

**Non-consolidated Financial Results**  
**for the Fiscal Year Ended December 31, 2021**  
**[Japanese GAAP]**

February 9, 2022

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 Scheduled date of Ordinary General Meeting of Shareholders: March 24, 2022  
 Scheduled filing date of securities report: March 25, 2022  
 Scheduled starting date of dividend payments: —  
 Supplementary briefing materials on financial results: No  
 Explanatory meeting on financial results: Yes (for securities analysts and institutional investors)

(Amounts of less than one million yen are rounded down)

**1. Financial Results for the Fiscal Year Ended December 31, 2021 (January 1, 2021 to December 31, 2021)**

(1) Operating results (% indicates changes from the previous corresponding period)

	Net sales		Operating income		Ordinary income		Net income	
	Million yen	%	Million yen	%	Million yen	%	Million yen	%
Fiscal Year ended December 31, 2021	9,365	(19.8)	4,418	(36.8)	4,774	(31.6)	3,606	(18.9)
Fiscal Year ended December 31, 2020	11,677	-	6,991	-	6,976	-	4,448	-

	Net income per share	Diluted net income per share	Return on equity	Ordinary income to total assets	Operating income to net sales
	Yen	Yen	%	%	%
Fiscal Year ended December 31, 2021	27.98	27.78	15.6	18.1	47.2
Fiscal Year ended December 31, 2020	35.40	34.26	23.4	31.6	59.9

(Reference) Equity in earnings (losses) of affiliates Fiscal Year ended December 31, 2021: (470) million yen  
 Fiscal Year ended December 31, 2020: (729) million yen

(Note) PeptiDream has changed its fiscal-year end from June 30 to December 31 starting from the fiscal year 2019 ended December 31, 2019. As the financial results for the fiscal year 2019 are for a six-month period only, changes from the previous corresponding period are not presented for the following fiscal year ended December 31, 2020.

(2) Financial position

	Total assets	Net assets	Equity ratio	Net assets per share
	Million yen	Million yen	%	Yen
As of December 31, 2021	26,619	24,998	93.8	192.39
As of December 31, 2020	26,266	21,217	80.5	168.10

(Reference) Equity As of December 31, 2021: 24,977 million yen  
 As of December 31, 2020: 21,132 million yen

(3) Cash flows

	Cash flow from operating activities	Cash flow from investing activities	Cash flow from financing activities	Balance of cash and cash equivalents
	Million yen	Million yen	Million yen	Million yen
Fiscal Year ended December 31, 2021	6,654	(2,283)	66	11,746
Fiscal Year ended December 31, 2020	1,732	(1,200)	(237)	7,149

## 2. Payment of Dividends

	Annual dividends					Total dividends (Annual)	Dividend payout ratio	Dividends to net assets
	1st quarter-end	2nd quarter-end	3rd quarter-end	Year-end	Total			
	Yen	Yen	Yen	Yen	Yen	Million yen	%	%
Fiscal Year ended December 31, 2020	-	0.00	-	0.00	0.00	-	-	-
Fiscal Year ended December 31, 2021	-	0.00	-	0.00	0.00	-	-	-
Fiscal Year ending December 31, 2022 (forecast)	-	0.00	-	0.00	0.00		-	

## 3. Financial Forecasts for the Fiscal Year Ending December 31, 2022 (January 1, 2022 to December 31, 2022)

	Net sales	Operating income	Ordinary income	Net income
	Million yen	Million yen	Million yen	Million yen
Fiscal Year ending December 31, 2022	13,000 or more	6,500 or more	6,200 or more	4,500 or more

### [Notes]

#### (1) Changes in accounting policies, changes in accounting estimates and retrospective restatements

- |  |        |
|--|--------|
| 1) Changes in accounting policies due to amendment to the accounting standards, etc. | : None |
| 2) Changes in accounting policies other than 1) above                                | : None |
| 3) Changes in accounting estimates   | : None |
| 4) Retrospective restatements  | : None |

#### (2) Number of shares issued (common stock)

- Number of shares issued at the end of the period (including treasury stock)
- Number of treasury stock at the end of the period
- Average number of shares during the period

As of December 31, 2021	130,010,400 Shares	As of December 31, 2020	125,910,400 Shares
As of December 31, 2021	182,964 shares	As of December 31, 2020	193,694 shares
Fiscal Year ended December 31, 2021	128,904,152 shares	Fiscal Year ended December 31, 2020	125,668,094 shares

(Note) The number of treasury shares at the end of the period includes shares in the Company held by the Custody Bank of Japan, Ltd. (Trust Account E) (193,600 shares as of December 31, 2020 and 182,800 shares as of December 31, 2021). In addition, the shares in the Company held by the Custody Bank of Japan, Ltd. (Trust Account E) are included in treasury shares excluded from calculating the average number of shares during the period (173,398 shares for the fiscal year ended December 31, 2020 and 186,934 shares for the fiscal year ended December 31, 2021).

\*These financial results are outside the scope of audit by a certified public accountant or an audit firm.

#### \*Explanation on the appropriate use of operating forecasts and other special instructions

##### (Caution regarding forward-looking statements)

Financial forecasts and other statements regarding the future presented in these materials are based on information currently available and certain assumptions deemed to be reasonable and are not meant to be taken as commitment of the Company to achieve such results. Actual performance may differ substantially due to various factors.

##### (Caution regarding forward-looking statements)

The Company plans to hold an explanatory meeting on financial results for institutional investors on February 10, 2022 and intends to publish the presentation materials on its website on the same day.

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## 1. Analysis of Operating Results and Financial Position

### (1) Overview of Business Results for the Fiscal Year Under Review

During the twelve months ended December 31, 2021 (from January 1, 2021 to December 31, 2021), PeptiDream Inc. (“the Company”) continued to make excellent progress in leveraging the PDPS (Peptide Discovery Platform System) technology, its proprietary drug finding platform, across its three business segments; 1) Collaboration Discovery and Development, 2) PDPS Technology Transfer, and 3) In-House/Strategic Discovery and Development.

As of December 31, 2021, the Company’s pipeline consisted of 123 discovery & development programs (representing a net increase of 3 program from the end of the prior fiscal quarter ending December 31, 2020).

The below table is a snapshot of the Company’s program(s) across the three drug discovery approaches at the end of the current fiscal quarter.

【Number of programs for each drug discovery approach】	As of December 31, 2021
Peptide drugs	76
Small molecule drugs	
Peptide drug conjugates (“PDCs”)	47
Total	123

The below table is a snapshot of the number of program(s) currently at each stage of the discovery and development process, compared to the end of the prior fiscal year.

【Number of programs at each stage of the discovery and development process】	As of September 30, 2021	As of December 31, 2021
Target Validation-to-Hit Stage	39	37
Hit-to-Lead Stage	56	56
Lead-to-GLP-Tox Stage	16	18
GLP-Tox-to-IND Stage	9	9
Phase I	3	3
Phase II	0	0
Phase III	0	0
Total	123	123

The figures in the above table include programs in the Collaboration Discovery and Development segment and the In-House/Strategic Discovery and Development segment, and DO NOT include programs in the PDPS Technology Transfer segment.

#### **In the Collaboration Discovery and Development Segment;**

During the current fiscal quarter under review there was no specific milestone events to which the Company was able to issue a press release without contractual restrictions in the Collaboration Discovery and Development segment.

The Company continues to receive various R&D support payments from its big pharma discovery and development partners, in addition to being eligible for potential pre-clinical and clinical milestones payments as the programs advance, as well as being eligible for commercial sales milestones and royalties on net sales of any commercialized products. The Company looks forward to announcing future updates as additional milestones are met, and as allowed by the partner companies. In addition, the Company continues to receive considerable interest from multiple big pharma companies interested in partnering with the Company on discovery and development programs.

#### **In the PDPS Technology Transfer Segment;**

As of December 31, 2021, the Company has non-exclusively licensed its PDPS technology to 10 companies; Bristol-Myers

Squibb (2013), Novartis (2015), Lilly (2016), Genentech (2016), Shionogi (2017), MSD (U.S.-Merck & Co. Kenilworth, NJ, USA) (2018), MiraBiologics (2018), Taiho Pharmaceutical (2020), Janssen (2020), and Ono Pharmaceutical (2021).

In accordance with all PDPS technology license agreements, the Company is not informed as to what specific discovery and development programs are being prosecuted by the licensee company until certain initial pre-clinical milestones are achieved. The Company continues to receive various technology license and management payments from the licensee companies, in addition to potential preclinical and clinical milestone payments as programs advance. In addition, the Company continues to receive interest from multiple companies interested in licensing the PDPS technology.

#### **In the In-House/Strategic Discovery and Development Segment;**

The Company continues to expand the number of In-House/Strategic Discovery and Development programs. The goal of these efforts is to develop the programs to at least the pre-Phase I stage, or potentially post-Phase I/II stage, before seeking to license these programs out to big pharma companies, leveraging the Company's existing network of partners, for significantly higher financials than can be attained from standard discovery and development deals. The Company has continually been expanding its capabilities in turning hit candidates identified from the PDPS technology into 1) peptide therapeutics, 2) small molecule therapeutics, and 3) peptide drug conjugates ("PDCs"). Programs being developed with Strategic partners, Strategic partners being companies that bring proprietary technology/know-how to combine with the Company's, are under a cost-sharing agreement, in which the costs of discovery and development are shared, allowing for the Company to have a far larger share in the program and future revenues if successful. In addition, the Company continues to pursue a number of in-house fully-owned programs and looks forward to providing future updates as these programs progress toward the clinic.

The Company has announced strategic partnerships with JCR Pharmaceuticals Co., Ltd. ("JCR Pharma"), Modulus Discovery, Inc. ("Modulus Discovery"), Heptares Therapeutics Ltd., ("Sosei-Heptares"), Kleo Pharmaceuticals, Inc. (now Biohaven Pharmaceutical Holding Company Ltd. ("Biohaven")), Nihon Medi-Physics Co., Ltd. ("NMP"), POLA Chemical Industries ("POLA"), Kawasaki Medical School, the Bill & Melinda Gates Foundation ("Gates Foundation"), JSR Corporation ("JSR"), Mitsubishi Corporation ("MC") (PeptiGrowth Inc. ("PeptiGrowth")), RayzeBio Inc. ("RayzeBio"), PeptiAID Inc. ("PeptiAID"), and Amolyt Pharma ("Amolyt").

The Company and JCR Pharma have successfully development a series of constrained peptides that bind to the transferrin receptor (TfR) and are capable of carrying various therapeutic payloads across the blood-brain barrier (BBB) for delivery/targeting to the brain, and for the delivery of therapeutic payloads to muscle, arising from the joint research collaboration between the companies initiated in February 2016. Most therapeutics do not readily cross the BBB into the brain, with only a small fraction of the drug ever entering the central nervous system (CNS), posing a significant challenge to the development of effective therapeutics for the treatment of CNS disorders. The developed peptide carriers, when conjugated to various therapeutic payloads (herein referred to as a peptide-drug conjugates or "PDC"), function to facilitate the transport of the payload across the BBB into the brain, thereby significantly increasing the amount of the therapeutic in the brain, and/or can function to deliver the therapeutic payloads specifically to muscle, thereby significantly increasing the amount of therapeutic targeted to muscle. Potential payloads range from antibody and protein therapeutics to nucleic acid, peptide, and small molecules drugs. The two companies are focusing on third-party licensing activities, with PeptiDream leading such activities from execution of agreement to supply of peptide carriers, with the Dec 22, 2020 announced collaborative research and exclusive license agreement to create PDCs for neuromuscular diseases with Takeda Pharmaceutical Company Limited, representing the first of such licensing deals. The Company announced on July 27, 2021, a further expansion of the collaborative research and license agreement with Takeda Pharmaceutical Company extending into CNS Diseases. The companies are looking to conjugate the peptide carriers to a number of Takeda payloads, and the collaboration has the potential to yield a number of therapeutics products in the neuromuscular, muscular, and CNS disease space. The Company continues to discuss additional potential research and license agreements with various companies. The companies will share related revenues from licensing activities.

