September 15, 2021

Business and Other Risks

The following are major risks which management believes may have a material impact on the financial condition, results of operations and cash flows of the consolidated companies. Although the Group (as defined below) recognizes these potential risks, and will strive to avoid them and respond to them if they occur, there is no guarantee that all risks can be avoided. In addition, this is not an exhaustive list of all risks associated with the Group.

Forward-looking statements herein are based on the judgment of the Group as of the end of the current consolidated fiscal year.

(1) Risks in the Fields of Somatic Stem Cell/iPSC Regenerative Medicine

1. Recording of Losses due to Long Development Periods and Possibility of Additional Financing

In addition to the field of iPSC regenerative medicine, the Company has been conducting research and development in the field of somatic stem cell regenerative medicine since January 2016, and relies on the future progress in its research and development as well as the success of its business development in both fields.

HLCM051, a therapeutic candidate in the field of somatic stem cell regenerative medicine, uses MultiStem®, a stem cell product developed by Athersys, for the treatment of the acute phase of cerebral infarction and acute respiratory distress syndrome (ARDS), and is undergoing clinical trials in anticipation of obtaining approval based on a new early approval system established under the revised law.

iPSC regenerative medicine therapeutic candidates are in the preclinical stage, and will require further steps before the products are able to be launched.

As a result, in the fields of somatic stem cell/iPSC regenerative medicine, it is expected that revenues will not be generated, and losses will continue to be incurred until the products are actually launched. Furthermore, the Company's research and development in the fields of somatic stem cell regenerative medicine and iPSC regenerative medicine require a substantial amount of money, and the Company may raise additional financing therefor. In these circumstances, if additional unexpected costs are incurred, or if the Company is unable to raise additional financing as anticipated, the results of operations and future business development of the Group (the Company and its affiliated companies) may be materially affected.

The Group has been implementing a hybrid strategy of developing HLCM051 first and targets using sales proceeds from it to fund development in the field of iPSC regenerative medicine. Patient enrollment in the clinical trial for the acute phase of cerebral infarction has been completed. In addition, the Company has released preliminary results of its clinical trial for ARDS. The Company plans to proceed with an application for manufacturing and sales approval through continued consultation with the regulatory authorities.

2. Reliance on Specific Partners

The Company has entered into a joint development agreement, a licensing agreement

and a joint venture agreement with Sumitomo Dainippon Pharma Co., Ltd. relating to the development of HLCR011, and has formulated its plans for the development of RPE cell products in Japan on the basis of these agreements. In addition, clinical trials for HLCM051 are ongoing under a license agreement with Athersys. The Company will outsource the commercial manufacturing of HLCM051 to a contract manufacturing organization (CMO). If the financial condition of Athersys deteriorates significantly, or there is any problem with the manufacturing and supply system of the CMO, the development or sales plans for HLCM051 may be seriously delayed or become difficult to continue.

Furthermore, the Company cannot rule out the possibility that these agreements will be terminated before the expiry of their term due to circumstances beyond the control of the Company, such as changes in the management policy of the other parties thereto. Termination of these agreements may materially affect the Group's results of operations and future business development.

The Group holds shares of Athersys for the purpose of strengthening its partnership with Athersys and establishing a cooperative framework for the development of HLCM051. In addition, the Group has dispatched a part-time director to support the proper business operations of Athersys.

3. Technological Innovation and Competition

The Company's research and development of iPSC regenerative medicine is in a field that is attracting interest both domestically and globally, and that is likely to create innovation through the discovery of new knowledge and technologies. Development of various therapies, including cell-based medicine derived from embryonic stem cells, is progressing.

In the field of somatic stem cell regenerative medicine, various research and development activities are already underway, especially in the United States, and more feasible technological innovations may be made.

If an early entrant or a potential competitor in these fields, including in adjacent fields, develops any new technology superior to the intellectual property rights held by the Company, and obtains a relevant patent or launches its product before the Company, or if the Group is unable to promptly respond to environmental changes due to its insufficient collection and analysis of the latest industry trends in the regenerative medicine field, the Group's results of operations and future business development may be materially affected.

