Supplementary Information for Financial Results Q2 FY12/22

Aug. 10, 2022

To accelerate drug discovery and development of mAb for therapeutics to overcome current medical unmet-needs

Chiome Bioscience Inc.



- 1. Overview of Q2 FY12/22 "Financial results"
- 2. Overview of Q2 FY12/22 "Operation highlights"

Appendix.

Corporate information Pipeline information



Overview of Q2 FY12/22 "Financial results"



(JPY in millions)

| | Q2 FY2021 | Q2 FY2022 | Increase (decrease) | Main reasons for increase / decrease |
|---------------------------------|-----------|-----------|------------------------|---|
| Net sales | 384 | 278 | (106) | |
| Drug Discovery & Development | 103 | 0 | (103) | Upfront payment of the out-licensing contract was recorded in FY12/21 |
| Drug Discovery Support | 281 | 278 | (3) | |
| COS/SGA | 800 | 1,057 | 257 | |
| R&D Expense | 459 | 690 | 231 | Expenses recorded for the completion of manufacturing of study drugs for CBA-1535 |
| Other costs | 340 | 366 | 25 | |
| Operating Loss | (415) | (779) | (363) | |
| Ordinary Loss | (409) | (768) | (359) | |
| Net Loss | (408) | (771) | (362) | |



(JPY in millions) As of Dec. 31, 2021 As of Jun. 30, 2022 2,216 1,792 Current assets 1,790 1,471 (Cash on hand in banks) 425 320 *1 (Other current assets) 122 128 Non-current assets Total assets 2,339 1,920 392 390 **Current Liabilities** 53 54 Non-current liabilities 446 444 Total liabilities 1,893 1,476 Total net assets 2,339 Total liabilities and net assets 1,920

Explanation of balance sheet

*1 Upon completion of manufacturing of study drugs for CBA-1535, advance payments were reversed and charged to the current period as an expense



| | | (JPY in millions) | |
|---|-----------|-------------------|----|
| | Q2 FY2020 | Q2 FY2021 | |
| Cash flows from operating activities | (560) | (660) | *1 |
| Cash flows from investing activities | - | _ | |
| Cash flows from financing activities | 176 | 341 | *2 |
| Net increase (decrease) in cash and cash equivalents | (384) | (319) | |
| Cash and cash equivalents as of the beginning of the year | 2,686 | 1,790 | |
| Cash and cash equivalents as of the end of the year | 2,301 | 1,471 | |

<u>*1 Cash flows from operating activities</u>

Expenses for clinical development for CBA-1205 and CBA-1535 and research for drug discovery, SG & A expenses.

*2 Cash flows from financing activities

Proceeds from issuance of shares resulting from exercise of 18th subscription rights to shares.



Overview of Q2 FY12/22 "Operation highlights"





In the first part of CBA-1205, during the course of the study, several patients who were refractory to standard treatments stayed on the study for more than 4 months due to the SD (stable disease) evaluations.

CBA-1535, dosing to the patient in the first Phase 1 clinical study of Tribody[™] started.

Amanitin based ADC technology was applied to anti-CDCP-1 antibody (Technology introduced by Heidelberg Pharma)

July 2022

In drug discovery projects, novel Tribody[™] antibodies were designed and generated. The patent application covering this molecule was filed.

A service agreement with option contract with Rohto Pharmaceutical Co. Ltd. has been concluded