The Company and Modulus Discovery are working to leverage the expertise of both companies to jointly discover and develop small molecule clinical candidates based on peptide hit candidates identified from the PDPS technology against high value targets. Modulus Discovery is utilizing its computational chemistry technology and expertise to design small molecule candidates in

collaboration with the Company and its internal efforts. The companies jointly share the costs of the discovery and development programs and will co-own any resulting products. The Company has already identified hit candidate peptides against a number of high-value kinase targets, that exhibit the desired inhibition activity independent of ATP-binding (allosteric inhibitors) and obtained a number of crystal structures of these candidates in complex with their respective kinase targets yielding the structural information needed to enable computational small molecule design efforts. Using this approach, the companies have now identified highly selective and potent small molecule lead compounds for a specific high value kinase target and have recently completed in vivo proof of concept studies validating the lead candidate's efficacy. The companies are jointly continuing preclinical development efforts with the plan to nominate a clinical candidate in 2022, and are actively discussing a variety of partnering and out-licensing options for the program.

The Company and Sosei-Heptares are working to discover, develop and commercialize novel therapeutics targeting Protease Activated Receptor 2 (PAR2), which is a well validated target for multiple indications in pain, cancer, and inflammatory disease. The strategic partnership brings together two powerful technologies, Sosei-Heptares's StaR platform for GPCR target protein production and the Company's PDPS hit finding technology, in addition to considerable preclinical and clinical development capabilities. Under the agreement, the companies will jointly share the costs and will co-own any resulting products. As announced on May 12, 2021, the companies have previously identified high affinity and selective inhibitors against PAR2 and those candidates have been optimized to be sufficiently stable in the gut for oral administration, and therefore are now considered lead candidates. The candidates are now advancing through preclinical studies with the objective of developing a novel oral peptide therapy to treat inflammation and pain in gastrointestinal (GI) disorders, such as Inflammatory Bowel Disease. The companies are actively discussing a variety of partnering and out-licensing options for the program.

The Company and Biohaven (As announced on January 4, 2021, Biohaven agreed to merge and take over full control of Kleo and its discovery and development programs) continue to work to co-discover and develop novel Antibody Recruiting Molecule ("ARMs") or Synthetic Antibody Mimic ("SyAMs") products in multiple indications. The Company will receive a tiered share of the proceeds of any products developed. Biohaven has taken over clinical development control of the 2 clinical candidates, both of which are referred to as CD38-ARMs (ARM<sup>TM</sup>), and currently termed "BHV-1100( KP1237, ARM) + Autologous NK cells" and "BHV-1100 (ARM)". The CD38-ARMs are designed to recruit endogenous antibodies to multiple myeloma ("MM") cancer cells, targeting them for destruction via the body's innate antibody-mediated immune mechanisms. CD38 is a validated "MM" target, which is also overexpressed in chronic lymphocytic leukemia and other cancers. "BHV-1100 (ARM) + Autologous NK cells" is a short-acting ARM, whereas "BHV-1100 (ARM)" is a long-acting ARM and intended for a larger market of MM patients relapsed / refractory to Daratumumab therapy. BHV-1100 (ARM) + Autologous NK cells received IND authorization from the US Food and Drug Administration ("FDA") on February 7, 2020, to initiate a safety and tolerability clinical study combining BHV-1100 with patients' own Natural Killer ("NK") cells to treat MM patients and received Orphan Drug Designation on September 8, 2020. BHV-1100 shows similar or better activity to Johnson & Johnson's Darzalex, with the significant advantage being that it does not deplete the patients CD38-expressing immune effector cells. While many recent advances have been made to benefit MM patients, most patients will unfortunately still relapse, and the Companies believe that BHV-1100 enabled NK cells will kill CD38-positive MM cells and recruit other immune effector cells to assist in reducing the tumor burden. As announced on October 27, 2021, the first patient has been enrolled in the Ph Ia/ Ib study (ClinicalTrials.gov Identifier: NCT04634435). The clinical trial will assess the safety and tolerability, as well as exploratory efficacy endpoints, in newly diagnosed MM who have tested positive for minimal residual disease (MRD+) in first remission prior to autologous stem cell transplant (ASCT).

The Company and NMP are working to discover, develop, and commercialize novel peptide-radioisotope (RI) conjugates for use as therapeutics and diagnostics. Company has been using its proprietary PDPS technology for the identification of novel peptides for use as Peptide-Drug Conjugates (PDCs). NMP has been pursuing the fusion of therapeutics with diagnostics; "Theranostics", and is a leader in the research, development, and manufacturing of radiopharmaceuticals. The two companies will work together across a variety of programs to conjugate Company's constrained peptides with NMP's RIs to create a new exciting class of therapeutic and diagnostic products. Under the terms of the deal, both companies will independently fund their efforts, and the development and commercialization rights will be shared between the companies under a cost-sharing structured arrangement. The lead program in the collaboration continues to make progress and advance to the nomination of a clinical candidate, expected

sometime in 2022. The companies will look to commercialize products in Japan & Asia, and potentially license out such products to the United States and Europe.

The Company and POLA Chemical Industries (“POLA”) are working to discover and development of dermatology focused peptide-based cosmetics, quasi-drugs, and therapeutics. The Company will identify candidates using its PDPS technology against applicable dermatological targets based on POLA’s extensive expertise in the field and work together to commercialize such products. The company would lead the development of any therapeutics, arising from the collaboration. In addition, the company will expand its application of the PDPS technology to the discovery and development of peptides for use as quasi-drugs and cosmetics which are led by POLA. The companies have identified a number of lead candidates that are now being tested in in-vitro and ex-vivo models for efficacy.

The Company and Kawasaki Medical School are working to develop a novel Myostatin peptide inhibitor for the treatment of Duchenne Muscular Dystrophy (“DMD”). DMD is the most common type of muscular dystrophy, a fatal hereditary genetic disorder characterized by progressive weakness. Due to mutations in the dystrophin gene, dystrophin, which is important for maintaining muscle cells, becomes deficient or abnormal, with rapid muscle weakness in skeletal muscle and diaphragm resulting in difficulty with jumping, running, and walking, and later effecting the heart and respiratory muscles, which can eventually cause acute respiratory failure. It is a rare and fatal disease in which patients’ quality of life is significantly reduced. Research and development efforts have largely focused on the discovery and development of antibody-based therapeutics and/or nucleic acid based therapeutics, such as gene therapy, exon skipping, stop codon read-through, and gene repair, spanning multiple mechanisms of action, and while exciting progress has been made, there is no current effective therapeutic that can be used to treat a wide range of patients and be considered as a first line therapy, therefore there remains a significant unmet medical need for more broadly effective therapies for DMD. Myostatin (also known as growth differentiation factor 8, or GDF8) is a protein produced and released by myocytes that acts on muscle cells to inhibit muscle cell growth and is widely distributed in blood and muscle tissue (including diaphragm and extremity muscles) in normal individuals. Animals either lacking myostatin or that have been treated with myostatin inhibitors exhibit significantly more muscle mass and strength, and therefore represents an attractive target to inhibit to promote muscle growth and improve muscle function (stop or slow muscle degeneration), in patients with DMD and other muscle wasting diseases. The partners believe the current candidate could have a broad beneficial impact to all DMD patients and significantly increase their quality of life. Efforts in the discovery and development of myostatin inhibitors, largely focused on antibody-based therapeutics, and while they have shown significant promise in animal models, that promise has yet to translate into therapeutic benefits in humans for a variety of reasons. A constrained macrocyclic peptide-based myostatin inhibitor approach represents a potentially attractive alternative, as the current clinical candidate exhibits a high level of both potency and exposure in muscle tissue, both of which are known to be key attributes for any myostatin inhibitor. The partners plan to engage PeptiStar Inc., for candidate scale up and production of GLP/GMP batches, with the intention of conducting long-term safety studies, anticipating an entry into the clinic in 2023. Since DMD has been designated as a rare and intractable disease, the partners will work with the related agencies to seek priority review and shorten development timelines. The partners have initiated discussions with multiple potential partners for the joint development/partnering and/or out-licensing of the program.

The Company and the Gates Foundation are working on discovery and development programs aimed at identifying novel therapeutic macrocyclic peptide candidates to treat Malaria and Tuberculosis, two infectious diseases that disproportionately affect people in the world’s poorest countries. On Nov 1, 2019, the Company announced that it had been awarded a second grant from the Gates Foundation to fund the next phase of development of a candidate series originally identified under the first grant, awarded in November 2017, for the potential treatment of Tuberculosis caused by Mycobacterium infection. The original grant provided funding for multiple discovery programs aimed at the original November 2017 grant provided funding for identifying novel therapeutic macrocyclic peptide candidates (“hit candidates”) to treat Malaria and Tuberculosis, and the second November 2019 grant provided funding for turning one of the most promising hit candidate series into lead candidates (“hit-to-lead development funding”) suitable for future preclinical development. The current lead candidate series is for the treatment of Tuberculosis, and the Company is currently focused on optimizing the lead candidates for orally bioavailability. One of the main advantages of the lead series is that it may be effective against dormant Tuberculosis. Bacterial infections are among the leading causes of morbidity and mortality globally. The global burden of tuberculosis is staggering, with up to one-third of the world’s population latently-

infected, and with 10.4 million new active cases and 1.8 million deaths occurring annually. Under the terms of the grant(s), any Gates Foundation-funded products will be made available by PeptiDream at an affordable price in lower middle-income countries (LMIC). PeptiDream will be able to merchandise each product in developed countries on its own, through licensees or a combination of both.

The Company and JSR are working to identify peptides suitable for use in affinity chromatography processes for the purification of certain biopharmaceuticals, namely antibody therapeutics. The manufacturing process for complex biopharmaceuticals, such as antibody therapeutics, generally consists of a target protein generation process, followed by a purification process that uses affinity chromatography to separate the target protein from the cells and various impurities by binding the proteins to a specific ligand or peptide. The development and commercialization of new affinity chromatography media based on unique, synthetic peptides has the potential to simplify the purification process and lower overall costs. This development effort will specifically focus on ensuring consistent quality and reliable mass production of ligands based on unique peptides that will enhance purification efficiency enabling the purification of biopharmaceuticals that are generally considered difficult to purify through conventional affinity chromatography.

The Company and MC established a joint venture company, PeptiGrowth to develop, produce and sell peptide alternatives to growth factors, key ingredients of cell culture, used in the manufacturing of cell therapy, regenerative medicines and other biopharmaceuticals. PeptiGrowth is 60.5% owned by MC and 39.5% by PeptiDream. PeptiGrowth will leverage expertise and know-how of both parent companies to work towards the advancement of cell therapy, regenerative medicines, and other biopharmaceuticals in the pharmaceutical industry. Growth factors are a class of proteins that are widely present in humans and other animals. In addition to playing important roles in cell growth and proliferation, they are crucially involved in induction of differentiation of stem cells (iPS cells, ES cells, etc.) into nerve, blood, and other types of cells. Currently, growth factors are mainly extracted from animal serum or produced by gene recombination technology, however, their production presents a number of challenges to the pharmaceutical industry, including safety risks due to contamination with impurities, variation in quality among production lots, and high production costs. PeptiGrowth will utilize PeptiDream's proprietary drug discovery platform system, PDPS (Peptide Discovery Platform System), to identify alternative peptides that perform the equivalent function as growth factors and develop a new chemical synthesis method that does not use animal serum or gene recombination technology. In addition, by establishing a commercial manufacturing process and system, PeptiGrowth will achieve high purity, less variation among production lots in terms of specification and quality, with lower costs. Dozens of growth factors have been identified to date, and in order to realize a completely Xeno-Free culture medium, multiple growth factors need to be replaced with chemically synthesized alternative compounds. This is a world-first in terms of the comprehensive development of chemically synthesized, peptide alternatives to multiple growth factors, and both MC and PeptiDream believe such an initiative is essential for further advancement of cell therapy and regenerative medicines in the industry. PeptiGrowth will fully leverage the MC Group's global network and its broad customer base to enhance marketing and sales functions. On July 29, 2021 the Company announced the initiation of marketing of PG-001, a peptide alternative to human growth hormone (HGF) that has equivalent capabilities for both receptor activation and cell proliferation as HGF, as the first product originating from PeptiGrowth. In addition, PeptiGrowth launched PG-002, a peptide inhibitor of TGF $\beta$ 1, in November 2021. PeptiGrowth is progressing a number of peptide alternative growth factor programs in parallel, with PG-003 expected to be launched in Q1, 2022, with additional products to follow. The Company is in active discussions with multiple potential partners regarding the therapeutic use of PG-001 and PG-002.

