Better Health, Brighter Future





# **Takeda Quarterly Financial Report**

For the Year Ended March 31, 2022

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# **Financial Highlights**

# **Selected Financial Results**

#### **Results of Operation**

_	Fiscal Year Ended	at March 31	Change versus the previous year	
(JPY millions)	2021	2022	JPY	%
Revenue	3,197,812	3,569,006	371,194	11.6 %
Operating profit	509,269	460,844	(48,424)	(9.5) %
Profit before tax	366,235	302,571	(63,665)	(17.4) %
Net profit for the period	376,171	230,166	(146,005)	(38.8) %
Net profit attributable to owners of the Company	376,005	230,059	(145,946)	(38.8) %
Earnings per share (JPY)				
Basic earnings per share	240.72	147.14	(93.58)	(38.9) %
Diluted earnings per share	238.96	145.87	(93.09)	(39.0) %

#### Non-IFRS Measures

Results of Operations

	Fiscal Year Ended	at March 31	Change versus the p	s the previous year	
(JPY billions)	2021	2022	JPY	%	
Underlying:					
Revenue Growth	+ 2.2%	+ 7.4%			
Core operating profit margin	30.3 %	27.9 %			
Core Operating Profit	967.9	955.2	(12.7)	(1.3) %	
Core EPS (yen)	420	425	5	1.2 %	
Free Cash Flow	1,237.8	943.7	(294.2)	(23.8) %	

Leverage				
	As of			
(JPY billions)	March 31, 2021	March 31, 2022		
Net debt	(3,429.4)	(3,233.8)		
Adjusted EBITDA (Last 12 months)	1,083.5	1,168.0		
Net debt/Adjusted EBITDA ratio	3.2 x	2.8 x		

Takeda uses certain non-IFRS measures to supplement the analysis of results of operations under International Financial Reporting Standards ("IFRS"). Refer to *Supplementary Information "<u>3. Definition of Non-IFRS Measures</u>" for the definition and "<u>4.</u> <u>Reconciliation</u>" for reconciliations of non-IFRS Measures.* 

#### **Consolidated Cash Flows**

	Fiscal Year Ended	at March 31	Change versus the previous year		
(JPY millions)	2021	2022	JPY	%	
Cash flows from (used in) operating activities	1,010,931	1,123,105	112,174	11.1 %	
Cash flows from (used in) investing activities	393,530	(198,125)	(591,655)	—	
Cash flows from (used in) financing activities	(1,088,354)	(1,070,265)	18,089	(1.7) %	

#### **Consolidated Financial Position**

	As of			orevious year
(JPY millions)	March 31, 2021	March 31, 2022	JPY	%
Non-current Assets	10,199,400	10,584,376	384,976	3.8 %
Current Assets	2,712,893	2,593,642	(119,251)	(4.4) %
Total Assets	12,912,293	13,178,018	265,725	2.1 %
Non-current Liabilities	5,961,940	5,348,764	(613,176)	(10.3) %
Current Liabilities	1,773,176	2,145,730	372,554	21.0 %
Total Liabilities	7,735,116	7,494,495	(240,621)	(3.1)%
Equity	5,177,177	5,683,523	506,346	9.8 %
Total liabilities and equity	12,912,293	13,178,018	265,725	2.1 %

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#### **Forecast and Management Guidance**

Forecast\*

(JPY billions)	FY2021 (Actual)	FY2022 (Forecast)	Change over the pro	evious year
Reported:				
Revenue	3,569.0	3,690.0	+121.0	+3.4 %
Operating profit	460.8	520.0	+59.2	+12.8 %
Profit before tax	302.6	411.0	+108.4	+35.8 %
Net profit for the year (attributable to owners of the Company)	230.1	292.0	+61.9	+26.9 %
EPS (JPY)	147.14	188.13	+40.99	+27.9 %
Non-IFRS Measures				
Core Operating Profit	955.2	1,100.0	+144.8	+15.2 %
Core EPS (JPY)	425	484	+60	+14.0 %
Free cash flow (including announced divestitures)	943.7	600.0 - 700.0		
Dividends per share (Yen)	180	180		<u> </u>

\*Refer to Analysis of Results of Operations, Financial Position, and Cash Flow "Outlook for the Fiscal Year Ending March 31, 2023" for details.

Management Guidance*	
	FY2022
Core Revenue Growth	Low-single-digit growth
Core Operating Profit Growth	High-single-digit growth
Core EPS Growth	High-single-digit growth

\*CER (Constant Exchange Rate) eliminates the effect of foreign exchange rates by translating results of operations using corresponding exchange rates in the same period of the previous fiscal year. Please refer to "*Analysis of Results of Operations, Financial Position, and Cash Flow - <u>Results of Operations (Underlying)</u>" and "Supplementary Information - <u>3. Definition of Non-IFRS Measures</u>" for the definition of Core performance measurements.* 

### **Revenue by Region**

		JPY (millions) Fiscal Year Ended March 31							
		Japan	United States	Europe and Canada	Asia (excluding Japan)	Latin America	Russia/CIS	Other	Total
	2021	559,748	1,567,931	666,177	156,240	121,638	57,560	68,518	3,197,812
	2022	658,983	1,714,421	739,168	196,964	128,467	62,057	68,945	3,569,006
Change versus the	JPY	99,236	146,489	72,991	40,724	6,829	4,497	428	371,194
previous year	%	17.7 %	9.3 %	11.0 %	26.1 %	5.6 %	7.8 %	0.6 %	11.6 %

previous year

"Other" includes the Middle East, Oceania and Africa. This disaggregation provides revenue attributable to countries or regions based on the customer location.

# **Revenue by Therapeutic Area and Product**

	JPY (millions)			
	Fiscal Year Ende	d March 31	Change versus the p	orevious year
	2021	2022	JPY	%
Gastroenterology:				
ENTYVIO	429,281	521,778	92,498	21.5 %
TAKECAB-F <sup>(1)</sup>	84,822	102,397	17,575	20.7 %
GATTEX/REVESTIVE	64,564	75,751	11,187	17.3 %
DEXILANT	55,572	50,763	(4,809)	(8.7)%
PANTOLOC/CONTROLOC <sup>(2)</sup>	43,120	40,275	(2,845)	(6.6)%
LIALDA/MEZAVANT	25,478	26,475	997	3.9 %
PENTASA	23,135	20,192	(2,943)	(12.7)%
AMITIZA	21,220	6,452	(14,769)	(69.6)%
RESOLOR/MOTEGRITY	11,239	12,992	1,753	15.6 %
ALOFISEL	784	1,843	1,059	135.1 %
Others	18,584	16,766	(1,818)	(9.8)%
Total Gastroenterology	777,800	875,685	97,885	12.6 %
Rare Diseases:				
Rare Metabolic:				
ELAPRASE	68,786	73,119	4,333	6.3 %
REPLAGAL	51,764	51,714	(50)	(0.1)%
VPRIV	38,518	42,408	3,890	10.1 %
NATPARA/NATPAR	3,552	5,353	1,801	50.7 %
Total Rare Metabolic	162,620	172,595	9,974	6.1 %
Rare Hematology:			,,,,,	0.1 70
ADVATE	128,535	118,491	(10,044)	(7.8)%
ADYNOVATE/ADYNOVI	58,070	60,726	2,656	4.6 %
FEIBA	44,495	39,162	(5,333)	(12.0)%
RECOMBINATE	13,389	12,297	(1,092)	(12.0) %
HEMOFIL/IMMUNATE/IMMUNINE	18,663	17,722	(1,052) (941)	(5.0)%
Other PDT Products	3,461	3,916	455	13.2 %
Others	23,186	31,375	8,189	35.3 %
Total Rare Hematology	289,799	283,689	(6,111)	(2.1)%
Hereditary Angioedema:	209,799	203,009	(0,111)	(2.1) /0
TAKHZYRO	86,718	103,242	16,524	19.1 %
FIRAZYR	26,824	26,691		
CINRYZE	20,824 21,869	19,297	(133) (2,572)	(0.5)%
KALBITOR				(11.8)%
Total Hereditary Angioedema	3,916	4,357	441	11.3 %
Others:	139,327	153,587	14,260	10.2 %
Total Rare Diseases	=	1,325	1,325	
PDT Immunology:	591,746	611,196	19,450	3.3 %
immunoglobulin	334,874	385,864	50,991	15.2 %
albumin				
Other	57,580	90,035	32,455	56.4 %
Total PDT Immunology	27,935	31,052	3,117	11.2 %
i otar i 12 i infiliuliology	420,389	506,951	86,563	20.6 %

	Fiscal Year En	ded March 31	Change versus the <b>p</b>	orevious year
	2021	2022	JPY	%
Oncology:				
VELCADE	101,112	110,046	8,933	8.8 %
LEUPLIN/ENANTONE	95,365	106,459	11,094	11.6 %
NINLARO	87,396	91,203	3,808	4.4 %
ADCETRIS	59,432	69,190	9,758	16.4 %
ICLUSIG	34,193	34,860	667	1.9 %
VECTIBIX	23,823	24,702	880	3.7 %
ALUNBRIG	8,806	13,644	4,837	54.9 %
Other	6,385	18,627	12,242	191.7 %
Total Oncology	416,512	468,730	52,219	12.5 %
Neuroscience:				
VYVANSE/ELVANSE	271,531	327,052	55,522	20.4 %
TRINTELLIX	68,869	82,315	13,446	19.5 %
INTUNIV	20,408	18,938	(1,471)	(7.2)%
ADDERALL XR	17,773	20,885	3,112	17.5 %
ROZEREM	12,017	11,667	(350)	(2.9)%
Other	26,699	21,437	(5,262)	(19.7)%
Total Neuroscience	417,297	482,294	64,997	15.6 %
Other:				
AZILVA-F <sup>(1)</sup>	82,205	76,297	(5,909)	(7.2)%
LOTRIGA	31,765	32,690	925	2.9 %
AIPHAGAN	15,913	14,899	(1,015)	-6.4 %
FOSRENOL	13,476	13,612	136	1.0 %
ACTOVEGIN	10,716	13,440	40 2,724	
Others <sup>(3)</sup>	419,992	473,213	53,221	12.7 %
Total Other	574,068	624,150	50,082	8.7 %
Total Revenue by Product	3,197,812	3,569,006	371,194	11.6 %

#### JPY (millions)

<sup>(1)</sup> The figures include the amounts of fixed dose combinations and blister packs. <sup>(2)</sup> Generic name: pantoprazole

<sup>(3)</sup> The figure for the Fiscal Year ended March 31, 2021 includes the revenue of Takeda Consumer Healthcare Company Limited, which was divested on March 31, 2021. The figure for the Fiscal Year ended March 31, 2022 includes the 133,043 million JPY selling price on sales of four diabetes products (NESINA, LIOVEL, INISYNC and ZAFATEK) in Japan to Teijin Pharma Limited recorded as revenue.

# **Recent Developments**

## **Business Development**

During the year-ended March 31, 2022 and through the issuance of its earnings release dated May 11, 2022, Takeda Pharmaceutical Company Limited ("Takeda", or the "Company") divested certain businesses and assets in non-core areas as part of its efforts to deleverage toward its target of 2x (i.e. "low-twos") net debt/adjusted EBITDA ratio by the fiscal year ending March 2024. Major divestment activities during the period are as follows:

- In April 2021, we completed the asset transfer associated with a portfolio of select non-core products in Japan to Teijin Pharma Limited for a total value of 133.0 billion JPY.
- In March 2022, we completed the sale of a portfolio of non-core prescription pharmaceutical products sold in China to Hasten Biopharmaceutic Co., Ltd. (China) for a total value of 230.0 million USD or 28.1 billion JPY<sup>\*1</sup>.

Note:

\*1 Calculated using the Japanese yen-U.S. dollar exchange rate of 122.2 JPY.

## Pipeline and R&D Activities

Research and development expenses for the year ended March 31, 2022 were 526.1 billion JPY.

The research and development (R&D) of pharmaceutical products is a lengthy and expensive process that can span more than 10 years. The process includes multiple studies to evaluate a product's efficacy and safety, followed by submission to regulatory authorities who review the data and decide whether to grant marketing approval. Only a small number of therapeutic candidates pass such rigorous investigation and become available for use in clinical treatment. Once approved, there is ongoing R&D support for marketed products, including medical affairs and other investments.

Clinical trials, which must comply with regional and international regulatory guidelines, generally take five to seven years or longer, and require substantial expenditures. In general, clinical trials are performed in accordance with the guidelines set by the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use. The relevant regional regulatory authorities are the Ministry of Health, Labour and Welfare (MHLW) for Japan, the Food and Drug Administration (FDA) for the United States, the European Medicines Agency (EMA) for the EU and National Medical Products Administration (NMPA) for China.

The three phases of human clinical trials, which may overlap with each other, are as follows:

Phase 1 ("P-1") clinical trials

Conducted using a small group of healthy adult volunteers in order to evaluate safety and absorption, distribution, metabolism and excretion of the drug.

Phase 2 ("P-2") clinical trials

Conducted using a small group of patient volunteers in order to evaluate safety, efficacy, dosage and administration methods. P-2 clinical trials may be divided into two sub- categories, P-2a and P-2b. P-2a are usually pilot studies designed to demonstrate clinical efficacy or biological activity. P-2b studies look to find the optimum dose at which the drug shows biological activity with minimal side-effects.

Phase 3 ("P-3") clinical trials

Conducted using a large number of patient volunteers in order to evaluate safety and efficacy in comparison to other medications already available or placebo.

Of these three phases, Phase 3 requires the largest expenditures and thus the decision to proceed with Phase 3 testing is a critical business decision in the drug development process. For those drug candidates that pass Phase 3 clinical trials, a New Drug Application ("NDA"), Biologics License Application ("BLA") or a Marketing Authorization Application ("MAA") is submitted to the relevant governmental authorities for approval, which if granted permits the subsequent launch of the drug. The preparation of an NDA, BLA or MAA submission involves considerable data collection, verification, analysis and expense. Even after the launch of the product, health authorities require post-marketing surveillance of adverse events, and they may request a post-marketing study to provide additional information regarding the risks and benefits of the product.

Takeda's R&D engine is focused on translating science into highly innovative, life-changing medicines that make a critical difference to patients. Takeda supports dedicated R&D efforts across three areas: Innovative Biopharma, Plasma-Derived Therapies ("PDT") and Vaccines. The R&D engine for Innovative Biopharma is the largest component of our R&D investment and has produced exciting new molecular entities ("NMEs") that represent potential best-in-class and/or first-in-class medicines in areas of high unmet medical need across our core therapeutic areas (oncology, rare genetics and hematology, neuroscience, and gastroenterology ("GI")). Over the past several years, including via our acquisition of Shire, we are working to harness the potential of cell and gene therapies by investing in new capabilities and next-generation platforms internally and through a network of partnerships.

Takeda's pipeline is positioned to support both the near-term and long-term sustained growth of the company. Once first approval of a product is achieved, Takeda R&D is equipped to support geographic expansions of such approval and approvals in additional indications, as well as post-marketing commitment and potential additional formulation work. Takeda's R&D team works closely with the commercial functions to maximize the value of marketed products and reflect commercial insights in its R&D strategies and portfolio.

