line chemotherapy treatments achieved CR. Two subjects achieved PRs (one with refractory melanoma previously treated with anti-PD-1 antibody/anti-CTLA-4 antibody, and the other one was with NSCLC) and five subjects achieved SDs (one with MCC, one with NSCLC, one with GEC, and two with melanoma). Based on current efficacy data, YH003 combined with toripalimab has shown encouraging anti-tumor activity and may provide an option for patients resistant to immunotherapies.

PK data: In the dose range of 0.1 to 1.0 mg/kg, YH003 exhibited more than dose-proportional PK, which is indicated by reduced systemic clearance and reduced volume of distribution at higher dose levels.

Further clinical development plan:

Biocytogen received the IND approval for the Ph II MRCT from the FDA, the TGA, the MedSafe, the NMPA and Taiwan FDA. The Ph II MRCT is an open-label, multicenter trial with primary endpoint of ORR. The Company expects to recruit 129 patients in total, including 60 patients in mainland China and 20 patients in the US.

Biocytogen is initiating its Ph I dose escalation trial of YH003 in mainland China to explore the safety, tolerability and PK of YH003 in Chinese population and to bridge the ethnic group difference. The Company has received the IND approval of the Ph I clinical trial from the NMPA in May 2021. In addition, Biocytogen also plans to apply for a Ph I dose escalation trial in Australia to evaluate the safety, tolerability, preliminary efficacy and pharmacokinetics of YH001 and YH003 in combination with Toripalimab in patients with advanced solid tumors. The Company will also further explore the expansion of YH003 for the treatment of other solid tumor indications.

YH001, a potential best-in-class anti-CTLA-4 monoclonal antibody

YH001 is another core product of Biocytogen, which is a recombinant humanized anti-CTLA-4 IgG1 mAb. Biocytogen is conducting a Ph I clinical trial in Australia of YH001 + Toripalimab in patients with advanced solid tumors, which reached the primary end-point, with the RP2D identified (YH001 1.0 mg/kg + Toripalimab 240 mg) in Apr 2021. A Ph II MRCT will be conducted in patients with advanced NSCLC or HCC to further investigate efficacy and safety of combination of YH001 and Toripalimab.

In Aug 2022, the Ph I/II trial of YH001 in combination with envafolimab and adriamycin has also obtained FDA approval. The trial will evaluate the safety and efficacy of YH001 + envafolimab for the treatment of rare alveolar soft part sarcoma and chondrosarcoma/

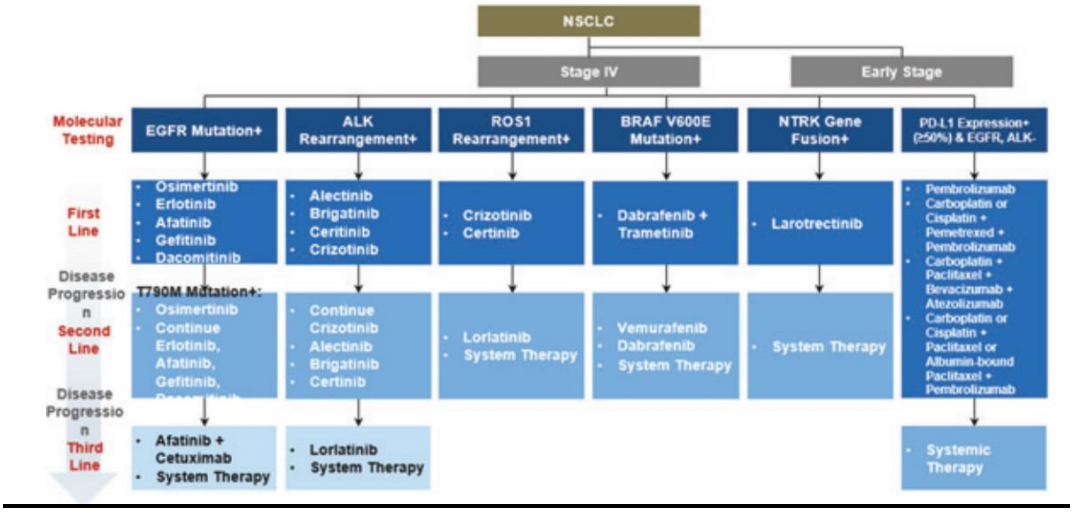
YH001 + envafolimab + adriamycin for the treatment of common leiomyosarcoma and dedifferentiated liposarcoma, respectively.

Indication selection of YH001:

Biocytgen is developing YH001 + Toripalimab as a second-line therapy for patients with HCC, and as a first-line therapy for patients with NSCLC. Multi-kinase inhibitors such as Sorafenib, Lenvatinib have been used as first- or second-line treatment for HCC. Since May 2020, Atezolizumab plus Bevacizumab combination (immunotherapy plus anti-VEGF) has become the new reference standard in first-line HCC treatment.

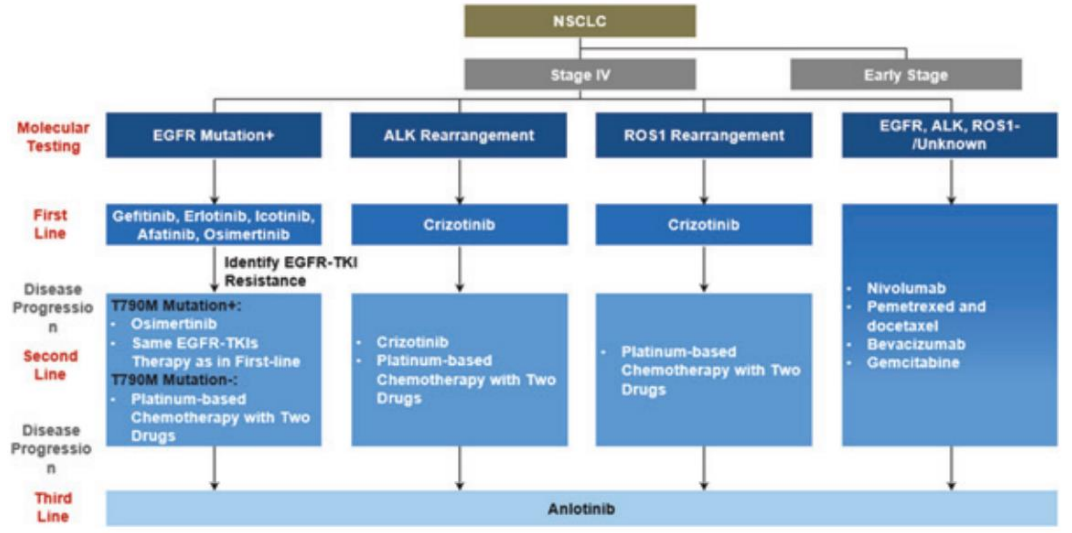
For advanced (stage IV) NSCLC, the treatment is further specified by different molecular testing with more treatment options in the US than in China.

Figure 23: Treatment for stage IV NSCLC in the US



Source: NCCN, CMBIGM

Figure 24: Treatment for stage IV NSCLC in China



Source: CSCO, CMBIGM

Competition landscape of CTLA-4 antibodies:

As of 13 Aug 2022, Ipilimumab (Yervoy) is the only marketed CTLA-4 antibody globally, which was approved as a monotherapy and as part of the combination therapy in melanoma and in RCC in the US. In China, Ipilimumab (Yervoy) was approved in Jun 2021.

From 2012 to 2020, the global sales revenue of Yervoy increased from US$706mn to US$1,682mn, according to F&S. However, the use of Yervoy has been limited due to its toxicity. According to FDA, the most common severe immune-mediated adverse reactions of Yervoy include enterocolitis, hepatitis, dermatitis (including toxic epidermal necrolysis), neuropathy, and endocrinopathy.

The recent trend in the oncology area is to discover combination therapies for checkpoint inhibitors. Due to the commercialization of CTLA-4/PD-1 combination therapies since the approval of Yervoy, the size of global and domestic CTLA-4 antibody market is increasing drastically, according to F&S.

Figure 25: Marketed anti-CTLA-4 antibody

Brand	Generic	Company	Indications approved	Year of initial approval	Authorities of approval
Yervoy	Ipilimumab	BMS	Unresectable or metastatic melanoma, advanced renal cell carcinoma in combo with Nivolumab, colorectal cancer in combo with Nivolumab, hepatocellular carcinoma in combo with Nivolumab, metastatic or recurrent NSCLC in combo with Nivolumab	2011	FDA
			Unresectable or metastatic melanoma in combo with Nivolumab, advanced renal cell carcinoma in combo with Nivolumab, metastatic NSCLC in combo with Nivolumab, unresectable malignant pleural mesothelioma, colorectal cancer in combo with Nivolumab	2011	EMA
			Unresectable non-epithelial malignant pleural mesothelioma in combo with Nivolumab	2021	NMPA

Source: FDA, EMA, NMPA, F&S, CMBIGM

According to F&S, combination therapies of anti-CTLA-4 mAbs with immune checkpoint inhibitors such as PD-1 and PD-L1 have become a recent global trend.

Figure 26: Global status of anti-CTLA-4 antibody candidates at clinical stage as of Apr 2022

Drug	Company	Type of treatment	Indication	Highest Phase	First post	Location
Tremelimumab (CP-675206)	AZ	+Durvalumab (PD-L1)	SCLC	Ph 3	Oct-18	Global
		+Durvalumab (PD-L1)	Advanced urothelial cancer	Ph 3	Sep-18	Global
		+Durvalumab (PD-L1)	HCC	Ph 3	Oct-17	Global
		+Durvalumab (PD-L1)	Pediatric malignancies	Ph 1/2	Feb-19	Global
		+Platinum-based Chemo	Advanced NSCLC	Ph 3	Apr-18	China
		+Platinum-based Chemo	Advanced SCLC	Ph 3	May-18	China
Quavonlimab	MSD/Eisai	+Pembrolizumab (PD-1), Lenvatinib	Advanced clear cell RCC	Ph 3	Feb-21	Global
	MSD	+Pembrolizumab (PD-1), Lenvatinib	Advanced HCC	Ph 2	Feb-21	Global
		+Pembrolizumab (PD-1)	MSI-H/dMMR advanced CRC	Ph 2	May-21	Global
		+Pembrolizumab	Advanced Solid Tumors	Ph 1/2	Jun-17	Global
YH-001	Biocytogen/ Eucure	+Toripalimab (PD-1)	HCC, NSCLC	Ph 2	Jan-22	Global
			Advanced solid tumor	Ph 1	Apr-20	Australia
		Mono	Advanced solid tumor	Ph 1	Dec-20	China
BMS-986218	BMS	With/Without Nivolumab and Docetaxel	Prostatic Neoplasms, Castration-Resistant	Ph 2	Dec-12	Global
		+Nivolumab (PD-1)	Advanced tumor	Ph 1/2	Apr-17	Global
BMS-986249		+Nivolumab (PD-1)	Advanced solid tumor	Ph 1/2	Dec-17	Global
AGEN1181	Agenus	+AGEN2034 (PD-1)	Advanced tumor	Ph 1/2	Mar-19	US
		+Balstilimab	Advanced cancer	Ph 1	Mar-19	US
AGEN1884		+AGEN2034 (PD-1)	Cervical cancer	Ph 1/2	Apr-18	Global
BT-001	Transgene, BioInvent	With/without Pembrolizumab (PD-1)	Solid tumor	Ph 1/2	Jan-21	Global
XTX101	Xilio/ MSD	+ Pembrolizumab (PD-1)	Advanced solid tumor	Ph 1/2	May-21	US
HBM4003	Harbour	Mono	Advanced solid tumor	Ph 1	Oct-19	Global
		+PD-1	NSCLC	Ph 1	Apr-21	China
		+Toripalimab (PD-1)	Advanced melanoma	Ph 1	Dec-20	China

Nurulimab (BCD-145)	Biocad	Mono	Melanoma	Ph 1	Mar-18	Russia
ONC-392	OncoC4	+Pembrolizumab (PD-1)	Advanced solid tumor, NSCLC	Ph 1	Oct-19	US
KN044	Alphamab	Mono	Advanced solid tumor	Ph 1	Jun-19	China
ADG126	Adagene	Mono	Advanced/ metastatic tumor	Ph 1	Nov-20	Australia
AdG116		Mono	Advanced solid tumor	Ph 1	Aug-20	Australia
		Mono			Oct-19	US
REGN4659	Regeneron	+Cemiplimab	Carcinoma, NSCLC	Ph I	Jul-18	US
Ipilimumab Biosimilar						
IBI310	Innovent	+Sintilimab (PD-1)	Acral melanoma after surgery	Ph 3	Feb-20	China
		+Sintilimab (PD-1)	Advanced HCC	Ph 3	Jan-21	China
		+Sintilimab (PD-1)	Advanced cervical cancer	Ph 2	Oct-20	China
HL06	Hualan Genetic	Mono	Unresectable/ metastatic melanoma	Ph 1/2	Sep-19	China
CS1002	Cstone	Mono	Advanced solid tumor	Ph 1	Dec-19	China
		+CS1003 (PD-1)	Advanced solid tumor	Ph 1	May-18	Australia
MV049	Mab-Venture	Mono	Advanced solid tumor	Ph 1	Jul-19	China

Source: ClinicalTrials, CDE, Company data, F&S, CMBIGM

In China, there are several ongoing trials evaluating combination therapies of anti-CTLA-4 mAbs with immune checkpoint inhibitors.