The Company and RayzeBio are working to discover and development peptide- RI conjugates for use as therapeutics (“Peptide Radiotherapeutics”). The two companies are working on a number of programs against targets mutually agreed to, with PeptiDream providing peptide candidates, identified and optimized using its proprietary Peptide Discovery Platform System (PDPS) technology, to RayzeBio for further development as radiotherapeutics, with RayzeBio holding exclusive worldwide development and commercialization rights to the program peptides for use with RIs. PeptiDream will lead preclinical discovery and optimization efforts, with RayzeBio leading translational biology efforts to further characterize peptide-RI conjugates and advance such conjugates into clinical development and commercialization activities. Under the terms of the agreement, PeptiDream will receive an equity interest in RayzeBio, as well as be eligible for certain payments associated with product development and commercial success, as well as royalties on future sales of any products that arise from the partnership. In October 2020, RayzeBio announced



the completion of their \$45 million Series A funding round, on December 2020, the completion of their \$105 million Series B funding round, and on June 15, 2021, the completion of their \$108 million Series C funding round. The Company received a milestone payment in November 2020 for the progress made across multiple programs in the discovery and development of peptide-radiotherapeutics, and announced a second milestone payment on June 10, 2021, as a number of programs make progress to the election of clinical candidates, with the Company expecting to announce the first clinical candidate in 1H, 2022.

The Company and PeptiAID, a joint venture with Fujitsu, Mizuho Capital, Takenaka Corporation, and Kishida Chemical established November 12, 2020, are working on the development of therapeutics for the treatment of COVID19 and potentially any future coronavirus diseases. The Company has been applying its proprietary PDPS technology in a multi-pronged strategy toward identifying peptide candidates targeting different sites/regions of the COVID19 viral “spike” protein, which is essential for coronavirus to enter human cells, and PeptiAID, has obtained some of Company’s COVID19 candidate compounds. On March 23, 2021, PeptiAID announced the initiation of preclinical studies of the Company’s PA-001 candidate which exhibits highly potent antiviral activity against conventional SARS-CoV-2, as well as mutant strains such as the Alpha, Beta, Gamma, Delta and Omicron mutant strains. An in vitro study also demonstrated high synergistic effectiveness when used in combination with drugs that are currently approved for emergency use against COVID-19. Preclinical studies of PA-001, consisting of toxicity, safety pharmacology, and genotoxicity studies have been completed and confirmed the safety of PA-001. The initiation of early-stage exploratory clinical research of PA-001 based on the Clinical Trials Act, was approved by the Clinical Research Review Board. Clinical research has started in February 2022 (jRCT (Japan Registry of Clinical Trials) Trial ID: jRCTs031210601). The Company and PeptiAID are actively in discussions with interested third parties on potential partnering or licensing of the program. PeptiAID raised additional JPY 803m in September 2021 and the Company holds a 39.4% equity stake in PeptiAID.

The Company and Amolyt entered into a strategic partnership and license option agreement, announced December 8, 2020, whereby both companies will work together to test and further optimize PeptiDream’s Growth Hormone Receptor Antagonist “GHRA” peptide candidates, with the goal of selecting a clinical candidate for development in acromegaly, a rare endocrine disorder with serious medical complications, to which Amolyt has an option to license the candidates for future clinical development. Under the terms of the agreement, PeptiDream will be eligible for certain payments associated with the licensing, development, and commercial success of any GHRA product(s), as well as be eligible for certain royalties on future net sales. On September 9, 2021, the Company announced that Amolyt had exercised its option to globally license a portfolio of macrocyclic peptide growth hormone receptor antagonists (GHRA) under the terms of the research collaboration agreement with the Company announced in December 2020. The identified, optimized drug candidate, AZP-3813, is being developed as a potential treatment for acromegaly to be used in combination with somatostatin analogues (SSAs) for patients who do not adequately respond to SSAs alone. Amolyt is currently working to advance AZP-3813 through IND-enabling studies with the goal of filing an IND and initiating the first clinical trial by the end of 2022. On September 16, 2021, Amolyt announced the closing of an \$80 million Series B round, with the funds to be used in part toward the development of AZP-3813.

The Company expects to continue to form strategic partnerships with select-technology-leading bioventures and leading institutions, both in Japan and abroad, to accelerate and expand our clinical pipeline of best-in-class and first-in-class medicines. The Company continues to pursue a number of in-house fully owned programs. Some basic highlights are presented below.

**The Hemagglutinin (HA) program for the treatment of influenza:** The Company has previously identified highly selective potent lead candidates for the treatment of influenza. The lead candidate (referred to as PD-001) binds to the highly conserved stalk region of the influenza viral envelope protein HA, and shows strong broad efficacy against group 1 strains, including the H5N1 strain, and further enhanced potency in combination with existing influenza treatments, such as Tamiflu, in vivo animal studies. The Company has identified no preclinical toxicity for the lead candidates. The Company is actively discussing a variety of partnering and out-licensing options for the program.

**IL17 and related inflammatory cytokine program(s) for inflammatory diseases:** The Company has previously identified several highly selective potent lead candidates against a variety of pro-inflammatory cytokines for the potential treatment of a variety of inflammatory diseases. The Company is continuing preclinical development efforts against a number of high value pro-inflammatory targets, and has been investigating combining various candidates into bifunctional/multi-functional molecules (by linking peptides together into heterodimeric/multimeric peptide conjugates), as there is growing clinical evidence that

antagonizing multiple pro-inflammatory pathways in parallel may represent a superior therapeutic strategy to the treatment of inflammatory disease, and the belief that peptides may represent a superior modality to bispecific antibodies toward this goal.

PDC programs for the treatment of cancer and other diseases: The Company has been actively working to develop a number of in-house fully owned peptide candidates to a variety of targets applicable to the treatment of cancer and/or specific tissue/organ targeting, for potential conjugation to radionuclide, siRNA, small molecule, etc., payloads, for use as PDCs. The Company now has a growing pipeline of promising candidates that have been optimized for high affinity, high selectivity, and stability, spanning a variety of cell membrane/receptor targets, with which the Company intends to take forward into in vivo bioimaging studies, which is critical to validating the effective targeting of such conjugates and their ability to effectively deliver the payload of interest. The recent Fujifilm Toyama Chemical radiopharmaceutical business acquisition, upon closing, will allow the Company to rapidly move the most promising candidates into such in vivo bioimaging studies, as the existing business has such capabilities, and based upon those results, the Company anticipates prioritizing the most promising programs with the goal of nominating clinical candidates for use in peptide-RI conjugates in 2H, 2022. Additionally, upon the in vivo cell/tissue targeting validation of candidates as peptide-RI conjugates, the Company intends to actively investigate other potential payloads, on its own or potentially in collaboration with various existing and/or new partners.

### **In the Radiopharmaceutical Business Segment;**

On September 2, 2021, the Company announced its intention to fully acquire a newly established company, PDRadiopharma Inc. (“New Company”) that succeeds the radiopharmaceutical business (“acquired company”) of Fujifilm Toyama Chemical through an absorption-type split, and to make the New Company a subsidiary of the Company under a share purchase agreement signed with FUJIFILM Corporation (“FUJIFILM”). The acquired Company, as part of FUJIFILM’s healthcare business, engages in research, development, manufacturing and marketing of radiodiagnostics and radiotherapeutics. It is one of the two leading companies in radiopharmaceuticals in Japan and offers radiodiagnostic agents for SPECT (Single Photon Emission Computed Tomography) and for PET (Positron Emission Tomography) and radiotherapeutics, such as, Lutathera® Injection, developed by the acquired company, which received marketing authorization on June 23, 2021 as a new therapeutic option against neuroendocrine tumors and became the first approved peptide-radionuclide conjugate or Peptide Receptor Radionuclide Therapy (PRRT) in Japan. In addition, the acquired company received marketing authorization of “Raiatt MIBG-I 131 injection” on June 23, 2021, a radiotherapeutic for the treatment of pheochromocytoma and paraganglioma, well known diseases that cannot be treated surgically. The acquired company has facilities in Chiba, Kawasaki (Kanagawa), and Ibaraki (Osaka), Japan, a staff of roughly 500 employees (across research, development, manufacturing, and marketing functions), and currently markets 24 approved radiodiagnostic products and 9 approved radiotherapeutic products and forecasts 2021 net sales of around 15 billion JPY (approximately \$140-150 million).

The Company has been employing its proprietary PDPS discovery platform, to identify highly potent and selective hit macrocyclic peptide candidates for use in peptide-drug conjugate (PDC) therapeutics. The Company has been actively engaged in the discovery and development of peptide-RI conjugates for use as radiodiagnostics and radiotherapeutics in collaboration with BMS (radiodiagnostics), Bayer (radiodiagnostics), NMP (radiodiagnostics/therapeutics), Novartis (radiodiagnostics/therapeutics), and RayzeBio (radiodiagnostics/therapeutics), and has established itself as one of the major players in the discovery and development of such products. In addition, the Company has also recently been working to develop an in-house pipeline of fully-owned peptide-RI conjugates, in addition to its in-house PDC efforts.

The Company anticipates significant synergies from the acquisition, as the acquired company possess advanced technologies and know-how in radionuclides, pre-clinical and clinical development, manufacturing, approval, and marketing capabilities, along with a track record of in-licensing and commercialization of radiopharmaceuticals from overseas partners. The Company possesses experience and know-how in discovering and developing the carrier peptides to deliver the radionuclides selectively to targeted cells and tissues, enabling the continuous discovery of next-generation radiopharmaceuticals to feed into the pipeline, and the ability to leverage its global network of partners (both existing and future) to strengthen and accelerate both in-licensing and out-licensing activities. By combining the strengths and capabilities of the two companies, the Company believes it can not only significantly accelerate its own in-house peptide-RI conjugates programs, leading to higher value out-licensing/partnering deals, while retaining Japan commercialization rights, but also leverage those programs to maximize in-licensing activities. The acquisition will not only strengthen the Company’s position in the radiopharmaceutical space, but also allow the Company to unlock more of its core value faster by enhancing all of its PDC programs (in which verification of specific cell or tissue targeting of the peptide conjugate in appropriate models, which is best done using RI payloads, represents a critical validation step for any PDC program, irrespective of payload), while providing the Company more control over the clinical development of its programs. Once the acquisition is completed, the Company intends to provide greater detail on the radiopharmaceutical business, including the discovery and development pipeline, in future quarterly reports.

The Company expects to close the deal in March 2022. As announced on October 26, 2021, the Company expects to finance the acquisition (30.5 billion yen) through a combination of long-term loans/borrowing from leading financial institutions.