The Group is constantly working to develop cutting-edge technologies in collaboration with universities and public research institutions.

4. Laws and Regulations Related to Regenerative Medicine Products

The Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices (the "Pharmaceuticals and Medical Devices Act"), which came into force in November 2014, ensures the safe and prompt provision of pharmaceuticals and medical devices. It establishes a new conditional and time limited approval system based on the early approval system for regenerative medicine products, including somatic stem cell/iPSC regenerative medicine. Although approvals have been given to some regenerative medicine products under such system, no approvals have been granted to allogeneic iPS cell-derived products, and there is a possibility that verification will be required that is different

from that of other cell-derived products. In addition, laws and regulations related to regenerative medicine products, including the Pharmaceuticals and Medical Devices Act, may be revised on an ongoing basis in response to the technological innovation situation and the occurrence of unforeseen circumstances. Other laws and regulations or revised laws may require the Company to make large capital expenditures or bear additional development expenses in order to meet quality control standards stricter than those approved before. If the Company is required to conduct more tests than expected, it may cause a significant delay in its development schedule. In these circumstances, the Group's results of operations and future business development may be materially affected.

The Group collects information, consults with the relevant regulatory authorities, and develops internal systems to respond to such circumstances as quickly as possible.

5. Product Characteristics of Somatic Stem Cell/iPSC Regenerative Medicine

Due to the fact that cells derived from human cells and tissues are transplanted in or administered to the human body, somatic stem cell and iPSC regenerative medicines have risks related to the safety of materials, and a possibility that various unforeseen side effects and medical accidents will occur. For this reason, these medicines are subject to strict legal regulations. It is difficult to entirely prevent the occurrence of unexpected events in the future, and if such events occur, the Group's results of operations and future business development may be materially affected.

In order to deal with such regulations and prevent accidents, the Group has been taking various initiatives, such as requesting the involvement of personnel with expertise in the field of regenerative medicine and experts well versed in pharmaceutical affairs systems.

6. Uncertainty about the Establishment of Manufacturing and Sales Systems

The Company's somatic stem cell and iPSC regenerative medicine business aims to not only produce good results in research and development activities, but also develop subsequent manufacturing and sales activities as a business. However, pharmaceutical development requires a wide variety of technologies, and if for any reason it becomes difficult to establish manufacturing methods or build manufacturing systems, the Group's results of operations and future business development may be materially affected.

The Group is focusing its efforts on establishing manufacturing methods, including the development of mass cell culture technology, together with its collaborating partner companies.

In terms of the sales system, the Company has yet to decide whether it will establish such system by itself or in alliance with pharmaceutical companies. If the Company has any trouble establishing the sales system in the future, and falls behind its schedule, the Group's results of operations and future business development may be materially affected.

Prior to the launch of the products under development, the Group has begun preparations for sale, including establishing sales and marketing organizations and concluding contracts with Japan’s major wholesalers of ethical pharmaceuticals.

7. Overseas Business Development

The Group believes that the iPSC regenerative medicines being developed by the

Company will be in demand by patients in Japan and around the world who suffer from intractable diseases. For this reason, the Group is taking steps to expand overseas by establishing its overseas subsidiary.

However, the Group's business expansion may be restricted in some way, such as experiencing difficulties establishing necessary business alliances or organizational structures due to unique legal regulations and business practices overseas, which may materially affect the Group's results of operations and future business development.

8. Clinical Trials

The Company is currently conducting clinical trials in the field of somatic stem cell regenerative medicine. Generally, when conducting clinical trials delays may occur due to various factors, including the inability to secure an appropriate number of patients necessary for clinical trials, or the failure to proceed with various procedures at clinical trial sites as planned. In addition, there is a risk that development will be suspended if an unacceptable safety issue arises or the expected efficacy may not be achieved. In such cases, the Group's results of operations and future business development may be materially affected.

The Group carries out clinical trials based on a detailed plan after prior consultation with the Pharmaceuticals and Medical Devices Agency (PMDA).