Figure 27: China status of anti-CTLA-4 antibody candidates at clinical stage as of Apr 2022

Drug	Company	Type of treatment	Indication	Highest phase	First post
Tremelimumab (CP-675206)	AZ	+Durvalumab (PD-L1)	NSCLC	Ph 3	Jan-17
		+Platinum-based Chemo	Advanced NSCLC	Ph 3	Apr-18
		+Platinum-based Chemo	Advanced SCLC	Ph 3	May-18
		+Durvalumab (PD-L1)	HCC	Ph 2	Jun-17
Quavonlimab	MSD	Lenvatinib	Advanced HCC	Ph 2	Aug-21
YH-001	Biocytogen/ Eucure	+Toripalimab (PD-1)	HCC, NSCLC	Ph 2	Mar-22
		Mono	Solid tumor	Ph 1	Dec-20
BAT4706	Bio-thea	Mono	Melanoma, Advanced solid tumor	Ph 1	Jul-21
HBM4003	Harbour	+Toripalimab (PD-1)	Advanced melanoma	Ph 1	20-Dec
		+Pembrolizumab (PD-1)	NSCLC	Ph 1	21-Apr
		Mono	Advanced solid tumor	Ph 1	21-Jan
		+Toripalimab (PD-1)	NEN	Ph 1	21-Oct
		+Toripalimab (PD-1)	Advanced HCC	Ph 1	21-Nov
ONC-392	OncoC4	Mono	NSCLC	Ph 1	Oct-20
KN044	Alphamab	Mono	Advanced solid tumor	Ph 1	Jun-19
JS007	Junshi	Mono	Advanced solid tumor	Ph 1	Aug-21
TWP-102	Therawisdom	Mono	Advanced tumor	Ph 1	Sep-21
IMM27M	ImmuneOnce	Mono	Advanced/ metastatic tumor	Ph 1	Jan-22
ADG126	Adagene	Mono	Advanced solid tumor	Ph 1	Mar-22
Ipilimumab Biosimilar					
IBI310	Innovent	+Sintilimab (PD-1)	Acral melanoma after surgery	Ph 3	Feb-20
		+Sintilimab (PD-1)	Advanced HCC	Ph 3	Jan-21
		+Sintilimab (PD-1)	Advanced cervical cancer	Ph 2	Oct-20
HL06	Hualan Genetic	Mono	Unresectable/ metastatic melanoma	Ph 1/2	Sep-19
CS1002	Cstone	Mono	Advanced solid tumor	Ph 1	Dec-19
MV049	Mab-Venture	Mono	Advanced solid tumor	Ph 1	Jul-19

Source: ClinicalTrials, CDE, F&S, CMBIGM

Since 2015, the FDA has approved various combined therapies. Ipilimumab and Nivolumab combination therapy has received breakthrough designation from FDA for advanced HCC.

In light of the recent success, combined therapy of anti-PD-1 and anti-CTLA-4 mAbs possess a greater potential than PD-1 monotherapy. With advancing technologies, anti-CTLA-4 mAbs are expected to show greater efficacy on more indications and are expected to show great potential in combination with other immuno-oncology therapies, not limited to PD-1 combo therapy.

Figure 28: Approval history of anti-CTLA-4 mAbs and its combination with PD-1

Approval date	Indications approved		Therapy (Combo/Mono vs. SOC)
Oct-2020	Previously untreated unresectable malignant pleural mesothelioma	1st line	Combo w. Nivolumab vs. Platinum-based SOC
May-2020	Metastatic/recurrent NSCLC	1st line	Combo w. Nivolumab vs. Chemo
May-2020	Metastatic NSCLC with PD-L1 express >=1%	1st line	Combo w. Nivolumab vs. Chemo
Mar-2020	Sorafenib previously treated HCC	2nd line	Combo w. Nivolumab vs. Nivulumab
Jul-2018	Previously treated MSI-H/dMMR metastatic colorectal cance	2nd line	Combo w. Nivolumab vs. Chemo
Apr-2018	Intermediate and poor-risk advanced RCC	1st line	Combo w. Nivolumab vs. Sunitinib
Jan-2016	Unresectable/metastatic melanoma across BRAF status	1st line	Combo w. Nivolumab vs. Nivolumab
Oct-2015	BRAF V600 wild-type melanoma	1st line	Combo w. Nivolumab vs. Ipilimumab
Mar-2011	Late-stage melanoma	1st line	Mono vs. gp100

Source: FDA, F&S, CMBIGM

Summary of phase I trial in Australia:

Trial design & status: The first-in-human Ph I trial is a multicenter, open-label, dose-escalation study of YH001+Toripalimab in subjects with advanced solid tumors, which is currently ongoing in Australia. The study has a run-in phase to explore the safety and tolerability of YH001 as a single agent for 21 days as a DLT observation period, then followed by a combination phase to further explore the safety and tolerability of YH001 + Toripalimab for each dose level during dose escalation, using the standard 3+3 design. Subjects with advanced solid tumors received YH001 by IV administration at 0.05 mg/kg, 0.1 mg/kg, 0.3 mg/kg, 1.0 mg/kg, 2.0 mg/ kg, 4.0 mg/kg and 6.0 mg/kg for one cycle (21 days) then in combination with Toripalimab at 240 mg Q3W for four cycles. RP2D was determined of YH001 dose level of 1.0 mg/kg + toripalimab dose level of 240 mg.

As of the data cut-off date of 31 May 2021, dose escalation is ongoing at a dose level of 2.0 mg/kg, 16 patients were enrolled and treated at 0.05 mg/kg (n=2), 0.1 mg/kg (n=3), 0.3 mg/kg (n=3), 1 mg/kg (n=5) and 2 mg/kg (n=3). All patients enrolled progressed after a median of two prior lines of available standard therapy including three patients who progressed after immunotherapy of anti-PD-1 antibody.

Safety data: As of the data cut-off date of 31 May 2022, nine Grade 3 or above TRAEs have been reported, including two Grade 3 colitis, one Grade 3 Aplasia pure red cell, one Grade 4 thrombocytopenia, one Grade 3 Myocarditis, one Grade 3 Enterocolitis, one Grade 3 Rash, one Grade 3 Pruritus and one Grade 3 hepatitis.

Efficacy data: As of the data cut-off date of 31 May 2022, among the 25 subjects having imaging tumor assessment by RECIST v1.1, there were five PRs which occurred at 0.3 mg/kg with gastroesophageal junction cancer, 2.0mg/kg with urothelial carcinoma progressed after prior anti-PD-1 antibody, 2.0mg/kg with uterine carcinosarcoma, 6.0mg/kg with vulva adenocarcinoma and endometrial cancer respectively; and nine SD, including two tongue cancer at 0.05 mg/kg and 1.0 mg/kg group respectively, three nasopharyngeal carcinoma at 0.1mg/kg, 1.0 mg/kg and 4.0 mg/kg group respectively, one uterus leiomyosarcoma at 0.3 mg/kg group, one NSCLC at 1.0 mg/kg group, one colon carcinoma at 1.0 mg/kg group, one skin cancer at 4.0 mg/kg group.

Summary of phase I trial in China:

Trial design & status: An initial accelerated titration dose followed by a traditional 3+3 dose escalation design was utilized to identify MTD and/or RP2D. The DLT observation period is defined as the first cycle (21 days). All subjects will have cleared the DLT evaluation period at any given dose level before subjects are allowed to enroll at the next higher dose level. A single subject is enrolled at the 0.3 mg/kg dose level. Three to six subjects will be enrolled at subsequent dose levels of 1.0 mg/kg, 2.0 mg/kg, 4.0 mg/kg and 6.0 mg/kg.

As of the data cut-off date of 31 May 2022, dose level escalated to maximum administered dose 6.0 mg/kg, 17 patients were enrolled and treated at 0.3 mg/kg (n=1), 1.0 mg/kg (n=3), 2.0 mg/kg (n=3) 4.0 mg/kg (n=4) and 6.0 mg/kg (n=6). All subjects in this study had experienced disease progression after at least one line of anti-cancer treatment, including 14 subjects progressed after immunotherapy of anti-PD-1 antibody.

Safety data: As of the data cut-off date of 31 May 2022, eight Grade 3 or above TRAEs have been reported, including one Grade 3 anemia, one Grade 4 immune hepatitis, one Grade 3 hypocalcemia, one Grade 3 immune nephritis, one Grade 3 hypokalemia, one Grade 4 myelosuppression, one Grade 3 hyponatremia and one Grade 3 lipase increased.

Efficacy data: As of the data cut-off date of 31 May 2022, among the 14 patients having imaging tumor, four subjects achieved SDs.

Clinical development plan:

Biocytogen expects to initiate a Ph II MRCT of YH001 + Toripalimab for the treatment of advanced NSCLC or HCC in the US, China, Taiwan and Australia. The Company expects to commence first-patient-in in Taiwan, the US, China, and Australia in 4Q22, respectively. Biocytogen will also explore the expansion of YH001+PD-1 antibodies for the treatment of other solid tumor indications, and intends to conduct a clinical trial of YH001 + YH002 in patients with advanced solid tumors in China and Australia. Moreover, the Company also plans to initiate a Ph I dose escalation in Australia of YH001 + YH003 + Toripalimab in patients with advanced solid tumors, and will also further explore the expansion of YH001 for the treatment of other solid tumor indications.

Collaboration with TRACON:

On 8 Oct 2021, Biocytogen entered into an exclusive license agreement with TRACON, a Nasdaq listed company (TCON US), concerning the development and commercialization of YH001, in regions of the US, Canada and Mexico and in the field of sarcoma, microsatellite stable colorectal cancer (mssCRC), renal cell carcinoma (RCC), K-ras positive NSCLC only. Pursuant to the Agreement, Tracon received an exclusive, non-transferable, royalty-bearing license, in the Tracon Territories, for the development and commercialization of YH001 in the Tracon Field. Biocytogen may receive escalating tiered royalties ranging from 25% to 40%, based on the amount of annual net sales from the Tracon Territories and a one-time launch success milestone payment of US$9mn if the net sales for YH001 in the Tracon Territories in the first full calendar year following first commercial launch exceeds US$100mn.

In Aug 2022, the clinical trial of YH001 in combination with envafolimab and adriamycin, a project jointly developed by Biocytogen and Tracon, has obtained IND approval from the FDA. This PhI/II trial will evaluate the safety and efficacy of YH001 in combination with envafolimab for the treatment of patients with rare alveolar soft part sarcoma and chondrosarcoma; and will evaluate the safety and efficacy of YH001 in combination with

envafolimab and adriamycin for the treatment of common leiomyosarcoma and dedifferentiated liposarcoma. The Company expects to commence FPI of this trial by 4Q22.

YH002, a potential first-in-class anti-OX40 monoclonal antibody in China

YH002 is a recombinant humanized IgG1 antibody that targets the human OX40 receptor. Biocytogen is currently conducting a first-in-human, multicenter, open-label, Ph I dose-escalation study in Australia to determine the MTD/RP2D of YH002 in subjects with advanced solid malignancies. Preliminary data from the Ph I trial have demonstrated a favorable safety profile of YH002.

Competition landscape of OX40 antibodies:

According to F&S, there is no approved or commercialized anti-OX40 antibody globally. All the OX40 antibody candidates are at an early phase of development.

Figure 29: Global status of OX40 antibody candidates at clinical stage as of Jul 2021

Drug name	Company	Type of treatment	Indication	Highest phase	First post	Location
PF-04518600	Pfizer	Avelumab (PD-L1)	Advanced cancer	Ph 1b/2	Sep-2015	Global
INCAGN01949	Incyte	Nivolumab (PD- 1), Ipilimumab (CTLA-4)	Advanced cancer	Ph 1/2	Aug-2017	US
BMS 986178	BMS	Nivolumab (PD- 1), Ipilimumab (CTLA-4)	Advanced solid tumor	Ph 1/2	Apr-2016	Global
YH002	Biocytogen/ Eucure	/	Advanced solid tumor	Ph 1	Apr-2020	Australia
			Advanced solid tumor	Ph 1	Jun-2021	China
INBRX-106	Inhibrx/MSD	Pembrolizumab (PD-1)	Advanced solid tumor	Ph 1	Dec-2019	US
MEDI0562	MedImmune	Durvalumab (PD-L1)	Advanced solid tumor	Ph 1	Mar-2016	Global
BGB-A445	BeiGene	Tislelizumab (PD-1)	Advanced solid tumor	Ph 1	Jan-2020	Australia
GSK3174998	GSK/MSD	Pembrolizumab (PD-1)	Advanced solid tumor	Ph 1	Aug-2015	Global
IBI101	Innovent	Sintilimab (PD-1)	Advanced solid tumor	Ph 1	Oct-2018	China
MOXR0916	Genentech	Atezolizumab (PD-L1)	Advanced solid tumor	Ph 1	Apr-2015	Global

Source: ClinicalTrials, CDE, F&S, CMBIGM

Biocytogen was the first to discover the effectiveness of combination therapy using anti-OX40 and anti-CTLA-4 mAbs in inhibiting tumor growth in animal models. Emerging data showed that CTLA-4 and OX40 expressed at highest density on tumor-infiltrating Treg cells in mouse and human (Arce Vargas et al., 2018, Cancer Cell).

YH002 monotherapy exhibited a favorable safety profile in the ongoing Ph I trial in Australia. Although not from a head-to-head study, the safety profile of YH002 is consistent with that of other anti-OX40 antibodies under clinical development, which reported adverse events such as lymphopenia, fatigue, rash, infusion-related reactions, pyrexia, and pneumonitis. In the Ph I clinical trial of YH002, infusion-related reactions and pyrexia were not observed among the 13 subjects enrolled.

Summary of clinical trial:

Biocytogen is currently conducting a Ph I dose escalation clinical trial of YH002 as a single agent in patients with advanced solid malignancies in Australia. Preliminary data from the Ph I clinical trial showed that YH002 has a favorable safety profile.

Trial design & status: The trial is a multicenter, open-label, dose escalation Ph I study to evaluate the clinical safety, tolerability and PK of YH002 in approximately 48 subjects with

advanced solid tumor. An initial accelerated titration followed by a traditional 3+3 dose escalation algorithm will be utilized to determine the MTD and/or RP2D. As of the data cut-off date of 31 May 2022, 15 subjects were enrolled and treated at 0.01 mg/kg (n=1), 0.03 mg/kg (n=1), 0.1 mg/kg (n=1), 0.3 mg/kg (n=3), 1 mg/kg (n=3), 3 mg/kg (n=3) and 2 mg/kg (n=3).

Safety data: As of the data cut-off date of 31 May 2022, one case of DLT was observed in the 3.0 mg/kg dose group. Seven subjects (46.7%) had 25 drug-related AEs of any level, including three subjects had drug-related SAE, diarrhea, enteritis and pneumonitis, all subjects received YH002 3mg/kg on CID1. Six cases of Grade 2 AEs, such as fatigue, pneumonitis, diarrhea and vomiting. There was no death due to drug-related AE.