Our key in-house R&D facilities include:

- Shonan Heath Innovation Park: Located in Fujisawa and Kamakura in Kanagawa Prefecture in Japan, the Shonan Health Innovation Park ("Shonan iPark") was established in 2011 as the Shonan Research Center and is our primary location for neuroscience research. In April 2018, we launched Shonan iPark to enhance scientific innovation and establish a life science ecosystem with diverse external parties. To attract more diverse partners and to further the success of the Shonan iPark, in April 2020 Takeda transferred ownership rights of Shonan iPark to a trustee and Takeda, as a flagship tenant, has signed a 20-year lease agreement with the trustee and is committed to invigorating life science research in Japan.
- Greater Boston Area Research and Development Site: Our Boston R&D site is located in Cambridge, Massachusetts
  in the United States. It is the center of our global oncology, GI, and rare genetics and hematology R&D, and also
  supports R&D in other areas including plasma-derived therapies and vaccines, as well as research in
  immunomodulation and biologics. The site is home to the Takeda Cell Therapy engine with a recently opened stateof-the-art cell therapy manufacturing facility.
- San Diego Research and Development Site: Our R&D site located in San Diego, California in the United States supports R&D in the GI and neuroscience areas. The San Diego research center operates as a "biotech-like" site and leverages internal capabilities such as structural biology and biophysics to catalyze research internally and externally.
- *Vienna, Austria Research and Development Site*: Our R&D sites, located in Vienna and nearby Orth, Austria, support R&D in PDT and Gene Therapy. The research centers contain manufacturing sites for plasma derived products and gene therapy products.

Major progress on R&D events since April 2021 are listed as follows:

#### R&D pipeline

#### Oncology

In Oncology, Takeda endeavors to deliver novel medicines to patients with cancer worldwide through a commitment to breakthrough innovation and a passion for improving the lives of patients. Takeda focuses on three key areas in oncology: (1) building on its foundational expertise in hematologic malignancies through continued investment in lifecycle management programs for marketed products NINLARO, ADCETRIS, and ICLUSIG, as well as in pipeline assets in Multiple Myeloma and other blood cancers; (2) further developing its portfolio in lung cancer with the marketed products ALUNBRIG, EXKIVITY, and development programs in targeted lung cancer populations; and (3) pursuing novel immuno-oncology targets and next-generation platforms harnessing the power of the innate immune system, internally and through external partnerships.

#### NINLARO / Generic name: ixazomib

In May 2021, Takeda announced that it received approval from the Japanese Ministry of Health, Labour and Welfare (MHLW) for a partial amendment to the manufacturing and marketing approval of NINLARO to expand the eligible patient population for this medicine to those requiring a maintenance therapy after first-line treatment for multiple myeloma without prior stem cell transplant. The approval is based primarily on the results of the TOURMALINE-MM4 study, a randomized and placebo-controlled double-blind multicenter international Phase 3 clinical trial. The study achieved its primary endpoint, demonstrating a statistically significant improvement in

progression-free survival (PFS) in adult patients with multiple myeloma receiving NINLARO maintenance who had not undergone stem cell transplantation. The safety profile of NINLARO as a maintenance therapy is similar to its established safety profile in the monotherapy setting, and, notably, no new concerns were identified in the TOURMALINE-MM4 study.

#### ICLUSIG / Generic name: ponatinib

In June 2021, Takeda presented primary analysis data from the Phase 2 OPTIC (Optimizing Ponatinib Treatment in CML) trial during an oral session at the virtual 57<sup>th</sup> American Society of Clinical Oncology (ASCO) Annual Meeting, and as an oral session at the virtual 26<sup>th</sup> European Hematology Association (EHA) Annual Meeting. The OPTIC trial, which evaluated treatment in patients with resistant disease, with and without mutations, met its primary endpoint. The study demonstrated that the optimal benefit-risk profile for ICLUSIG in patients with CP-CML is achieved with a daily starting dose of 45-mg and, upon achieving ≤1% BCR-ABL1<sup>IS</sup>, dose reduction to 15-mg. The results also suggest a clinically manageable safety and arterial occlusive event (AOE) profile for ICLUSIG.

#### ALUNBRIG / Generic name: brigatinib

- In June 2021, Takeda announced that ALUNBRIG can be used for first-line treatment of patients with non-small cell lung cancer (NSCLC) who are ALK fusion gene positive (ALK-positive) as determined by the companion diagnostic ALK fusion protein kit, Ventana OptiView ALK (D5F3) (Ventana) in Japan. Ventana, developed by Roche Diagnostics, which uses as its assay principle the immunohistochemical staining method (IHC method), received an additional indication through a partial change of the drug's manufacturing and marketing approval to include its use to ALUNBRIG. The additional approval of ALUNBRIG for the indication of Ventana, in addition to the Fluorescence *In Situ* Hybridization (FISH) diagnostic, will provide a wider range of ALK-positive NSCLC patients with the opportunity to be treated with ALUNBRIG.
- In March 2022, Takeda announced that the National Medical Products Administration (NMPA) of China approved ALUNBRIG as a monotherapy for the treatment of patients with anaplastic lymphoma kinase-positive (ALK+) locally advanced or metastatic non-small cell lung cancer (NSCLC). In the US, it has been listed as a preferred firstline therapy by the National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology and also listed in the Chinese Society of Clinical Oncology (CSCO) Guidelines for Diagnosis and Treatment of Non-Small Cell Lung Cancer. Alunbrig is Takeda's first lung cancer drug approved in China.

#### ADCETRIS / Generic name: brentuximab vedotin

In September 2021, Takeda announced that it submitted a Supplemental New Drug Application (sNDA) of ADCETRIS in the first-line treatment of CD30-positive Hodgkin lymphoma in pediatric patients in Japan. This application is based on the results of a global Phase 1/2 trial (C25004 Trial) evaluating the efficacy and safety of ADCETRIS in combination with AVD (doxorubicin, vinblastine and dacarbazine) as a first-line therapy in pediatric patients with previously untreated advanced-stage Hodgkin lymphoma.

#### CABOMETYX / Generic name: cabozantinib

In August 2021, Takeda and Ono Pharmaceutical (Ono) announced that the companies received an approval from the Japanese Ministry of Health. Labour and Welfare (MHLW) for CABOMETYX and Ono's OPDIVO (nivolumab), a human anti-human PD-1 monoclonal antibody, in combination therapy for the treatment of unresectable or metastatic renal cell carcinoma (RCC), for a partial change in approved items of the manufacturing and marketing approval. This approval is based on results from the global, multi-center, randomized, open-label Phase 3 CheckMate-9ER study, evaluating OPDIVO and CABOMETYX combination therapy versus sunitinib alone in patients with previously untreated advanced or metastatic RCC. In this study, OPDIVO and CABOMETYX combination therapy demonstrated a significant and clinically meaningful improvement in the primary endpoint of progression-free survival (PFS) as assessed by the blind independent central review (BICR), compared to sunitinib alone at the final analysis, as well as the secondary endpoints of overall survival (OS) and objective response rate (ORR) as assessed by the BICR. The safety profiles of OPDIVO and CABOMETYX combination therapy observed in the study were consistent with the previously reported safety profile of each product.

#### ZEJULA / Generic name: niraparib

In September 2021, Takeda announced that it has received approval from the Japanese Ministry of Health. Labour and Welfare (MHLW) to manufacture and market ZEJULA tablets 100mg (ZEJULA tablets) as an additional formulation for ZEJULA capsules 100mg (ZEJULA capsules), an oral poly (ADP-ribose) polymerase (PARP) inhibitor. The approval was granted based on the results of a human bioequivalence trial (3000-01-004 trial) and a dissolution study that confirmed the equivalence of ZEJULA capsules and ZEJULA tablets. ZEJULA capsules require refrigerated storage, however the newly approved ZEULA tablets can be stored at room temperature.

#### EXKIVITY / Generic name: mobocertinib

- In May 2021, Takeda announced updated data from the Phase 1/2 trial of mobocertinib in patients with epidermal growth factor receptor (EGFR) Exon20 insertion mutation-positive (insertion+) metastatic non-small cell lung cancer (mNSCLC) who received prior platinum-based chemotherapy. The results showed mobocertinib continued to demonstrate clinically meaningful benefit after over a year of follow up and were presented at the virtual 57th American Society of Clinical Oncology (ASCO) Annual Meeting. Results showed a median overall survival (OS) of 24 months with a median follow up of 14 months, and responses were observed across diverse EGFR Exon20 insertion variants. Other key data points such as confirmed objective response rate (ORR), a median duration of response (DoR) and a disease control rate (DCR), remained consistent with previously reported data. The safety profile observed was manageable and consistent with previous findings.
- In July 2021, Takeda announced that Center for Drug Evaluation (CDE) of the National Medical Products Administration of China (NMPA) has accepted the New Drug Application (NDA) for mobocertinib and granted priority review for this Class-1 innovative drug, for the treatment of adult patients with non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) Exon20 insertion mutations.
- In September 2021, Takeda announced that the U.S. Food and Drug Administration (FDA) has approved EXKIVITY for the treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 20 insertion mutations as detected by an FDA-approved test, whose disease has progressed on or after platinum-based chemotherapy. The FDA approval is based on results from the platinum-pretreated population in the Phase 1/2 trial of EXKIVITY, which consisted of 114 patients with EGFR Exon20 insertion+ NSCLC who received prior platinum-based therapy and were treated at the 160 mg dose once- daily. EXKIVITY, which was granted priority review and received Breakthrough Therapy Designation, Fast Track Designation and Orphan Drug Designation from the FDA, is the first and only approved oral therapy specifically designed to target EGFR Exon20 insertion mutations. This indication is approved under Accelerated Approval based on overall response rate (ORR) and duration of response (DoR). Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial. The FDA simultaneously approved Thermo Fisher Scientific's Oncomine Dx Target Test as a next-generation sequencing (NGS) companion diagnostic for EXKIVITY to identify NSCLC patients with EGFR Exon20 insertions.

#### VECTIBIX / Generic name: panitumumab

In March 2022, Takeda announced that the PARADIGM trial (Panitumumab and RAS, Diagnostically useful Gene Mutation for mCRC), a Phase 3 clinical study of VECTIBIX conducted in Japan, has met its primary endpoint. The PARADIGM trial is a randomized Phase 3 study designed to compare the efficacy and safety of VECTIBIX versus Bevacizumab, both used in combination with mFOLFOX6, in patients with RAS wild-type metastatic colorectal cancer (mCRC) who are previously untreated with chemotherapy. The PARADIGM trial is the first prospective study to evaluate the optimal treatment for patients with left-sided primary tumors (descending colon, sigmoid colon, rectum), RAS wild-type mCRC. The topline results of the trial demonstrated that VECTIBIX plus mFOLFOX6 arm resulted in statistically significant overall survival (OS) improvement, the primary endpoint of this study, in both left-sided primary tumor population and intent-to-treat population, compared to the bevacizumab plus mFOLFOX6 arm. The safety profile of VECTIBIX in this study was consistent with the current package insert.

#### Development code: TAK-924 / Generic name: pevonedistat

In September 2021, Takeda announced the Phase 3 PANTHER (Pevonedistat-3001) study did not achieve predefined statistical significance for the primary endpoint of event-free survival (EFS). The trial evaluated whether the combination of pevonedistat plus azacitidine as first-line treatment for patients with higher-risk myelodysplastic syndromes (MDS), chronic myelomonocytic leukemia (CMML) and low-blast acute myeloid leukemia (AML) improved EFS versus azacitidine alone. An event in the trial was defined as death or transformation to AML in participants with higher-risk MDS or CMML, whichever occurred first, and death in participants with AML. Takeda discontinued all research and development.

#### **Rare Genetics & Hematology**

In Rare Genetics & Hematology, Takeda focuses on several areas of high unmet medical need. In hereditary angioedema, Takeda aspires to transform the treatment paradigm, including through TAKHZYRO, with continued investment in lifecycle management programs including evaluating TAKHZYRO in Bradykinin-mediated angioedema with normal C1-inhibitor. In rare hematology, Takeda focuses on addressing today's needs in the treatment of bleeding disorders, including through ADVATE and ADYNOVATE/ADYNOVI, as well as on the development of pipeline assets including TAK-755 for the treatment of immune thrombotic thrombocytopenic purpura (iTTP) and congenital thrombotic thrombocytopenic purpura (cTTP). In rare genetics and others, Takeda is developing treatments for lysosomal storage disorders (LSDs), with a portfolio that includes commercial products such as ELAPRASE and REPLAGAL, and late-stage investigational therapies and pipeline candidates like pabinafusp alfa for Hunter Syndrome. In addition, Takeda aims to redefine the management of post-transplant cytomegalovirus (CMV) infection/disease with LIVTENCITY. We are also building differentiated gene therapy capabilities for the development and delivery of functional cures to patients with rare diseases.

#### TAKHZYRO / Generic name: lanadelumab

- In July 2021, Takeda announced the results from two final analyses from the Phase 3 HELP (Hereditary Angioedema Long-term Prophylaxis) Study<sup>™</sup> Open-label Extension (OLE), which evaluated the long-term safety (primary endpoint) and efficacy of TAKHZYRO (lanadelumab) 300 mg every two weeks for up to 2.5 years. In the first analysis, the mean (min, max) reduction in the attack rate compared to baseline observed in the study population (N=212) was of 87.4 percent (-100; 852.8), and the median reduction was 97.7 percent and patients received treatment for a mean (standard deviation) duration of 29.6 (8.2) months. At steady state day 70 to the end of the treatment period attack rates were further reduced to a mean of 92.4 percent and a median reduction of 98.2 percent. An additional analysis further suggests TAKHZYRO was a well-tolerated treatment that prevented HAE attacks over an extended planned 132 week treatment period across specific HAE patient demographic and disease characteristic subgroups. These data were presented at the 2021 European Academy of Allergy and Clinical Immunology (EAACI) Hybrid Congress.
- In February 2022, Takeda announced the U.S. Food and Drug Administration (FDA) approval of the TAKHZYRO injection single-dose prefilled syringe (PFS) to prevent attacks of hereditary angioedema (HAE) in adult and pediatric patients 12 years of age and older. The PFS is ready to use and requires fewer preparation steps than the current TAKHZYRO vial injection, while also reducing supplies and waste.
- In February 2022, Takeda announced that it presented four abstracts including interim real-world data from the observational Phase 4 EMPOWER study of TAKHZYRO as a treatment for people with Hereditary Angioedema (HAE) Type I or II in North America, as well as findings from a post-hoc analysis of the Phase 3 HELP Open Label Extension (OLE) study of long-term safety and efficacy of TAKHZYRO in HAE patients 12 years of age and older at the American Academy of Allergy, Asthma and Immunology (AAAAI) 78th Annual Meeting. Interim real-world data from Phase 4 EMPOWER study showed attack rate reduction and improvement in treatment satisfaction and other patient-reported outcome scores. The interim patient-reported outcomes showed a reduction of monthly attack rates in new users and showed sustained angioedema control in established users over twelve-months using the angioedema control test (AECT). In addition, a post-hoc analysis of global Phase 3 HELP and HELP OLE showed that reduction of attack rates with TAKHZYRO were similar for patients previously on androgen treatments.
- In March 2022, Takeda announced that it has received approval from the Japanese Ministry of Health, Labour and Welfare (MHLW) for TAKHZYRO subcutaneous injection 300mg syringes for prophylaxis against acute attacks of hereditary angioedema (HAE) in adult and pediatric patients 12 years of age and older in Japan. The approval is primarily based on results of the global Phase 3 HELP Study and the Phase 3 HELP Study Open Label Extension (OLE), in addition to results of a Phase 3 study evaluating the efficacy and safety of TAKHZYRO in Japanese

patients. Combined, these studies have demonstrated the efficacy and safety profile of TAKHZYRO as a preventive treatment for HAE attacks.

In April 2022, Takeda announced that the Phase 3 SHP643-301 study evaluating the safety profile and pharmacokinetics of TAKHZYRO in patients 2 to <12 years of age is complete and has met its objectives. The safety profile was consistent with that seen in the clinical program for patients 12 years of age and older; there were no serious adverse events and no dropouts due to adverse events. The study also successfully reached the secondary objective evaluating the clinical activity/outcome of TAKHZYRO in preventing hereditary angioedema (HAE) attacks as well as characterizing the pharmacodynamics of TAKHZYRO in pediatric subjects 2 to <12 years of age.</p>

#### REPLAGAL / Generic name: agalsidase alfa

In November 2021, Takeda and Sumitomo Dainippon Pharma Co., Ltd. (Sumitomo Dainippon Pharma) announced that Takeda will assume the manufacturing and marketing authorization (and the marketing rights) of REPLAGAL 3.5mg for Fabry disease, an α-galactosidase enzyme intravenous (IV) infusion, from Sumitomo Dainippon Pharma as of February 15, 2022 in Japan.