### **Other Information Related to the Company;**

The Company has previously announced, along with Shionogi & Co., and Sekisui Chemical Co., Ltd, the formation of PeptiStar Inc., a Contract Development and Manufacturing Organization (“CDMO”) for the research and commercial manufacture of peptide therapeutics. PeptiStar brings together the most cutting-edge technologies and innovations in large-scale peptide production from various companies throughout Japan in order to manufacture therapeutic peptides of the highest quality and purity, while simultaneously driving down the cost of production. It is anticipated that PeptiStar will become the go-to CMO for all of the Company’s discovery and development partners, in addition to the Company’s own in-house/strategic partnered programs. The PeptiStar manufacturing facility is located in Osaka and became fully operational from October of 2019. On Dec 6, 2019, PeptiStar Inc., and AMED (The Japan Agency for Medical Research and Development) announced they had accomplished the CiCLE project goal, “establishment of a global leading contract manufacturing organization (CMO) for constrained peptide medicines”. On Dec 1, 2020, PeptiStar announced that it had successfully raised funds totaling 1,790 million yen through a third-party allotment.

The Company continues its commitment to promoting ESG (Environmental, Social, and Governance) initiatives and its sustainability efforts including focus areas, ten most material issues, relevant policies and data are proactively disclosed on the corporate website ([https://www.peptidream.com/esg/data\\_en.html](https://www.peptidream.com/esg/data_en.html)). The Company will continue to strive to meet the highest standards for environmental responsibility, social promotion, and good corporate governance. On June 15 2021, the Company announced that the Sustainability and Governance Committee was established to further promote these ESG efforts at the core of management and continue to deliberate and monitor issues related to sustainability and governance from a medium- to long-term perspective.

In order to ensure that the 2°C goal under the Paris Agreement is achieved, the Company had set a goal to decrease GHG emissions (Scope 1 and Scope 2) per employee by 50%, compared to the fiscal year ended June 2018, by the year 2030. The Company newly adopted the RCP8.5 scenario (IPCC), which is the highest scenario for future climate change, with reference to the recommendations made by the Task Force on Climate-related Financial Disclosures (TCFD) and conducted an analysis on the impact of climate change from a medium-term perspective until 2026. The Company will continue to strengthen governance on measures to address climate change, implement scenario analysis based on risks/opportunities analysis and their financial impact, respond to climate change risks and opportunities, and engage in further enhancement of disclosure, with the goal to achieve "carbon neutral" within its operations by 2026. As GHG (greenhouse gas) emissions (Scope 1+2) produced by our business operations mainly derive from electronic power consumption, the Company has selected an electricity supplier which proactively promotes the shift towards renewable energy. To further take this initiative, the Company has decided to introduce CO<sub>2</sub> (carbon dioxide)-free power from its supplier for use at our head office and laboratory. This means that we will achieve our medium-term goal of the realization of “carbon-neutral” business operations 4 years earlier than originally planned. In addition, for the first time, the Company participated in the Climate Change Program of CDP (Carbon Disclosure Project), an organization engaged in environmental information disclosure initiatives, and received a score of B (management level) in 2021.

On September 14, 2021, the Company announced selection to apply to the new market segment “Prime Market” on the Tokyo Stock Exchange (TSE). The Company filed an application in November 2021 and the results were published by TSE on January 11, 2022, and our new market segmentation after April 4, 2022 was determined to be the "prime market."

On September 17, 2021, the Company announced that it was successful in its bid for Lots 2-11 and 2-12 (Address: 3-chome, Tonomachi, Kawasaki-ku, Kawasaki City, Kanagawa) in the public tender for land that was conducted by the Urban Renaissance Agency as follows: Location: 102-20 and 102-21, 3-chome, Tonomachi, Kawasaki-ku, Kawasaki City, Kanagawa, Land area: 11,635.60 m<sup>2</sup>, Bid-winning price: 3.2 billion yen. KING SKYFRONT has been designated as an international strategic zone and the Keihin-Rinkai Life Innovation Comprehensive Global Strategic Special Zone. It is an open innovation hub for the creation of new industries based on world-class R&D in life science fields that are expected to grow globally. Following the successful bid, the Company will conclude a land purchase agreement with the Urban Renaissance Agency. The Company plans to expand the Company's head office and research laboratory on the land, and to strengthen and expand its drug discovery and development functions, in light of strong growth across its collaboration, strategic partnership, and in-house discovery and development businesses. Details of the plan will be announced as soon as they are finalized. The Company intends to finance the purchase of

the land and the construction of the future building using funds on hand and long-term loans from financial institutions.

As of December 31, 2021, the Company had a total of 170 employees (177 employees when including executive officers, approximately 35% of employees are women), representing an addition of 20 employee during the fiscal year ended December 31, 2021. The Company also has the equivalent of 20 chemists in China, through a contract research organization (“CRO”), working on amino acid and small molecule chemistry.

The Company reported net sales of 9,365,964 thousand yen (decreased 2,311,289 thousand yen year on year), operating income of 4,418,143 thousand yen (decreased 2,573,180 thousand yen year on year), ordinary income of 4,774,477 thousand yen (decreased 2,201,799 thousand yen year on year), and net income of 3,606,407 thousand yen (decreased 841,949 thousand yen year on year) for the fiscal year ended December 31, 2021.

Net sales, operating income, and ordinary income did not achieve the initial forecasts for the fiscal year under review, mainly due to the timing of the conclusion of a new joint drug discovery research and development agreement, which was anticipated during the fiscal year, being delayed compared to the performance forecasts announced on February 10, 2021. On the other hand, net income was in line with the results forecast at the beginning of the fiscal year due to the accumulation of various cost reductions and other measures.

The Company operates in a single business segment, and thus statements for segment information are omitted.

## (2) Overview of Financial Position for the Fiscal Year Under Review

Total assets at the end of the fiscal year under review increased by 352,439 thousand yen from the end of the previous fiscal year to 26,619,168 thousand yen. This was mainly because of an increase of 4,597,171 thousand yen in cash and deposits and an increase of 943,265 thousand yen in shares of subsidiaries and associates, despite a decrease of 4,844,642 thousand yen in accounts receivable - trade.

Liabilities decreased by 3,429,151 thousand yen from the end of the previous fiscal year to 1,620,573 thousand yen. This was mainly because of a decrease of 1,581,632 thousand yen in accounts payable - other, and a decrease of 1,666,804 thousand yen in income taxes payable.

Net assets increased by 3,781,590 thousand yen from the end of the previous fiscal year to 24,998,595 thousand yen. This was mainly because retained earnings increased by 3,606,407 thousand yen.

### (3) Overview of Cash Flows for the Fiscal Year Under Review

Cash and cash equivalents for the fiscal year under review increased by 4,597,171 thousand yen from the end of the previous fiscal year to 11,746,529 thousand yen.

Status of cash flows and related factors during the current fiscal year are described below.

#### (Cash flow from operating activities)

Cash flow from operating activities resulted in a cash inflow of 6,654,708 thousand yen (a 4,921,974 thousand yen increase in inflow year on year). This was mainly due to the recording of income before income taxes of 4,823,652 thousand yen for the year and a decrease in notes and accounts receivable – trade of 4,844,642 thousand yen, despite income taxes paid amounting to 2,391,619 thousand yen.

#### (Cash flow from investing activities)

Cash flow from investing activities resulted in a cash outflow of 2,283,450 thousand yen (a 1,083,424 thousand yen increase in outflow year on year). This was mainly due to an outflow of 943,265 thousand yen for purchase of shares of subsidiaries and associates and an outflow of 1,185,973 thousand yen for purchase of property, plant and equipment.

#### (Cash flow from financing activities)

Cash flow from financing activities resulted in a cash inflow of 66,067 thousand yen (an outflow of 237,244 thousand yen in the same period of the previous fiscal year). This was mainly due to proceeds from issuance of shares resulting from exercise of subscription rights to shares amounting to 44,940 thousand yen and proceeds from issuance of subscription rights to shares amounting to 21,490 thousand yen.

#### (Reference) Cash flow-related indices

	Fiscal Year ended June 30, 2018	Fiscal Year ended June 30, 2019	Fiscal Year ended Dec. 31, 2019	Fiscal Year ended Dec. 31, 2020	Fiscal Year ended Dec. 31, 2021
Equity ratio (%)	88.6	86.6	94.8	80.5	93.8
Equity ratio based on market capitalization (%)	3,428.1	3,445.4	3,938.5	2,507.9	1,241.3
Ratio of interest-bearing liabilities to cash flows (%)	—	—	—	—	—
Interest coverage ratio (%)	—	—	—	—	—

Equity ratio: Shareholders' equity / total assets

Equity ratio based on market capitalization: Market capitalization of shares / total assets

Ratio of interest-bearing liabilities to cash flows: Interest-bearing liabilities / cash flows

Interest coverage ratio: Cash flows / interest expense

#### (Notes)

1. Market capitalization of shares is calculated by multiplying the closing share price at the end of the period by the number of shares issued at the end of the period (excluding treasury stock). It should be noted that the Company does not hold treasury stock.
2. For cash flows, operating cash flows are used.
3. Figures of ratio of interest-bearing liabilities to cash flows and interest coverage ratio for the fiscal years ended June 30, 2018 through December 31, 2021 are not stated because the Company did not hold interest-bearing liabilities.

#### (4) Efforts to Tackle COVID19, Financial Forecasts and Other Forward-looking Information

The COVID19 pandemic has had a certain impact on the Company's operations. Although the Company has returned to the normal business operation after the state of emergency was lifted, it has been continuing the utmost efforts to reduce the risk of corona virus infection for its employees, business partners and their families, by continuing to implement both clean/hygienic conditions/practices within office premises and various measures for social distancing to avoid "close contact" with one another.

Further to the Company's efforts to contribute to the discovery and development of therapeutics for the treatment of COVID19, on June 12, 2020, the Company announced a new discovery and development collaboration with MSD to develop peptide therapeutics capable of neutralizing both COVID19 and potential future CoV outbreaks. On November 12, 2020, the Company also announced the establishment of a joint venture PeptiAID, aimed at the development of therapeutics for the treatment of COVID19 and potentially any future coronavirus diseases. On November 11, 2021, PeptiAID announced the completion of preclinical studies of the Company's PA-001 candidate. On February, PeptiAID announced initiation of clinical research of PA-001. The Company will continue to strive to prevent the spread of infection within the Company and, through the development of effective therapeutic treatments, contribute to overcoming the threat of COVID19 and/or any other future coronavirus pandemic to society as a whole.

With regards to the Company's financial results for the fiscal year ending December 31, 2022 (January 1, 2022 – December 31, 2022), the Company forecasts net sales of 13,000 million yen or more (+38.8%), operating income of 6,500 million yen or more (47.1%), ordinary income of 6,200 million yen or more (29.9%), and net income of 4,500 million yen or more (+24.8%).

The future forecasts announced in the same period of the previous year was based on the optimistic assumption that the infections of COVID 19 would gradually curb from the second half of 2021 onwards. However, given the fact that the pandemic has prolonged more than expected, the current harsh market environment is assumed to continue during the fiscal year ending December 2022. Under such circumstances, we will maintain a medium-term growth trend and steadily promote each R&D program and business activities in preparation for future market environment opportunities.

As such, the Company forecasts an increase in R&D expenses by 418 million (+25.5%) compared to the prior fiscal year. In addition, the Company will continue to actively recruit the best and brightest, expecting to increase total employees by 28 (+15.8%) over the previous year in order to continue to strengthen our core capabilities and further build out our R&D teams, an important foundation for future growth.

The Company will, in the current fiscal year (January 1 – December 31, 2022), continue to focus on the following three areas:

##### 1. Continued focus on moving late-stage research programs into clinical development

In the fiscal year ending December 2021, the impact of COVID19 has been widespread not only across our business but the pharmaceutical sector in general, with slowdowns, delays, and work from home rules all contributing to delays in the majority of our late-stage research programs moving into clinical trials. The Company believes these delays are only temporary and the Company was happy to report the Biohaven partnered program finally moving into the clinic in 2021 after a significant delay. While these delays have been unfortunate, the Company has also seen some important technology breakthroughs that should lead to a further acceleration and expansion of programs moving into the clinic, such as breakthroughs in oral formulation technologies for our peptides, strengthening of internal technologies and capabilities, and in increase in knowhow and expertise in translational science and early clinical development, all of which should have broad lasting impacts on the Company's pipeline. In the current fiscal year, the Company will continue to work closely with discovery and collaboration partners to advance late stage research programs into clinical development, and offer our ever expanding technologies, capabilities, and knowhow to all our partners across all of our programs toward this goal.