July 2022



Drug Discovery and Development – Pipeline

| CBA-1205 Humanized afucosylated anti-DLK1 antibody | Enrollment to the first part of Phase I clinical trial has been completed. Decision was made to move to the second half of Phase I trial. Dosing to a Hepatocellular Carcinoma patient started in the second part of the Phase 1. |
|---|--|
| CBA-1535 | ✓ The application of the clinical study plan was submitted to the Pharmaceutical and |
| Humanized anti 5T4 & CD3 | Medical Devices Agency (PMDA) as of February 16, 2022. ✓ Dosing to the patients with solid tumors has started. Study sites are National |
| trispecific antibody | Cancer Center Hospital and Shizuoka Cancer Center. |
| PCDC humanized anti-CDCP1 antibody | ✓ Promoting out-licensing activities mainly in the field of ADC applications. A data package using amanitin in ADC is also added to our out-licensing activities. |
| Discovery | ✓ Research progressed on a drug discovery project of Tribody[™] with a new molecular |
| Projects | combination. Filed a patent application for this project in June 2022. |

Pipeline - Out-Licensed programs

| LIV-2008 Humanized anti-TROP2 antibody | ✓ Henlius, which we out-licensed, considers multiple development plans for future IND applications. |
|---|--|
| ADCT-701 | ADCT and the National Cancer Institute entered a collaboration for the development of ADCT-701. Preparation for IND applications and clinical studies in 2022 is in progress. |



Drug Discovery Support Business

| Deals with pharmaceutical companies | Carrying out business development with new pharmaceutical companies as well as strengthening businesses with existing clients. A new contract (a service agreement with an option contract) with Rohto Pharmaceutical Co. Ltd. has been concluded as of July 11, 2022. | | |
|---|---|--|--|
| | ✓ Launch of the 3rd diagnostic kit developed with ADLib[®] antibodies by Fujirevio Inc. | | |
| Core Technology | | | |
| ADLib [®] system Tribody™ | Participating in a research program supported by a grant from the Japan Agency for Medical Research and Development (AMED), (Research on infectious diseases; and improvement of ADLib[®] system). Subsidy income of 16 million yen in FY2022 in the field of infectious diseases research. ADLib[®] Notice of Allowance Patent for a method of promoting diversification of the variable region of antibodies (Japan) Antibody acquisition methods (Europe) | | |
| | ✓ Publication of the paper: Research results on cancer immunotherapy using Tribody[™] technology <u>https://www.mdpi.com/1422-0067/23/7/3466</u> ✓ Conference presentation: A research group led by Associate Professor, Naoya Yamashita, from the Faculty of Applied Bioscience, Kanagawa Institute of Technology presented "Construction of the ELISA assay to quantify Semaphorin 3A in the adult brain". The antibody was obtained using our ADLib[®]system. | | |

Drug Discovery and Development - Pipeline



Out-Licensed Product

| Code | Target | Therapeutic Area | Basic research, Drug Discovery | Preclinical Study | Phase 1 | Partner |
|----------------------------|--------|---------------------|-----------------------------------|----------------------|---------|-----------------------------|
| ADCT-701 (LIV-1205 ADC) | DLK-1 | Oncology /ADC | | | | |
| LIV-2008 /2008b | TROP-2 | Oncology | | | | 2021.1~ Q Henlius |

In-house developed product

| In-house developed product | | | ★ First in class ★★ World first de moving into a | | lrug discovery modality clinical phase | |
|------------------------------|-----------------|---------------------|--|----------------------|--|---------|
| Code | Target | Therapeutic Area | Basic research, Drug Discovery | Preclinical Study | Phase 1 | Status |
| CBA-1205 (ADCC enhanced) | DLK-1 | Oncology | | : : | | Phase 1 |
| *★ CBA-1535 (Tribody™) | 5T4×CD3 ×5T4 | Oncology | | : : | | Phase 1 |

License candidate and drug discovery project

| Code | Target | Therapeutic Area | Basic research, Drug Discovery | Preclinical Study | Phase 1 | Status |
|---|-------------|--|-----------------------------------|---------------------------------|--|-----------------------|
| * ВМАА | SEMA3A | undisclosed | | | | Licensing opportunity |
| * PCDC | CDCP1 | Oncology /ADC | | | | Licensing opportunity |
| Discovery PJ/ Drug discovery research | Undisclosed | Oncology, CNS, autoimmune diseases, etc. | | *Co appl * proje proje | mpleted new patent ications for the oncology ect, one of the priority ects and Tribody project. | _ |

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Enrollment to the first part of Phase I clinical trial has been completed. Decision was made to move to the second half of Phase I trial.