#### FIRAZYR / Generic name: icatibant

In December 2021, Takeda announced that it has submitted an application for a revision to the marketing approval for the selective bradykinin B2 receptor blocker FIRAZYR for the treatment of pediatric patients with hereditary angioedema (HAE) in Japan. This application is based primarily on a Japanese Phase 3 open-label study and an overseas Phase 3 open-label study evaluating the safety, efficacy and pharmacokinetics of subcutaneous administration of FIRAZYR in children mainly aged between two and 18 years. The Japanese pediatric treatment response in the Japanese Phase 3 open-label study was similar to the pediatric treatment response in Japanese and overseas adults and in the overseas Phase 3 open-label study.

#### VONVENDI / Generic name: von Willebrand factor (Recombinant)

In January 2022, Takeda announced that the U.S. Food & Drug Administration (FDA) approved VONVENDI for routine prophylaxis to reduce the frequency of bleeding episodes in patients with severe Type 3 von Willebrand disease (VWD) receiving on-demand therapy. The approval is based on data from a prospective, open-label, international multicenter study to evaluate efficacy and safety of prophylactic treatment of VONVENDI in reducing the frequency of bleeding episodes in 10 adult patients diagnosed with severe Type 3 VWD who were previously treated on-demand. VONVENDI is now indicated for routine prophylaxis in adults with severe Type 3 VWD receiving on-demand therapy, as well as on-demand and perioperative bleed management in adults with VWD.

#### LIVTENCITY / Generic name: maribavir

- In June 2021, Takeda announced the results from a new subgroup analysis of SOT recipients in the Phase 3 TAK-620-303 (SOLSTICE) trial, for the investigational drug maribavir, at the American Transplant Congress (ATC) 2021 Virtual Connect. More than twice (55.6%, 79/142) as many SOT recipients with R/R CMV infection at baseline treated with maribavir achieved confirmed CMV viremia clearance at Study Week 8 (end of treatment phase) compared to those treated with conventional antiviral therapies (26.1%, 18/69) (investigator assigned treatment; IAT consists of one or a combination of ganciclovir, valganciclovir, foscarnet or cidofovir) (adjusted difference [95% CI]: 30.5% [17.3, 43.6]). The results presented showed consistent efficacy in SOT recipients receiving maribavir in heart, lung and kidney transplants.
- In October 2021, Takeda announced that the U.S. Food and Drug Administration (FDA) Antimicrobial Drugs Advisory Committee (AMDAC) voted unanimously to recommend use of maribavir for the treatment of refractory cytomegalovirus (CMV) infection and disease with genotypic resistance to ganciclovir, valganciclovir, foscarnet or cidofovir in transplant recipients. The committee also voted unanimously to recommend use of maribavir for the treatment of refractory CMV infection and disease without genotypic resistance to ganciclovir, valganciclovir, foscarnet or cidofovir in transplant recipients. Both recommendations were based on the results of the Phase 2 and Phase 3 TAK-620-303 (SOLSTICE) trials. The New Drug Application (NDA) for maribavir is currently under Priority Review by the FDA.

- In November 2021, Takeda announced that the U.S. Food and Drug Administration (FDA) approved LIVTENCITY for the treatment of adults and pediatric patients (12 years of age or older and weighing at least 35 kg) with post-transplant cytomegalovirus (CMV) infection/disease that is refractory to treatment (with or without genotypic resistance) with ganciclovir, valganciclovir, cidofovir, or foscarnet. Prior to FDA approval, LIVTENCITY was granted Orphan Drug Designation by the FDA for treatment of clinically significant CMV viremia and disease in at-risk patients, as well as Breakthrough Therapy Designation as a treatment for CMV infection and disease in transplant patients resistant or refractory to prior therapy. Takeda is also investigating LIVTENCITY as a first-line treatment of CMV in hematopoietic stem cell transplant recipients in an ongoing Phase 3 clinical trial.
- In December 2021, Takeda announced that the data from the pivotal Phase 3 SOLSTICE clinical trial of LIVTENCITY in post-transplant refractory CMV infections with or without resistance (R/R) were published in the journal of Clinical Infectious Diseases. The SOLSTICE study primary endpoint was met, with 55.7% (131/235) of adult patients on LIVTENCITY achieving confirmed CMV DNA level below the lower limit of quantification (<LLOQ, i.e. <137 IU/mL) at the end of Study Week 8 (end of treatment phase) in comparison with 23.9% (28/117) of patients on conventional antiviral therapies (one or a combination of ganciclovir, valganciclovir, foscarnet or cidofovir); adjusted difference [95% CI]: 32.8% [22.80 to 42.74]; P<0.001. The key secondary endpoint of the composite achievement of CMV DNA level <LLOQ and symptom control at Week 8 maintained through Week 16 was met, with a higher proportion of patients in the LIVTENCITY arm (18.7%, 44/235) meeting the endpoint compared to those on conventional antiviral therapies (10.3%, 12/117); adjusted difference [95% CI]: 9.5% [2.02 to 16.88]; P=0.013.</p>
- In March 2022, Takeda announced that it has received Orphan Drug Designation from the Japanese Ministry of Health, Labour and Welfare (MHLW) for maribavir for the expected indications of cytomegalovirus (CMV) infection following organ transplantation (including hematopoietic stem cell transplantation). Maribavir is the first and only orally administrable CMV antiviral compound that targets and inhibits the pUL97 kinase as well as its natural substrates, and a Phase 3 clinical trial in post-transplant CMV infection/disease is ongoing in Japan.
- In April 2022, Takeda announced that it presented four company-sponsored abstracts on LIVTENCITY at the Tandem Transplantation & Cellular Therapy Meetings in Salt Lake City, Utah, and the 32nd European Congress of Clinical Microbiology and Infectious Diseases (ECCMID) in Lisbon, Portugal. The abstracts include an exploratory analysis of the Phase 3 SOLSTICE trial showing LIVTENCITY-treated patients with post-transplant cytomegalovirus (CMV) infections/disease had reductions in hospitalizations (34.8%; p=0.021) and length of hospital stay (53.8%; p=0.029), compared to those treated with conventional antiviral therapies. In addition, a post-hoc, sub-group analysis of the Phase 3 SOLSTICE trial showed shorter time to first confirmed CMV DNA level less than the lower limit of quantification (<LLOQ) with LIVTENCITY, compared to conventional antiviral therapies, which was consistent with previously reported findings.</p>

#### Neuroscience

In Neuroscience, Takeda is focusing its R&D investments on potentially transformative treatments for neurological and neuromuscular diseases of high unmet need, and building its pipeline through a combination of in-house expertise and partnerships. By harnessing advances in disease biology understanding, translational tools, and innovative modalities, Takeda is primarily focusing on rare neurology, in particular, on potential investigative therapies for sleep-wake disorders such as narcolepsy and idiopathic hypersomnia with a franchise of orexin-2 receptor agonists (TAK-994, TAK-861, TAK-925, etc.), and rare epilepsies with soticlestat (TAK-935). Additionally, Takeda also makes targeted investments to investigate well-defined segments of neuromuscular diseases, neurodegenerative diseases and movement disorders.

#### Development code: TAK-994

- In July 2021, Takeda announced that the U.S. Food and Drug Administration (FDA) granted Breakthrough Therapy Designation (BTD) to TAK-994, its Phase 2 investigational oral orexin agonist, which is designed to selectively target orexin 2 receptors. TAK-994 is currently being studied in an ongoing Phase 2 (TAK-994-1501) study for the treatment of excessive daytime sleepiness (EDS) in patients with narcolepsy type 1 (NT1), a chronic neurological disorder that alters the sleep-wake cycle. The TAK-994 BTD was based, in part, on early phase and preliminary clinical data that indicates Takeda's investigational oral orexin agonist may demonstrate substantially improved objective and subjective measurements of daytime wakefulness in NT1 patients.
- In October 2021, Takeda announced that a safety signal has emerged in Phase 2 studies of TAK-994 (TAK-994-1501 study and TAK-994-1504 study). As an immediate precautionary measure, Takeda has suspended dosing of patients

and has decided to stop both Phase 2 studies early. This allows for the timely interpretation of the benefit/risk profile of TAK-994 and to determine next steps for the program.

#### Development code: TAK-935 /Generic name: soticlestat

In February 2022, Takeda announced that it has received Orphan Drug Designation from the Japanese Ministry of Health, Labour and Welfare (MHLW) for the cholesterol 24 hydroxylase (CH24H) inhibitor soticlestat for the expected indications of Dravet Syndrome (DS) and Lennox-Gastaut Syndrome (LGS). DS and LGS are forms of developmental epileptic encephalopathy (DEE) and are both specified in Japan as intractable diseases. Soticlestat is expected to improve the symptoms of DS and LGS by inhibition of CH24H and following reduction of 24Shydroxycholesterol (24HC) levels in neurons. Phase 3 clinical trials in DS and LGS are currently ongoing.

#### Gastroenterology (GI)

In Gastroenterology, Takeda focuses on delivering innovative, life-changing therapeutics for patients with gastrointestinal and liver diseases. Takeda is maximizing the potential of our inflammatory bowel disease ("IBD") franchise around ENTYVIO, including development of a subcutaneous formulation, a needle free device, and expanding into other indications such as active chronic pouchitis. Takeda is also expanding its position with GATTEX / REVESTIVE and ALOFISEL, which are in ongoing and planned Phase 3 trials to support further potential geographic expansion, including in the U.S. Furthermore, Takeda is progressing a pipeline built through partnerships exploring opportunities in IBD, celiac disease, select liver diseases, and motility disorders. TAK-999 is an example of an addition through partnership and a potential first-in-class RNAi for alpha-1 antitrypsin-deficiency associated liver disease in late-stage development.

#### ENTYVIO / Generic name: vedolizumab

- In October 2021, Takeda announced the update on the U.S. development program for the investigational subcutaneous (SC) formulation of ENTYVIO as a maintenance therapy in adults with moderate to severe ulcerative colitis (UC). Through our ongoing interactions with the U.S. Food and Drug Administration (FDA), Takeda has received feedback which has provided clarity on the regulatory package and critical elements for the resubmission of the Biologics License Application (BLA) for Entyvio SC, and we are moving forward accordingly. We are reviewing our development program timelines and currently anticipate potential approval in FY 2023.
- In December 2021, Takeda announced that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has recommended the approval of intravenous (IV) ENTYVIO for the treatment of adult patients with moderately to severely active chronic pouchitis, who have undergone proctocolectomy and ileal pouch-anal anastomosis for ulcerative colitis, and have had an inadequate response with or lost response to antibiotic therapy. The positive opinion from the CHMP was based on the EARNEST trial, recently presented at the United European Gastroenterology's annual meeting, UEG Week Virtual 2021, which assessed the safety and efficacy of ENTYVIO IV in the treatment of active chronic pouchitis. Moreover, information from a number of retrospective studies of historical data indicating that ENTYVIO can have a positive impact on patients with inflammation of the pouch was also included in the application. In January 2022, European Commission (EC) approved ENTYVIO as the first treatment indicated for active chronic pouchitis across the European Union.

#### *GATTEX / REVESTIVE / Generic name: teduglutide*

- In June 2021, Takeda announced that it obtained approval from the Japanese Ministry of Health, Labour and Welfare (MHLW) to manufacture and market REVESTIVE 3.8 mg for subcutaneous injection as a treatment for short bowel syndrome. The approval is mainly based on the results of several trials conducted overseas, as well as Phase 3 clinical trials (SHP633-302, SHP633-305, SHP633-306, and SHP633-307) conducted in pediatric and adult patients in Japan.
- In November 2021, Takeda announced that it submitted the New Drug Application to the Japanese Ministry of Health, Labour and Welfare (MHLW) for the low dose formulation (0.95 mg) as an additional dosage for REVESTIVE as a treatment for short bowel syndrome (SBS). This new formulation would allow REVESTIVE to be administered to SBS patients weighing less than 10 kg, or less than 20 kg with moderate or severe renal impairment (creatinine clearance of less than 50 mL/min), who cannot be dosed with the 3.8 mg formulation.

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#### ALOFISEL / Generic name: darvadstrocel

- In September 2021, Takeda announced that it has received approval from the Japanese Ministry of Health, Labour and Welfare (MHLW) to manufacture and market ALOFISEL for the treatment of complex perianal fistulas in patients with non-active or mildly active luminal Crohn's disease (CD). This product is indicated for the treatment of patients who have shown an inadequate response to at least one existing medicinal treatment. The approval is based on data from two trials, the Japanese Study Darvadstrocel-3002 and the ADMIRE-CD trial, conducted in Europe and Israel. ALOFISEL is the first expanded human allogeneic adipose-derived mesenchymal stem cell therapy to be approved in Japan, which exhibits immunomodulatory and local anti-inflammatory effects at the site of inflammation.
- In February 2022, Takeda announced the first six-month interim analysis results from INSPIRE Study at the European Crohn's and Colitis Organisation (ECCO) 2022 Congress. INSPIRE is a European, observational, multicenter, post-approval, open-enrollment study evaluating the real-world effectiveness and safety of ALOFISEL in patients with Crohn's disease (CD) and complex perianal fistulas. As of September 2021, 230 patients had enrolled in the ongoing study. 138 patients in the All Treated (AT) cohort and 120 patients in the Treated Per Protocol (PP) cohort were sixmonths post treatment and 66% for AT (92/138) and 58% for PP (69/120) had a six-month visit completed. Among them, 85% (78/92) of the AT cohort and 100% (69/69) of the PP cohort had clinical outcome data available at sixmonths. In this interim analysis, clinical response was observed in 73% (57/78) and 74% (51/69) of patients in the AT and PP cohorts, respectively. Clinical remission was observed in 65% of patients in both cohorts (AT cohort: 51/78; PP cohort: 45/69). Changes in CD activity, assessed using the Harvey–Bradshaw Index, post-treatment were minimal. Of the 205 patients with complete treatment data, 20% (41/205) had one or more adverse event and 9.3% (19/205) had one or more serious adverse event. There were no reports of ectopic tissue formation and no deaths. These results are consistent with the pivotal Phase 3 ADMIRE-CD study in terms of efficacy and safety.

#### Development code: TAK-721 (Planned trade name: Eohilia) / Generic name: budesonide oral suspension

In December 2021, Takeda announced that it has received a Complete Response Letter (CRL) from the U.S. Food and Drug Administration (FDA) in response to its New Drug Application (NDA) for TAK-721 for the treatment of eosinophilic esophagitis, a chronic inflammatory disease of the esophagus. The CRL indicates the FDA has completed its review of the TAK-721 NDA and determined that it cannot be approved in its present form. In addition, the FDA recommended an additional clinical study in order to help resolve FDA feedback. Takeda announced the discontinuation of this program in February 2022.

#### **Plasma-Derived Therapies (PDT)**

Takeda has created a dedicated PDT business unit with a focus to manage the business end-to-end, from plasma collection to manufacturing, R&D, and commercialization. In PDT, we aspire to develop life-saving plasma derived treatments which are essential for patients with a variety of rare and complex chronic diseases. The dedicated R&D organization in PDT is charged with maximizing the value of existing therapies, identifying new targeted therapies, and optimizing efficiencies of current product manufacturing. Near-term, our priority is focused on delivering value from our broad immunoglobulin portfolio (HYQVIA, CUVITRU, GAMMAGARD and GAMMAGARD S/D) through pursuit of new indications, geographic expansions, and enhanced patient experience through integrated healthcare technologies. In our hematology and specialty care portfolio, our priority is pursuing new indication and formulation development opportunities for PROTHROMPLEX (4F-PCC), FEIBA, CEPROTIN and ARALAST. Additionally, we are developing next generation immunoglobulin products with 20% fSCIg (TAK-881), IgG Low IgA (TAK-880) and pursuing other early-stage opportunities that would add to our diversified commercial portfolio of more than 20 therapeutic products distributed worldwide.