##### 2. Continued expansion of PDC programs

In the fiscal year ending December 2021, we continued to expand our network of partner companies in the PDC space, adding brain/BBB-targeting peptide conjugate programs and muscle targeting peptide conjugate programs a leading large pharma company in Takeda, along with siRNA-peptide conjugate programs with the global leader in siRNA Alnylam, to our already existing radionuclide-peptide conjugate program efforts with Novartis, RayzeBio, and NMP. Our strategy of a "hub and spoke" model,

where the Company is the “hub” supplying the targeting peptide to then be conjugated with various payloads provided by the “spoke” partner companies for them to then develop is starting to show significant promise and putting the Company in a leading role and the go to company for PDC discovery and development. The company expects to expand the number of programs and announce new collaboration partners in each of these payload areas in the coming fiscal year. In addition, the Company has continued to look to expand further the PDC space, investigating a wide range of other payloads, such as antibodies, small molecules, and other therapeutic payloads of interest, and expects to see further progress in these newer areas as well. A single peptide developed by the Company can be used to deliver multiple payloads and multiple types of payloads potentially resulting in multiple commercial products for the Company, and thus this modular nature provides a variety of ways for the Company to maximize value. The Company will continue and further expand efforts to discover and develop innovative peptides against the highest value targets for use in such PDC applications, which should allow for a wide range of PDC products to progress forward across a growing number of partners.

### 3. Further expansion of strategic partnerships and investments

The Company has a growing number of strategic partnerships and also strategic investments, holding equity stakes in PeptiStar, Modulus, Rayzebio, PeptiGrowth, and PeptiAID. In the fiscal year ending December 2021, the Company announced the acquisition of the Radiopharmaceuticals Business from Fujifilm Toyama Chemical Co., Ltd. The radiopharmaceutical space is one of the most rapidly growing spaces, and the use of peptides as the ideal targeting ligand for these molecules is gaining considerable traction quickly, in part, due to the Company’s role in supplying such peptides to major players in the space, such as Novartis, RayzeBio, and Bayer. With this acquisition, the Company will build an integrated Japan radiopharm platform from discovery and development through commercialization and sales, allowing the Company to not only accelerate the discovery and development of novel and innovative radionuclide-peptide conjugate drugs, but also to maximize the value of each discovered product.

In addition, in the fiscal year ending December 2021, PeptiGrowth began manufacturing and marketing two products (peptide alternatives to growth factors) for use in ex-vivo applications, such as the growing field of regenerative medicine. In the fiscal year ending December 2022, the Company plans to launch multiple additional products through PeptiGrowth, allowing the company to grow and become profitable as a peripheral healthcare business.

As the Company’s strategic and resource partners have increased over the years, so has the Company’s peptide drug discovery technologies, knowhow and capabilities, which is one of the sources of the Company’s competitive advantage. The Company will continue to look to maximize the value of its existing strategic relationships, while actively discussing potential new strategic partnerships, with a focus on continuing to expand and build its partnership network around its core platform business, toward its goal of reaching its Mid-term targets by the end of 2026.

The Company is in robust financial condition with no interest-bearing debt, a capital adequacy ratio of 93.8%, and cash and cash equivalents of 11,746 million yen (as of the end of December 2021), more than sufficient to maintain research and development activities, as well as strategic investments in further business growth. From a medium-term perspective, the Company expects to maintain its growth trend in both sales and profits while sustainably increasing its corporate value.



**【Company Performance (Prior Six Fiscal Years and Current Forecast for Fiscal Year 2022)】**

	Fiscal Year ended June 30, 2017	Fiscal Year ended June 30, 2018	Fiscal Year ended June 30, 2019	Fiscal Year ended Dec 31, 2019	Fiscal Year ended Dec 31, 2020	Fiscal Year ended Dec 31, 2021	Fiscal Year ending Dec 31, 2022
	2016/July ~ 2017/June	2017/July ~ 2018/June	2018/July ~ 2019/June	2019/July ~ 2019/Dec	2020/Jan ~ 2020/Dec	2021/Jan ~ 2021/Dec	2022/Jan ~ 2022/Dec
Net sales (JPY millions)	4,895	6,426	7,216	1,037	11,677	9,365	13,000 or more
Changes from the previous corresponding period (%)	13.1	31.3	12.3	—	—	(19.8)	38.8
Operating profit (JPY millions)	2,490	2,910	3,579	(887)	6,991	4,418	6,500 or more
Changes from the previous corresponding period (%)	(2.3)	16.9	23.0	—	—	(36.8)	47.1
Operating income to net sales (%)	50.9	45.3	49.6	(85.5)	59.9	47.2	50.0

\* PeptiDream has changed its fiscal-year end in fiscal 2019 from June 30 to December 31. Therefore, changes from the previous corresponding period for the fiscal year ended December 31, 2019 and 2020 are not presented.

**【Other key indices】**

	Fiscal Year ended June 30, 2017	Fiscal Year ended June 30, 2018	Fiscal Year ended June 30, 2019	Fiscal Year ended Dec 31, 2019	Fiscal Year ended Dec 31, 2020	Fiscal Year ended Dec 31, 2021	Fiscal Year ending Dec 31, 2022
	2016/July ~ 2017/June	2017/July ~ 2018/June	2018/July ~ 2019/June	2019/July ~ 2019/Dec	2020/Jan ~ 2020/Dec	2021/Jan ~ 2021/Dec	2022/Jan ~ 2022/Dec
Capital Expenditures (JPY millions)	1,890	2,436	185	140	566	1,300	6,960
Depreciation Expense (JPY millions)	174	493	501	246	559	633	653
Research and Development Expenses (JPY millions)	362	921	1,141	893	1,460	1,638	2,056
Year-end headcount (people)	74	99	127	130	157	177	205

- (Notes)
1. The amount that will actually be paid is shown for capital expenditures.
  2. Capital Expenditures of fiscal year ending December 31, 2021, includes advance payments (644 million yen) for the purchase of the land.
  3. Capital Expenditures of fiscal year ending December 31, 2022, includes balance for the purchase of the land, and advance payments for the construction of the future building.

The Company announced a new Mid-Term Management Targets on March 25, 2021 for the period from the fiscal year ending December 31, 2021 to the fiscal year ending December 31, 2026. Specifically, the Company anticipates 4 or more new therapeutic drugs (not including diagnostics) to be launched (approved), 32 or more programs to be in clinical development, and 160 or more programs to be in preclinical development, by the end of FY2026. In order to fully support and promote these targets, the Company will continue to actively expand through the hiring of highly skilled and talented professionals. In addition, in order to realize our goal of being a global “Drug Discovery Powerhouse”, the Company will continue to expand our partnership network and our leading position as the hub in the global peptide-based drug discovery ecosystem.

Mid-Term Targets by the end of FY2026		As of December 31, 2021
(1) New drugs* launched (approved)	4 or more	0
(2) Number of clinical programs	32 or more	3
(3) Number of preclinical drug discovery programs	160 or more	120
(4) Number of employees	220 or more	177
(5) Establishing foundation as a “Drug Discovery Powerhouse”		

\*Diagnostic agents and products other than therapeutics are not included.

Regarding the 5<sup>th</sup> target, the aim to solidify PeptiDream’s position and reputation as a global “Drug Discovery Powerhouse”, we will particularly focus our efforts on the following five initiatives:

- ① To further lead the expansion of the global peptide-based drug discovery eco-system and our partnership network through expanding our role as the central hub.
- ② To continue to expand the number of licensees of our proprietary PDPS technology and its position as “the most widely-used peptide-based drug discovery platform”.
- ③ To create a healthy, safe, and diverse work environment where all employees can maximize their abilities, have equal opportunities, and be considered a “best place to work”
- ④ To strive toward a “transparent, responsive, and balanced corporate governance structure”, ensure the highest business ethical standards, and maintain a continuous and open dialogue with all internal and external stakeholders.
- ⑤ To promote operational efficiency for the sustainable growth of society, minimize our environmental impact with a focus on water, waste, and energy efficiency, and become “carbon neutral” in our operations by 2026.

#### (5) Basic Policy for Profit Distribution and Dividends for the Fiscal Year under Review and the Following Fiscal Year

The Company acknowledges that returning profits to shareholders is an essential management issue and intends to consider profit distribution taking into account its operating results and financial position. However, for the time being the Company is focusing on maintaining internal reserves and placing priority on securing research and development funds.

## (6) Business Risks

The following are matters that could potentially become major risk factors associated with the business development and/or other activities of the Company. For the purpose of proactive information disclosure to investors, the Company has also included risks that are not necessarily perceived to be material to the Company and risks that are less likely to materialize, as long as they are thought to be significant from the perspective of investment decisions by the investor or for better understanding the business activities of the Company. Upon recognizing the possibility of these risks, the Company has set its policy to make every effort to prevent such risks from materializing and to minimize their impact when they occur, but does not guarantee that such risks will be prevented altogether. It should also be noted that the following is by no means an exhaustive list of all possible risks facing the Company.

Forward-looking statements hereunder are based on the Company's judgment as of the date this document was submitted and involve inherent uncertainties, and therefore the actual results may differ.

### 1) Risks arising from business environment

#### (i) Potential of nonstandard constrained/macrocyclic peptides as pharmaceuticals

The nonstandard constrained/macrocyclic peptides of the Company include not only the 20 L-amino acids that are used to naturally make proteins, but also D-amino acids, N-methyl amino acids, and other amino acid derivatives, etc. collectively referred to as nonstandard amino acids. This ability enables the Company to create various highly diverse nonstandard constrained/macrocyclic peptide libraries from which nonstandard constrained/macrocyclic peptides that exhibit high affinity and specificity against the target protein, which maintain high in-vivo stability and cell membrane permeability, can be identified.

Owing to this feature, the nonstandard constrained/macrocyclic peptides of the Company are expected to represent a new therapeutic class of molecules, and such expectations have led to and continue to lead to discovery and development agreements with pharmaceutical companies.

The Peptide Discovery Platform System (PDPS) of the Company arose in 2010. Pharmaceuticals, in general, require a significant amount of development costs and time (10 years or more) from basic research until obtaining marketing authorizations, etc. It has not been long since the Company's nonstandard constrained/macrocyclic peptide drug discovery and development technology was created and thus to date, no novel drug generated from nonstandard constrained/macrocyclic peptides of the Company has been approved. (However, novel drugs generated from organic compounds incorporating nonstandard amino acids that exist in nature have been approved. For example, in 1983, Sandoz Pharmaceuticals AG of Switzerland launched an immunosuppressive drug named "Sandimmune," and this was created by a peptide (cyclosporine) with a nonstandard structure, produced by a fungus found in the soil of the Hardanger Plateau in southern Norway).

In the event novel drugs cannot be developed from nonstandard constrained/macrocyclic peptides of the Company, or in cases where the Company's nonstandard constrained/macrocyclic peptide drug discovery and development technology cannot beneficially contribute to the clients' drug development efforts, the Company's business strategies and operating results may be negatively impacted.

(ii) Technology innovation

The Peptide Discovery Platform System (PDPS) of the Company incorporates a variety of technologies that are necessary for using nonstandard constrained/macrocylic peptides as therapeutic candidates (i.e., technologies (A) to produce nonstandard constrained/macrocylic peptides, (B) to generate/produce libraries with high diversity compared with low-molecular weight pharmaceuticals and antibody pharmaceuticals and (C) to rapidly conduct screening). The Company considers that the technologies (A) to (C) are all superior to those technologies of other companies that also discover and develop peptides as therapeutic candidates.

However, technology is always evolving, and there is always a chance that a technology superior to the PDPS of the Company will be developed, by utilizing a technology that does not conflict with the patented technology of the Company.