CBA-1205 Out-licensing plan





Expectations for a surplus in a single year by out-licensing in early-stage or after P1



Dosing for patients started in CBA-1535 Phase I study

| 202 | 21 | 2022 | 2023 | 2024 |
|----------------------------|--|--|--|---|
| CMC develop Preclinical | CMC development and Preclinical studies | | rted end June e 1 study (First part) | |
| | | | Phase 1 Bus lie | study (Second part) iness alliances and censing activities |
| Study design | First part Target: Soli • Starting steps to can be s • Evaluate | t (single agent) d cancer patients to administer a low dose in find the maximum dose that afely administered. initial drug efficacy signals | Second part (combined immunotherapy drugter) Target: Solid cancer Administer the dose safe in the first part Find the maximum of administered when of immunotherapy drugtered Evaluate early drugtered | bined use with cancer ugs) batients that was confirmed to be in steps in increments. lose that can be safely combined with cancer use (IOs) efficacy signals when |

Aims of this development plan

- This study is designed to confirm if CBA-1535 satisfies clinical needs such like safety and efficacy fastest by adopting combination use of IO in Phase 1
- ➤ Confirmation of safety in this study as a T Cell engager will be a milestone in the drug discovery using Tribody[™] platform.

Potential applications for Tribody™



By targeting the disease related antigen other than 5T4, Tribody™ technology opens the door to new pipelines

Candidate for new development



PCDC Technology Introduction and Out-licensing Policy



Introducing technology: ADC with amanitin

- Amanitin technology was introduced from Heidelberg Pharma, Germany. Amanitin is a toxin found in mushrooms that suppress tumor growth by inhibiting RNA Polymerase II.
- ✓ Characteristics and expectations of amanitin
 - High drug efficacy and the effect on current ADC-resistant cancer are expected
 - Heme, ocular and neurotoxicity that are observed in current ADC are low





※Heidelberg Pharma HP (<u>https://heidelberg-pharma.com/en/research-and-development/adc-technology</u>)

Out-licensing strategy and target clients of PCDC

- 1. Pharmaceutical companies wishing to expand their pipeline as ADC
 - Our company will pay license fees to Heidelberg Pharma if PCDC is determined to be outlicensed as therapeutic antibodies using amanitin
- 2. Pharmaceutical companies already own ADC technology but are looking for antibodies for ADC



Sales increase in contracted services

- > Net sales for the six months under review were 278 million yen (a decrease of 3 million yen year-on-year)
- Despite the decrease compared to the same period last year, steady transactions with existing clients have been carried out, mainly domestic pharmaceutical companies.
- Service agreement with option contract with Rohto Pharmaceutical Co. Ltd. concluded in July 2022 on therapeutic antibody generation. In case the candidate antibody proceeds to the commercialization/development stage, an option contract will be exercised (the duration of the option agreement is for five years, starting from the completion of tasks under this agreement).



| Major clients | Contract date |
|---|---------------|
| Chugai Pharmaceutical Co., Ltd. | Jun. 2011 |
| Chugai Pharmabody Research Pte. Ltd | Aug. 2012 |
| Mitsubishi Tanabe Pharma Co., Ltd. TANABE RESEARCH Laboratories U.S.A., Inc. | Dec. 2016 |
| Ono Pharmaceutical Co., Ltd. | Oct. 2018 |
| Kyowa Kirin Co., Ltd. | Jul. 2019 |
| | |



Appendix. Corporate information

Corporate Overview



Biotech company dedicating to satisfy unmet medical needs



Management principle

- Place the highest priority on sound management and credibility and aim to become a corporation that grows with society.
- With creativity and science, develop therapeutic drugs for unmet medical needs, and contribute to the health of patients.
- Achieve successive product pipelines and improvement of corporate value through collaboration with external institutions.