# Development code: CoVIg-19 (previously TAK-888) / Generic name: anti-SARS-CoV-2 polyclonal hyperimmune immunoglobulin

In April 2021, The CoVIg-19 Plasma Alliance announced that the Phase 3 Inpatient Treatment with Anti-Coronavirus Immunoglobulin (ITAC) clinical trial sponsored and funded by the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health (NIH), did not meet its endpoints. No serious safety signals were raised in the trial. The study aimed to determine whether an investigational anti-coronavirus hyperimmune intravenous immunoglobulin (H-Ig) medicine could reduce the risk of disease progression when added to standard of care treatment including remdesivir in hospitalized adult patients at risk for serious complications. Following the outcome of the ITAC trial, the CoVIg-19 Plasma Alliance's work has now concluded. The full dataset from ITAC clinical trial has been published in The Lancet.

#### Vaccine

In Vaccines, Takeda is applying innovation to tackle some of the world's most challenging infectious diseases such as dengue, COVID-19 and zika. To support the expansion of our pipeline and the development of our programs, we have entered into partnerships with government organizations in Japan and the U.S., and leading global institutions. Such partnerships have been essential in building the critical capabilities that will be necessary to deliver on our programs and realize their full potential.

# SPIKEVAX (formerly COVID-19 Vaccine Moderna) Intramuscular Injection / Development code: mRNA-1273 (Japanese development code: TAK-919)

- In May 2021, Takeda announced positive interim results from the ongoing Phase 1/2 immunogenicity and safety clinical trial of TAK-919 in Japan have been submitted to the Japan Pharmaceuticals and Medical Devices Agency (PMDA). Takeda currently has a three-way agreement with Moderna, Inc. (Moderna) and the Government of Japan's Ministry of Health Labour and Welfare (MHLW) to import and distribute 50 million doses of TAK-919 in Japan. This interim analysis showed binding antibody and neutralizing antibody titres were elevated at 28 days after the second dose in 100% of people vaccinated with two 0.5ml doses of TAK-919 given 28 days apart. The vaccine candidate was generally well-tolerated with no significant safety concerns reported. The study results were submitted to the Japan Pharmaceuticals and Medical Devices Agency (PMDA) to be evaluated as part of the New Drug Application submitted in March 2021, which also includes safety and efficacy results from Moderna's pivotal Phase 3 COVE trial conducted in the U.S.
- In May 2021, Takeda announced that the Japanese Ministry of Health, Labour and Welfare (MHLW) granted special approval under article 14-3 of the Pharmaceuticals and Medical Devices Act for emergency use of COVID-19 Vaccine Moderna Intramuscular Injection in Japan. The approval is based on positive clinical data from Takeda's Phase 1/2 immunogenicity and safety clinical trial of COVID-19 Vaccine Moderna Intramuscular Injection in Japan, which showed an immune response consistent with results from Moderna's pivotal Phase 3 COVE trial conducted in the United States. Takeda has started distribution in Japan.
- In July 2021, Takeda announced an additional agreement with Moderna and the Government of Japan's Ministry of Health, Labour and Welfare (MHLW) to import and distribute an additional 50 million doses of COVID-19 Vaccine Moderna Intramuscular Injection in Japan from as early as the beginning of 2022. This agreement includes the potential to secure and supply vaccines corresponding to COVID-19 variants or booster products, should they be successfully developed by Moderna and licensed by the MHLW. Takeda will import and distribute the totaling 100 million doses including the additional 50 million doses in 2022 and 50 million doses announced in October 2020.
- In July 2021, Takeda announced that the Japanese Ministry of Health, Labour and Welfare (MHLW) accepted the change in age indication in the package insert for COVID-19 Vaccine Moderna Intramuscular Injection to expand to 12 years of age and older. This change is based on the results of Moderna's Phase 2/3 study conducted in 3,732 subjects aged 12 to 17 years in the United States. The serum neutralizing antibody titer and neutralizing antibody titer response rate 28 days after the second vaccination of adolescents (12 to 17 years old), which are the primary endpoints, showed non-inferiority to young adults (18 to 25 years old) in the overseas phase 3 study (mRNA-1273-P301 study). Additionally, the results indicating a high preventive effect at the vaccine efficacy rate 2 weeks after the second vaccination, which was set as a secondary endpoint. No significant safety concerns were reported, as was the case with the results of clinical studies in patients aged 18 years or older.
- In December 2021, Takeda announced that Japan's Ministry of Health, Labour and Welfare (MHLW) has granted regulatory approval for a 50 µg booster dose of SPIKEVAX Intramuscular Injection, previously known as COVID-19 Vaccine Moderna Intramuscular Injection, in Japan for administration at least six months after completion of the primary series in those who are 18 years and older. The approval is based on previously-reported positive Moderna Phase 2 study results. Moderna's Phase 2 study was amended to offer a 50 µg booster dose to interested participants aged 18 years and older six to eight months following their second dose of the primary series of Moderna's COVID-19 vaccine. The results showed that a booster dose of the vaccine greatly increased neutralizing titers measured against the original virus strain compared to pre-boost levels. The reactogenicity profile observed following the booster dose was similar to the second dose of the primary series and the safety profile was also similar to that following any dose of Moderna's COVID-19 vaccine of the primary series.
- In December 2021, Takeda announced a third agreement with Japan's Ministry of Health, Labour and Welfare (MHLW) and Moderna to import and distribute 18 million additional doses of SPIKEVAX Intramuscular Injection in Japan in 2022. Takeda previously announced a three-way agreement with Moderna and MHLW to distribute 50 million doses of SPIKEVAX in Japan in 2021, and announced a second agreement for Takeda to import and

distribute an additional 50 million doses in 2022, totaling 100 million doses between the two agreements. Due to the approval of the 50 microgram booster dose described in the foregoing paragraph, which is half of the dosage level used in the initial two-dose series of the vaccine (100 microgram per dose), the doses per vial for the second 50 million doses will increase, meaning Takeda will be able to deliver 75 million booster doses (at 15 doses per vial). With this third agreement for 18 million doses (at 15 doses per vial), Takeda will now deliver a total of 93 million doses to Japan in 2022.

#### NUVAXOVID Intramuscular Injection / Development code: NVX-CoV2373 (Japanese development code: TAK-019)

- In September 2021, Takeda announced the agreement that the Japanese Ministry of Health, Labour and Welfare (MHLW) will purchase 150 million doses of Novavax, Inc. (Novavax)'s vaccine candidate (TAK-019 in Japan) manufactured in Japan by Takeda subject to licensing and approval. Takeda is establishing the capability to manufacture TAK-019 at its facilities in Japan and aims to begin distribution in early calendar year 2022. Novavax is licensing and transferring manufacturing technologies to enable Takeda to manufacture the vaccine antigen and is supplying the Matrix-M<sup>TM</sup> adjuvant to Takeda for fill/finish together with the antigen. Takeda is responsible for the Japanese clinical trial and regulatory submission and will distribute TAK-019 in Japan should it be approved by the MHLW.
- In April 2022, Takeda announced that it has received manufacturing and marketing approval from the Japanese Ministry of Health, Labour and Welfare (MHLW) for NUVAXOVID Intramuscular Injection (NUVAXOVID), a novel recombinant protein-based COVID-19 vaccine, for primary and booster immunization in individuals aged 18 and older. The approval is based on interim results from a Phase 1/2 study conducted by Takeda in Japan and several studies conducted by Novavax, including two pivotal Phase 3 clinical trials in the U.K., the U.S. and Mexico, Phase 1/2 studies in Australia and the U.S., as well as safety and efficacy data from outside of Japan which was subsequently submitted for review. Interim results from the Phase 1/2 study in Japan were positive and consistent with previously reported clinical trial results. No serious adverse events were reported in the NUVAXOVID treatment group, and the vaccine candidate was well-tolerated. Additionally, studies conducted by Novavax, including Phase 1/2 studies conducted in Australia and the U.S. as well as a Phase 2 study conducted in South Africa, evaluated safety and efficacy of booster immunization. In these studies, subjects received a booster dose 6 months after primary immunization, and compared to pre-booster levels, a significant elevation of antibody titer was observed without major safety concerns.

#### Development code: TAK-003 / Generic name: Dengue vaccine

In May 2021, Takeda announced that TAK-003 demonstrated continued protection against dengue illness and hospitalization, regardless of an individual's previous dengue exposure, with no important safety risks identified through three years after vaccination in the ongoing pivotal Phase 3 Tetravalent Immunization against Dengue Efficacy Study (TIDES) trial. TIDES enrolled more than 20,000 healthy children and adolescents ages four to 16 years in dengue-endemic countries in Latin America and Asia. Safety and efficacy results from the 36-month follow-up exploratory analysis of TIDES were presented at the 17th Conference of the International Society of Travel Medicine (CISTM). Through three years (36 months after the second dose), observations of varied vaccine efficacy by serotype remained consistent with previously reported results. No evidence of disease enhancement was observed. TAK-003 was generally well tolerated, and there were no important safety risks observed. TIDES safety and efficacy data through 36-months follow-up was included in regulatory submissions to the European Union and dengue-endemic countries and will be part of additional future filings, including in the United States.

#### Building a sustainable research platform / Enhancing R&D collaboration

In addition to our concentrated efforts to increase our in-house R&D capabilities, external partnerships with third-party partners are a key component of our strategy for enhancing our R&D pipeline. Our strategy to expand and diversify our external partnerships allows us to take part in research of a wide variety of new products and increases the chances that we will be able to take part in a major research-related breakthrough.

In July 2021, Takeda and PeptiDream Inc. announced an expansion of its research collaboration and exclusive license agreement, announced in December 2020, to create peptide-drug conjugates (PDCs) for several central nervous system (CNS) targets, which play important roles in chronic neurodegenerative diseases. This new collaboration expands the use of the TfR1 binding peptide ligands for CNS targets associated with neurodegeneration allowing Takeda to conjugate the peptides with therapeutic cargoes optimized to cross the bloodbrain barrier (BBB). A significant challenge to the development of effective medicines for neurodegenerative

diseases is the ability to deliver therapeutic molecules across the BBB into the brain. Peptide carriers that bind to TfR1 when conjugated to various therapeutic payloads facilitate the transport of the payload across the BBB into the brain, and thereby significantly improve functional benefit. This TfR1 BBB shuttle approach has the potential to accelerate the development of therapies for which BBB penetration remains challenging. This approach may also enable broad brain region biodistribution that is frequently needed to effectively treat many neurodegenerative diseases for which few, if any, effective drugs currently exist.

- In July 2021, Takeda and Frazier Healthcare Partners announced a collaboration to launch HilleVax, Inc. (HilleVax), a biopharmaceutical company to develop and commercialize Takeda's norovirus vaccine candidate. Takeda has granted a license to HilleVax for the exclusive development and commercialization rights to its norovirus vaccine candidate, HIL-214 (formerly TAK-214), worldwide outside of Japan, in exchange for upfront consideration, as well as future cash milestones and royalties on net sales. Takeda will retain commercialization rights in Japan and HilleVax will integrate certain Japan development activities into its global development. HIL-214, which is a virus-like particle (VLP) based vaccine candidate, completed a randomized, placebo-controlled Phase 2b field efficacy study in 4,712 adult subjects in which HIL-214 was well-tolerated and demonstrated clinical proof of concept in preventing moderate-to-severe cases of acute gastroenteritis from norovirus infection. As of July 2021, the candidate has been studied in nine human clinical trials with safety data from over 4,500 subjects and immunogenicity data from over 2,000 subjects.
- In September 2021, Takeda and Mirum Pharmaceuticals, Inc. (Mirum) announced that the companies have entered into an exclusive licensing agreement for the development and commercialization of maralixibat chloride (maralixibat) (US trade name: LIVMARLI), an apical sodium dependent bile acid transporter (ASBT) inhibitor, in Japan for Alagille syndrome (ALGS), progressive familial intrahepatic cholestasis (PFIC), and biliary atresia (BA). Maralixibat, an investigational, orally administered medication, is being evaluated globally in ALGS, PFIC, and BA. Under the terms of the agreement, Takeda will be responsible for regulatory approval and commercialization of maralixibat in Japan. Takeda will also be responsible for development, including conducting clinical studies in cholestatic indications.
- In September 2021, Takeda and JCR Pharmaceuticals Co., Ltd. (JCR) announced a geographically-focused exclusive collaboration and license agreement to commercialize JR-141 (pabinafusp alfa), an investigational, next-generation recombinant fusion protein of an antibody against the human transferrin receptor and iduronate-2-sulfatase (IDS) enzyme for the treatment of Hunter syndrome (also known as Mucopolysaccharidosis type II or MPS II). JR-141, applied with J-Brain Cargo, JCR's proprietary blood-brain barrier (BBB) technology, is engineered to transport the therapeutic enzyme across the BBB to directly reach the brain and address both the somatic and neuronopathic manifestations of the disease, which can lead to progressive cognitive decline. Under the terms of the exclusive collaboration and license agreement, Takeda will exclusively commercialize JR-141 outside of the United States, including Canada, Europe, and other regions (excluding Japan and certain other Asia-Pacific countries). The two companies will collaborate to bring this therapy to patients as quickly as possible upon completion of the global Phase 3 program, which will be conducted by JCR. Takeda receives an option under a separate option agreement, which allows Takeda to acquire an exclusive license to commercialize JR-141 in the U.S. upon completion of the Phase 3 program.
- In October 2021, Takeda announced the exercise of its option to acquire GammaDelta Therapeutics Limited ("GammaDelta"), a company focused on exploiting the unique properties of gamma delta (γδ) T cells for immunotherapy. Through the acquisition, Takeda will obtain GammaDelta's allogeneic variable delta 1 (Vδ1) gamma-delta (γδ) T cell therapy platforms, which includes both blood-derived and tissue-derived platforms, in addition to early-stage cell therapy programs. The transaction was completed in April 2022.
- In January 2022, Takeda announced the exercise of its option to acquire Adaptate Biotherapeutics Ltd. ("Adaptate"), a UK company focused on developing antibody-based therapeutics for the modulation of variable delta 1 (V $\delta$ 1) gamma delta ( $\gamma\delta$ ) T cells. Through the acquisition, Takeda will acquire Adaptate's antibody-based  $\gamma\delta$  T cell engager platform, including pre-clinical candidate and discovery pipeline programs. Adaptate's  $\gamma\delta$  T cell engagers are designed to specifically modulate  $\gamma\delta$  T cell-mediated immune responses at tumor sites while sparing damage to healthy cells. The planned acquisition of Adaptate follows Takeda's recently exercised option to acquire GammaDelta Therapeutics and is intended to further accelerate the development of innovative  $\gamma\delta$  T cell-based therapies. The transaction was completed in April 2022.

# Analysis of Results of Operations, Financial Position, and Cash Flow

# **Results of Operations (Reported)**

## Consolidated Financial Results (April 1, 2021 to March 31, 2022)

			Billion JPY	or percentage
	For the fiscal ye March 3			
	2021	2022	Change versus the	previous year
Revenue	3,197.8	3,569.0	371.2	11.6 %
Cost of sales	(994.3)	(1,106.8)	(112.5)	11.3 %
Selling, general and administrative expenses	(875.7)	(886.4)	(10.7)	1.2 %
Research and development expenses	(455.8)	(526.1)	(70.3)	15.4 %
Amortization and impairment losses on intangible assets associated with products	(421.9)	(472.9)	(51.1)	12.1 %
Other operating income	318.0	43.1	(274.9)	(86.4)%
Other operating expenses	(258.9)	(159.1)	99.8	(38.6)%
Operating profit	509.3	460.8	(48.4)	(9.5)%
Finance income and (expenses), net	(143.1)	(142.9)	0.2	(0.1)%
Share of profit (loss) of investments accounted for using the equity method	0.1	(15.4)	(15.4)	_
Profit before tax	366.2	302.6	(63.7)	(17.4)%
Income tax (expenses) benefit	9.9	(72.4)	(82.3)	—
Net profit for the year	376.2	230.2	(146.0)	(38.8)%

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*Revenue*. Revenue for the fiscal year ended March 31, 2022 was 3,569.0 billion JPY, an increase of 371.2 billion JPY, or 11.6%, compared to the previous fiscal year. Excluding the impact from fluctuations in foreign exchange rates, which was calculated by translating revenue of the fiscal year ended March 31, 2022, using corresponding exchange rates in the previous fiscal year, the increase in revenue was 6.3%. In April 2021, Takeda completed the sale of a portfolio of diabetes products in Japan to Teijin Pharma Limited for 133.0 billion JPY, which was recorded as revenue and accounted for 4.2 percentage points ("pp") of the increase in revenue. Excluding this selling price from revenue for the fiscal year ended March 31, 2022, the increase was 7.4%.