9. Uncertainties about the Results of Analysis and Evaluation of Clinical Trial Data and the Application for Approval

The Company is conducting a clinical trial of HLCM051 for the acute phase of cerebral infarction. In August 2021, the Company announced the completion of patient enrollment after confirming for a certain period of time after administering HLCM051 to patients that there were no dropouts that would affect the efficacy analysis.

Data analysis and evaluation of clinical trial results is scheduled to be conducted following the follow-up period of the patients enrolled in the clinical trial. The Company aims to obtain the preliminary data analysis during the fourth quarter of the fiscal year ending December 31, 2021. However, there is no assurance that clinical trials will proceed as expected or that data analysis and evaluation will be conducted on schedule as they depend on various factors including the progress and results of consultation with the PMDA.

It is difficult for the Company to predict with certainty the results of analysis and evaluation of future clinical trial data, and the Company may see unexpected results. In these cases, the Group's future business development may be materially affected.

A clinical trial of HLCM051 is also underway for the treatment of ARDS. In August 2021, the Company announced in its preliminary report that the analysis of the data in relation to certain endpoints showed favorable results in terms of efficacy and safety.

The Company will continue to analyze the data from this clinical trial, and prepare for the application for manufacturing and sales approval through continued consultation with the PMDA, targeting to submit such application by the first quarter of the fiscal year ending December 31, 2022. However, there is no assurance that the Company will be able to submit such application according to the targeted timing. If the schedule is severely delayed due to unforeseen circumstances in the process of the application, the Group's future business

development may be adversely affected.

10. Risks Related to Investment

The Group is constantly working on developing cutting-edge technologies. In order to stay ahead of early entrants in the Group's business, including in adjacent fields, and potential competitors, the Group may form alliances with companies that possess relevant technologies and patents in the form of equity investments or M&As (acquisitions, mergers, business transfers/successions). Besides, the Company has been providing growth funding in the field of biotechnology both in and outside Japan through Saisei Ventures LLC.

If an unforeseen problem arises on the part of its collaboration partner or investee company, or research and development does not proceed as expected, the Group's results of operations and future business development may be materially affected.

The Group carefully considers the selection of collaboration partners and the appropriateness of the investment prices by obtaining valuations from third-party organizations.

(2) Risks Related to Pharmaceutical Research and Development in General

1. Revisions of Laws and Regulations on Pharmaceutical Prices

Amid the global trend of reducing medical expenses, if pharmaceutical prices or insurance reimbursement prices become less than the product values estimated by the Company due to revisions of laws and regulations on pharmaceutical prices, the Group's results of operations and future business development may be materially affected.

2. Product Liability

If a pharmaceutical product developed by the Company causes any health problem or other issue, or any inappropriate clinical trial, manufacturing or sale is discovered, the Company may become subject to product liability claims, which may materially affect the Group's results of operations and future business development.

(3) Risks Related to Human Resources and Organization

1. Reliance on Specific Individuals

The Group is a small organization, and Hardy TS Kagimoto, Chairman and CEO, plays an important role in the Group's business activities, including guiding research and development, making decisions on management policies and strategies, and building relationships with collaboration partners. The Group is working to strengthen its organizational management structure that does not overly rely on any specific individuals. However, if for any reason it becomes difficult for Hardy TS Kagimoto to continue with the Group's business, the Group's results of operations and future business development may be materially affected.

2. Internal Control System

Due to the nature of its business, the Group relies heavily on the expertise, technique and experience of its other officers and employees. Although the Group intends to increase its personnel and improve its internal control system in line with its business growth, if the Group

fails to secure human resources as planned or loses its personnel, or its internal control system becomes insufficient, it will be difficult to promote research and development or establish relationships with external parties, which may materially affect the Group's results of operations and future business development.

(4) Other Business Risks

1. Relationships with Universities and Other Public Research Institutions

The Company has been actively engaged in research and development activities in collaboration with, and through the conclusion of patent licensing agreements with, public research institutions. However, as a result of the transformation of national universities into independent administrative institutions, universities are changing their approach toward intellectual property rights. If it becomes difficult for the Company to enter into or renew patent licensing agreements with such public research institutions, the Group's results of operations and future business development may be materially affected.