Founded:

February 2005

- Listed on the stock exchange: Dec.2011 (Tokyo Stock Exchange Growth Section)
- President and Chief Executive Officer: Shigeru Kobayashi, M.E.

\blacksquare Location :

- <Head Office and Research Laboratories> 3-12-1Honmachi, Shibuya-ku, Tokyo <Drug Discovery Laboratories>
- 2-13-3 Nogawahonchou, Miyamae-ku, Kawasaki-city, Kanagawa
- Number of Employees :62 (As of Jun. 30, 2022)
- Business :
- Chiome Bioscience (4583.T), is a public company leveraging a proprietary monoclonal antibody generating technology, for drug discovery and development, as well as providing drug discovery supports.

Chiome's business

Antibody drug discovery for diseases where high unmet medical needs exist

- Intractable diseases for which effective treatment is not available
- Diseases for which some treatments are available, but not a drug
- Effective drugs are available, but are not easy to use or accompanies with hard side effects
- Difficult for a big pharma to focus on due to small number of patient







Drug Discovery and Development Business

This is business to obtain revenues such as upfront, milestone, and royalty payments relating to out-licensing of patents of pipeline product and drug candidates, and also, income from collaborative research. It drives our future growth.

Drug Discovery Support business

This is business to obtain revenues from antibody generation service by using platform technology that Chiome possesses to support drug discovery research at pharmaceutical companies, or for diagnostic and research purposes at academia or institutes on fee-for-service scheme. It secures constant revenue stream.



Technology Platform (Chiome's mAb Discovery Engine)



Chiome possesses antibody platforms including its proprietary technology, and extensive knowhows and experiences in protein/antibody engineering to streamline the process of drug discovery.



Core technology : Human ADLib[®]System



One-stop-order platform for antibody drug discovery



The ADLib®system offers a platform library with unique array space that adds seamless Affinity maturation function. It is a one stop order drug discovery and research tool that can complete all the steps necessary for antibody drug discovery such as selection, full-length IgG expression, humanization, and affinity maturation on 1 platform.

Core technology that support 2 businesses: ADLib[®] System

<u>Generating method of human antibodies in cultured cells (in vitro) without living</u> <u>organisms (animals)</u>



- Acquire human antibodies in a short period of time
- Unlike immunization methods using individual animals, not affected by immune tolerance
- By utilizing the feature of autonomous genetic diversification, a high affinity of antibodies can be achieved in sequence
- Acquire antibodies as early as possible leads to early application for patents





The Tribody[™] technology enables the generation of multi-specific antibody products. This unique technology overcomes the key shortcomings of conventional mono- as well as of currently developed bi-specific antibody formats.

Discover drug candidates utilizing Tribody™ technology



One of the binding sites can be designed to recruit immune cells (effector cells) with cytotoxic activity, such as T cells and NK cells, and the remaining 2 sites can be designed to bind to different epitopes of a cancer-specific antigen or to recognize different antigens expressed on the cancer cell surface.

By combining targets and the number of binding,

it is expected to generate antibodies to targets that could not be made into drugs in the past, and that have characteristics that will free patients from the need to administer multiple drugs in combination.



Drug development process and Chiome's revenue model



Business strategy for the future growth



Create candidate of innovative antibody drugs for unmet medical needs and pay maximum efforts to increase the corporate value by developing and licensing highly valuable antibodies.