Clinical development plan:

Biocytogen has received IND approvals from the NMPA and the FDA for Ph I trial of YH002 as a single agent in China and the US. The Company plans to conduct a clinical trial of YH002 in combination with YH001 in patients with advanced solid tumors in China and Australia. Biocytogen may conduct a Ph II MRCT to evaluate YH002 in combination with YH001 for the treatment of soft tissue sarcomas, SCLC and other solid tumor indications in China, the US, Australia and potentially, other countries or regions.

YH004, a potential best-in-class agonistic mAb targeting 4-1BB (IgG1)

YH004 is a humanized IgG1 anti-4-1BB Agonists. Biocytogen has initiated a Ph I clinical trial of YH004 in Australia and has completed the dosing of the FPI in Dec 2021.

Competition landscape of 4-1BB antibodies:

According to F&S, anti-4-1BB monoclonal antibodies are currently being developed for treatment of multiple indications such as lymphoma, nasopharyngeal carcinoma, ovarian cancer and other solid tumors globally. Combination therapies of anti-4-1BB mAbs with immune checkpoint inhibitors such as PD-1 and PD-L1 have become a global trend.

Figure 30: Global status of clinical-stage anti-4-1BB antibody candidates as of Jul 2021

Drug name	Company	Type of treatment	Indication	Highest phase	First post	Location
ADG106	Adagene	Toripalimab (PD-1)	Advanced solid tumor, R/R NHL	Ph 1b/2	Jan-21	China
		Mono	Advanced solid tumor	Ph 1	Oct-18	US
Utomilumab (PF-05082566)	Pfizer	MK-3475 (PD-L1)	Advanced solid tumor	Ph 1	Jul-14	US
ATOR-1017	Alligator Bioscience	Mono	Advanced solid tumor	Ph 1	Oct-19	Sweden
AGEN2373	Agenus	Balstilimab (PD-1)	Advanced solid tumor	Ph 1	Oct-19	US
LVGN6051	Lyvgen Biopharma	Pembrolizumab (PD-1)	Advanced tumor	Ph 1	Oct-19	US
		Pembrolizumab (PD-1)	Advanced tumor	Ph 1	Feb-21	China
CTX-471	Compass Therapeutics	Mono	Advanced solid tumor	Ph 1	Mar-19	US

Source: ClinicalTrials, CDE, F&S, CMBIGM

Clinical development plan of YH004:

Biocytogen has initiated a Ph I clinical trial of YH004 in Australia and has completed the dosing of the first patient in Dec 2021. The Ph I trial is a first-in-human, multi-center, open-label, dose escalation study of YH004 as a single agent and YH004 + Toripalimab in subjects with advanced solid tumors or relapsed/refractory NHL. As of 13 Aug 2022, the

Company has completed first cohort at 0.01mg/kg (N=1) and second cohort at 0.03mg/kg (N=1). As of the data cut-off date of 31 May 2022, DLT was not observed in 0.01 mg/ kg and 0.03 mg/kg cohorts. Eight SAE occurred but none of them was drug-related. We have completed first cohort at 0.01mg/kg (N=1), second cohort at 0.03mg/kg, and third cohort at cohort 0.1mg/kg (N=3).

Biocytogen is also applying for a Ph I clinical trial of YH004 in combination with Toripalimab in China, and has received the approval for the IND applications by the NMPA on 7 Jan 2022. Depending on the results of the Ph I clinical trial, a Ph II MRCT may also be conducted to evaluate YH004 + PD-1 for the treatment of solid tumors in China, the US, Australia and potentially, other countries or regions.

Pre-clinical stage candidates

In addition to clinical stage assets, Biocytogen has six drug candidates at pre-clinical stage, including YH008, YH009, YH006, YH010, YH012 and YH013. The Company is also exploring the development of innovative antibody drug for animals, including an anti-PD-1 canine mAb candidate at pre-clinical CMC stage for the treatment of animal tumors.

Figure 31: Biocytogen's pre-clinical stage candidates

候選藥物 Candidate		靶點 Target	聯合用藥 Combination	適應症 Indication	臨床前 Pre-clinical	IND	I期 Phase I	II期 Phase II	III期 Phase III	權益 Rights
臨床前候選藥物 Preclinical Drug Candidates	YH008	PD-1/CD40 (雙抗) PD-1/CD40 (bispecific antibody)		實體瘤 Solid tumors	CMC					全球 Global
	YH006	CTLA-4/OX40 (雙抗) CTLA-4/OX40 (bispecific antibody)		實體瘤 Solid tumors	CMC					全球 Global
	YH009	RSV		預防／治療RSV感染 Prevention/ Treatment for RSV infection	CMC					全球 Global
	YH010	PD-L1/IL12		實體瘤 Solid tumors	藥物發現 Discovery					全球 Global
	YH011	PD-L1／細胞因子 PD-L1/cytokine		實體瘤 Solid tumors	藥物發現 Discovery					3
	YH012	TROP2/HER2 雙抗ADC TROP2/HER2 bispecific antibody ADC		實體瘤 Solid tumors	CMC					全球 Global
	YH013	MET/EGFR 雙抗ADC MET/EGFR bispecific antibody ADC		實體瘤 Solid tumors	CMC					全球 Global

註： 核心產品 Core Product　合作開發藥物 Co-development　已授權轉讓藥物 Out-licensing　腫瘤管線 Oncology　非腫瘤管線 Non-oncology
Notes:

Source: Company data, CMBIGM
Notes: Biocytogen is entitled to collect licensing fee from GeneQuantum for PD-L1 antibody and co-own the IP rights

YH008, a potential first-in-class anti-PD-1/CD40 bi-specific antibody: YH008 is an anti-PD-1/CD40 bi-specific antibody for the treatment of solid tumors. YH008 activates CD40 while simultaneously inhibiting PD-1. The results of in vitro and in vivo experiments show that the activation of the CD40 pathway by YH008 depends on the cross-linking effect of PD-1, avoiding non-specific activation outside the tumor microenvironment. YH008 is currently at CMC stage.

YH009, an innovative mAb for the prevention and treatment of RSV infection: YH009 is an innovative monoclonal antibody developed for the prevention and treatment of RSV infection. YH009 demonstrates a strong neutralization effect on RSV and a good binding affinity with the F protein of different RSV subtype strains. YH009 is currently at CMC stage.

***YH006, a CTLA-4/OX40 bi-specific antibody*:** YH006 is currently at CMC stage, which is for the treatment of solid tumors. YH006 simultaneously binds both CTLA-4 and OX40 to enhance the antineoplastic activity while at the same time decreasing the adverse effects

of immunotherapy. Biocytogen expects to submit the IND applications in the next 12 to 18 months.

YH010, a fully human PD-L1/IL-12 bi-specific antibody: YH010 simultaneously activates the IL-12 signaling pathway while inhibiting PD-L1 binding to PD-1. YH010 also has the potential to further enhance the specific killing activity of T cells by tethering IL-12R positive T cells with PD-L1 positive tumor cells. YH010 is currently at discovery stage, and Biocytogen expects to submit the IND applications in the next 18 to 24 months.

YH012 and YH013, bi-specific ADCs developed via RenLite platform: YH012 and YH013 are intended for the treatment of solid tumor, and the two drugs are currently at discovery stage. Bi-specific ADCs can be used to effectively target two tumor-associated antigens and deliver the payload specifically to tumor cells, which overcomes the non-tumor cytotoxicity of traditional ADC drugs. YH012 and YH013 are currently at discovery stage, and Biocytogen expects to submit the IND applications in the next 12 to 18 months.

Out-licensed product candidates

YH005, out-licensed to RemeGen for developing Claudin 18.2 ADC (RC118): YH005 is an anti-Claudin 18.2 antibody generated using Biocytogen's Claudin 18.2 knock-out mice, which global rights has been transferred to RemeGen in 2017. RemeGen has developed a potentially first-in-class Claudin18.2 ADC, RC118, based on YH005. To date, RC118 has obtained TGA approval for clinical trials in Australia and is currently under IND application process in China.

Pursuant to the agreement, Biocytogen is responsible for providing anti-Claudin 18.2 antibody and pre-clinical support to RemeGen, and is entitled to upfront payment and milestone payment for total RMB50mn and royalties for ex-China revenue of RC118. Currently, Biocytogen has received RMB15mn as upfront payment after delivering all related antibody and data in Oct 2017, RMB25mn after RC118 received IND approval in Oct 2021, and will receive RMB10mn after BLA approval is obtained. When the first international licensing or transfer of RC118 occurs, Biocytogen shall be entitled to no more than 10% of the revenue obtained by RemeGen through the licensing or transfer.

YH011, out-licensed to GeneQuantum to co-develop PD-L1/cytokine bifunctional molecules: YH011 is PD-L1/cytokine bifunctional molecules, which is currently at discovery stage and is expected to qualify for IND application in the next 15-18 months. On 20 Nov 2020, Biocytogen entered into an exclusive agreement which out-licensed its PD-L1 antibody to GeneQuantum to co-develop PD-L1/cytokine bifunctional molecules globally.

Pursuant to the agreement, Biocytogen is responsible for the in vivo and in vitro screening as well as the pre-clinical efficacy study of PD-L1/cytokine bifunctional molecules. GeneQuantum is responsible for CMC development, safety evaluation and IND application in China. Biocytogen is entitled to an upfront payment of RMB5mn after the agreement is in force, 16.7% of the interest of the PD-L1/cytokine bifunctional molecules during the IND stage and before its IND approval and 10% royalties for third parties out-licensed revenue before IND filing stage. The two companies co-own the intellectual property rights and share the interests of YH011.

Fast growing pre-clinical research service business

Biocytogen's pre-clinical research services primarily include services related to 1) gene editing, 2) preclinical pharmacology and efficacy evaluation, 3) animal models selling. In past years, pre-clinical research services contributed the majority of the Company's revenue.

Leading gene editing platforms

Advanced gene editing technologies

Biocytogen has developed powerful gene editing platforms, including SUPCE, CRISPR/EGE, and ESC/HR. Compared with other common gene editing technologies that can only edit gene fragments of less than 30,000 bases at a time using plasmid, Biocytogen's unparalleled in-house developed SUPCE technology allows megabase-scale chromosomal editing. Developed based on the CRISPR/Cas9 gene targeting platform, Biocytogen's innovative Extreme Genome Editing (EGE) system is site-specific, while ~20-fold more efficient than CRISPR/Cas9, at knocking in DNA fragments. Moreover, Biocytogen has also mastered Embryonic Stem Cell/Homologous Recombination (ESC/HR) platform, based on years of accumulation.

Figure 32: Biocytogen's gene editing platforms

Editing technology	Description	Biocytogen's advantages	Model	Service term
Size-unlimited and Precise Chromosome Engineering System (SUPCE) technology	SUPCE is a genetic manipulation technique for targeted modification of genomic DNA at megabase scale. It can break the limitation of gene length by other common gene editing techniques using plasmid and realize the modification of large segments (Mb (Mega base pair) level) of gene clusters, which can be used for special purposes such as humanized mouse preparation.	Achieved Mb (Mega base pair) level ultralong chromosome fragment transformation, and can improve success rate of germline transmission.	Mouse	Internal use, no external gene editing services
CRISPR/EGE-based gene editing technology	This technology is developed and optimized on the basis of CRISPR/Cas9 principles, which greatly improves the efficiency of homologous recombination and more convenient.	Biocytogen's EGE technology can improve homologous recombination efficiency by approximately 20x, making gene editing faster and more convenient. Biocytogen's EGE technology can precisely edit DNA sequences at almost any genomiclocus, which is ideal for preparing a variety of gene editing animal models.	Rat/Mouse	6~8 months
ESC/HR-based gene editing technology	Through the principle of DNA homologous recombination, targeted gene-edited embryonic stem cells are obtained, which depend on cellular totipotency to develop into mouse models with the desired genotype.	Biocytogen's self-developed C57BL/6 ES cell demonstrated germline transmission capabilities for more than 70 generations.	Mouse	7~11 months

Source: Company data, CMBIGM

Leveraging advanced gene editing technologies, Biocytogen has completed ~3,500 customized gene editing projects for clients and self-developed ~2,500 gene edited animal and cell models. The Company's clients include research institutes, academic institutions and pharmaceutical companies engaged in basic life science research and new drug development, based in China and abroad.

Customized gene editing services

Biocytogen mainly provides customized gene editing services based on rat/mouse and cell lines. The final products include 1) animal or cell line models with specific genotypes, 2) genotype detection reports and project closure reports, and 3) gene editing experimental services (such as sgRNA plasmid construction and sgRNA activity detection).

Animal-based gene editing services. Biocytogen provides customized gene editing services for rat/mouse using mature and stable ESC/HR-based and CRISPR/ EGE-based gene editing technologies. The Company performs gene editing modification based on several rat/mouse strains (mouse strains mainly include C57BL/6, BALB/c, DBA2 and NOD-scid; rat strains mainly include Sprague Dawley and Wistar).

Cell line based gene editing services. Biocytogen provides a variety of cell line gene editing services using ESC/ HR-based and CRISPR/EGE-based gene editing technologies. Compared with gene editing animal models, cell line models have the advantages of convenience, short cycle time and low cost.

Gene editing experimental services. 1) sgRNA plasmid construction: Biocytogen provides sgRNA plasmid construction services to ensure CRISPR/Cas9 gene editing under high specificity and high activity conditions, 2) sgRNA activity assay: Biocytogen independently developed a UCA assay for sensitive, convenient and high throughput in vitro determination of sgRNA activity to screen out highly active sgRNAs for gene editing, 3) donor plasmid construction: Biocytogen provides targeting vectors for ESC/HR-based and CRISPR/EGE-based gene editing and vector construction services for Tol2 transgenesis.