Each of our core therapeutic areas in the business (i.e. Gastroenterology ("GI"), Rare Diseases, Plasma-Derived Therapies ("PDT") Immunology, Oncology, and Neuroscience) contributed to positive revenue growth; however, Rare Diseases would have declined if not for the positive impact of the depreciation of the yen. Intensified competition impacted some products in this area, especially treatments for Rare Hematology. Although the impact of the global spread of COVID-19 did not have a material effect on our overall consolidated revenue for the fiscal year ended March 31, 2022, we have experienced some disruption to certain products in the second half of the fiscal year due to the spread of the Omicron variant, including shipping delays and fewer diagnostic procedures.

During the third quarter of the fiscal year ended March 31, 2022, LIVTENCITY (for post-transplant cytomegalovirus ("CMV") infection/disease) was launched in the U.S. in December 2021, following the launch of EXKIVITY (for non-small cell lung cancer) in the U.S. in September 2021.

Revenue outside of our core therapeutic areas increased by 50.1 billion JPY, or 8.7%, compared to the previous fiscal year to 624.1 billion JPY, due to the 133.0 billion JPY selling price of the diabetes portfolio in Japan and other increases including revenue from distributing Moderna's COVID-19 vaccine, SPIKEVAX Intramuscular Injection, in Japan, offsetting the impact from prior divestitures.

Year-on-year change in revenue for this fiscal year in each of our main therapeutic areas was primarily attributable to the following products:

GI. In Gastroenterology, revenue was 875.7 billion JPY, a year-on-year increase of 97.9 billion JPY, or 12.6%. Growth was driven by Takeda's top-selling product ENTYVIO (for ulcerative colitis ("UC") and Crohn's disease ("CD")), with sales of 521.8 billion JPY, a year-on-year increase of 92.5 billion JPY, or 21.5%. Sales in the U.S. increased by 55.2 billion JPY, or 18.8%, to 349.5 billion JPY driven by increases in the first line biologic inflammatory bowel disease ("IBD")

population both in UC and CD. Sales in Europe and Canada increased by 27.0 billion JPY, or 24.8%, to 136.0 billion JPY. In Growth and Emerging Markets, sales increased by 7.8 billion JPY, or 45.7%, to 25.0 billion JPY, primarily driven by increased sales in Brazil and China. Sales of TAKECAB (for acid-related diseases) were 102.4 billion JPY, an increase of 17.6 billion JPY, or 20.7%, versus the previous fiscal year. This increase was mainly driven by the expansion of new prescriptions in the Japanese market due to TAKECAB's efficacy in reflux esophagitis and the prevention of recurrence of gastric and duodenal ulcers during low-dose aspirin administration. Sales of GATTEX/REVESTIVE (for short bowel syndrome) were 75.8 billion JPY, an increase of 11.2 billion JPY, or 17.3%, primarily due to increased market penetration and new country launches including Japan. Sales of AMITIZA (for chronic constipation) decreased by 14.8 billion JPY, or 69.6%, to 6.5 billion JPY, due to generic entrants in the U.S. in January 2021.

Rare Diseases. In Rare Diseases, revenue was 611.2 billion JPY, a year-on-year increase of 19.5 billion JPY, or 3.3%.

Revenue in Rare Metabolic increased by 10.0 billion JPY, or 6.1%, compared to the previous fiscal year to 172.6 billion JPY. Sales of enzyme replacement therapies ELAPRASE (for Hunter syndrome) and VPRIV (for Gaucher diseases) increased primarily in Europe and Growth and Emerging Markets, and in the U.S., Europe and Growth and Emerging Markets, respectively.

Revenue in Rare Hematology decreased by 6.1 billion JPY, or 2.1%, to 283.7 billion JPY. Sales of ADVATE decreased by 10.0 billion JPY, or 7.8%, to 118.5 billion JPY. Sales of ADYNOVATE/ADYNOVI increased by 2.7 billion JPY, or 4.6%, to 60.7 billion JPY. Both products were impacted by the competitive landscape in the hemophilia A non-inhibitors market in the U.S. FEIBA sales decreased by 5.3 billion JPY, or 12.0%, to 39.2 billion JPY, negatively impacted by the difference in timing of government tenders in Growth and Emerging Markets.

Revenue in Hereditary Angioedema ("HAE") was 153.6 billion JPY, a year-on-year increase of 14.3 billion JPY, or 10.2%. Sales of TAKHZYRO were 103.2 billion JPY, an increase of 16.5 billion JPY, or 19.1%, versus the previous fiscal year primarily due to expansion of the prophylactic market, continued geographic expansion and strong patient uptake. Sales of CINRYZE decreased by 2.6 billion JPY, or 11.8%, to 19.3 billion JPY, primarily due to conversion to TAKHZYRO and a shift to newer agents marketed by competitors.

- *PDT Immunology*. In Plasma-Derived Therapies ("PDT") Immunology, revenue increased by 86.6 billion JPY, or 20.6%, compared to the previous fiscal year to 507.0 billion JPY. Aggregate sales of immunoglobulin products were 385.9 billion JPY, an increase of 51.0 billion JPY, or 15.2%, compared to the previous fiscal year. In particular, sales of GAMMAGARD LIQUID/KIOVIG (for the treatment of primary immunodeficiency ("PID") and multifocal motor neuropathy ("MMN")) increased due to continued strong demand globally and enabled by growing supply. In addition, CUVITRU and HYQVIA, which are SCIG (subcutaneous immunoglobulin) therapies, marked double digit percentage of revenue growth. Aggregate sales of albumin products including HUMAN ALBUMIN and FLEXBUMIN (primarily used for hypovolemia and hypoalbuminemia) were 90.0 billion JPY, an increase of 32.5 billion JPY, or 56.4%, versus the previous fiscal year driven by higher sales following the resolution of the supply interruption which impacted HUMAN ALBUMIN for release in China in the second half of the previous fiscal year, in addition to strong FLEXBUMIN demand in China and the U.S.
- Oncology. In Oncology, revenue was 468.7 billion JPY, a year-on-year increase of 52.2 billion JPY, or 12.5%. Sales of VELCADE (for multiple myeloma) increased by 8.9 billion JPY, or 8.8% versus the previous fiscal year to 110.0 billion JPY. This growth was driven by an increase in U.S. sales of 10.4 billion JPY, or 10.8%, versus the previous fiscal year. This reflects a rebound in demand after lower sales in the first quarter of the previous fiscal year, when prescribers favored orally administered products over infusions or injections early in the COVID-19 pandemic. In addition, increased use of VELCADE as part of initial treatment for new patients contributed to the growth this year in the U.S. Royalty income outside the U.S. decreased due to continued generic erosion. Sales of LEUPLIN/ENANTONE (generic name: leuprorelin) (for endometriosis, uterine fibroids, premenopausal breast cancer, prostatic cancer, etc.), an off-patented product, increased by 11.1 billion JPY, or 11.6%, versus the previous fiscal year to 106.5 billion JPY mainly driven by an increased supply in the U.S. which was partially offset by a decrease in Japan due to generic erosion and competition. Sales of NINLARO (for multiple myeloma) were 91.2 billion JPY, an increase of 3.8 billion JPY, or 4.4%, versus the previous fiscal year. In the U.S., NINLARO growth was adversely impacted by a temporary demand increase favoring oral options early in the previous fiscal year due to COVID-19, and by demand slow-downs in the fourth quarter of the current fiscal year. There has been continued strong growth in other regions, particularly in China and Japan. Sales of ADCETRIS (for malignant lymphomas) increased by 9.8 billion JPY, or 16.4% versus the previous fiscal year to 69.2 billion JPY, led by strong growth in sales in Growth and Emerging Markets, particularly in China where it was approved in May 2020. Sales of ALUNBRIG (for non-small cell lung cancer) were 13.6 billion JPY, an increase of 4.8 billion JPY, or 54.9% due to new launches and market penetration around the world.
  - *Neuroscience*. In Neuroscience, revenue was 482.3 billion JPY, a year-on-year increase of 65.0 billion JPY, or 15.6%. Sales of VYVANSE/ELVANSE (for attention deficit hyperactivity disorder ("ADHD")) were 327.1 billion JPY, an

increase of 55.5 billion JPY, or 20.4%, versus the previous fiscal year. VYVANSE/ELVANSE has been negatively affected by COVID-19 during the course of the pandemic, most notably during periods when stay-at-home restrictions have been in place reducing patient visits, subsequent diagnoses and creating temporary discontinuation of medication. While the trend has been fluctuating since 2020, overall there has been a positive impact from increasing prescriptions in the current fiscal year. Sales of TRINTELLIX (for major depressive disorder ("MDD")) were 82.3 billion JPY, an increase of 13.4 billion JPY, or 19.5%, versus the previous fiscal year, due to increasing prescriptions in the U.S. and in Japan. The increase of these products was partially offset by the decrease of other neuroscience products such as REMINYL (for Alzheimer's disease), attributable to the continued impact of competition from generic products in Japan.

Dillion IDV: percentages are the properties to total revenue

Revenue by Geographic Region:

		the fiscal year end	es are the proportion to nded March 31	total revenue
Revenue:	2021	the listal year of	2022	
Japan <sup>*1</sup>	559.7	17.5 %	659.0	18.5 %
United States	1,567.9	49.0 %	1,714.4	48.0 %
Europe and Canada	666.2	20.8 %	739.2	20.7 %
Asia (excluding Japan)	156.2	4.9 %	197.0	5.5 %
Latin America	121.6	3.8 %	128.5	3.6 %
Russia/CIS	57.6	1.8 %	62.1	1.7 %
Other <sup>*2</sup>	68.5	2.1 %	68.9	1.9 %
Total	3,197.8	100.0 %	3,569.0	100.0 %

\*1 The 133.0 billion JPY selling price of the sale of diabetes portfolio in Japan is included in the fiscal year ended March 31, 2022.

\*2 Other includes the Middle East, Oceania and Africa.

*Cost of Sales.* Cost of Sales increased by 112.5 billion JPY, or 11.3%, to 1,106.8 billion JPY. The increase was primarily due to the depreciation of the yen and a sales increase of products with higher cost of sales ratio for the fiscal year ended March 31, 2022. The increase was partially offset by a 46.5 billion JPY decrease in non-cash charges related to the unwind of the fair value step up on acquired inventory recognized in connection with the acquisition of Shire as well as a decrease of cost of sales from divested products of the previous fiscal year.

*Selling, General and Administrative (SG&A) expenses.* SG&A expenses increased by 10.7 billion JPY, or 1.2%, to 886.4 billion JPY for the fiscal year ended March 31, 2022, mainly due to the impact from the depreciation of the yen in the current fiscal year.

**Research and Development (R&D) expenses.** R&D expenses increased by 70.3 billion JPY, or 15.4%, to 526.1 billion JPY for the fiscal year ended March 31, 2022, mainly due to further investment in prioritized new molecular entities as well as the impact from the depreciation of the yen in the current fiscal year.

*Amortization and Impairment Losses on Intangible Assets Associated with Products.* Amortization and Impairment Losses on Intangible Assets Associated with Products increased by 51.1 billion JPY, or 12.1%, to 472.9 billion JPY for the fiscal year ended March 31, 2022 mainly due to impairment charges of certain in-process R&D assets including TAK-721 due to discontinuation of the program and intangible assets related to NATPARA resulting from the reassessment of the recoverable amount and recorded in the current fiscal year.

*Other Operating Income.* Other Operating Income was 43.1 billion JPY, a decrease of 274.9 billion JPY, or 86.4%, for the fiscal year ended March 31, 2022, predominantly driven by the effect of a 228.9 billion JPY divestiture gain in the previous fiscal year. This included a 139.5 billion JPY gain on sale of shares and relevant assets of Takeda Consumer Healthcare Company Ltd., and other non-core assets amounting to 89.4 billion JPY. The decrease is also due to a 60.2 billion JPY revaluation gain recorded in the previous fiscal year, triggered by an update to previously recognized liabilities for pipeline compound SHP647 and certain associated rights ("SHP647"), to reflect management's decision to terminate the clinical trial program following the European Commission's decision in May 2020 to release Takeda's obligation to divest SHP647.

*Other Operating Expenses.* Other Operating Expenses were 159.1 billion JPY, a decrease of 99.8 billion JPY, or 38.6%, for the fiscal year ended March 31, 2022. This is mainly attributable to a 72.9 billion JPY loss recognized in the previous year from

changes in the fair value of financial assets associated with contingent consideration arrangements from the divestment of XIIDRA and a 32.0 billion JPY decrease in restructuring expenses mainly attributable to the decrease in Shire integration costs.

*Operating Profit*. As a result of the above factors, Operating Profit decreased by 48.4 billion JPY, or 9.5%, for the fiscal year ended March 31, 2022 to 460.8 billion JPY.

*Net Finance Expenses.* Net Finance Expenses were 142.9 billion JPY for the fiscal year ended March 31, 2022, a decrease of 0.2 billion JPY, or 0.1%, compared to the previous fiscal year. These results include a negative impact from the remeasurement of a warrant to purchase stocks of a company held by Takeda that was offset by factors including a gain on prior equity method investments related to the acquisition of Maverick Therapeutics, Inc. in April 2021 recorded in the current fiscal year and a decrease in net interest expense primarily driven by the reduction in outstanding balances of bonds and loans.

*Share of Loss of Investments Accounted for Using the Equity Method.* Share of Loss of Investments Accounted for Using the Equity Method was 15.4 billion JPY, a decrease of 15.4 billion JPY compared to Share of Profit of Investments Accounted for Using the Equity Method of 0.1 billion JPY for the previous fiscal year, mainly due to the negative impact from Takeda's share of loss on an investment held by Takeda Ventures, Inc. This negative impact was partially offset by a decrease of Takeda's share of impairment loss recognized by Teva Takeda Pharma Ltd.

*Income Tax Expenses.* Income Tax Expenses were 72.4 billion JPY for the fiscal year ended March 31, 2022, compared to income tax benefit of 9.9 billion JPY for the previous fiscal year. This was primarily due to a decrease of tax benefits from internal entity restructuring transactions and a current fiscal year's tax charge of 65.4 billion JPY for tax and interest, net of 0.5 billion JPY of associated tax benefit, arising from tax assessment involving Irish taxation of the break fee Shire received from AbbVie in connection with the terminated offer to acquire Shire made by AbbVie in 2014. There was also a decrease in tax benefits from the recognition of previously unrecognized deferred tax assets. These unfavorable changes were partially offset by a tax charge on divestitures in the previous fiscal year, decreased deferred tax liability for unremitted earnings in foreign subsidiaries, and lower pretax earnings.

*Net Profit for the Year.* Net Profit for the Year decreased by 146.0 billion JPY, or 38.8%, for the fiscal year ended March 31, 2022 to 230.2 billion JPY.

# Results of Operations (Underlying) (April 1, 2021 to March 31, 2022)

#### Definition of Core and Underlying Growth

Takeda uses the concept of Underlying Growth for internal planning and performance evaluation purposes.