Appendix. Pipeline information



| ADCT-701* (F | Iumanized anti-DLK1 antibody ADC) | • |
|------------------|--|---|
| Therapeutic Area | Liver cancer, lung cancer, neuroblastoma etc. | |
| Origin | An Antibody Drug Conjugate (ADC) form of LIV-1205 that was licensed out to Switzerland-based ADC Therapeutics SA in September 2017. | C |
| Patent | Granted in Japan, US, EU, China etc. (Humanized anti-DLK1 antibody) $% \left($ | |

- ✓ ADCT-701 is an antibody-drug conjugate of the antibody LIV-1205 developed by Chiome and PBD* (*Pyrrolobenzodiazepine : Drug with anti-tumor properties)
- ✓ ADCT is preparing for the Clinical study for ADCT-701 with National Cancer Institute (NCI) in neuroendocrine cancer.



Chiome has right to develop ADCs other than PBD, and it opened up the possibility of strategic development of anti-DLK-1 antibody.

Drug Discovery and Development - Pipeline



ADC Therapeutics entered into a collaboration with the National Cancer Institute (NCI) for the development of ADCT-701, targeting DLK-1.

- ✓ ADC Therapeutics and the National Cancer Institute (NCI) started a collaboration aimed at the continued development of ADCT-701, targeting DLK-1, in neuroendocrine malignancies.
- ✓ Chiome granted ADCT a worldwide exclusive license with a right to sublicense, develop, manufacture, and commercialize an ADC format of LIV-1205 and PBD conjugate.

ADC Therapeutics Inc.

ADC Therapeutics is based in Switzerland and is focused on the development of proprietary antibody drug conjugates for the treatment of both solid and hematological cancers. ADC Therapeutics' CD19-directed ADC ZYNLONTA® is approved by the FDA, and it has multiple PBD-based ADCs in ongoing clinical studies in the US and in Europe.



About National Cancer Institute(NCI)

The NCI is part of the National Institutes of Health (NIH) in the United States and is one of eight organizations that constitute the Department of Public Health and Human Services. NCI is involved in much of the development of anti-cancer drugs in the United States, and in addition to having a large research program within the organization, it is also actively funding cancer researchers in the United States.



| LIV-2008 (Humanized anti-TROP2 antibody) | | | | | |
|--|---|----------|--|--|--|
| Therapeutic Area | Breast cancer (TNBC), lung cancer, colorectal can | cer etc. | | | |
| Expectation | LIV-2008 is a humanized monoclonal antibody targeting cell surface antigen "TROP-2" which is overexpressed in breast cancer, colon cancer, lung cancer and several types of solid cancers and is also expected to play a key role against the proliferation of cancer cells. | | | | |
| Patent | Granted in Japan, US, EU, China etc. | | | | |

- Chiome grants an exclusive license, with sublicensing rights, to Henlius for development, manufacturing and marketing of LIV-2008/2008b and its derivatives in China (including Hong Kong Special Administrative Region, Macau Special Administrative Region, and Taiwan region)
- Chiome also grants to Henlius an option right to develop, manufacture and sale in the rest of the world other than the initial territory.

(Henlius Company website : <u>HKEX-EPS_20210114_9583899_0.PDF (windows.net)</u>)

Conditions

Upon exercise of the above option rights to develop, manufacture and market the product on a worldwide basis, there is an agreement for a total of up to approximately US\$122.5 million in upfront payments and milestone payments based on progress in development and sales. In addition, royalty income at a fixed rate based on the sales value will be paid if the product is launched.



First in class

CBA-1205 (Humanized afucosylated anti-DLK1 antibody)

| Origin | A humanized antibody generated by hybridoma technology in Livtech which Chiome acquired in 2015. |
|---------------------|--|
| ADCC | GlymaxX (ProBioGen) |
| Therapeutic Area | Liver cancer, lung cancer, neuroblastoma etc. |
| Expectation | First-in-class therapeutic antibody targeting intractable cancers. Providing new therapeutics for highly malignant tumors that are without effective therapeutic drugs including hepatocellular carcinoma. |
| Patent | Granted in Japan, US, Europe, China etc. |

Phase I clinical study

First part: Evaluate the safety in patients

Enrollment completed.