Integrated pre-clinical pharmacology and efficacy evaluation capabilities

Biocytogen's pharmacology team (based in China and the US) has built significant expertise in testing novel therapeutics for various diseases, in supporting drug discovery and development worldwide. The Company's services utilize a large collection of genetically humanized mouse models for checkpoint inhibitors and cytokine/cytokine receptors, highly immune-deficient B-NDG mice and their variants, including CDX (cell derived xenograft) models and engineered cell line models, among others. Biocytogen's pharmacology services include in vivo efficacy, PK/PD, biomarker assessments, toxicology and safety evaluation, in vitro immune cell and cytokine profiling and cell functional assays.

***In vivo* pharmacology capabilities**

Biocytogen's *in vivo* pharmacology team has successfully developed and validated hundreds of syngeneic and xenogeneic tumor models, including internally generated humanized mice and cell lines carrying functional human genes. Employing the humanized cell lines and the humanized mice results in a tailored therapeutic strategy with a complete biology to evaluate the efficacy of different types of human therapeutic molecules against the therapeutic targets of interest. Furthermore, tumor cell implantation through different routes including orthotopic injection delivers favorite translatable data to support clinical studies.

All these models cover broad immune-therapeutic areas and greatly increase translation from pre-clinical research to clinical studies for drug development. Besides the tumor models, *in vivo* pharmacology services have also developed several translatable immune and autoimmune inflammatory disease models and metabolic disease models in both wild-type and humanized mice.

Biocytogen's model-based *in vivo* efficacy services have high throughput screening capabilities to support lead molecule selection, best-in-class drug comparison, or first-in-class drug evaluation by *in vivo* activity assessment. Complementary its *in vivo* capabilities, the Company's *in vitro* pharmacology services include immune cell profiling, cytokine profiling, primary T, NK, and macrophage cell-based functional assays, among others. The integrated *in vivo* capabilities and *in vitro* pharmacology capabilities enable Biocytogen to provide a complete PoC and MoA for drug development.

Pharmacokinetics (PK) & Pharmacodynamics (PD)

Since human antibodies have different affinities to the targets, and FcRn expressed in animal species differ from that expressed in human, the PK profile of human antibodies from animals may not be translatable to human. Biocytogen's humanized mice could express human therapeutic targets, and FcRn humanized mice enable more translatable evaluation of human antibody PK in mice. Due to the growing limited availability of non-human primates, humanized mice may have increased value in non-clinical PK and toxicity studies for biologic drug development.

Utilizing target humanized mice and FcRn humanized mice, Biocytogen has established a comprehensive PK/PD service platform to support drug development and clinical trials. The PK/PD evaluation is also supported by its *in vitro* capabilities including human IgG antibody ELISA detection SOPs, bi-specific antibody ELISA SOPs, MSD platform for more sensitive and accurate measurement of drug's concentration. Also, cell-based assays including antibody-dependent cytotoxicity (ADCC) and complement-dependent cytotoxicity (CDC) assist with ex vivo or *in vitro* PD evaluation and identification of the MoA.

Small animal toxicology and safety study

Humanized mice can provide favorite translatable results in the toxicology and safety evaluation of drug candidates and are recommended by the FDA. Biocytogen has established toxicology and safety evaluation platforms using humanized mice and highly immune deficient B-NDG mice. The Company's comprehensive toxicology and safety readouts include blood biochemistry liver and renal function evaluation, histopathology evaluation, cytokine release syndrome (CRS) evaluation, anti-drug antibody (ADA) test and more. As of 13 Aug 2022 Biocytogen has completed over 500 drug evaluation projects for more than 200 partners worldwide.

Comprehensive animal model platform

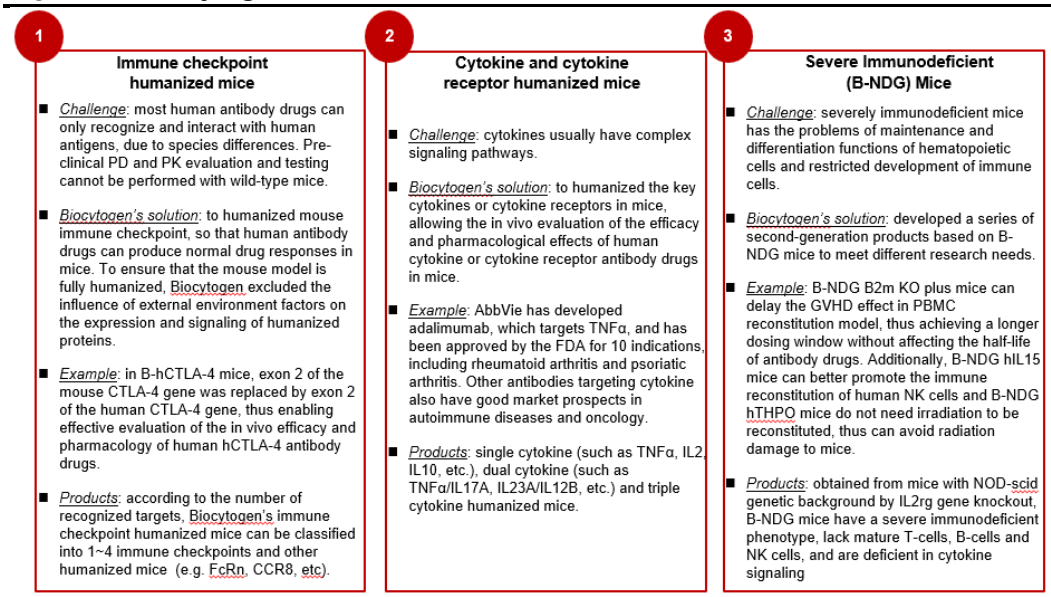
Biocytogen has created the most comprehensive set of antibody discovery and disease mouse models worldwide (~2,500 gene-edited mouse/cell line projects). The combination of an extensive portfolio of animal models and large-scale animal production and in vivo efficacy studies has enabled Biocytogen to conduct large-scale in vivo antibody discovery and screening for its internal pipeline as well as providing disease animal models and in vivo pharmacology services to biotechnology and large pharmaceutical company clients worldwide.

The Company also established world-class model animal production centers, including three animal facilities encompassing a total of ~55,500 square meters of animal facilities, with annual supply capacity of 800,000 gene edited mice. Moreover, as of 13 Aug, Biocytogen has a team of more than 380 members focusing on the feeding, research and development of animal models.

Biocytogen's animal models mainly consist of 1) disease models and 2) research models:

Disease models that mimic human pathological environments through the modification of key genes are essential tools in the current drug development process. Drug evaluations using these models are considered the “gold standard” for validating the efficacy of pre-clinical drugs. Based on the gene editing humanized mouse model, Biocytogen has developed mouse models for tumor and autoimmune diseases, which are used for gene function research and drug development. In addition to tumor and autoimmune diseases, Biocytogen is further expanding the disease areas of animal models, such as neurological, cardiovascular and metabolic diseases, to provide preclinical in vivo and in vitro drug efficacy testing for drug development.

Figure 33: Biocytogen’ disease mouse models



Source: Company data, CMBIGM

In order to solve the problems of maintenance and differentiation functions of hematopoietic cells and restricted development of immune cells in severely immunodeficient mice, Biocytogen has also developed a series of second-generation products based on B-NDG mice to meet different research needs. For example, B-NDG B2m KO plus mice can delay the GVHD effect in PBMC reconstitution model, thus achieving a longer dosing window without affecting the half-life of antibody drugs. Additionally, B-NDG hIL15 mice can better promote the immune reconstitution of human NK cells and B-NDG hTHPO mice do not need irradiation to be reconstituted, thus can avoid radiation damage to mice.

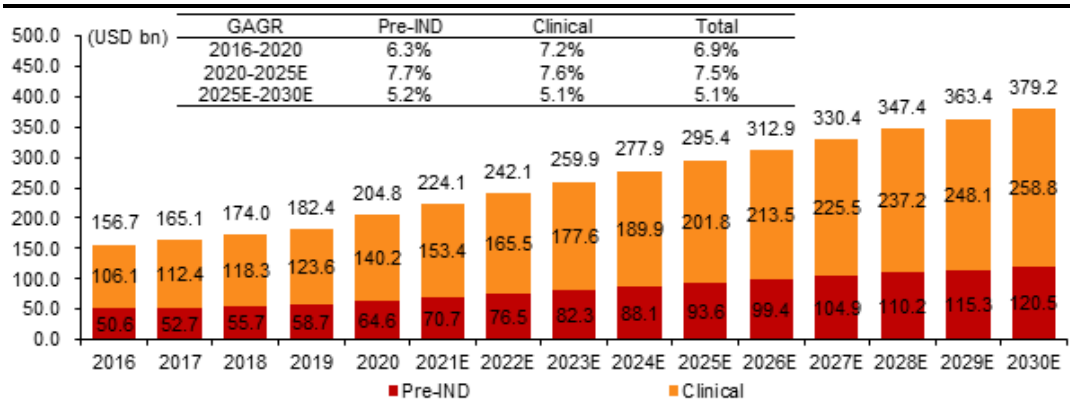
Overview of pharmaceutical research & development

Overview of pharmaceutical R&D expenditure

The research and development of biologics can generally be divided into the following stages: pre-IND stage (drug discovery stage and pre-clinical study stage), clinical trials stage and post-market research stage.

Global pharmaceutical research and development expenditure increased from US$156.7bn in 2016 to US$204.8bn in 2020, representing a CAGR of 6.9%, and is expected to increase to US$295.4bn in 2025E, representing a CAGR of 7.6%, and to further increase to US$379.2bn in 2030E, representing a CAGR of 5.1%. Pre-IND stage expenditures were US$64.6bn in 2020, and is expected to increase to US$93.6bn in 2025E, representing a CAGR of 7.7%, and to further increase to US$120.5bn in 2030E, representing a CAGR of 5.2%.

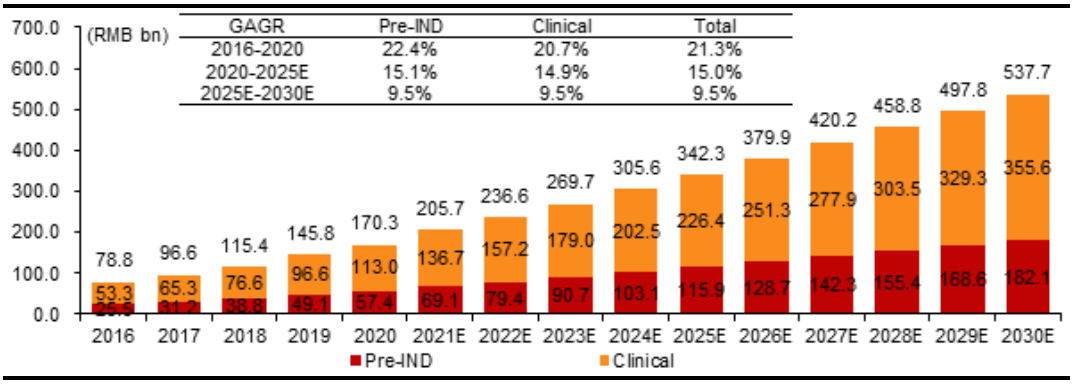
Figure 34: Global pharmaceutical R&D expenditure by Pre-IND and Clinical, 2016-2030E



Source: F&S, CMBIGM

Pharmaceutical research and development expenditure in China increased from RMB78.8bn in 2016 to RMB170.3bn in 2020, representing a CAGR of 21.3%, and is expected to increase to RMB342.3bn in 2025E, representing a CAGR of 15.0%, and further increase to RMB537.7bn in 2030E, representing a CAGR of 9.5%. Research and development expenditures in the pre-IND stage was RMB57.4bn in 2020, and is expected to increase to RMB115.9bn in 2025E, representing a CAGR of 15.1%, and to further increase to RMB182.1bn in 2030E, representing a CAGR of 9.5%.

Figure 35: Pharmaceutical R&D expenditure by Pre-IND and Clinical in China, 2016-2030E



Source: F&S, CMBIGM

Overview of antibody research and development market

Advantages of fully human antibody mouse

Phage display technology and fully human antibody mouse platform technology are the two main technologies currently used to produce fully human antibodies. Different from phage display technology, the fully human antibody mouse platform technology introduces human immunoglobulin gene sequences into the genome of a gene-edited mouse model, allowing the mouse's immune system to naturally produce a diverse range of human antibodies. This technology results in a wider variety of antibodies that are non-immunogenic in humans and have higher affinity, stability, solubility and other drug-forming properties. According to F&S, approximately 70% of fully human mAbs have been derived from mouse platform technology.

Figure 36: Comparison of two technology platforms for producing human antibody

Technology	Companies	Advantages	Disadvantages
Phage display technology	Cambridge Antibody Technology (CAT) MorphoSys Dyax	Fast screening	Produces low-affinity antibodies
		Automated	Involved in intellectual property disputes
		Generate multiple target screens simultaneously	Inappropriate for difficult-to- express antigens
		Generates diverse antibodies	
Fully humanized mouse	Cell Genesys/ Abgenix GenePharm/ Medarex Genmab	Fast optimization (*in vivo* optimization)	May be biased: all antibodies produced are directed against only one region of the antigen
		Produces high-affinity antibodies	Only one target at a time
		No need for "humanization"	Difficult to automate
		Production flexibility	Unsuitable for antigens with weak immunogenicity
		Easy transition from R&D to production	

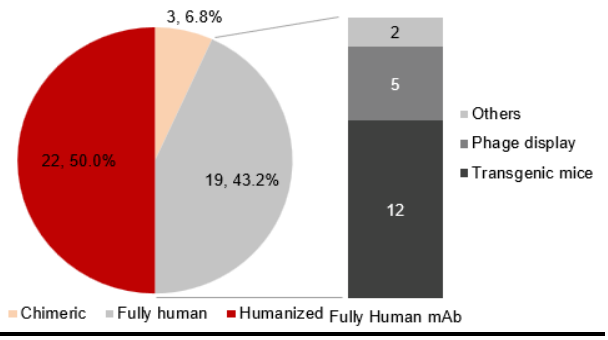
Source: F&S, CMBIGM

Antibodies approved by FDA and NMPA

Out of the 44 innovative monoclonal antibodies approved by the FDA from 2016 to June 2021, 19 are fully human mAbs, accounting for 43.2% of the total mAbs approved. As fully human antibodies have lower immunogenicity as compared to murine, chimeric or humanized mAbs, it is likely the preferred type of monoclonal antibody-drug going forward.