Underlying Growth compares two periods (fiscal quarters or years) of financial results under a common basis and is used by management to assess the business. These financial results are calculated on a constant currency basis using a full year plan rate and exclude the impacts of divestitures and other amounts that are unusual, non-recurring items or unrelated to our ongoing operations. Although these are not measures defined by IFRS, Takeda believes Underlying Growth is useful to investors as it provides a consistent measure of our performance.

Takeda uses "Underlying Revenue Growth", "Underlying Core Operating Profit Growth", and "Underlying Core EPS Growth" as key financial metrics.

Underlying Revenue represents revenue on a constant currency basis and excluding non-recurring items and the impact of divestitures that occurred during the reported periods presented.

Underlying Core Operating Profit represents Core Operating Profit (as defined below) on a constant currency basis and further adjusted to exclude the impacts of divestitures that occurred during the reporting periods presented.

Underlying Core EPS represents net profit based on a constant currency basis, adjusted to exclude the impact of divestitures, items excluded in the calculation of Core EPS (as defined below), divided by the outstanding shares (excluding treasury shares) as of the end of the comparative period.

Core Revenue represents revenue adjusted to exclude significant items unrelated to Takeda's core operations.

Core Operating Profit represents net profit adjusted to exclude income tax expenses, the share of profit or loss of investments accounted for using the equity method, finance expenses and income, other operating expenses and income, amortization and impairment losses on acquired intangible assets and other items unrelated to Takeda's core operations, such as non-recurring items, purchase accounting effects and transaction related costs.

Core EPS represents net profit adjusted to exclude the impact of items excluded in the calculation of Core Operating Profit, and other non-operating items (e.g. amongst other items, fair value adjustments and the imputed financial charge related to contingent consideration) that are unusual, non-recurring in nature or unrelated to Takeda's ongoing operations and the tax effect of each of the adjustments, divided by the average outstanding shares (excluding treasury shares) of the reporting periods presented.

#### **Underlying Results**

#### For the fiscal year ended March 31, 2022

Underlying Revenue Growth	+7.4%
Underlying Core Operating Profit Growth	+5.4%
Underlying Core Operating Profit Margin	28.0%
Underlying Core EPS Growth	+9.4%

*Underlying Revenue Growth* was 7.4% compared to the previous fiscal year, driven by our diverse portfolio of global products as well as new product launches. Underlying revenue attributable to Takeda's 14 global brands\* grew by 12.0%, which constitute approximately 42% of the total Underlying revenue.

\* Takeda's 14 global brands
 GI: ENTYVIO, GATTEX/REVESTIVE, ALOFISEL
 Rare Diseases: NATPARA/NATPAR, ADYNOVATE/ADYNOVI, TAKHZYRO, ELAPRASE, VPRIV
 PDT Immunology: GAMMAGARD LIQUID/KIOVIG, HYQVIA, CUVITRU, HUMAN ALUBUMIN/FLEXBUMIN
 Oncology: NINLARO, ALUNBRIG

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#### Underlying Revenue Growth by Therapeutic Area

GI	+6.8%
Rare Diseases	-1.4%
Rare Metabolic	+2.4%
Rare Hematology	-6.7%
Hereditary Angioedema	+4.3%
PDT Immunology	+13.6%
Oncology	+7.6%
Neuroscience	+9.5%
Other	+12.8%
Total	+7.4%

(Note) Underlying Revenue represents revenue on a constant currency basis and excluding non-recurring items and the impact of divestitures. Please refer to "<u>3. Definition of Non-IFRS Measures</u>" for the definition and "<u>Results of Operations (Reported)</u>" for the revenue of each core therapeutic area and sales of major products before underlying adjustments.

The impact of major non-recurring items and divestitures\* excluded to calculate Underlying Revenue:

- Revenue of select over-the-counter and non-core products in Asia Pacific is excluded from the previous fiscal year as the divestiture was completed in November 2020.
- Revenue of select non-core prescription pharmaceutical products predominantly in Europe is excluded from the previous fiscal year as the divestiture was completed in December 2020.
- Revenue of select over-the-counter and non-core products in Latin America is excluded from the previous fiscal year as the divestiture was completed in January 2021.
- Net sales from TACHOSIL, a surgical patch, are excluded from the previous fiscal year as the divestiture was completed in January 2021.
- Revenue of select over-the-counter and non-core products predominantly in Europe is excluded from the previous fiscal year as the divestiture was completed in March 2021.
- Revenue of the former subsidiary, Takeda Consumer Healthcare Company Limited, is excluded from the previous fiscal year as the divestiture was completed in March 2021.
- Net sales from a portfolio of diabetes products in Japan (NESINA, LIOVEL, INISYNC and ZAFATEK) are excluded from the previous fiscal year as the divestiture was completed at the beginning of April 2021. In addition, the non-recurring item of the 133.0 billion JPY selling price as the result of the completion of the divestiture is excluded from the current fiscal year.
  - \*Revenue of select non-core prescription pharmaceutical products in China had been excluded from both the current fiscal year and the previous fiscal year until the third quarter of the fiscal year ended March 31, 2022. However, as the divestiture was completed at the end of March 2022, the current fiscal year and the previous fiscal year are comparable, thus, in this quarter, no exclusion of its divestiture impact has been made for either fiscal year.

#### Underlying Core Operating Profit Growth was 5.4%, attributable to Underlying Revenue Growth.

Core Operating Profit for the current fiscal year, which excludes items unrelated to Takeda's core operations such as the sale of a portfolio of diabetes products in Japan, was 955.2 billion JPY.

Underlying Core Operating Profit Margin for the current fiscal year was 28.0%.

Underlying Core EPS Growth for the current fiscal year was 9.4%.

## **Consolidated Financial Position**

*Assets.* Total Assets as of March 31, 2022 were 13,178.0 billion JPY, reflecting an increase of 265.7 billion JPY compared to the previous fiscal year-end. Goodwill increased by 373.8 billion JPY mainly due to the effect of foreign currency translation. In addition, Property, Plant and Equipment increased by 128.9 billion JPY due to the effect of foreign currency translation as well as acquisitions, and Inventories increased by 99.3 billion JPY. These increases were partially offset by a decrease in Cash and Cash Equivalents of 116.5 billion JPY and a decrease in Intangible Assets of 90.6 billion JPY mainly due to amortization. In addition, Trade and Other Receivables decreased by 86.4 billion JPY mainly due to the trade receivables sales program put in place in the current fiscal year.

*Liabilities.* Total Liabilities as of March 31, 2022 were 7,494.5 billion JPY, reflecting a decrease of 240.6 billion JPY compared to the previous fiscal year-end. Bonds and Loans decreased by 290.0 billion JPY to 4,345.4 billion JPY<sup>\*</sup> primarily as a result of the repayment of loans and the redemption of bonds. In addition, Deferred Tax Liabilities decreased by 91.3 billion JPY. These decreases were partially offset by an increase in Trade and Other Payables of 172.5 billion JPY.

The carrying amount of Bonds was 3,637.4 billion JPY and Loans was 708.1 billion JPY as of March 31, 2022. Breakdown of Bonds and Loans carrying amount is as follows.

#### Bonds:

Name of Bond (Face Value if Denominated in Foreign Currency)	Issuance	Maturity	Carrying Amount (Billion JPY)
Unsecured US dollar denominated senior notes (1,520 million USD)	June 2015	June 2022 ~ June 2045	186.0
Unsecured US dollar denominated senior notes (4,000 million USD)	September 2016	September 2023 ~ September 2026	466.0
Unsecured Euro denominated senior notes (3,750 million EUR)	November 2018	November 2022 ~ November 2030	507.2
Unsecured US dollar denominated senior notes (3,250 million USD)	November 2018	November 2023 ~ November 2028	395.3
Hybrid bonds (subordinated bonds)	June 2019	June 2079	498.2
Unsecured US dollar denominated senior notes (7,000 million USD)	July 2020	March 2030 ~ July 2060	849.4
Unsecured Euro denominated senior notes (3,600 million EUR)	July 2020	July 2027 ~ July 2040	486.0
Unsecured JPY denominated senior bonds	October 2021	October 2031	249.4
Total			3,637.4

Loans:

Name of Loan (Face Value if Denominated in Foreign Currency)	Execution	Maturity	Carrying Amount (Billion JPY)
Syndicated loans	April 2016	April 2023 ~ April 2026	200.0
Syndicated loans	April 2017	April 2027	113.5
Syndicated loans (1,500 million USD)	April 2017	April 2027	183.0
Bilateral loans	March 2016 ~ April 2017	March 2023 ~ March 2026	210.0
Other			1.5
Total			708.1

On May 17, 2021, Takeda redeemed the remaining 200 million USD of unsecured U.S. dollar-denominated senior notes issued in July 2017 in advance of their original maturity date of January 18, 2022. Following this, on June 11, 2021, Takeda prepaid 2,000 million USD of the Japan Bank for International Cooperation loan ("JBIC Loan") amount of 3,700 million USD (that was entered into on December 3, 2018) in advance of its original maturity date of December 11, 2025. On August 10, 2021, Takeda redeemed 1,500 million EUR of unsecured senior notes issued in November 2018 in advance of their original maturity date of November 21, 2022. On October 14, 2021, Takeda issued 10-year unsecured senior bonds with an aggregate principal amount of 250 billion JPY and a maturity date of October 14, 2031. Following this, on December 13, 2021 Takeda prepaid the remaining 1,700 million USD amount outstanding on the JBIC Loan in advance of its original maturity date of December 11, 2025. Furthermore, on March 24, 2022, Takeda redeemed 1,500 million USD of unsecured senior notes issued in September 2016 in advance of their original maturity date of September 23, 2023.

On April 23, 2022, Takeda redeemed 219 million USD of unsecured U.S. dollar-denominated senior notes issued in June 2015 in advance of their original maturity date of June 23, 2022.

*Equity.* Total Equity as of March 31, 2022 was 5,683.5 billion JPY, an increase of 506.3 billion JPY compared to the previous fiscal year-end. This was mainly due to an increase of 568.1 billion JPY in Other Components of Equity mainly due to fluctuation in currency translation adjustments reflecting the depreciation of yen. This increase was partially offset by an increase in Treasury Shares of 56.5 billion JPY mainly due to the share buybacks conducted in the current fiscal year and a decrease in Retained Earnings of 30.2 billion JPY. The decrease in Retained Earnings reflects primarily dividend payments of 284.2 billion JPY despite the recording of Net Profit for the Year.

## **Consolidated Cash Flow**

Billion JPY

	For the fiscal year ended March 31,		
	2021	2022	
Net cash from (used in) operating activities	1,010.9	1,123.1	
Net cash from (used in) investing activities	393.5	(198.1)	
Net cash from (used in) financing activities	(1,088.4)	(1,070.3)	
Net increase (decrease) in cash and cash equivalents	316.1	(145.3)	
Cash and cash equivalents at the beginning of the year	637.6	966.2	
Effects of exchange rate changes on cash and cash equivalents	12.5	28.8	
Cash and cash equivalents at the end of the year	966.2	849.7	

*Net cash from operating activities* was 1,123.1 billion JPY for the fiscal year ended March 31, 2022 compared to 1,010.9 billion JPY for the fiscal year ended March 31, 2021. The increase of 112.2 billion JPY was primarily driven by higher net profit for the period adjusted for non-cash items and other adjustments, including gain on divestment of business and subsidiaries as well as the income relating to the release from the obligation to divest the pipeline compound SHP 647 and certain associated rights in the previous fiscal year. In addition, there was a decrease in trade and other receivables mainly due to the trade receivables sales program put in place in the current fiscal year. These favorable impacts were partially offset by a decrease of other financial liabilities primarily attributable to an decrease of deposits restricted to certain vaccine operations and a decrease in provisions due to payments.

*Net cash used in investing activities* was 198.1 billion JPY for the fiscal year ended March 31, 2022 compared to net cash from investing activities of 393.5 billion JPY for the fiscal year ended March 31, 2021. This increase in net cash used of 591.7 billion JPY was mainly due to a decrease of 502.2 billion JPY in proceeds from sales of business (net of cash and cash equivalents divested) reflecting the sales of the non-core assets in the previous fiscal year, a decrease of 57.7 billion JPY in proceeds from sales and redemptions of investments, an increase of 49.7 billion JPY in the acquisition of businesses (net of cash and cash equivalents acquired), and a decrease of 44.6 billion JPY in proceeds from sales of property, plant and equipment. These were partially offset by a decrease of 62.5 billion JPY in acquisition of intangible assets .

*Net cash used in financing activities* was 1,070.3 billion JPY for the fiscal year ended March 31, 2022 compared to 1,088.4 billion JPY for the fiscal year ended March 31, 2021. The decrease of 18.1 billion JPY was mainly due to a net increase in short-term loans and commercial papers of 149.0 billion JPY and a decrease in payments for settlement of forward rate agreements related to bonds of 34.8 billion JPY, partially offset by an increase in repayments of bonds and long-term loans, net of proceeds from issuance of bonds upon refinancing, of 88.6 billion JPY and increase in purchase of treasury shares by 75.4 billion JPY mainly due to the share buybacks conducted in the current fiscal year.

# **Impact of the Spread of the Novel Coronavirus Infectious Disease (COVID-19) and Takeda's Initiatives in Response**

#### (i) Impact of COVID-19 on Takeda's Operations and Financial Condition

Takeda continues to respond to the COVID-19 pandemic and provide industry support in a number of ways. While vaccines are becoming more broadly available, we continue to strictly adhere to local public health guidance across our geographies in addition to the internal protocols we have put in place, and monitor any potential impacts of the effects and evolution of COVID-19, including new variants, on our business activities.

In monitoring demand for our products, we have seen limited impact as many of our medicines are for severe chronic or lifethreatening diseases, without the requirement of a hospital elective procedure. In terms of our global supply chain, based on current assessments, we have not seen, nor do we anticipate, any material potential supply distribution issues due to the COVID-19 pandemic. Where appropriate and in accordance with local public health guidance and regulations, our field employees have resumed some face-to-face engagements with customers. Clinical trial activities that were temporarily paused during the previous fiscal year have generally been resumed while we continue to monitor the evolution of the pandemic.

As we continue to monitor developments in the financial markets, we currently do not anticipate any material liquidity or funding-related issues.

#### (ii) Takeda's Initiatives to Mitigate the Impact of COVID-19

Guided by our values, Takeda's response to COVID-19 continues to focus on protecting the health and safety of our employees, our ability to ensure our medicines are available to patients who rely on them and playing our part to reduce transmission and support the communities where our employees live and work.

Major updates to Takeda's initiatives in response to the spread of COVID-19 in the current fiscal year are as below.

- The highly contagious Omicron variant has temporarily slowed the roll out of a new hybrid working model in parts of the business. Moving forward, implementation of this model will vary by job function, and on the local level, given differences in public health guidance and regulations, changes in population and epidemiology over time and standards of practice in the community.
- After over two years of providing support for Takeda's global pandemic response, Takeda's firmwide COVID-19 Global Crisis Management Committee was discontinued and Takeda has shifted to an operating model in which regional crisis management committees will provide guidance based on regional information from public health authorities.
- Takeda has undertaken a number of efforts to help the world respond to COVID-19. This includes bringing COVID-19 vaccines to Japan through two partnerships. The first partnership is with Novavax, for the development, manufacturing, and commercialization of its COVID-19 vaccine in Japan. In September 2021, Takeda concluded an agreement with the Government of Japan's Ministry of Health, Labour and Welfare (MHLW) to provide 150 million doses of Novavax' COVID-19 vaccine manufactured in Japan by Takeda. In April 2022, Takeda received manufacturing and marketing approval from the MHLW for NUVAXOVID Intramuscular Injection, a novel recombinant protein-based COVID-19 vaccine, for primary and booster immunization in Japan.