No serious adverse reaction reported.

During the course of the study, several patients who were refractory to standard treatments stayed on the study for more than 4 months due to the SD (stable disease) evaluations.

Second part: Evaluate the safety and efficacy of the drug in patients with hepatocellular carcinoma.

Poster presentation at the annual meeting of the American Association for Cancer Research (AACR)Title : CBA-1205, a novel glycoengineered humanized antibody targeting DLK-1 exhibits potent anti-tumor
activity in DLK-1 expressing tumor xenograft modelshttps://www.abstractsonline.com/pp8/#!/6812/presentation/2425(April 2019)



A patent application, "Combination of CBA-1205 and Lenvatinib" filed in 2019 is published

Mouse xenograft study: Hep3B hepatoma model CBA-1205 + Lenvatinib



Patent: WO/2020/204033

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CBA-1535 (Humanized anti 5T4 & CD3 trispecific antibody)

| Origin | CBA-1535 is a T-cell engager, trispecific antibody, directed against the 5T4 tumor antigen, a protein found on various solid tumors and is thought to be involved in metastasis. |
|---------------------|--|
| Therapeutic Area | Malignant mesothelioma, small cell lung cancer, non small cell lung cancer, TNBC etc. |
| Expectation | First-in-class therapeutic antibody with trispecific format Offer a new treatment option for a disease which has poor prognosis and where there are only a few effective treatments. |
| Patent | Granted in Japan, UK, US, China. Pending in Europe etc. |

Phase I study: Dosing for patients has started in the first part for safety and initial drug efficacy evaluation. Study sites: National Cancer Center Hospital

Shizuoka Cancer Center





First in class

BMAA (Humanized anti-Semaphorin3A antibody)

| Origin | A humanized antibody generated using the ADLib [®] System. Demonstrated as a selective antibody possessing functional inhibitory activity through collaboration with Professor Yoshio Goshima in Yokohama City University. |
|---------------------|--|
| Therapeutic Area | Undisclosed |
| Expectation | To be applied in a wide range of disease areas including inflammatory and CNS diseases which involve SEMA3A. Providing treatment methods for patients who do not respond to traditional therapeutics for diabetic retinopathy, which is the primary medical condition causing loss of sight in adulthood. |
| Patent | Granted in Japan, US and Europe etc. |

- Completion of a research collaboration with an overseas research institute aimed at diseases involving Semaphorin 3A.
- The data obtained so far on Semaphorin 3A and the exploratory research data (Semaphorin family) will be used for future business development activities.



PCDC (humanized anti-CDCP1 antibody for antibody drug conjugate)

| Origin | Humanized anti-CDCP1 antibody discovered by Chiome's proprietary antibody technologies. |
|-----------------------|---|
| Potential indication | Solid tumors (lung, colorectal, pancreatic, breast, ovarian etc.) |
| Opportunities | CDCP1 is a First-in-class therapeutic target highly expressed in broad range of solid tumors, including standard-of-care resistant cases. High efficacy and safety expected from binding and toxicological profiles of the antibody. |
| Patent application | "ANTI-CDCP1 ANTIBODY" : The international patent application is filed under the PCT. |

- Promoting out-licensing activities, mainly in the field of ADC
- ✓ Out-licensing strategy/target
 - 1. Pharmaceutical companies wishing to expand their pipeline as ADC
 - 2. Pharmaceutical companies already own ADC technology but are looking for antibodies for ADC
- Pharmacological data of animal model drug efficacy using amanitin from Heidelberg Pharma has been added to out-licensing data packages and out-licensing activities are in full speed.



Pipeline -Licensing-



A patent application for PCDC "Anti-CDCP1 antibody" is published ~The antibody for highly effective antibody-drug conjugate against various solid tumors ~



Shine light on unmet needs. Bring a brighter future to patients.

To accelerate drug discovery and development of mAb for therapeutics to overcome current medical unmet-needs



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