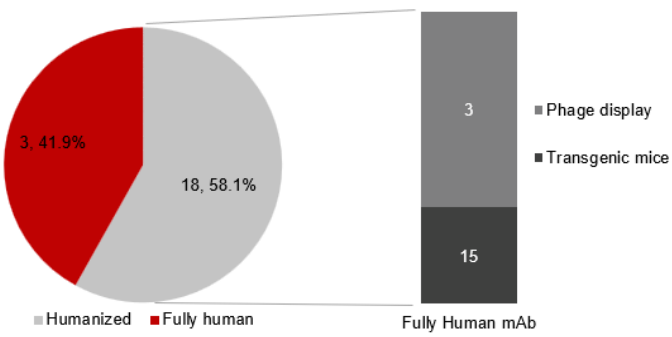
Among fully human innovative mAbs, transgenic mice technique is the major technique. 12 innovative conventional fully human mAb drugs have been developed by transgenic mice. In China, 18 out of the 31 innovative monoclonal antibodies approved by the NMPA from 2016 to Jun 2021 are fully human antibodies, accounting for 58.1% of the total.

Figure 37: FDA approved antibody drugs, 2016-2021



Source: FDA, F&S, CMBIGM

Figure 38: NMPA approved antibody drugs, 2016-2021



Source: NMPA, F&S, CMBIGM

Notes: 1) By July 2021, 2) Only innovative conventional mAb drugs are included, not including approved biosimilars, BsAb drugs, ADCs, fusion proteins, 3) Others: Aduhelm and Ebanga were derived by single B cell.

R&D strategies for fully human mouse

Gene editing technology of fully human transgenic mouse can be divided into random insertion and in situ replacement. Random insertion has the advantages of being fast, convenient and relatively low cost, but there are many disadvantages and uncertain factors. In situ replacement has the advantages of high accuracy and few uncertainties, but takes longer and has relatively higher costs.

Figure 38: Advantages and disadvantages of random insertion and in situ replacement

Technology	Advantages	Disadvantages
Random insertion	• Fast, convenient and low cost.	The risk of random insertion is relatively high and there are many uncertain factors: • When multiple insertions occur, much unnecessary protein will be produced. • Insertion into critical genes could be lethal, infertility or tumorigenesis in mice models. • If insertion occurs in a non-functional area, the mice model will be invalid; If insertion occurs in functional regulation genes, the model will not be as effective as expected. • It may affect the expression of changed genes or/and original endogenous genes.
*In situ R*eplacement	• High accuracy and few uncertainties. • Mice's original genomic environment is preserved, such as 3' end enhancer, regulatory region between J and C domain, and other regulatory regions which not yet been fully studied. Thus, mice antibody genes' regulatory functions are preserved maximally that ensure normal production of antibodies.	• High cost and cumbersome • It takes a lot of time to screen the correctly gene humanized cell clones.

Source: F&S, CMBIGM

Currently, only three transgenic engineering platforms are using in situ replacement technology worldwide.

Figure 39: Global competitive landscape of in situ replacement technology platforms

Platform	Company	Characteristics
RenMab	Biocytogen	• Mouse constant region remains to ensure normal immune cell population, development and maturation. • Mouse variable region is deleted. • Full human heavy chain and κ light chain V(D)J loci substitution in situ. The gene regulation is as similar as that of human as possible.
VelocImmune	Regeneron	• Mouse constant region is preserved to ensure normal immune cell population, development and maturation. • Mouse variable region is deleted. • The variable region sequence of the human antibody genes introduced into mice is not 100% complete, κ light chain contains only one Vκ copy of human.
Kymouse	Kymab	• Mouse constant region is preserved to ensure normal immune cell population, development and maturation. • Mouse variable region is inactivated by inversion rather than deletion. Some of the antibodies produced may still contain the mouse peptide sequence. • The variable region sequence of the human antibody genes introduced into mice is not 100% complete, a proximal and a distal Vκ copy of human genes introduced into κ light chain.

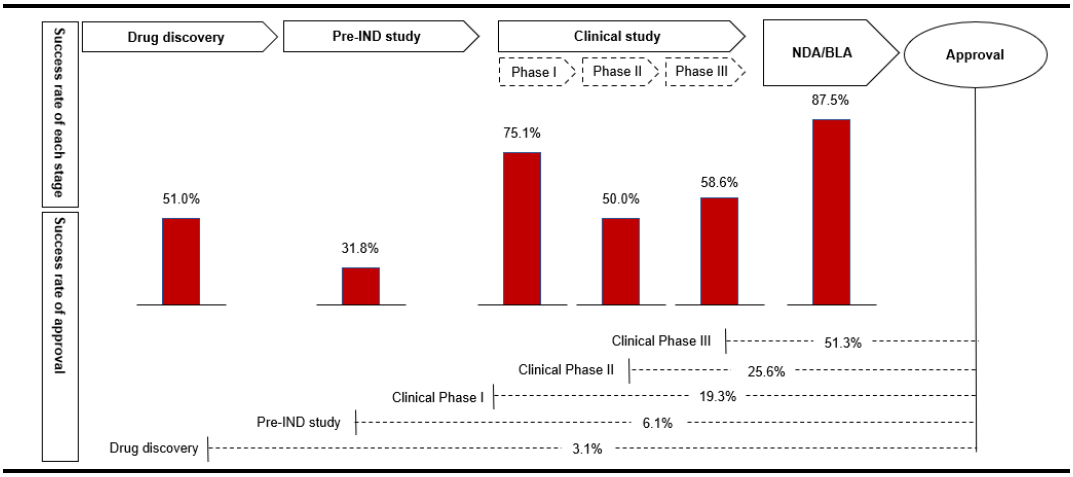
Source: F&S, CMBIGM

Overview of antibody drug development market

Antibody drug R&D process and success rate

Antibodies' development and approval is time- and resource-consuming. According to F&S, it takes ten years or more to bring a drug to the market at a cost of US$2.6bn, on average. The later the candidate drug fails, the more time and resources are wasted.

Figure 40: Success rate in each stage of antibody drug R&D



Source: F&S, CMBIGM

The pain points of antibody development mainly include:

1) The choice of target. Targets of antibodies approved are relatively few, mainly focusing on TNF, PD-1/ L1, VEGF, and EGFR, and other popular targets with complete basic scientific research. Moreover, the selection of targets under research are relatively concentrated, such as VEGF, PD-1 and TNF, with relatively good drug ability.

2) Bispecific antibody. Rational target selection determines the MOA of bsAb and is the most important step for success. However, lowering the off-target toxicity is still the pain point in target selection of bsAb development. Secondly, the safety and effectiveness of the two targets need to be balanced and coordinated in bsAb development. In general, the conventional animal models are difficult to evaluate bsAb candidates since they have different target binding characteristics than humans. These difficulties in pre-clinical evaluation models increase the difficulties of evaluating the rationality of the target design. Finally, bsAb is mainly formed by combining two different H chains and two different L chains. This random combination method can produce 16 different combinations, of which only 12.5% shows the required double specificity as designed. Thus, it is difficult to isolate the bsAb candidates from 16 different combinations.

3) Experimental design. Experimental design defects include adopting a less rigorous design and having an insufficient understanding of disease mechanisms and pathways, which is very common in early drug development, especially for first-in-class drugs. Other issues include retrospective subgroup analysis and a wrong biomarker selection, as well as a wrong judgment of dose and an improper choice of administration method, or dosage form/excipients.

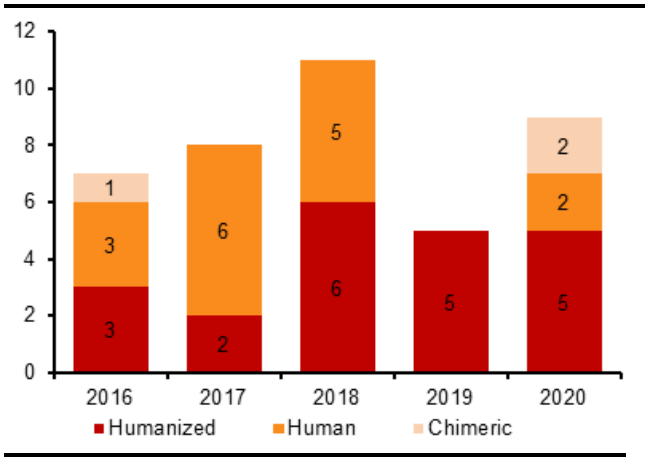
Antibodies approved by FDA and NMPA

Since the FDA approved the first mAb, Muromonab, in 1986, a total of 87 conventional mAbs have been approved by the FDA and 40 innovative conventional mAbs have been

approved from 2016 to 2020, accounting for 46.0% of the total. In recent years, the number of mAbs approved worldwide has been on the rise. In the past five years, the FDA has approved an average of 9.8 mAbs annually.

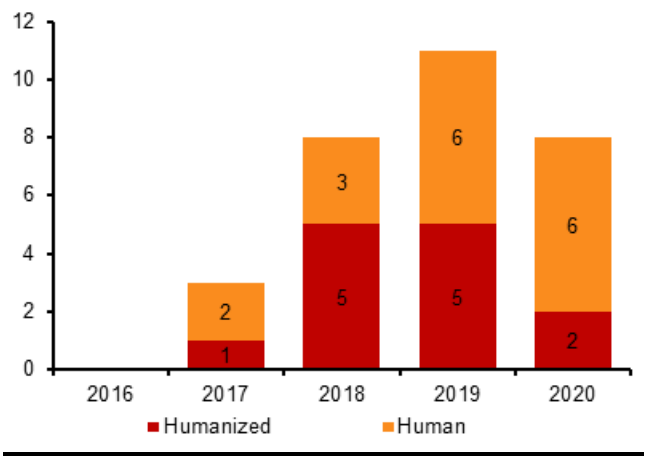
With increasing clinical demand and government support for biologics, the annual approval rate of biologics in China has been faster than ever. However, before 2018, mAbs accounted for only a small part of all approved biologics. In the past three years, the approval for mAbs has accelerated significantly. From 2016 to July 2021, the NMPA had approved 31 innovative monoclonal antibodies, including 18 fully human antibodies, which accounted for 58.1% of the total innovative mAbs approved.

Figure 41: Number of innovative mAbs approved by FDA, 2016-2020



Source: FDA, EMA, F&S, CMBIGM

Figure 42: Number of innovative mAbs approved by NMPA, 2016-2020



Source: NMPA, F&S, CMBIGM

Notes: Only innovative conventional mAb drugs are included, not including approved biosimilars, BsAb drugs, ADCs, fusion proteins.

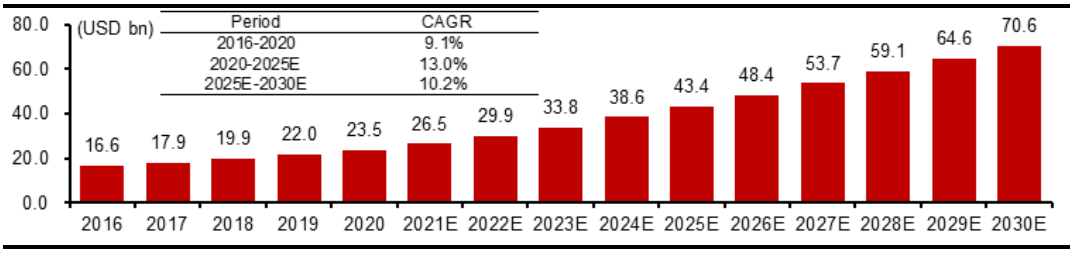
To reduce immunogenicity, the developing platforms of mAbs have undergone the process from murine to chimeric, humanized and fully human. As fully human antibodies carry a lower risk for inducing immune responses, it is expected that fully human is the future trend of mAbs. With the rapid development of DNA recombination technology, major breakthroughs have been made in antibody screening, scFc engineering and other aspects. The diversity of antibodies has been greatly enriched, such as bispecific antibody (BsAb), heavy chain antibody (HCAb) and single-chain variable fragment (ScFV). These diversified drug formats would be beneficial to suit respective functional needs. The development of antibodies is gradually developing towards humanization, functionalization, miniaturization, and specialization.

Overview of pre-IND CRO market

The pharmaceutical pre-IND CRO industry is mainly composed of CRO services prior to IND, which include drug discovery and pre-clinical services. Drug discovery is a systematical process that requires interdisciplinary efforts to design effective and commercially feasible drugs, and early drug discovery is the fundamental of drug discovery. It starts with initial steps of target identification and moves to the later stages of lead optimization. Pre-clinical CRO services include solution-based approaches by leveraging highly experienced program development directors and project managers to help guide strategic decisions and manage development in an integrated, streamlined manner, which help to improve success rate and reduce costs.

The pharmaceutical pre-IND CRO market is growing steadily. The global pharmaceutical pre-IND CRO market is expected to grow at a CAGR of 13.0% from 2020 to 2025E, and further grow at a CAGR of 10.2% from 2025E to 2030E, reaching approximately US$70.6bn in 2030E.

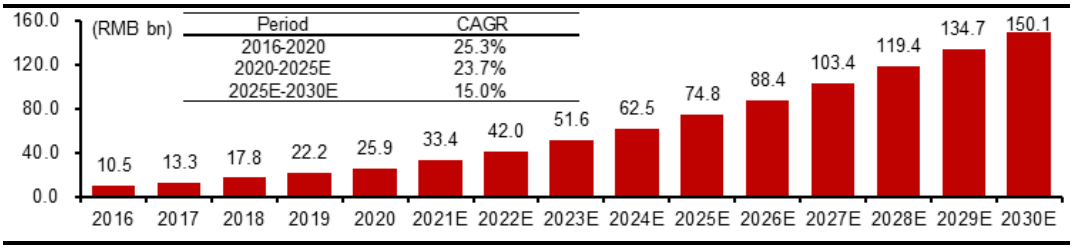
Figure 43: Global pre-IND CRO market, 2016-2030E



Source: F&S, CMBIGM

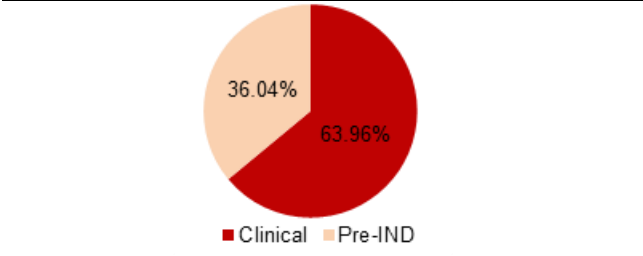
In China, the pharmaceutical pre-IND CRO market is expected to grow at a CAGR of 23.7% from 2020 to 2025E, and further grow at a CAGR of 15.0% from 2025E to 2030E, reaching approximately RMB150.1bn in 2030E.