2. Intellectual Property Rights

The Group may use intellectual property rights owned by third parties in performing its business. Although the Group uses intellectual property rights in accordance with legal procedures, a dispute may arise in connection with a third party's intellectual property rights. To avoid the infringement of such intellectual property rights, the Group conducts investigations, reviews and assessments from time to time, and enters into license agreements promptly when needed, but the Group expects such risks to increase in the future as its business expands.

The Group intends to further strengthen its intellectual property right management system. However, if a lawsuit is filed against the Group, the Group's results of operations and future business development may be adversely affected.

In addition, intellectual property rights owned by the Group may be infringed by third parties. If infringed, the Group will consider taking legal action necessary to protect its intellectual property rights. However, the Group cannot rule out the possibility that it will decide not to take any legal action in light of cost-effectiveness and the possibility that a third party will attempt to invalidate the relevant patents of the Group. In that case, such third party may operate a business that competes with the Group, which may materially affect the Group's results of operations and future business development.

3. Reputational Issues

The Group is committed to ensuring the safety of its development activities, complying with laws and regulations, and managing intellectual property rights and personal information. However, if the Group suffers any reputational damage due to unfounded reports in the media, the Group's results of operations and future business development may be materially affected.

4. Uncertainty about the Occurrence of Disasters

In the event of a natural disaster or other accident, including a fire, in an area where the Group conducts its business activities, the Group may suffer severe damage to its facilities and equipment, leading to the suspension of all or part of their operations, and delays to its

research and development activities. In addition, the Group may incur substantial costs for repairing its damaged facilities and equipment, which may materially affect the Group's results of operations and future business development.

5. Financing

Biotechnology companies such as the Group tend to record operating losses continuously during their development period due to research and development expenses, resulting in negative cash flows from operating activities. The Group will strive to secure funds from upfront payments and milestone revenues from new collaboration partners, subsidies, as well as borrowings from financial institutions and other lenders, and will raise funds by way of capital increases if necessary. However, if for any reason the Group fails to secure such funds, the Group's results of operations and future business development may be materially affected.

6. Dividend Policy

The Group has not distributed any retained earnings (*jouyokin no bunpai*) to its shareholders since its foundation. The Group recognizes the return of profits to its shareholders as an important business task, and intends to consider the distribution of retained earnings in the future, taking into account its results of operations and financial condition. As retained earnings brought forward (*kurikoshi rieki jouyokin*) are negative at present, the Group does not intend to pay dividends for the time being, giving priority to securing funds for its continuous research and development activities.

7. Dilution of Stock Value Following Exercise of Stock Acquisition Rights (*shinkabu yoyakuken*)

The Company has granted stock acquisition rights to its officers and employees and certain other people to enhance their motivation. In addition, the Company has issued bonds with stock acquisition rights to meet its funding needs for pipeline development and new technology development.

If these stock acquisition rights are exercised, the Company's new shares will be issued, which may dilute the stock value and voting right ratios of its existing shareholders. As of June 30, 2021, the number of dilutive shares underlying these stock acquisition rights was 6,806,335 shares, or 13.2% of the sum of the total number of issued shares and the number of dilutive shares.

8. Foreign Exchange Fluctuation Risk

The Company has established subsidiaries overseas, and there is a possibility that foreign currency transactions will increase in the future in connection with the conclusion of license agreements with foreign companies, and overseas research and development activities. If a foreign exchange risk is materialized due to rapid exchange rate fluctuations, the Group's results of operations and future business development may be materially affected.

9. Risks due to COVID-19

The Company is conducting clinical trials in Japan, using HLCM051, for the acute phase of cerebral infarction (trial name: TREASURE study) and acute respiratory distress syndrome (ARDS) (trial name: ONE-BRIDGE study). As for patient enrollment in these two

clinical trials, the rapid spread of infection due to the third wave of COVID-19 caused medical resources to be allocated to the treatment of COVID-19 at the hospitals conducting the clinical trials, and the pace of patient enrollment in the clinical trials was slower than expected since December 2020, causing delays in the progress of both clinical trials.

If medical institutions have no choice but to continue to prioritize the response to COVID-19, there could be further delays in the progress of the Company's clinical trials, which may materially affect the Company's development schedule and future business development.