The second partnership is with Moderna and the MHLW to import and distribute Moderna's mRNA COVID-19 vaccine (SPIKEVAX Intramuscular Injection (former product name: COVID-19 Vaccine Moderna Intramuscular Injection)) in Japan. Since May 2021, Takeda has been distributing the Moderna COVID-19 vaccine in Japan. In October 2021, Takeda and Moderna published an investigation report prompted by the recall of three lots of the Moderna COVID-19 vaccine in Japan based on the observation of foreign particles in unpunctured vials from a single lot. The report concluded that the event does not pose an undue risk to patient safety or adversely affect the benefit/risk profile of the product.

In December 2021, the parties reached to an agreement to import and distribute 18 million additional doses of Moderna's COVID-19 vaccine, bringing the total to 93 million doses in 2022. Takeda started to import and distribute these booster doses from January 2022.

#### (iii) Business risks associated with the continued global spread of COVID-19

Depending on the severity and duration of the impacts resulting from the COVID-19 pandemic, and despite our various efforts, we may experience further adverse effects on our business including, but not limited to, disruptions to our ability to procure raw materials or to supply products, additional disruptions to our clinical trial programs, or disruptions to our ability to observe regulations applicable to us. While vaccines, including those used for additional vaccination, are becoming widely available across the globe, it remains unclear how long the pandemic of COVID-19, including the impact of new variants, and measures intended to stop or slow its spread will last in many regions worldwide.

We will continue to closely monitor the situation and take necessary measures to minimize any future business risks, but our business, financial condition and results of our operations could be adversely affected depending on the future status of the COVID-19 pandemic.

#### (iv) FY2021 financial impact from COVID-19

Overall, the global spread of COVID-19 did not have a material effect on our financials for the fiscal year ended March 31, 2022. Over the course of the pandemic, there have been adverse effects due to COVID-19 observed in certain therapeutic areas, especially in Neuroscience during periods when stay-at-home restrictions have been in place, reducing patient visits to medical care providers. This was notable especially in the early months of the previous fiscal year. The trend has occurred intermittently since then, and we have not yet seen a full recovery to pre-COVID-19 levels, however, a certain number of our life-saving medicines have shown resilience and have grown even under such an environment. Although it was financially immaterial, we have experienced some disruption to certain products in the second half of the fiscal year due to the spread of the Omicron variant, including shipping delays and fewer diagnostic procedures.

## Takeda's Operations in Ukraine and Russia

Our commitment to patients, regardless of where they live, and to our people is unwavering and is even more important in times of crisis. Takeda is making every effort to protect our colleagues in Ukraine and to continue to supply patients in Ukraine and in the region with much needed treatments.

We are supporting the global humanitarian efforts by contributing 300 million JPY (approx. \$2.6 million USD) to The International Federation of Red Cross and Red Crescent Societies, which is actively providing urgent local humanitarian support to people displaced and impacted by the conflict. We are also donating medicines to hospitals working to provide care around the clock to patients in need.

Takeda has taken further action to discontinue activities in Russia that are not essential to maintaining the supply of medicines to patients and providing ongoing support to our employees. This includes suspending all new investments, suspending advertising and promotion, not initiating new clinical trials and stopping enrollment of new patients in ongoing clinical trials.

Our focus only on essential activities is consistent with our values and ethical responsibility to our patients in Ukraine, Russia and the region who depend on our treatments. This commitment notwithstanding, we are adhering to all international sanctions imposed on Russia.

We will be increasing our humanitarian relief efforts, including monetary and medicine donations to benefit people affected by the conflict in Ukraine, and we will continue to assess new ways to provide support as we look to meet the needs of patients across the region.

Takeda will continue to monitor the situation closely and take appropriate actions grounded in our values.

In the fiscal year ended March 31, 2022, revenue attributable to Russia/CIS represented 1.7% of Takeda's total consolidated revenue of 3,569.0 billion JPY, as indicated in the Revenue by Geographic Region in 1. Financial Highlights for the Fiscal Year Ended March 31, 2022, (1) Business Performance, (ii) Consolidated Financial Results (April 1, 2021 to March 31, 2022). There was no material financial impact on Takeda's financial results for the current fiscal year resulting from the crisis in these countries. However, depending on the future status of the crisis, our results of operations and financial conditions could be adversely affected.

# **Outlook for the Fiscal Year Ending March 31, 2023**

The full year consolidated reported forecast for fiscal 2022 is as below:

## Full Year Reported Forecast for the Fiscal Year Ending March 31, 2023 (FY2022)

			Billion JPY or percentage	
	FY2021	FY2022	Change over the	e previous year
Revenue	3,569.0	3,690.0	+121.0	+3.4 %
Operating profit	460.8	520.0	+59.2	+12.8 %
Profit before tax	302.6	411.0	+108.4	+35.8 %
Net profit for the year (attributable to owners of the Company)	230.1	292.0	+61.9	+26.9 %
EPS (JPY)	147.14	188.13	+40.99	+27.9 %
Core Revenue	3,420.5	3,690.0	+269.5	+7.9 %
Core Operating Profit	955.2	1,100.0	+144.8	+15.2 %
Core EPS (JPY)	425	484	+60	+14.0 %

#### [Revenue]

Takeda expects FY2022 revenue to be 3,690.0 billion JPY, an increase of 121.0 billion JPY or 3.4% from FY2021. Continued acceleration of our Growth and Launch Products such as ENTYVIO, TAKHZYRO, immunoglobulin, albumin, and recently launched LIVTENCITY and EXKIVITY, in addition to a favorable impact from foreign exchange rates, is expected to fully offset the impact from loss of exclusivity of VELCADE in the U.S. and the non-recurrence of 133.0 billion JPY from the sale of a diabetes portfolio in Japan recorded as revenue in FY2021. This portfolio sale was excluded from Core revenue in FY2021, and in FY2022, Takeda does not include any such non-core items that requires adjustment in its revenue forecast; therefore, the Core revenue forecast for FY2022 is the same as the reported revenue forecast at 3,690.0 billion JPY.

#### [Operating Profit]

Operating Profit is expected to increase by 59.2 billion JPY, or 12.8%, to 520.0 billion JPY, reflecting business momentum and lower restructuring expenses, combined with a positive impact from foreign exchange rates. Core Operating Profit, adjusted to exclude items unrelated to Takeda's core operations, is expected to be 1,100.0 billion JPY, an increase of 144.8 billion JPY, or 15.2%.

[Net profit for the year (attributable to owners of the Company)]

Net profit for the year (attributable to owners of the Company) is expected to be 292.0 billion JPY, an increase of 61.9 billion JPY, or 26.9%. In addition to the Operating Profit growth of 59.2 billion JPY, net finance expenses are expected to decrease by 35.9 billion JPY, including a decrease in net interest expenses. For these main reasons, Profit Before Tax is expected to increase by 108.4 billion JPY, or 35.8%, to 411.0 billion JPY. The assumption for the effective tax rate is approximately 29%, which is applied to the Profit Before Tax forecast.

Core EPS is expected to be 484 JPY, an increase of 60 JPY, or +14.0%.

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### Major assumptions used in preparing the FY2022 Reported Forecast

	FY2021	Billion JPY or percentage FY2022
FX rates	1 USD = 112 JPY 1 Euro = 131 JPY 1 RUB = 1.5 JPY 1 BRL = 20.9 JPY 1 CNY = 17.4 JPY	1 USD = 119 JPY 1 Euro = 133 JPY 1 RUB = 1.3 JPY 1 BRL = 24.0 JPY 1 CNY = 18.8 JPY
R&D expenses	(526.1)	(570.0)
Amortization of intangible assets associated with products	(418.8)	(438.0)
Of which Shire acquisition related	(339.7)	(358.0)
Impairment of intangible assets associated with products	(54.1)	(50.0)
Other operating income	43.1	12.0
Other operating expenses	(159.1)	(73.0)
Japan diabetes portfolio divestiture gain	131.4	
Other Core Operating Profit adjustments	(36.9)	(31.0)
Of which Shire acquisition related to unwind of inventories step-up	(31.9)	(22.0)
Finance income/expenses	(142.9)	(107.0)
Free cash flow	943.7	600.0 - 700.0
Capital expenditures (cash flow base)	(186.0)	(260.0 - 310.0)
Depreciation and amortization (excluding intangible assets associated with products)	(161.0)	(150.0)
Cash tax rate on adjusted EBITDA (excluding divestitures)	~12%	Mid-teen %

#### **Management Guidance at CER\***

Beginning with FY2022, Takeda will now use growth in its Core financial measures on a Constant Exchange Rate basis ("Core Growth at CER") to provide its Management Guidance. Previously, Takeda used Underlying financial measures for its Management Guidance, which also adjusted for the impact of divestitures. Because Takeda now anticipates that all the major divestitures following its acquisition of Shire have been completed, we will no longer use Underlying financial measures going forward in our financial reporting.

	FY2022
Core Revenue Growth	Low-single-digit growth
Core Operating Profit Growth	High-single-digit growth
Core EPS Growth	High-single-digit growth

\* CER (Constant Exchange Rate) eliminates the effect of foreign exchange rates by translating results of operations using corresponding exchange rates in the same period of the previous fiscal year. Please refer to "<u>Results of</u> <u>Operations (Underlying)</u>" and "Supplementary Information - <u>3. Definition of Non-IFRS Measures</u>" for the definition of Core performance measurements.

#### Other assumptions used in preparing the FY2022 Reported Forecast and the Management Guidance

- Based on currently available information, Takeda expects that its financial results for FY2022 will not be materially affected by COVID-19 or the crisis in Ukraine and Russia and, accordingly, Takeda's FY2022 reported forecast and the management guidance reflect this expectation.
- The FY2022 reported forecast and the management guidance include approximately 50.0 billion JPY revenue contribution from COVID-19 vaccines.

#### **Forward looking statements**

All forecasts in this document are based on information currently available to management, and do not represent a promise or guarantee to achieve these forecasts. Various uncertain factors could cause actual results to differ, such as changes in the business environment and fluctuations in foreign exchange rates. Should any significant event occur which requires the forecast to be revised, the Company will disclose it in a timely manner.

# Capital Allocation Policy and Dividends for the Fiscal Year Ended March 31, 2022 and Ending March 31, 2023

#### (i) Capital Allocation Policy

Takeda is delivering on its financial commitments and has a strong cash flow outlook driven by revenue growth and strong margins. Guided by our values and our commitment to Patients, People and Planet, we will allocate capital to maximize value for patients and shareholders.

Takeda's policy in the allocation of capital is as follows:

- Invest in growth drivers;
- Deleverage rapidly; and
- Shareholder returns.

In respect of "Invest in growth drivers", Takeda makes disciplined and focused investments in value-creating business opportunities including R&D, new product launches, including in China, and plasma-derived therapies. With regard to "Deleverage rapidly", Takeda is targeting a 2x (i.e. "low-twos") net debt/adjusted EBITDA ratio by the fiscal year ending March 2024 and has committed to maintaining solid investment grade credit ratings. In respect of "Shareholder returns", Takeda maintains its well-established dividend policy of 180 yen per share annually, alongside share buybacks when appropriate. We believe we are positioned for revenue and profit growth over the medium-term.

#### (ii) Dividend

Takeda is strongly committed to shareholder returns with the dividend as a key component.

[FY2021] 180 yen per share

Year-end dividend per share: 90 yen Together with the interim dividend of 90 yen per share, the annual dividend will be 180 yen per share.

[FY2022 guidance] 180 yen per share

# **Consolidated Financial Statements [IFRS]**

# (1) Consolidated Statements of Profit or Loss

	JPY (millions, except per share data)			USD (millions) <sup>(*)</sup>	
	]	For the year ended	For the year ended March 31,		
		2021	2022	2022	
Revenue	¥	3,197,812 ¥	3,569,006	\$ 29,389	
Cost of sales		(994,308)	(1,106,846)	(9,114)	
Selling, general and administrative expenses		(875,663)	(886,361)	(7,299)	
Research and development expenses		(455,833)	(526,087)	(4,332)	
Amortization and impairment losses on intangible assets associated with products		(421,864)	(472,915)	(3,894)	
Other operating income		318,020	43,123	355	
Other operating expenses		(258,895)	(159,075)	(1,310)	
Operating profit		509,269	460,844	3,795	
Finance income		105,521	23,700	195	
Finance expenses		(248,631)	(166,607)	(1,372)	
Share of profit (loss) of investments accounted for using the equity method		76	(15,367)	(127)	
Profit before tax		366,235	302,571	2,492	
Income tax (expenses) benefit		9,936	(72,405)	(596)	
Net profit for the year		376,171	230,166	1,895	
Attributable to:					
Owners of the Company		376,005	230,059	1,894	
Non-controlling interests		166	107	1	
Net profit for the year		376,171	230,166	1,895	
Earnings per share (JPY)					
Basic earnings per share		240.72	147.14	1.21	
Diluted earnings per share		238.96	145.87	1.20	

(\*) Consolidated statements of profit or loss have been translated solely for the convenience of the reader at an exchange rate of 1USD = 121.44 JPY, the Noon Buying Rate certified by the Federal Reserve Bank of New York on March 31, 2022. The rate and methodologies used for the convenience translations differ from the currency exchange rates and translation methodologies under IFRS used for the preparation of the consolidated financial statements. The translation should not be construed as a representation that the Japanese yen amounts could be converted into U.S. dollars at the above or any other rate.

# (2) Consolidated Statements of Comprehensive Income

	JPY (millions) For the year ended March 31,			)	USD (millions) <sup>(*)</sup>	
				For the year ended March 31,		
		2021		2022		2022
Net profit for the year	¥	376,171	¥	230,166	\$	1,895
Other comprehensive income (loss)						
Items that will not be reclassified to profit or loss:						
Changes in fair value of financial assets measured at fair value through other comprehensive income		61,866		(14,626)		(120)
Remeasurement of defined benefit pension plans		4,866		20,783		171
		66,732		6,158		51
Items that may be reclassified subsequently to profit or loss:						
Exchange differences on translation of foreign operations		309,304		583,969		4,809
Cash flow hedges		(45,345)		2,173		18
Hedging cost		(9,147)		2,457		20
Share of other comprehensive loss of investments						
accounted for using the equity method		(299)		(497)		(4)
		254,513		588,103		4,843
Other comprehensive income for the year, net of tax		321,245		594,261		4,893
Total comprehensive income for the year		697,416		824,427		6,789
Attributable to:						
Owners of the Company		697,202		824,258		6,787
Non-controlling interests		214		168		1
Total comprehensive income for the year		697,416		824,427		6,789

(\*) Consolidated statements of comprehensive income have been translated solely for the convenience of the reader at an exchange rate of 1USD = 121.44 JPY, the Noon Buying Rate certified by the Federal Reserve Bank of New York on March 31, 2022. The rate and methodologies used for the convenience translations differ from the currency exchange rates and translation methodologies under IFRS used for the preparation of the consolidated financial statements. The translation should not be construed as a representation that the Japanese yen amounts could be converted into U.S. dollars at the above or any other rate.