Figure 44: Pre-IND CRO market in China, 2016-2030E



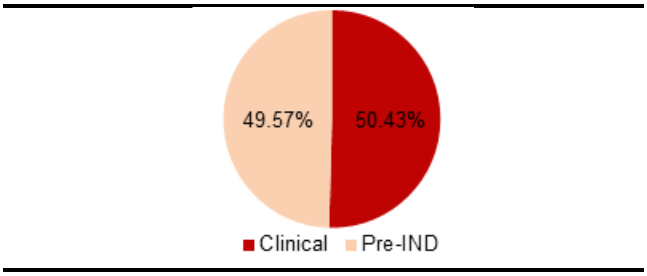
Source: F&S, CMBIGM

Figure 45: Global market share of pre-IND CRO market, 2020



Source: F&S, CMBIGM

Figure 46: Market share of pre-IND CRO market in China, 2020



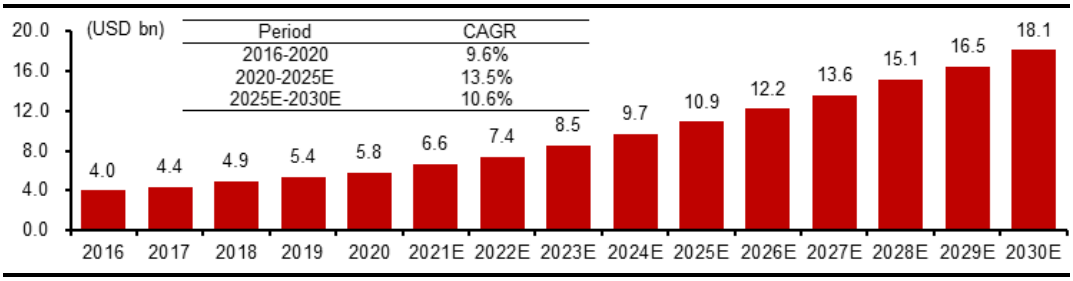
Source: F&S, CMBIGM

Overview of pre-IND pharmacological efficacy evaluation service market

Pre-IND pharmacological efficacy evaluation assesses the drug's therapeutic efficacy and toxicity through both *in vitro* and *in vivo* studies. It studies a drug's MOA, dose-effect relationship, time-effect relationship and efficacy characteristics through *in vivo* and *in vitro* experiments, as well as PD/PK tests that combine the characteristics of drug metabolism (to study the relationship between drug concentration and efficacy *in vivo*), including preliminary effectiveness tests to explore the therapeutic effect and dose-effect relationship for specific disease state and the main pharmacodynamic research to evaluate the therapeutic effect and action characteristics of drugs for specific disease state.

The pre-IND pharmacological efficacy evaluation service market is growing steadily. The global pre-IND pharmacological efficacy evaluation service market is expected to grow at a CAGR of 13.5% from 2020 to 2025E, and further grow at a CAGR of 10.6% from 2025E to 2030E, reaching approximately US$18.1bn in 2030E.

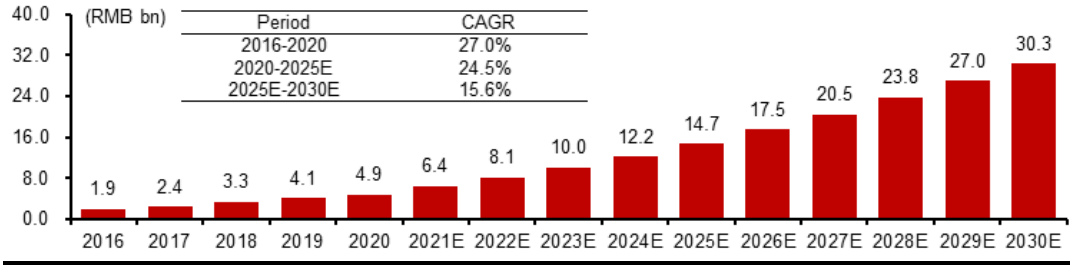
Figure 47: Global pre-IND pharmacological efficacy evaluation service market, 2016-2030E



Source: F&S, CMBIGM

In China, the pre-IND pharmacological efficacy evaluation service market is expected to grow at a CAGR of 24.5% from 2020 to 2025E, and further grow at a CAGR of 15.6% from 2025E to 2030E, reaching approximately RMB30.3bn in 2030E.

Figure 48: China pre-IND pharmacological efficacy evaluation service market, 2016-2030E



Source: F&S, CMBIGM

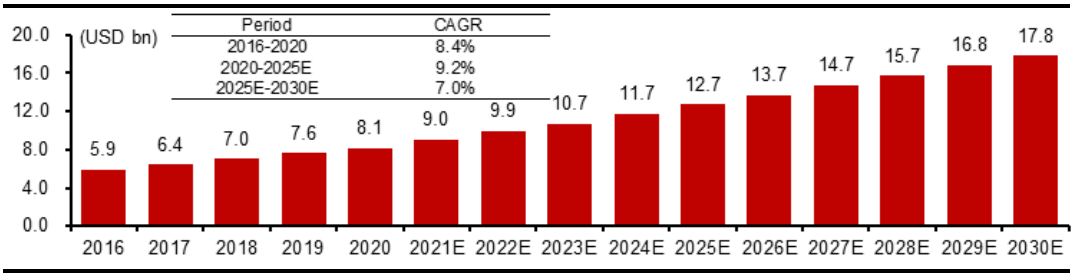
Overview of mice model market

Mice model created through gene editing and humanization serve as excellent research platforms for exploring the pathogenesis of special diseases and evaluating the efficacy of drug candidates at an early stage of drug development. Common disease mice models mainly include, 1) humanized mice with immune checkpoints (single, double, or triple immune points), 2) severe immunodeficiency (B-NDG) mice for use in human cell or tissue transplantation, tumor and tumor stem cell research, ES and iPS cell research, among

others, 3) cytokine humanized mice (single, double, or triple cytokine) and 4) other genetically modified mice.

The mice model market is growing steadily. The global mice model market is expected to grow at a CAGR of 9.2% from 2020 to 2025E, and further grow at a CAGR of 7.0% from 2025E to 2030E, reaching US$17.8bn in 2030E.

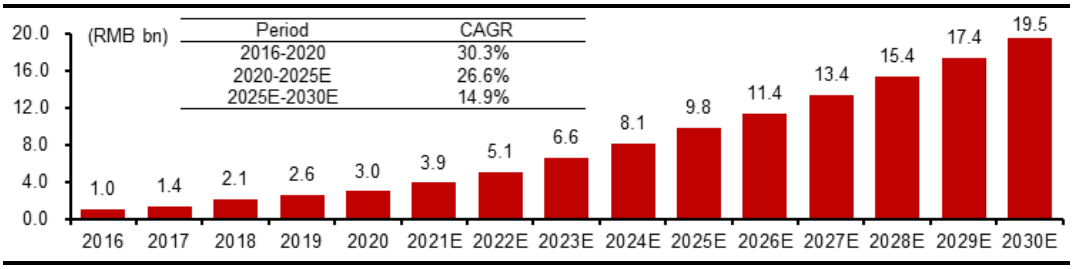
Figure 49: Global mice model market, 2016-2030E



Source: F&S, CMBIGM

In China, the mice model market size is expected to grow at a CAGR of 26.6% from 2020 to 2025E, and further grow at a CAGR of 14.9% from 2025E to 2030E, reaching RMB19.5bn in 2030E.

Figure 50: China mice model market, 2016-2030E



Source: F&S, CMBIGM

Figure 51: Competitive landscape of humanized mice model market

Company	Technology	Representatives
Biocytogen	• Developed on the C57BL/6 genetic background	• Humanized Immune-Checkpoint Mice • Humanized Cytokines Mice • Humanized GPCR Mice
Charles River	• NCG triple-immunodeficient mouse model	• Humanized CD34+ (huCD34) Mouse Models • Humanized PBMC (huPBMC) Mouse Models • Knock-in Humanized Mouse Models
CrownBio	• PDX Platform • HuPrime®, HuKemia®, HuBase™, HuMark™, HuTrial™, and HuSignature Platform.	• Hematopoietic Stem Cell (HSC)-PDX • MiXeno models • Human peripheral blood mononucleated cell (PBMC)-humanized mouse models
Cyagen	• CRISPR-Pro • TurboKnockout • ESC-Based Gene Editing • Transgenes	• Humanized immune checkpoint mouse models • Humanized pk/pd study mouse model
Taconic Biosciences	• CRISPR-cas	• Humanized Immune System Mouse Model
The Jackson Labatory	• NA	• Humanized CD34+ mice • JAX FcRn Model (huPBMC Mouse Model) • hu-NSG Mouse Model
Shanghai Model Organisms	• CRISPR-/CAS9 • Piggybac • ES Cell Targetting	• Humanized immune checkpoint mouse models • Humanized gene mouse models • Humanized immune deficient mouse model
GemPharmatech	• CRISPR/Cas9, TALEN, ZFN, ES	• Humanized Mouse Model

Source: Company Websites, F&S, CMBIGM

Figure 52: Competitive landscape of the animal models selling market in China

Company	Strain quantity	Application field	Hot strains	AAALAC
Biocytogen	Provide more than 2,500 gene-edited models.	Immune checkpoint humanized mice, severely immunodeficient (B-NDG) mice, humanized tumor cell lines, reporter gene cell lines, Cre tool mice, cytokine humanized mice.	• B-NSG severely immunodeficient mice • Immune checkpoint humanized mouse, Cytokine Humanized Mice and other humanized mouse	Yes
GemPharmatech	More than 14,000 lines in sale, more than 29,000 lines under research.	Tumor immune (CD3e humanized mice, immune checkpoint humanized mice, immunodeficiency/reconstruction), autoimmune disease, spontaneous tumor, neuropathy, neurodegenerative disease, tool mice (scissors mice), report mice, live gene-edited mice.	• B6/J Gpt • NCG • Nu • NOD-Scid • ICR • BALB/CJ	Yes
Shanghai Model Organisms	More than 3,000 finished mouse models.	Tumor, immune system, nervous system, blood system, reproductive system, cardiovascular, metabolism, aging, development.	• M-NSG severely immunodeficient mice • PD-1 humanized mice • PD-L1 humanized mice • Hemophilia mice	Yes
Cyagen	The "Red Rat" CRISPR-AI Knockout Mouse Resource Library contains 16,000 strains of knockout live mice.	Metabolic diseases, neuroscience, immunity and inflammation, tumors, m6A methylation modification and related diseases.	• Fgf21 Sirt3 Sirt5 Nfe2l2 Park2 Trem2 Ifnar1 Il17a Ythdf3 Ythdf1 knockout mice	Yes
Charles River	More than 20 common mouse strains.	Pharmacology and toxicology research, production and verification of drugs and biologicals, development of transgenic/gene knockout models. Heredity, development, blood, cardiovascular, nerve, metabolism, tumor, immunity.	• CD-1(ICR) IGS • NU/NU • C57BL/6N	Yes

Source: Company Website, F&S, CMBIGM

Overview of gene-edited animal customized service market

Gene-editing technologies allow the insertion, deletion or modification of DNA within a living organism, which can also be used to create animal models that replicate a particular diseased state, allowing more accurate assessment of drug safety and efficacy. The two main gene technologies on the global market include ES targeting technology and CRISPR/Cas9 technology. Compared with traditional CRISPR/Cas9, EGE technology can use fertilized eggs for genetic modification, so it is no longer limited to embryonic stem cells, which greatly broadens the application range of gene editing.

Figure 53: Competitive landscape of gene-edited customized service market

Company	Technology	Strategies
BioCytogen	• CRISPR/EGE™-based Gene Editing • ESC-Based Gene Editing • SUPCE Technology	• Conditional Knockout/Knockin • Conventional Knockout/Knockin • Point Mutation Knockin • rosa26 locus Knockin • Tag and Reporter Genes • Tol2 Transgenic
GemPharmatech	• CRISPR/Cas Platform	• Conditional Knockout/Knockin • Conventional Knockout/Knockin • Point Mutation Knockin
Shanghai Model Organisms	• CRISPR/Cas Platform • ESC-Based Gene Editing	• Conditional Knockout/Knockin • Conventional Knockout/Knockin • Point Mutation Knockin
Cyagen	• CRISPR-Pro • ESC-Based Gene Editing • TurboKnockout	• Conditional Knockout/Knockin • Conventional Knockout/Knockin • Point Mutation Knockin
Creative Biolabs	• CRISPR/Cas9 Platform	• Knock in/out services
AlstemBio	• CRISPR/Cas9 technology	• Permanent/ conditional knockout • Point Mutation/ insertion

Source: F&S, CMBIGM

Financial Analysis

Expect net profit breakeven in 2025E

We expect total revenue to grow 73%/ 43%/ 43% YoY to RMB613mn/ RMB879mn/ RMB1,253mn in FY22E/ 23E/ 24E, mainly driven by fast growth of its pre-clinical research services and antibody development business.