The Company intends to continue to actively perform research and development and to endeavor to secure intellectual property rights necessary for the PDPS technology, for the continued upgrade and evolution of the PDPS technology. However, if a technology superior to the PDPS is developed, the Company's competitive advantage will decrease and, as a result, the Company's business strategies and operating results may be negatively impacted, with more of such cases where agreements under conditions desired by the Company can no longer be entered into with the clients.

2) Risks arising from business

(i) Business based on nonstandard constrained/macrocylic peptide pharmaceuticals

The Company has been conducting its business operations specializing in nonstandard constrained/macrocylic peptide pharmaceuticals. Therefore, nonstandard constrained/macrocylic peptides produced by the Peptide Discovery Platform System (PDPS) of the Company have novelty and inventiveness leading to high originality, thus the Company believes that it is unlikely that alternative technologies could be easily developed to put the existence value of the Company at risk. However, in cases where pharmaceutical companies' views change regarding the value of nonstandard constrained/macrocylic peptides and also in cases where the Company's nonstandard constrained/macrocylic peptide drug discovery and development technology cannot contribute to the clients' drug development efforts, the Company's business strategies and operating results may be negatively impacted.

Recently, by using nonstandard constrained/macrocylic peptides as search markers, it has become apparent that this can lead to development of low-molecular weight pharmaceuticals, and the range of applicability for PDPS has significantly widened. As a result, business operations that specialized in nonstandard constrained/macrocylic peptides is undergoing change, and while making inroads into the industry with PDPS as a foundation in drug discovery and development based on nonstandard constrained/macrocylic peptides, the Company is attempting to expand use into development of low-molecular weight pharmaceuticals, in addition to nonstandard constrained/macrocylic peptides. In cases where the Company cannot contribute to the development of low-molecular weight pharmaceuticals, the Company's business strategies and operating results may be negatively impacted.

(ii) Conducting joint research and development with multiple pharmaceutical companies

As of the date this document was submitted, the Company has joint research and development agreements with more than one company. Each pharmaceutical company has its specific target(s) for drug discovery and development, for which the Company will prosecute by receiving proposals concerning the research and development of, but in rare cases, the target for drug discovery and development may be requested by multiple pharmaceutical companies. Whenever such cases arise, the Company has a formal process for determining which pharmaceutical company has priority. Until now, no issue with this process has occurred.

However, in cases hereafter where this kind of coordination becomes difficult, the Company will not be able to enter into new joint research and development agreements and to acquire new target proteins, and thus the Company's business strategies and operating results may be negatively impacted.

(iii) Revenue recognition

The sales category of the Company for joint research and development agreements is, in principle, composed sequentially of (A) upfront payments (technological access fees), (B) funding for research and development, (C) funding for additional research and development, (D) premiums for drug discovery and development (E) incentives for reaching preclinical and/or clinical development goals (milestones), (F) royalties on net sales, and (G) incentives for reaching sales targets.

Although (A) upfront payments (technological access fees), (B) funding for research and development, and (C) funding for additional research and development significantly rely on the operational success of the Company, for (B) and (C) in particular, project termination resulting from client's policy changes, can result in a situation where ongoing revenue cannot be recognized, as the research and development activities cease. As for (A), whose amount is often relatively larger than that of (B) and (C), such revenue is recognized at one time, which means that the operating results of the Company could be negatively impacted by (A).

(D) Premiums for drug discovery and development and (E) milestones significantly rely on the business progress and strategy of the client, which are sales categories that are largely out of the control of the Company.

Therefore, in cases where the client's development progress is slowed, deprioritized or delayed, or in cases where the client's development strategy is changed, etc., the Company's business strategies and operating results may be negatively impacted.

(iv) Possibility of legal disputes

The Company, during the course of conducting its business operations, in cases where it violates the rights or interests of a third party or in cases where the counterparty considers that it did, even though it actually did not, legal disputes such as lawsuits for damages, etc. may occur.

As of the date this document was submitted, no legal dispute has occurred nor has any formal litigation initiated. In the future, however, when a legal dispute occurs between a third party and the Company, dispute resolution may require certain resources in addition to time and money and the Company can also be exposed to reputation risks resulting from the legal dispute, regardless of the final outcome. In such cases, the Company's business strategies and operating results may be negatively impacted.

In the course of future business operations, conflicts with patent rights, etc. of other companies may limit the Company's business, and in such cases, the Company's business strategies and operating results may be negatively impacted.

Furthermore, there exist no examples of the Company's nonstandard constrained/macrocytic peptide pharmaceuticals researched and developed jointly by the Company and a pharmaceutical company commercially launched as pharmaceuticals to date. Therefore, in the unlikely event that the pharmaceutical researched and developed jointly by the Company causes unforeseen health problems, the negative image/reputation may adversely affect the reliability of the Company and its Peptide Discovery Platform System (PDPS) and thus the Company's business strategies and operating results may be negatively impacted.

(v) Material business agreements

As for agreements considered to be important or material to the Company's business operations, in cases where such agreements are terminated or in cases where changes are made to the counterparty's strategic plans, the Company's business strategies and operating results may be negatively impacted.

Further, revenue/funding related to joint research and development agreements (corresponding to or represented as sales for the Company) are, in principle, received as advances to the Company, which in turn is not obligated to return the money even in cases of early termination of the agreements. In exchange for this benefit, the counterparty holds the right to terminate the agreement at its discretion.

(vi) Dependence on counterparties of joint research and development agreements

Revenue in the Alliance business of the Company is mostly from counterparties of joint research and development

agreements (clients). In the event the joint research and development for novel target molecules are not commenced with the clients or in cases where results of the joint research and development do not meet the criteria required by the clients, the Company's business strategies and operating results may be negatively impacted.

In addition, for lead compounds licensed out by the Company, the client conducts the clinical trials and applies for regulatory approval and thus their progress and results significantly affect the Company's business strategies and operating results. Although the Company will support the client even after licensing out, clinical trials and applications for approval should be carried out by the client and those are beyond the control of the Company. Therefore, the possibility that the progress of clinical trials and/or applications for regulatory approval might be delayed due to reasons unexpected by the Company and that clinical trials and applications for approval might be terminated for various reasons, exists.

Furthermore, marketing plans after obtaining approval for manufacturing and sale rest solely with the clients, and thus there are possibilities such that marketing plan targets cannot be achieved due to factors such as changes in the clients' management policies or marketing plans and deterioration in the business environment.

Furthermore, as significant funds are required for the research and development of drugs, organizational restructuring and M&A are active in this industry. Clients may restructure organization or acquire competing firms (or acquired by competing firms), causing the competitive landscape within the industry to be changed drastically within short periods of time. If such large-scale corporate organizational restructuring occurs at the Company's clients, the Company's business strategies and operating results may be negatively impacted.

(vii) Product pipeline of the Company (in-house drug discovery programs)

The Company is promoting research and development of its own in-house product pipeline (in-house drug discovery programs) utilizing the characteristics of nonstandard constrained/macrocyclic peptides.

As things stand, the Company takes a two-pronged approach to development: Use of nonstandard constrained/macrocyclic peptides as pharmaceuticals, and development of PDC for use in combination with other drugs, leveraging the excellent selectivity of nonstandard constrained/macrocyclic peptides. In addition, through using nonstandard constrained/macrocyclic peptides as search markers, this can lead to development of low-molecular weight pharmaceuticals, and the Company has begun development of low-molecular weight pharmaceuticals in its internal pipeline.

With regard to the in-house product pipeline, if research and development progress smoothly and pre-clinical trials are conducted at the Company's expense, the Company may find itself incurring significant development costs. However, if progress in research and development of the in-house product pipeline is not smooth, there is a risk of losing certain options for future commercialization.

(viii) About strategic alliances with other companies and success or failure of corporate acquisitions, etc.

With the intent of strengthening competitiveness and expanding business scope, etc., the Company may make strategic alliances, etc. through transferring business divisions from other companies, acquiring other companies, entering into business alliances with other companies, establishing joint ventures, or making investments in other companies (hereinafter "Strategic alliances, etc.") Regarding such Strategic alliances, etc., there are possibilities such as the possibility that the alliance or integration does not proceed smoothly with the partner company due to differing views, the possibility that initially expected results cannot be attained, and the possibility that the investment amount cannot be recovered, either in part or in whole. Additionally, there is the possibility that the partner company may make decision that conflicts with the Company's benefit, and in cases such as when the partner company makes changes to its business strategy, there is the possibility that it may become difficult for the Company to maintain the relationship under the Strategic alliance, etc., and the Company's business strategies and operating results may be negatively impacted.

### 3) Intellectual property rights

(i) Acquisition of and application for patents

The Company engages in various inventions and patent rights in the course of its business, some of which have already

been granted to the Company, the University of Tokyo or the State University of New York, while others are at various stages of the patent process.

However, it is possible that not all of the pending applications will be granted. In addition, even after receiving grant of patent rights, there remains the possibility that the item requested may be nullified via the patent objection claim system. There is also the possibility that a legal dispute concerning the patent right might arise, such as the filing of a patent violation lawsuit or request for a hearing on patent invalidation, resulting in some adverse effect to the right implemented by the Company.

There are other possibilities that the technology included in the patent right held by the Company might become obsolete due to emergence of a technology superior to the patent right held by the Company. When such a situation occurs, the Company's business strategies and operating results may be negatively impacted. In addition, the Company has obtained, through an agreement, the exclusive license, with the right to sublicense to a third party, with regard to various inventions or patent rights which the University of Tokyo or the State University of New York is the applicant. In such cases where the contents of the said agreement are subject to alterations or the agreement is terminated due to expiration or cancellation, etc., the Company's business strategies and operating results may be negatively impacted.

(ii) Internal assignment of employee inventions

When the Company receives a right to obtain a patent for an invention by an officer or employee, etc. of the Company, the Company will pay "reasonable consideration" that is provided for in the Patent Act to the said officer or employee, etc. who is the inventor of that invention. The Company has established rules for its handling in the internal rules, etc. and ensured awareness of them among executives and employees, etc. as well as strengthened operations. However, if issues such as payment claims for reasonable consideration arise in handling employee inventions, the Company's business strategies and operating results may be negatively impacted.

4) Risks related to the pharmaceutical research and development business

(i) Uncertainties in pharmaceutical development

Pharmaceutical development in general, not only requires a considerable amount of research and development investment and time, but also has a notably low success rate compared with other industries. Even for compounds considered to be promising at the early stages of research and development, research and development can fall behind schedule due to reasons such that useful effects are not discovered in the course of pre-clinical studies and clinical trials, leading to extension or cancellation of the development. When the development is extended, additional funding may be required and the remaining patent life will be shortened, affecting the recovery of funds invested. In addition, when the development is cancelled, the funds invested in the research and development may not be recovered.

(ii) Risks related to occurrence of adverse drug reactions

Pharmaceuticals can cause unexpected adverse drug reactions starting from the clinical trial stage to post-marketing. When such unexpected adverse drug reactions occur, claim litigation and loss of creditworthiness, etc. are all possible, to which the Company's business strategies and operating results may be negatively impacted.

(iii) Regulations concerning pharmaceutical affairs including the Pharmaceutical Affairs Act

The pharmaceutical industry is subject to various regulations including the Pharmaceutical Affairs Act of each country (the "Law on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices" in Japan) and other related laws and regulations regarding business activities of research, development, manufacturing and sales.

The product pipeline of the Company is now at the discovery and development, with no product yet having been approved for sale by the Ministry of Health, Labour and Welfare of Japan, U.S. Food and Drug Administration (FDA) and European Medicines Agency (EMA). However, the Company intends to apply for regulatory approval for manufacturing and sales of pharmaceuticals pursuant to various regulations of the Pharmaceutical Affairs Act of each country and to obtain such approval in the future.

Therefore, the Company is required to prepare an internal system that meets and adheres to the regulations from the various regulatory entities mentioned above. Moreover, the Pharmaceutical Affairs Act of each country and other related laws and regulations are subject to change from time to time, and it is possible that these changes can affect the class of peptides Company is developing in either a positive or negative way, and that further improvement and amendment of the internal system might become necessary.

Compliance with such regulations shall affect the Company's business strategies and operating results.

(iv) Product liability

Development and manufacturing of pharmaceuticals are subject to the underlying risks of product liability. If any developed pharmaceutical causes adverse health issues or unintended side effects are found, whether in the course of clinical trials, manufacturing, operating or sales, in the future, the Company shall bear product liability and thus the Company's business strategies and operating results may be negatively impacted.

In addition, the negative image resulting from the product liability compensation claim can adversely affect the credibility of the Company and its pharmaceuticals, and thus the Company's business strategies and operating results may be negatively impacted.

(v) Drug administration

The selling prices of drugs for medical use are affected by the regulations relating to drug prices of Japan and the governments of other countries. Thus far, the Company has not conducted an in-house clinical trial, and has adopted a policy of licensing out candidates for early development to clients. As a result, the Company's drug price strategy depends on its clients, and is indirectly affected by the drug price policies of Japan and the governments of other countries. In the event that the Company's development candidates are brought to market, if there are negative amendments to drug prices for the relevant drugs, or other amendments to medical insurance systems, the Company's financial position and operating results may be negatively impacted.

5) Risks associated with human resources and the organization

The Company believes that securing superior human resources with expert knowledge and experience in the research and development field is indispensable for elevating its drug discovery platform technology and advancing its drug discovery research and development. Should the Company encounter any obstacles in securing its human resources as planned, or lose any of its superior human resources, the Company's business strategies and operating results may be negatively impacted.



## 6) Other risks

### (i) Dilution of the Company's stock value due to the exercise of stock acquisition rights

The Company has granted stock acquisition rights to its officers and employees. Should such stock acquisition rights be exercised, the Company's number of shares outstanding would increase, and the value of the shares held by existing shareholders and the ratio of voting rights may become diluted. As of the date this document was submitted, the number of dilutive shares to be increased by the exercisable subscription rights to shares was 0 shares, which is equivalent to 0% of the aggregate number of shares issued and dilutive shares.

### (ii) Dividend policy

The Company recognizes returning profits to shareholders through dividends as one of its important management tasks.

Once steady predictable revenues have been attained, and enough revenue exists to cover the costs of research and development, upon comprehensively taking into account the necessity of enhancing internal reserves in preparation for future research and development activities, the Company will consider the profit distribution to its shareholders.

### (iii) Information security

The Company's business involves receiving information on targeted proteins from client pharmaceutical companies. For this reason, the Company makes every effort to prevent the leakage of corporate information by requiring its employees to sign confidentiality agreements relating to corporate information including customer information.

However, should a leak of corporate information including customer information occur, the Company may face a loss of public confidence and the Company's businesses, etc. may be negatively impacted.

### (iv) Cyberattacks

The technology used in cyberattacks is becoming more sophisticated than ever, and their modus operandi have become more diverse and elaborate in recent years. In light of this situation, the Company regards cyber security-related risk as one of its most material risks. The Company has taken various measures against cyberattacks such as monitoring networks and facilities primarily and is making every possible effort to manage the risk.

However, should cyberattacks cause serious system failure and interrupt business de facto despite these measures, the Company's business, etc. may be negatively impacted.

### (v) Fluctuation of foreign exchange rates

Due to the large number of overseas pharmaceutical companies among the Company's clients, much of its sales are denominated in foreign currencies (mainly in US dollar) and affected by fluctuations of foreign exchange rates. Therefore, should fluctuations in foreign exchange rates occur, the Company's operating results and financial position may be negatively impacted.

### (vi) Breakout of infectious diseases, etc.

The facilities and functions necessary for the Company's business activities and research and development activities are concentrated at its headquarters and research facilities. As the Company now has its employees work from home, etc., work that can be continued away from the headquarters and research facilities is limited to some administrative work. The Company has been continuing the utmost efforts to reduce the risk of infection for its employees, business partners and their families, by continuing to implement both clean/hygienic conditions/practices within office premises and various measures for social distancing to avoid "close contact" with one another as infection countermeasures. However, should a designated infectious disease break out, causing unexpected circumstances such as temporary closure of the headquarters and research facilities, the Company's business activities and operating results may be negatively impacted.

(vii) Environmental safety, natural disasters, and climate change etc

Chemical substances used in our R&D process include substances that adversely affect the human body and the environment. We are monitoring environmental pollutants used in R&D activities, but pollutant exposure to humans, soil pollution, air pollution, water pollution, etc. may affect our business strategies and performance.

The Company has headquarters and research facilities in Tonomachi, Kawasaki, in Kanagawa Prefecture, and facilities and personnel relating to the Company's business activities and research and development activities are concentrated in the present location. With the Tama River flowing nearby, if there is a natural disaster, such as a flood, tsunami or other water-related incidents associated with climate change, causing unexpected circumstances to occur, such as damage to the Company's facilities or supply restrictions from different types of infrastructure, the Company's business strategies and operating results may be negatively impacted.

(viii) Establishment of a CDMO (Contract Development and Manufacturing Organization)

In September 2017, the Company established a CDMO (trade name: "PeptiStar, Inc."; hereinafter, "PeptiStar") as a joint venture with Shionogi & Co., Ltd. and Sekisui Chemical Co., Ltd. in Settsu, Osaka Prefecture.

At present, the research and development of nonstandard peptide pharmaceuticals is conducted by pharmaceutical companies in Japan and overseas, but even on a global level, there is no CDMO that can provide a stable supply of high quality raw materials for nonstandard peptides at a low cost. Under these circumstances, the Company believes that establishing a CDMO with specialist technology relating to nonstandard peptide pharmaceuticals can contribute to promoting the Company's business and, by extension, expanding the market for nonstandard peptide pharmaceuticals. By strategically consolidating the state-of-the-art technology held by each of the domestic companies participating in the PeptiStar joint venture, the Company aims to eliminate bottlenecks relating to the development and sale of nonstandard peptide pharmaceuticals.

The Company has invested 1.9 billion yen into PeptiStar, and has an ownership stake of 14.9% in PeptiStar, equal to that of both Shionogi and Sekisui Chemical. In addition, the Company has guaranteed PeptiStar's debt, thereby making PeptiStar an affiliate of the Company. As a result, if PeptiStar cannot develop its business in the manner forecast by the Company at the time of investment, the Company's financial position and operating results may be negatively impacted, including an impairment of shares.

ix) The investment securities that the Company holds

The Company holds investment securities for the purpose of accelerating collaboration discovery and development. Since the values of the investment securities are determined by the circumstances of the stock issuing companies such as their financial conditions, operating results, etc., in the event that decreases in their real values call for an impairment, loss on valuation of investment securities will be posted, and thus the Company's operating results may be negatively impacted.

x) Harmful rumors

Should negative rumors about the Company, or the Company's related parties or business partners be spread by Analyst report and media coverage or be posted on the Internet, public confidence of the Company may be affected, regardless of whether there was any truth in the rumors. Should negative rumors about the Company, or the Company's related parties or business partners be spread, the credibility of the Company may be adversely affected due to the negative image, and the Company's financial position and operating results may be negatively impacted.

## 2. Management Policies

### (1) Basic Management Policy

The Company's basic management policy is to leverage its proprietary PDPS (Peptide Discovery Platform System) to discover and develop nonstandard constrained/macrocytic peptide pharmaceuticals in order to address unmet medical needs (medical needs for which there are no effective treatments) and to improve the quality of life of patients worldwide. To this end, the Company will contribute to the creation of a market for "nonstandard constrained/macrocytic peptide pharmaceuticals" as a third major market following "low-molecular weight pharmaceuticals" and "antibody pharmaceuticals," and contribute to the progress of medicine around the world.

### (2) Medium- to Long-term Management Strategies

Please refer to "Efforts to Tackle COVID19, Financial Forecasts and Other Forward-looking Information" for details of medium- to long-term management strategies.

### (3) Issues to be Addressed

The Company leverages its proprietary PDPS (Peptide Discovery Platform System) to conclude joint research and development agreements with pharmaceutical companies both in Japan and abroad for the purpose of conducting development of drugs that utilize nonstandard constrained/macrocytic peptides.

The Company recognizes the following as issues that need to be addressed in order to sustain growth as a going concern.

(Issues associated with sales activities)

The Company has built relationships (joint research and development systems) that are mutually amicable and economically beneficial with pharmaceutical companies both in Japan and abroad, and the Company projects the conclusion of further joint research and development agreements in the future. The Company believes that in order to maintain and expand a smooth joint research and development system, strategic sales activities that move in step with establishment and enrichment of the research and development system are important.

(Issues associated with research and development activities)

The Company maintains and utilizes PDPS and believes this system at the moment has huge technological advantages. Additionally, there are significant possibilities for the use of nonstandard constrained/macrocytic peptides that are created via PDPS. To continue to uphold the advantage of this in-house technology, the Company is committed to strengthening its in-house research and development system while undertaking joint research with pharmaceutical companies and research institutions, etc. in Japan and overseas.

(Issues associated with internal management and controls)

The Company recognizes the reinforcement of its corporate governance as a major issue that needs to be addressed in order to develop its corporate structure as a going concern. The Company is aware that enhancement of the efficiency, soundness and transparency of management, and the long-term, stable and continuous improvement of its share value will be indispensable in winning the trust of each stakeholder, including its shareholders. The Company will, therefore, make every effort to develop an organization equipped with agility and company-level efficiency while keeping in mind the adequacy of business execution, and the efficiency and efficacy of its management functions.

## 3. Basic Approach to Accounting Standards

Effective from the three months ending March 31, 2022, the Company voluntarily adopts the International Financial Reporting Standards (IFRS) with the aim of facilitating international comparisons of financial data in capital markets and further improving the level of business management, among others.

## 4. Financial Statements

### (1) Balance Sheets

(Thousands of yen)

	As of December 31, 2020	As of December 31, 2021
<b>Assets</b>		
Current assets		
Cash and deposits	7,149,358	11,746,529
Accounts receivable - trade	5,655,460	810,818
Raw materials and stocks	585,981	925,138
Prepaid expenses	253,843	62,891
Short-term loans receivable from subsidiaries and associates	-	62,805
Other	1,996,877	255,119
<b>Total current assets</b>	<b>15,641,520</b>	<b>13,863,303</b>
Non-current assets		
Property, plant and equipment		
Buildings	4,155,352	4,157,788
Accumulated depreciation	(531,363)	(688,676)
Buildings, net	3,623,989	3,469,112
Structures	192,138	192,138
Accumulated depreciation	(43,434)	(55,975)
Structures, net	148,703	136,162
Tools, furniture and fixtures	2,688,588	3,303,330
Accumulated depreciation	(1,599,053)	(2,020,483)
Tools, furniture and fixtures, net	1,089,535	1,282,847
Land	904,628	904,628
Construction in progress	-	644,400
<b>Total property, plant and equipment</b>	<b>5,766,856</b>	<b>6,437,151</b>
Intangible assets		
Software	77,192	47,256
Other	1,491	28,245
<b>Total intangible assets</b>	<b>78,683</b>	<b>75,502</b>
Investments and other assets		
Investment securities	3,413,342	4,003,553
Shares of subsidiaries and associates	691,445	1,634,710
Long-term loans receivable	89,598	83,355
Long-term loans receivable from subsidiaries and associates	62,805	414,097
Long-term prepaid expenses	8,921	2,379
Deferred tax assets	505,013	93,956
Other	8,541	11,159
<b>Total investments and other assets</b>	<b>4,779,667</b>	<b>6,243,212</b>
<b>Total non-current assets</b>	<b>10,625,208</b>	<b>12,755,865</b>
<b>Total assets</b>	<b>26,266,729</b>	<b>26,619,168</b>

(Thousands of yen)