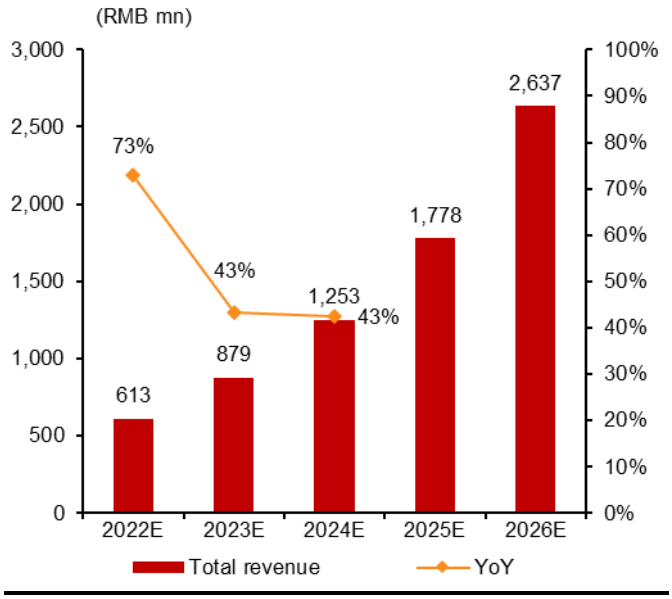
We expect pre-clinical pharmacology & efficacy evaluation, animal models selling and antibody development will contribute the majority of revenue during 2022-24E. Especially, we highlight the revenue growth of antibody development business may grow 151%/ 43%/ 45% YoY to RMB223mn/ RMB318mn/ RMB461mn in FY22E/ 23E/ 24E, respectively.

Figure 54: Revenue forecasts (2022-2026E)

(YE 31 Dec) (RMB mn)	2022E	2023E	2024E	2025E	2026E
Gene editing	**53**	**54**	**56**	**58**	**59**
YoY	*3%*	*3%*	*3%*	*3%*	*3%*
Pre-clinical pharmacology	**158**	**230**	**322**	**434**	**564**
YoY	*50%*	*45%*	*40%*	*35%*	*30%*
Animal models selling	**177**	**275**	**413**	**598**	**838**
YoY	*65%*	*55%*	*50%*	*45%*	*40%*
Antibody development	**223**	**318**	**461**	**597**	**783**
YoY	*151%*	*43%*	*45%*	*30%*	*31%*
Innovative drugs risk adj. revenue	**0**	**0**	**0**	**89**	**391**
YoY	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*
Others	**2**	**2**	**2**	**2**	**2**
YoY	*0%*	*0%*	*0%*	*0%*	*0%*
Total revenue	**613**	**879**	**1,253**	**1,778**	**2,637**
YoY	*73%*	*43%*	*43%*	*42%*	*48%*

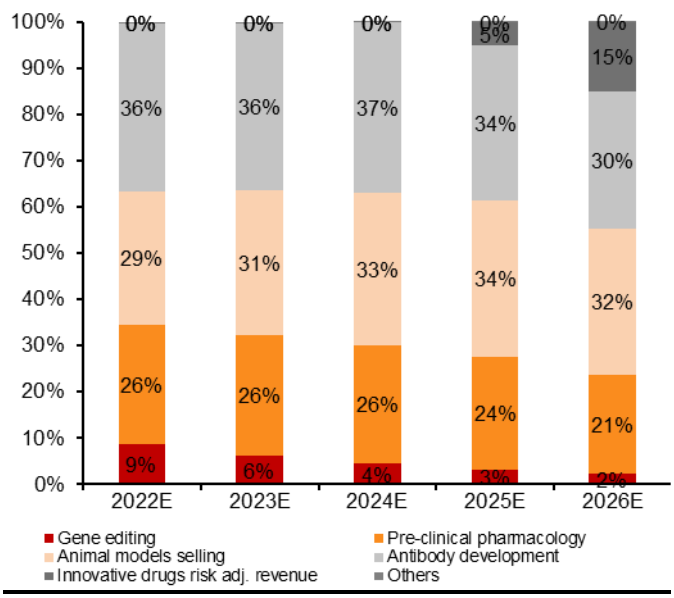
Source: Company data, CMBIGM estimates

Figure 55: Total revenue forecasts (2022-2026E)



Source: Company data, CMBIGM estimates

Figure 56: Revenue breakdown (2022-2026E)



Source: Company data, CMBIGM estimates

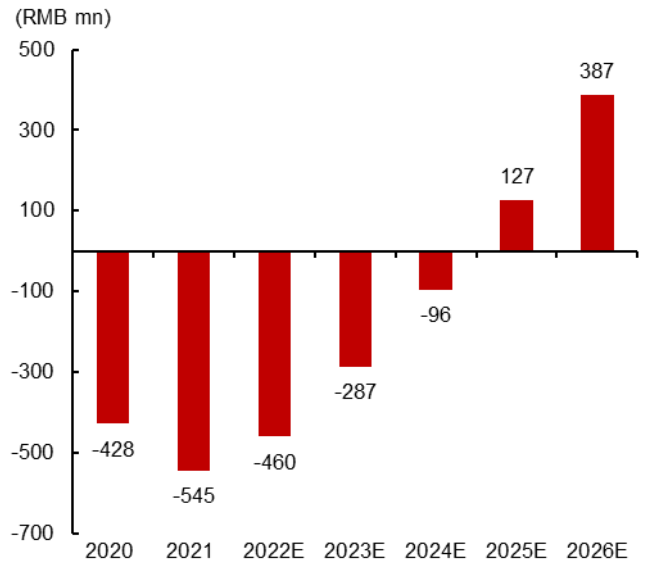
Biocytogen recorded attributable net losses of RMB428mn/ RMB546mn/ RMB272mn in 2020/ 2021/ 1H22. We expect its attributable net loss to gradually narrow to RMB460mn/ RMB287mn/ RMB96mn in FY22E/ 23E/ 24E and we expect the Company to generate net profit from FY25E.

Figure 57: P&L forecasts

(YE 31 Dec) (RMB mn)	2020	2021	2022E	2023E	2024E	2025E	2026E
Revenue	**254**	**355**	**613**	**879**	**1,253**	**1,778**	**2,637**
YoY	*49.3%*	*39.8%*	*72.9%*	*43.4%*	*42.5%*	*41.9%*	*48.3%*
Cost of services	-87	-107	-169	-232	-323	-448	-641
% of revenue	*-34.1%*	*-30.2%*	*-27.5%*	*-26.4%*	*-25.7%*	*-25.2%*	*-24.3%*
Gross profit	**167**	**247**	**444**	**647**	**930**	**1,330**	**1,996**
GPM	*65.9%*	*69.8%*	*72.5%*	*73.6%*	*74.3%*	*74.8%*	*75.7%*
General and administrative expenses	-245	-188	-215	-246	-288	-320	-422
% of revenue	*-96.8%*	*-53.1%*	*-35.0%*	*-28.0%*	*-23.0%*	*-18.0%*	*-16.0%*
Research and development expenses	-276	-558	-613	-571	-564	-622	-791
% of revenue	*-109.0%*	*-157.5%*	*-100.0%*	*-65.0%*	*-45.0%*	*-35.0%*	*-30.0%*
Selling & marketing expenses	-32	-42	-71	-101	-141	-193	-281
% of revenue	*-12%*	*-12%*	*-12%*	*-11%*	*-11%*	*-11%*	*-11%*
Other gains & losses, net	9	26	20	18	20	20	20
% of revenue	*3.5%*	*7.2%*	*3.2%*	*2.0%*	*1.6%*	*1.1%*	*0.7%*
Operating profit (loss)	**-358**	**-506**	**-435**	**-253**	**-43**	**215**	**522**
Finance costs	-23	-39	-25	-34	-53	-66	-66
% of revenue	*-8.9%*	*-11.1%*	*-4.2%*	*-3.9%*	*-4.3%*	*-3.7%*	*-2.5%*
Profit before tax	**-477**	**-546**	**-460**	**-287**	**-96**	**150**	**456**
Income tax expense	0	0	0	0	0	-22	-68
Total net profit	**-477**	**-546**	**-460**	**-287**	**-96**	**127**	**387**
Minority interests	-49	-0	0	0	0	0	0
Net profit attributable to shareholders	**-428**	**-546**	**-460**	**-287**	**-96**	**127**	**387**
NMP	*-168.9%*	*-153.8%*	*-75.1%*	*-32.7%*	*-7.7%*	*7.1%*	*14.7%*

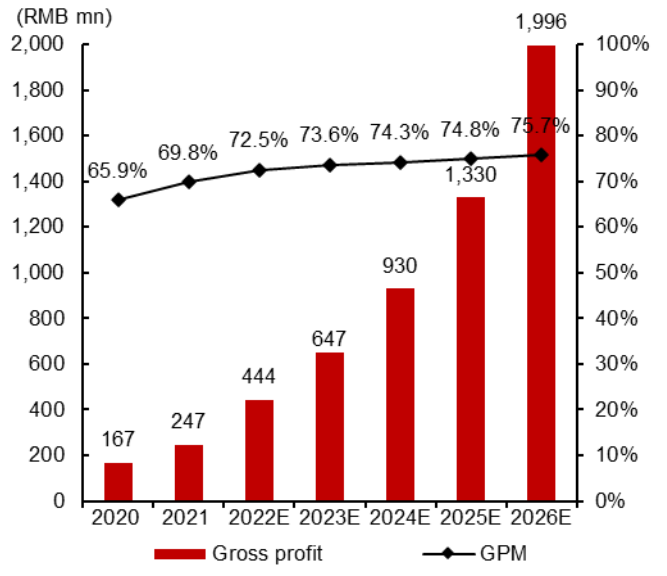
Source: Company data, CMBIGM estimates

Figure 58: Net profit forecasts



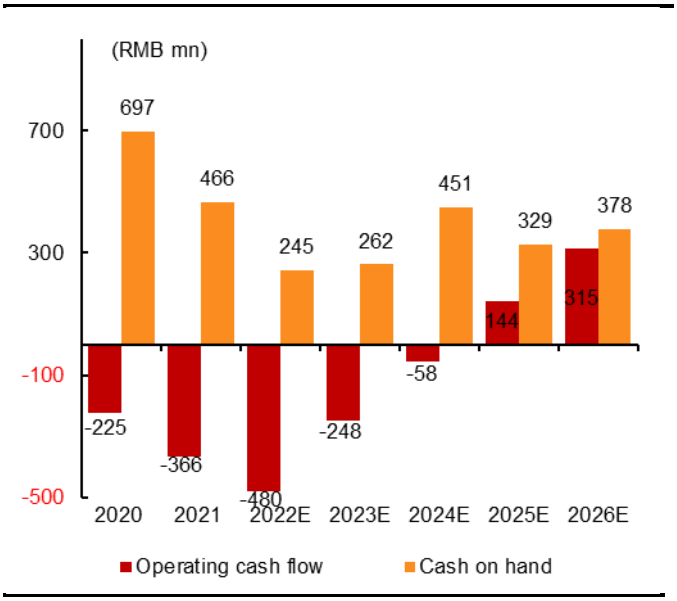
Source: Company data, CMBIGM estimates

Figure 59: Gross profit & GPM forecast



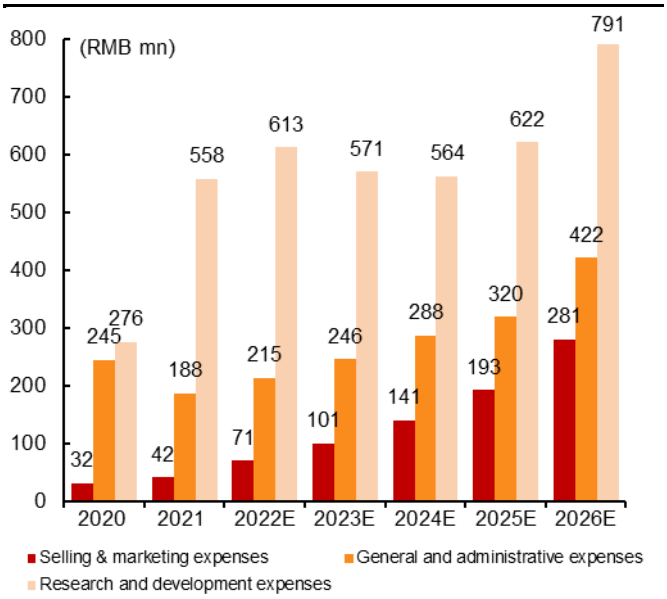
Source: Company data, CMBIGM estimates

Figure 60: Cash on hand and operating cash flows



Source: Company data, CMBIGM estimates

Figure 61: Operating expense forecasts



Source: Company data, CMBIGM estimates

Valuation

Initiate at BUY with TP of HK$43.85

Given that Biocytogen's future cash flows will mainly rely on fast growth of its pre-clinical research services and antibody development business, we believe DCF would be a reasonable method to value the Company. We derive our target price of HK$43.85 based on a 14-year DCF model (WACC: 11.8%, terminal growth rate: 2.0%).

Figure 62: Base case risk-adjusted DCF valuation (terminal growth rate: 2.0%)

DCF Valuation (in Rmb mn)	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E	2034E	2035E
EBIT	-442	-258	-50	208	515	1,119	1,627	2,195	2,828	3,463	4,021	4,600	5,131	5,647
Tax rate	0.0%	0.0%	0.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%
EBIT*(1-tax rate)	-442	-258	-50	177	437	951	1,383	1,866	2,404	2,944	3,417	3,910	4,361	4,800
+ D&A	71	76	82	88	94	99	104	109	113	118	122	126	130	133
- Change in working capital	-116	-71	-97	-137	-232	-233	-295	-286	-325	-290	-236	-228	-181	-157
- Capex	-200	-200	-200	-200	-200	-200	-200	-200	-200	-200	-200	-200	-200	-200
FCFF	**-687**	**-453**	**-265**	**-73**	**99**	**618**	**992**	**1,489**	**1,992**	**2,572**	**3,103**	**3,608**	**4,110**	**4,576**
Terminal value														**47,498**

Terminal value (RMB mn)	9,931
Total PV (RMB mn)	**15,491**
Net debt (RMB mn)	74
Minority interest (RMB mn)	5
Equity value (RMB mn)	**15,412**
# of shares (mn)	399
Price per share (Rmb per share)	38.6
Price per share (HK$ per share)	**43.85**

Terminal growth rate	**2.0%**
WACC	**11.8%**
Cost of Equity	15.1%
Cost of Debt	5.0%
Equity Beta	1.15
Risk Free Rate	3.00%
Market Risk Premium	10.50%
Target Debt to Asset ratio	30.0%
Effective Corporate Tax Rate	15.0%

Source: CMBIGM estimates

Figure 63: Sensitivity analysis (HK$)

	WACC				
Terminal growth rate	**10.8%**	**11.3%**	**11.8%**	**12.3%**	**12.8%**
3.0%	58.11	52.37	47.36	42.97	39.09
2.5%	55.49	50.17	45.51	41.40	37.76
2.0%	53.16	48.21	**43.85**	39.98	36.54
1.5%	51.08	46.45	42.35	38.70	35.44
1.0%	49.21	44.86	40.99	37.53	34.43

Source: CMBIGM estimates

Investment Risks

Risks relating to the research and development of drug candidates

The development and commercialization of new drugs is highly competitive. Biocytogen faces competition from major pharmaceutical companies, specialty pharmaceutical companies and biopharmaceutical companies worldwide.