	As of December 31, 2020	As of December 31, 2021
<b>Liabilities</b>		
Current liabilities		
Accounts payable - trade	55,276	100,868
Accounts payable - other	1,895,157	313,524
Accrued expenses	589,546	448,605
Income taxes payable	1,709,327	42,523
Advances received	319,944	244,063
Deposits received	136,777	122,093
<b>Total current liabilities</b>	<b>4,706,030</b>	<b>1,271,679</b>
Non-current liabilities		
Provision for employee stock ownership plan trust	59,743	68,021
Provision for directors' share benefits	283,951	280,873
<b>Total non-current liabilities</b>	<b>343,694</b>	<b>348,894</b>
<b>Total liabilities</b>	<b>5,049,724</b>	<b>1,620,573</b>
<b>Net assets</b>		
Shareholders' equity		
Capital stock	3,933,885	3,956,738
Capital surplus		
Legal capital surplus	3,930,167	3,953,020
<b>Total capital surplus</b>	<b>3,930,167</b>	<b>3,953,020</b>
Retained earnings		
Other retained earnings		
Retained earnings brought forward	13,936,858	17,543,266
<b>Total retained earnings</b>	<b>13,936,858</b>	<b>17,543,266</b>
Treasury stock	(655,383)	(620,123)
<b>Total shareholders' equity</b>	<b>21,145,528</b>	<b>24,832,900</b>
Valuation and translation adjustments		
Valuation difference on available-for-sale securities	(13,128)	144,204
<b>Total valuation and translation adjustments</b>	<b>(13,128)</b>	<b>144,204</b>
Subscription rights to shares	84,604	21,490
<b>Total net assets</b>	<b>21,217,004</b>	<b>24,998,595</b>
<b>Total liabilities and net assets</b>	<b>26,266,729</b>	<b>26,619,168</b>

## (2) Statements of Income

(Thousands of yen)

	Fiscal year ended December 31, 2020	Fiscal year ended December 31, 2021
Net sales	11,677,253	9,365,964
Cost of sales	2,147,904	2,358,013
Gross profit	9,529,349	7,007,950
Selling, general and administrative expenses	2,538,025	2,589,807
Operating income	6,991,323	4,418,143
Non-operating income		
Interest income	2,167	283
Foreign exchange gains	-	309,617
Operation consignment fee	101,500	-
Subsidies for employment adjustment	16,875	8,010
Other	1,836	38,614
Total non-operating income	122,379	356,525
Non-operating expenses		
Foreign exchange losses	133,266	-
Share issuance cost	30	159
Other	4,128	31
Total non-operating expenses	137,426	191
Ordinary income	6,976,277	4,774,477
Extraordinary income		
Gain on reversal of subscription rights to shares	-	84,000
Total extraordinary income	-	84,000
Extraordinary losses		
Loss on sales of investment securities	-	34,825
Loss on valuation of investment securities	956,251	-
Total extraordinary losses	956,251	34,825
Income before income taxes	6,020,025	4,823,652
Income taxes - current	1,600,250	806,187
Income taxes - deferred	(28,582)	411,057
Total income taxes	1,571,668	1,217,244
Net income	4,448,357	3,606,407

### (3) Statements of Changes in Equity

Fiscal year ended December 31, 2020

(Thousands of yen)

	Shareholders' equity						
	Capital stock	Capital surplus		Retained earnings		Treasury stock	Total shareholders' equity
		Legal capital surplus	Total capital surplus	Other retained earnings Retained earnings brought forward	Total retained earnings		
Balance at the beginning of current period	3,930,541	3,926,823	3,926,823	9,488,501	9,488,501	(411,570)	16,934,296
Changes of items during period							
Issuance of new shares	3,344	3,344	3,344				6,688
Net income				4,448,357	4,448,357		4,448,357
Acquisition of treasury stock						(243,813)	(243,813)
Disposal of treasury stock							-
Net changes of items other than shareholders' equity							
Total changes of items during period	3,344	3,344	3,344	4,448,357	4,448,357	(243,813)	4,211,232
Balance at the end of current period	3,933,885	3,930,167	3,930,167	13,936,858	13,936,858	(655,383)	21,145,528

	Valuation and translation adjustments		Subscription rights to shares	Total net assets
	Valuation difference on available-for-sale securities	Total valuation and translation adjustments		
Balance at the beginning of current period	(40,700)	(40,700)	84,693	16,978,289
Changes of items during period				
Issuance of new shares				6,688
Net income				4,448,357
Acquisition of treasury stock				(243,813)
Disposal of treasury stock				-
Net changes of items other than shareholders' equity	27,571	27,571	(88)	27,482
Total changes of items during period	27,571	27,571	(88)	4,238,714
Balance at the end of current period	(13,128)	(13,128)	84,604	21,217,004

Fiscal year ended December 31, 2021

(Thousands of yen)

	Shareholders' equity						
	Capital stock	Capital surplus		Retained earnings		Treasury stock	Total shareholders' equity
		Legal capital surplus	Total capital surplus	Other retained earnings Retained earnings brought forward	Total retained earnings		
Balance at the beginning of current period	3,933,885	3,930,167	3,930,167	13,936,858	13,936,858	(655,383)	21,145,528
Changes of items during period							
Issuance of new shares	22,852	22,852	22,852				45,704
Net income				3,606,407	3,606,407		3,606,407
Acquisition of treasury stock						(362)	(362)
Disposal of treasury stock						35,622	35,622
Net changes of items other than shareholders' equity							
Total changes of items during period	22,852	22,852	22,852	3,606,407	3,606,407	35,260	3,687,372
Balance at the end of current period	3,956,738	3,953,020	3,953,020	17,543,266	17,543,266	(620,123)	24,832,900

	Valuation and translation adjustments		Subscription rights to shares	Total net assets
	Valuation difference on available-for-sale securities	Total valuation and translation adjustments		
Balance at the beginning of current period	(13,128)	(13,128)	84,604	21,217,004
Changes of items during period				
Issuance of new shares				45,704
Net income				3,606,407
Acquisition of treasury stock				(362)
Disposal of treasury stock				35,622
Net changes of items other than shareholders' equity	157,333	157,333	(63,114)	94,218
Total changes of items during period	157,333	157,333	(63,114)	3,781,590
Balance at the end of current period	144,204	144,204	21,490	24,998,595



## (4) Statements of Cash Flows

(Thousands of yen)

	Fiscal year ended December 31, 2020	Fiscal year ended December 31, 2021
<b>Cash flow from operating activities</b>		
Income before income taxes	6,020,025	4,823,652
Depreciation	559,201	633,006
Amortization of goodwill	11,815	-
Increase (decrease) in provision for directors' share benefits	139,214	27,500
Interest and dividend income	(2,167)	(283)
Foreign exchange losses (gains)	132,827	(159,845)
Share issuance cost	30	159
Subsidy income	-	(748)
Loss (gain) on valuation of investment securities	956,251	-
Loss (gain) on sales of investment securities	-	34,825
Gain on reversal of subscription rights to shares	-	(84,000)
Decrease (increase) in notes and accounts receivable - trade	(5,342,968)	4,844,642
Decrease (increase) in inventories	(244,665)	(339,157)
Decrease (increase) in prepaid expenses	(94,827)	197,493
Decrease (increase) in accounts receivable - other	(1,738,800)	1,738,800
Increase (decrease) in notes and accounts payable - trade	16,680	45,591
Increase (decrease) in accounts payable - other	1,788,258	(1,667,072)
Increase (decrease) in accrued expenses	518,692	(140,941)
Increase (decrease) in advances received	7,020	(75,881)
Increase (decrease) in deposits received	124,410	(14,683)
Other, net	(1,109,874)	(817,145)
Subtotal	1,741,127	9,045,912
Interest and dividend income received	2,167	283
Income taxes paid	(10,725)	(2,391,619)
Income taxes refund	164	131
Net cash provided by (used in) operating activities	1,732,733	6,654,708
<b>Cash flow from investing activities</b>		
Proceeds from sales of investment securities	-	145,222
Purchase of shares of subsidiaries and associates	(691,445)	(943,265)
Loan advances to subsidiaries and associates	(62,805)	(414,097)
Collection of loans receivable	4,160	6,241
Subsidies received	136,323	137,071
Purchase of property, plant and equipment	(575,910)	(1,185,973)
Purchase of intangible assets	(10,350)	(28,705)
Other, net	-	55
Net cash provided by (used in) investing activities	(1,200,025)	(2,283,450)
<b>Cash flow from financing activities</b>		
Proceeds from issuance of shares resulting from exercise of subscription rights to shares	6,569	44,940
Proceeds from issuance of subscription rights to shares	-	21,490
Purchase of treasury shares	(243,813)	(362)
Net cash provided by (used in) financing activities	(237,244)	66,067
Effect of exchange rate change on cash and cash equivalents	(132,827)	159,845
Net increase (decrease) in cash and cash equivalents	162,636	4,597,171
Cash and cash equivalents at beginning of period	6,986,722	7,149,358
Cash and cash equivalents at end of period	7,149,358	11,746,529

(5) Notes to Financial Statements

(Notes regarding going concern assumption)

Not applicable.

(Segment information, etc.)

The Company operates in a single business segment, the Alliance business segment. As such, statements for segment information are omitted because of immateriality.

(Equity in earnings and losses, etc.)

(Thousands of yen)

	Fiscal year ended December 31, 2020	Fiscal year ended December 31, 2021
Investments in affiliates	691,445	1,634,710
Investments accounted for using the equity method	294,927	596,810
Losses on investments accounted for using the equity method	729,057	470,053

(Per share information)

	Fiscal year ended December 31, 2020	Fiscal year ended December 31, 2021
Net assets per share	168.10yen	192.39 yen
Net income per share	35.40yen	27.98 yen
Diluted net income per share	34.26yen	27.78 yen

(Notes) 1. Shares in the Company remaining in the trust and reported as treasury shares under shareholders' equity are included in treasury shares excluded when calculating the average number of shares during the period for the calculation of net income per share. In addition, these shares are included in the number of treasury shares excluded from the total number of shares issued at the end of the period for the calculation of net assets per share.

When calculating net income per share and diluted net income per share, the average number of treasury shares during the period that is excluded is 173,454 shares for the fiscal year ended December 31, 2020 and 187,069 shares for the fiscal year ended December 31, 2021. When calculating net assets per share, the number of shares of treasury stock at the end of the period that is excluded is 193,694 shares for the fiscal year ended December 31, 2020 and 182,964 shares for the fiscal year ended December 31, 2021.

2. Net income per share and diluted net income per share are calculated based on the following basis:

Items	Fiscal year ended December 31, 2020	Fiscal year ended December 31, 2021
Net income per share		
Net income (thousands of yen)	4,448,357	3,606,407
Net income not attributable to common shareholders (thousands of yen)	—	—
Net income related to common stock (thousands of yen)	4,448,357	3,606,407
Average number of common stock during the period (shares)	125,668,094	128,904,152
Diluted net income per share		
Adjustments for net income (thousands of yen)	—	—
Number of increase of common stock (shares)	4,159,153	917,292
(Subscription rights to shares)	(4,159,153)	(917,292)
Dilutive shares that do not have a diluting effect and thus were not included in the calculation of diluted net income per share	Seventh series stock acquisition rights (Number of stock acquisition rights: 24,000)	Eighth series stock acquisition rights (Number of stock acquisition rights: 30,700)

3. Net assets per share are calculated based on the following basis:

Items	As of December 31, 2020	As of December 31, 2021
Total net assets (thousands of yen)	21,217,004	24,998,595
Amounts deducted from total net assets (thousands of yen)	84,604	21,490
(Subscription rights to shares) (thousands of yen)	(84,604)	(21,490)
Amounts of net assets related to common stock at the end of the period (thousands of yen)	21,132,399	24,977,105
Number of common stock at the end of the period used for the calculation of net assets per share (shares)	125,716,706	129,827,436

(Significant subsequent events)

Not applicable.