The Company's business and prospects depend substantially on the success of Project Integrum. If the Company is unable to discover and develop new antibody drugs or successfully monetize the antibody molecules screened and selected, its business and profitability may be affected.

Risks relating to extensive government regulation

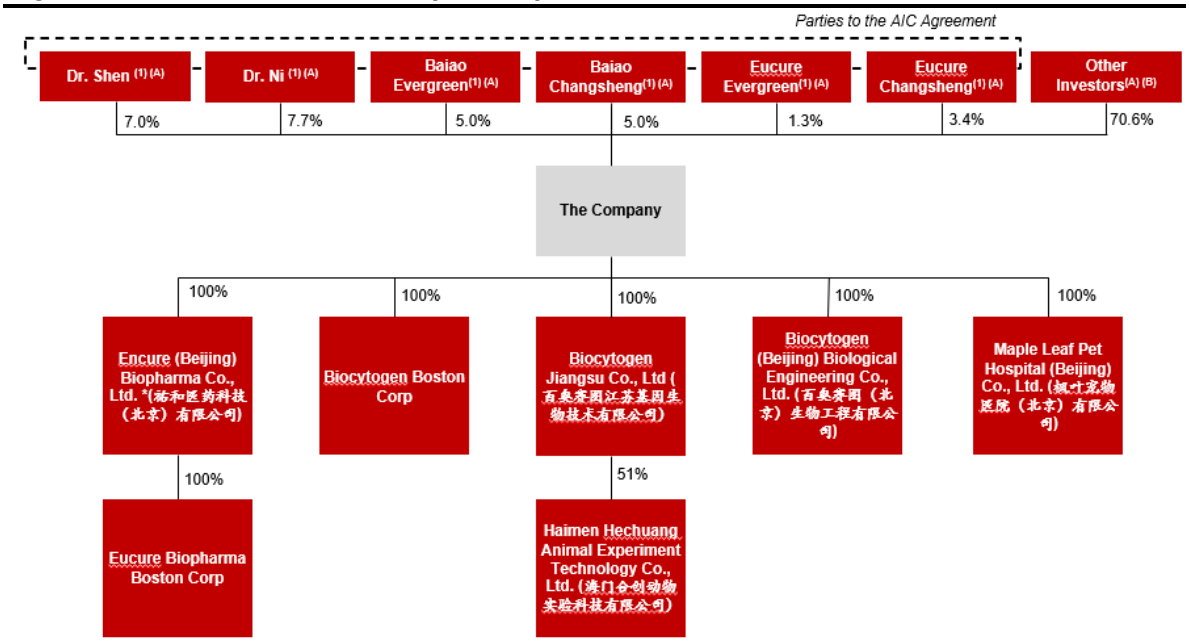
The time required to obtain approval by the NMPA, FDA, TFDA, TGA, MFDS and other comparable regulatory authorities is unpredictable but typically takes 10-15 years following the commencement of pre-clinical studies and clinical trials and depends on numerous factors, including the substantial discretion of the regulatory authorities. Biocytogen's drug candidates could fail to receive regulatory approval for many reasons, including: 1) failure to begin or complete clinical trials due to disagreements with regulatory authorities; 2) failure to demonstrate that a drug candidate is safe and effective or, if it is a biologic, that it is safe, pure and potent for its proposed indication; 3) failure of clinical trial results to meet the level of statistical significance required for approval; 4) data integrity issues related to clinical trials; and 5) disagreement with interpretation of data from pre-clinical studies or clinical trials.

Failure in protecting intellectual property rights

The absence of patent linkage, patent term extension and data and market exclusivity for NMPA-approved pharmaceutical products could increase the risk of early generic competition with Biocytogen's products in China.

Appendix: Company Profile

Figure 64: Shareholder structure (Pre-IPO)



Source: Company data, CMBIGM
Notes: 1. Dr. Shen, Dr. Ni and Baiao Evergreen, Baiao Changsheng, Eucure Evergreen and Eucure Changsheng are parties to the AIC Agreement. 2. Owned as to 49% by Jiangsu Dongbuzhou Science and Technology Park Group Co., Ltd.* (江苏东布州科技园集团有限公司), an independent third party. A. The Shares held by these Shareholders are Domestic Shares. B. The Shares held by these Shareholders are Domestic Shares, except for 26,088,480 Shares, 20,291,400 Shares, 6,920,640 Shares, 4,665,600 Shares, 4,665,600 Shares, 4,043,520 Shares, 933,120 Shares, and 622,080 Shares, held by Astral, Bioveda, COWIN CHINA Fund I, LBC, CPE-CbioMice, Octagon, CTW, and OrbiMed, respectively, being Unlisted Foreign Shares.

Figure 65: Management profile

Name	Age	Date of Joining	Position	Roles and responsibilities
Dr. Shen Yuelei (沈月雷)	52	13 Nov 2009	Chairman of the Board, executive Director, CEO and general manager	Responsible for the overall strategic planning of the Group
Dr. Yang Yi (杨毅)	44	4 Nov 2016	Deputy general manager, CSO	Oversees the research and development of innovative drug
Dr. Guo Chaoshe (郭朝设)	51	23 Oct 2013	Deputy general manager	Responsible for the formulation and implementation of the Company's marketing and business strategies and objectives
Mr. Liu Bin (刘斌)	53	20 Apr 2020	CFO	Supervises the financial operations of the Company
Dr. Chen Zhaorong (陈兆荣)	64	7 Jun 2021	Deputy general manager and CMO	Responsible for formulation of research and development strategy and global clinical research
Mr. Wang Yongliang (王永亮)	37	17 Jul 2017	Deputy general manager, Chief secretariat officer	Responsible for financing and investment of the Company and devising the Company's strategic development and internal control

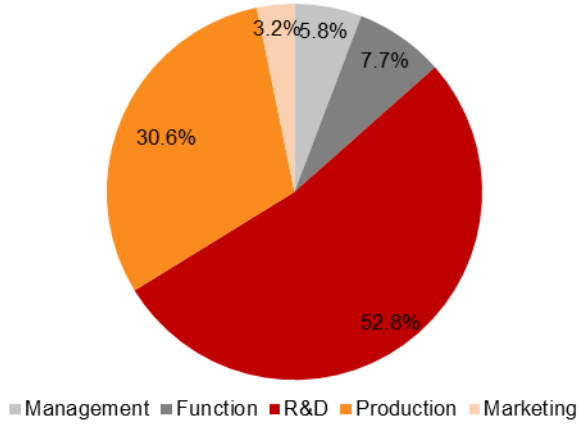
Source: Company data, CMBIGM

Figure 66: Employee structure

Function	# of staff	% of total
Management	99	5.8%
Function	131	7.7%
R&D	904	52.7%
Production	525	30.6%
Marketing	55	3.2%
Total	**1,714**	**100.0%**

Source: Company data (as of 13 Aug 2022), CMBIGM

Figure 67: Employee number breakdown



Source: Company data (as of 13 Aug 2022), CMBIGM

Financial Summary

INCOME STATEMENT	2019A	2020A	2021A	2022E	2023E	2024E
YE 31 Dec (RMB mn)						
Revenue	**170**	**254**	**355**	**613**	**879**	**1,253**
Cost of goods sold	(73)	(87)	(107)	(169)	(232)	(323)
Gross profit	**97**	**167**	**247**	**444**	**647**	**930**
Operating expenses	**(318)**	**(525)**	**(753)**	**(879)**	**(900)**	**(973)**
Selling expense	(29)	(32)	(42)	(71)	(101)	(141)
Admin expense	(140)	(245)	(188)	(215)	(246)	(288)
R&D expense	(159)	(276)	(558)	(613)	(571)	(564)
Others	(2)	19	10	0	0	0
Operating profit	**(221)**	**(358)**	**(506)**	**(435)**	**(253)**	**(43)**
Other expense	(85)	(118)	(39)	(25)	(34)	(53)
Other gains/(losses)	11	9	26	20	18	20
Share of (losses)/profits of associates/JV	0	0	(0)	0	0	0
Pre-tax profit	**(306)**	**(477)**	**(546)**	**(460)**	**(287)**	**(96)**
Income tax	0	0	0	0	0	0
After tax profit	**(306)**	**(477)**	**(546)**	**(460)**	**(287)**	**(96)**
Minority interest	(43)	(49)	(0)	0	0	0
Net profit	**(263)**	**(428)**	**(546)**	**(460)**	**(287)**	**(96)**

BALANCE SHEET	2019A	2020A	2021A	2022E	2023E	2024E
YE 31 Dec (RMB mn)						
Current assets	**672**	**1,148**	**874**	**772**	**924**	**1,300**
Cash & equivalents	246	750	466	245	262	451
Account receivables	58	115	183	294	419	594
Inventories	3	8	15	24	33	46
Other current assets	344	254	168	168	168	168
Contract obtaining costs	20	21	42	42	42	42
Non-current assets	**551**	**1,179**	**1,429**	**1,557**	**1,681**	**1,799**
PP&E	533	1,136	1,391	1,521	1,645	1,763
Intangibles	2	2	6	4	4	4
Other non-current assets	15	41	32	32	32	32
Total assets	**1,222**	**2,327**	**2,303**	**2,330**	**2,605**	**3,099**
Current liabilities	**1,410**	**328**	**447**	**450**	**513**	**604**
Account payables	18	88	102	139	190	265
Tax payable	2	14	27	27	27	27
Other current liabilities	1,262	0	0	0	0	0
Lease liabilities	90	179	256	256	256	256
Contract liabilities	38	48	62	29	40	56
Non-current liabilities	**318**	**540**	**604**	**604**	**1,104**	**1,604**
Long-term borrowings	0	0	0	0	500	1,000
Deferred income	91	90	93	93	93	93
Other non-current liabilities	227	450	511	511	511	511
Total liabilities	**1,728**	**868**	**1,051**	**1,055**	**1,617**	**2,208**
Share capital	37	360	375	375	375	375
Other reserves	(542)	1,098	877	900	613	517
Total shareholders equity	**(505)**	**1,458**	**1,252**	**1,275**	**988**	**892**
Total equity and liabilities	**1,222**	**2,327**	**2,303**	**2,330**	**2,605**	**3,099**

CASH FLOW	2019A	2020A	2021A	2022E	2023E	2024E
YE 31 Dec (RMB mn)						
Operating						
Profit before taxation	**(306)**	**(477)**	**(546)**	**(460)**	**(287)**	**(96)**
Depreciation & amortization	28	43	128	71	0	82
Tax paid	0	0	0	0	0	0
Change in working capital	79	(29)	(10)	(116)	(71)	(97)
Others	162	237	62	25	110	53
Net cash from operations	**(37)**	**(225)**	**(366)**	**(480)**	**(248)**	**(58)**
Investing						
Capital expenditure	(153)	(296)	(199)	(200)	(200)	(200)
Net proceeds from disposal of short-term investments	59	1,393	650	0	0	0
Others	(310)	(1,285)	(535)	(25)	(34)	(53)
Net cash from investing	**(404)**	**(188)**	**(84)**	**(225)**	**(234)**	**(253)**
Financing						
Dividend paid	0	0	0	0	0	0
Proceeds from share issues	500	948	311	483	0	0
Others	(11)	(80)	(92)	0	500	500
Net cash from financing	**490**	**868**	**219**	**483**	**500**	**500**
Net change in cash						
Cash at the beginning of the year	(1)	(4)	697	466	245	262
Exchange difference	199	246	(0)	0	0	0
Cash at the end of the year	**246**	**697**	**466**	**245**	**262**	**451**

GROWTH	2019A	2020A	2021A	2022E	2023E	2024E
YE 31 Dec						
Revenue	na	49.3%	39.8%	72.9%	43.4%	42.5%
Gross profit	na	71.9%	48.2%	79.6%	45.7%	43.7%

PROFITABILITY	2019A	2020A	2021A	2022E	2023E	2024E
YE 31 Dec						
Gross profit margin	57.2%	65.9%	69.8%	72.5%	73.6%	74.3%
Operating margin	(130.2%)	(141.4%)	(142.7%)	(70.9%)	(28.8%)	(3.4%)
Return on equity (ROE)	na	(89.8%)	(40.3%)	(36.4%)	(25.4%)	(10.3%)

GEARING/LIQUIDITY/ACTIVITIES	2019A	2020A	2021A	2022E	2023E	2024E
YE 31 Dec						
Current ratio (x)	0.5	3.5	2.0	1.7	1.8	2.2
Receivable turnover days	77.9	96.8	106.1	100.0	99.0	98.0
Inventory turnover days	0.0	33.7	51.6	51.6	51.6	51.6
Payable turnover days	88.0	221.7	323.8	300.0	300.0	300.0

VALUATION	2019A	2020A	2021A	2022E	2023E	2024E
YE 31 Dec						
P/S (x)	**na**	**na**	**na**	14.6	10.2	7.2
P/B (x)	**na**	**na**	**na**	7.0	9.1	10.1

Source: Company data, CMBIGM estimates. Note: The calculation of net cash includes financial assets.

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