# (3) Consolidated Statements of Financial Position

		JPY (millions)			USD (millions) <sup>(*)</sup>	
	As o	As of March 31, 2021		f March 31, 2022	As of	March 31, 2022
ASSETS						
Non-current assets:						
Property, plant and equipment	¥	1,453,917	¥	1,582,800	\$	13,034
Goodwill		4,033,917		4,407,749		36,296
Intangible assets		3,909,106		3,818,544		31,444
Investments accounted for using the equity method		112,468		96,579		795
Other financial assets		235,882		233,554		1,923
Other non-current assets		100,341		82,611		680
Deferred tax assets		353,769		362,539	_	2,985
Total non-current assets		10,199,400		10,584,376		87,157
Current assets:						
Inventories		753,881		853,167		7,025
Trade and other receivables		783,091		696,644		5,737
Other financial assets		36,598		25,305		208
Income taxes receivable		29,623		27,733		228
Other current assets		122,789		141,099		1,162
Cash and cash equivalents		966,222		849,695		6,997
Assets held for sale		20,689			_	
Total current assets		2,712,893		2,593,642		21,357
Total assets		12,912,293		13,178,018		108,515
LIABILITIES AND EQUITY						
LIABILITIES						
Non-current liabilities:						
Bonds and loans		4,613,218		4,141,418		34,103
Other financial liabilities		517,677		468,943		3,862
Net defined benefit liabilities		158,857		145,847		1,201
Income taxes payable		33,690		21,634		178
Provisions		38,748		52,199		430
Other non-current liabilities		56,898		67,214		553
Deferred tax liabilities		542,852		451,511		3,718
Total non-current liabilities		5,961,940		5,348,764		44,045
Current liabilities:						
Bonds and loans		22,153		203,993		1,680
Trade and other payables		343,838		516,297		4,251
Other financial liabilities		248,053		196,071		1,615
Income taxes payable		145,203		200,918		1,654
Provisions		471,278		443,502		3,652
Other current liabilities		542,651		584,949		4,817
Total current liabilities		1,773,176		2,145,730		17,669
Total liabilities		7,735,116		7,494,495		61,714

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	JPY (m	illions)	USD (millions) <sup>(*)</sup>
	As of March 31, 2021	As of March 31, 2022	As of March 31, 2022
EQUITY			
Share capital	1,668,145	1,676,263	13,803
Share premium	1,688,424	1,708,873	14,072
Treasury shares	(59,552)	(116,007)	(955)
Retained earnings	1,509,906	1,479,716	12,185
Other components of equity	366,114	934,173	7,692
Equity attributable to owners of the company	5,173,037	5,683,019	46,797
Non-controlling interests	4,140	504	4
Total equity	5,177,177	5,683,523	46,801
Total liabilities and equity	12,912,293	13,178,018	108,515

(\*) Consolidated statements of financial position have been translated solely for the convenience of the reader at an exchange rate of 1USD = 121.44 JPY, the Noon Buying Rate certified by the Federal Reserve Bank of New York on March 31, 2022. The rate and methodologies used for the convenience translations differ from the currency exchange rates and translation methodologies under IFRS used for the preparation of the consolidated financial statements. The translation should not be construed as a representation that the Japanese yen amounts could be converted into U.S. dollars at the above or any other rate.

# (4) Condensed Interim Consolidated Statements of Changes in Equity

			JPY (n	nillions)				
	Equity attributable to owners of the company							
					Other components of equity			
	Share capital	Share premium	Treasury shares	Retained earnings	Exchange differences on translation of foreign operations	Changes in fair value of financial assets measured at fair value through other comprehensive income		
As of April 1, 2020	1,668,123	1,680,287	(87,463)	1,369,972	91,848	22,891		
Net profit for the year				376,005				
Other comprehensive income (loss)					308,950	61,873		
Comprehensive income (loss) for the year		—	_	376,005	308,950	61,873		
Transactions with owners:								
Issuance of new shares	22	22						
Acquisition of treasury shares			(2,141)					
Disposal of treasury shares		(0)	2					
Dividends				(283,718)				
Transfers from other components of equity				47,647		(42,781)		
Share-based compensation		37,663						
Exercise of share-based awards		(29,548)	30,050					
Total transactions with owners	22	8,137	27,911	(236,071)		(42,781)		
As of March 31, 2021	1,668,145	1,688,424	(59,552)	1,509,906	400,798	41,983		

Equity attributable to owners of the company Other components of equity

	Cash flow hedges	Hedging cost	Remeasurement s of defined benefit pension plans	Total	Total	Non- controlling interests	Total equity
As of April 1, 2020	(22,730)	555		92,564	4,723,483	4,003	4,727,486
Net profit for the year				_	376,005	166	376,171
Other comprehensive income (loss)	(45,345)	(9,147)	4,866	321,197	321,197	48	321,245
Comprehensive income (loss) for the year	(45,345)	(9,147)	4,866	321,197	697,202	214	697,416
Transactions with owners:							
Issuance of new shares				—	44		44
Acquisition of treasury shares				—	(2,141)		(2,141)
Disposal of treasury shares				—	2		2
Dividends				_	(283,718)	(77)	(283,795)
Transfers from other components of equity			(4,866)	(47,647)	_		_
Share-based compensation				_	37,663		37,663
Exercise of share-based awards					502		502
Total transactions with owners		_	(4,866)	(47,647)	(247,648)	(77)	(247,725)
As of March 31, 2021	(68,075)	(8,592)		366,114	5,173,037	4,140	5,177,177

		JPY (millions) Equity attributable to owners of the company						
					Other comp	onents of equity		
	Share capital	Share premium	Treasury shares	<b>Retained</b> earnings	Exchange differences on translation of foreign operations	Changes in fair value of financial assets measured at fair value through other comprehensive income		
As of April 1, 2021	1,668,145	1,688,424	(59,552)	1,509,906	400,798	41,983		
Net profit for the year				230,059				
Other comprehensive income (loss)					583,343	(14,558)		
Comprehensive income (loss) for the year	_	—	—	230,059	583,343	(14,558)		
Transactions with owners:								
Issuance of new shares	8,118	14,036						
Acquisition of treasury shares			(79,447)					
Disposal of treasury shares		(0)	1					
Dividends				(284,246)				
Changes in ownership				(2,143)				
Transfers from other components of equity				26,141		(5,357)		
Share-based compensation		43,374						
Exercise of share-based awards		(36,960)	22,992					
Total transactions with owners	8,118	20,450	(56,454)	(260,249)	_	(5,357)		
As of March 31, 2022	1,676,263	1,708,873	(116,007)	1,479,716	984,141	22,068		

Equity attributable to owners of the company
Other components of equity

	Cash flow hedges	Hedging cost	Remeasurements of defined benefit pension plans	Total	Total	Non- controlling interests	Total equity
As of April 1, 2021	(68,075)	(8,592)		366,114	5,173,037	4,140	5,177,177
Net profit for the year				_	230,059	107	230,166
Other comprehensive income (loss)	2,173	2,457	20,783	594,200	594,200	61	594,261
Comprehensive income (loss) for the year	2,173	2,457	20,783	594,200	824,258	168	824,427
Transactions with owners:							
Issuance of new shares				_	22,154		22,154
Acquisition of treasury shares				_	(79,447)		(79,447)
Disposal of treasury shares				_	1		1
Dividends				—	(284,246)		(284,246)
Changes in ownership				—	(2,143)	(3,804)	(5,948)
Transfers from other components of equity			(20,783)	(26,141)	_		—
Share-based compensation				—	43,374		43,374
Exercise of share-based awards					(13,968)		(13,968)
Total transactions with owners			(20,783)	(26,141)	(314,276)	(3,804)	(318,080)
As of March 31, 2022	(65,901)	(6,135)		934,173	5,683,019	504	5,683,523

# (5) Consolidated Statements of Cash Flows

		JPY (millions) For the year ended March 31,		
	2021		2022	<u>31,</u> 2022
Cash flows from operating activities:				
Net profit for the year	¥ 376,1	71 ¥	230,166	\$ 1,895
Depreciation and amortization	559,6	71	583,151	4,802
Impairment losses	25,4	52	54,515	449
Equity-settled share-based compensation	37,6	63	43,374	357
Change in estimate of liabilities related to SHP647	(60,1	79)	_	_
Loss (gain) on sales and disposal of property, plant and equipment	(2,1	09)	655	5
Gain on divestment of business and subsidiaries	(229,9	93)	(7,829)	(64)
Change in fair value of financial assets and liabilities associated with contingent consideration arrangements, net	59,2	77	(11,195)	(92)
Finance (income) and expenses, net	143,1	10	142,907	1,177
Share of loss (profit) of investments accounted for using the equity method	(	76)	15,367	127
Income tax expenses (benefit)	(9,9	36)	72,405	596
Changes in assets and liabilities:				
Decrease (increase) in trade and other receivables	(9,3	16)	127,294	1,048
Decrease (increase) in inventories	25,9	78	(46,148)	(380)
Increase in trade and other payables	36,6	20	125,157	1,031
Increase (decrease) in provisions	49,0	99	(58,090)	(478)
Increase (decrease) in other financial liabilities	173,4	00	(49,608)	(408)
Other, net	37,7	86	41,409	341
Cash generated from operations	1,212,6	18	1,263,528	10,405
Income taxes paid	(235,8	01)	(147,724)	(1,216)
Tax refunds and interest on tax refunds received	34,1	14	7,301	60
Net cash from operating activities	1,010,9	31	1,123,105	9,248
Cash flows from investing activities:				
Interest received	1,1	05	2,919	24
Dividends received	3	87	3,401	28
Acquisition of property, plant and equipment	(111,2	06)	(123,252)	(1,015)
Proceeds from sales of property, plant and equipment	46,4	53	1,815	15
Acquisition of intangible assets	(125,2	62)	(62,785)	(517)
Acquisition of investments	(12,5	96)	(8,341)	(69)
Proceeds from sales and redemption of investments	74,6	04	16,921	139
Acquisition of businesses, net of cash and cash equivalents acquired			(49,672)	(409)
Proceeds from sales of business, net of cash and cash equivalents divested	530,3	88	28,196	232
Other, net	(10,3	43)	(7,328)	(60)
Net cash from (used in) investing activities	393,5	30	(198,125)	(1,631)

	JPY (mill	JPY (millions) For the year-ended March 31,		
	For the year-ende			
	2021	2022	2022	
Cash flows from financing activities:				
Net decrease in short-term loans and commercial papers	(149,043)	(2)	(0)	
Proceeds from issuance of bonds and long-term loans	1,179,515	249,334	2,053	
Repayments of bonds and long-term loans	(1,651,706)	(810,115)	(6,671)	
Payments for settlement of forward rate agreement related to bonds	(34,830)	—	—	
Acquisition of treasury shares	(2,141)	(77,531)	(638)	
Interest paid	(107,350)	(108,207)	(891)	
Dividends paid	(283,357)	(283,665)	(2,336)	
Repayments of lease liabilities	(39,270)	(39,694)	(327)	
Other, net	(172)	(385)	(3)	
Net cash used in financing activities	(1,088,354)	(1,070,265)	(8,813)	
Net increase (decrease) in cash and cash equivalents	316,107	(145,285)	(1,196)	
Cash and cash equivalents at the beginning of the year				
(Consolidated statements of financial position)	637,614	966,222	7,956	
Effects of exchange rate changes on cash and cash equivalents	12,501	28,758	237	
Cash and cash equivalents at the end of the year				
(Consolidated statements of financial position)	966,222	849,695	6,997	

(\*) Consolidated statements of cash flows have been translated solely for the convenience of the reader at an exchange rate of 1USD = 121.44 JPY, the Noon Buying Rate certified by the Federal Reserve Bank of New York on March 31, 2022. The rate and methodologies used for the convenience translations differ from the currency exchange rates and translation methodologies under IFRS used for the preparation of the consolidated financial statements. The translation should not be construed as a representation that the Japanese yen amounts could be converted into U.S. dollars at the above or any other rate.

#### (6) Other Information

(Significant Subsequent Events)

Not applicable.

# Supplementary Information

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### 1. Pipeline

#### I. Clinical Development Activities

- The following table lists the pipeline assets that we are clinically developing as of May 11, 2022. The assets in our pipeline are in various stages of development, and the contents of the pipeline may change as therapeutic candidates currently under development drop out and new therapeutic candidates are introduced. Whether the therapeutic candidates listed below are ever successfully released as products depends on various factors, including the results of pre-clinical and clinical trials, market conditions for various drugs and regulatory approvals.
- This table primarily shows the indications for which we are actively pursuing regulatory approval and those regulatory approvals granted during fiscal year 2021. We are also conducting additional studies of certain assets to examine their potential for use in further indications and in additional formulations.
- The listings in this table are limited to the U.S., EU and Japan and China, but we are also actively conducting development activities in other regions, including in Emerging Markets. Country/region column denotes where a pivotal clinical study is ongoing or a filing has been made with our specific intention to pursue approval in any of the U.S., EU, Japan or China. 'Global' refers to U.S., EU, Japan and China.
- Brand name and country/region indicate the brand name and country in which the specific asset has already been approved for any indication in any of the U.S., EU, Japan or China and Takeda has commercialization rights for such asset.
- Stage-ups are recognized in the table upon achievement of First Subject In.
- Modality of our pipeline assets in the following table is classified into either of the following categories: 'small molecule', 'peptide/oligonucleotide', 'cell and gene therapy', 'microbiome' or 'biologic and other.'

### **Oncology Pipeline**

Development code <generic name=""> Brand name (country/region)</generic>	Type of Drug (administration route)	Modality	Indications / additional formulations	Country/ Region	Stage
SGN-35 <sup>1</sup>  brentuximab vedotin> ADCETRIS 	CD30 monoclonal antibody-drug conjugate (injection)	Biologic and other	Cutaneous T cell lymphoma	China	Approved (Apr 2021)
 brigatinib> ALUNBRIG (Global)	ALK inhibitor (oral)	Small molecule	1L & 2L ALK-positive Non-Small Cell Lung Cancer 2L ALK-positive Non-Small Cell Lung Cancer (head-to-head with alectinib)	China U.S. EU	Approved (Mar 2022) P-III P-III
MLN9708 <ixazomib> NINLARO (Global)</ixazomib>	Proteasome inhibitor (oral)	Small molecule	Maintenance therapy in patients with newly diagnosed Multiple Myeloma not treated with stem cell transplant Maintenance therapy in patients with newly diagnosed Multiple Myeloma following autologous stem cell transplant	Japan U.S. EU China U.S. EU	Approved (May 2021) P-III P-III P-III P-III P-III

			1L Renal cell carcinoma in combination with nivolumab	Japan	Approved (Aug 2021)
<cabozantinib><sup>2</sup> CABOMETYX (Japan)</cabozantinib>	Multi-targeted kinase inhibitor (oral)	Small molecule	2L metastatic Non-Small Cell Lung Cancer in combination with atezolizumab <sup>3</sup>	Japan	P-III
			Metastatic Castration-Resistant Prostate Cancer in combination with atezolizumab <sup>4</sup>	Japan	P-III
<ponatinib> ICLUSIG (U.S.)</ponatinib>	BCR-ABL inhibitor (oral)	Small molecule	Front line Philadelphia chromosome-positive Acute Lymphoblastic Leukemia	U.S.	P-III
TAK-788	EGFR/HER2 exon 20	Small	Treatment Naïve Non-Small Cell Lung Cancer with EGFR exon 20 insertion	Global	P-III
<mobocertinib> EXKIVITY (U.S.)</mobocertinib>	nobocertinib> inhibitor (oral) molect	molecule	Previously treated Non-Small Cell Lung Cancer with EGFR exon 20 insertion <sup>5</sup>	U.S. China EU <sup>6</sup> Japan	Approved (Sep 2021) Filed (Jul 2021) Filed (Jul 2021) P-III
TAK-385 <relugolix></relugolix>	LH-RH antagonist (oral)	Small molecule	Prostate cancer	Japan China	P-III P-III
TAK-981 <subasumstat></subasumstat>	SUMO inhibitor (injection)	Small molecule	Multiple cancers	-	P-II
TAK-007 <sup>7</sup>	CD19 CAR-NK (injection)	Cell and gene therapy	Relapsed/refractory B cell malignancies	-	P-I/II
TAK-102 <sup>8</sup>	GPC3 CAR-T (injection)	Cell and gene therapy	Solid tumors	-	P-I
TAK-103 <sup>8</sup>	Mesothelin CAR-T (injection)	Cell and gene therapy	Solid tumors	-	P-I
TAK-573 <sup>9</sup> <modakafusp alfa=""></modakafusp>	Anti-CD38-targeted IgG4 genetically fused with an attenuated IFNα (injection)	Biologic and other	Relapsed/refractory Multiple Myeloma	-	P-I
TAK-605 <sup>10</sup>	Oncolytic virus (intra- tumoral administration)	Biologic and other	Solid tumors	-	P-I
TAK-676	STING agonist (injection)	Small molecule	Solid tumors	-	P-I
TAK-500	STING agonist antibody drug conjugate (injection)	Biologic and other	Solid tumors		P-I
TAK-940 <sup>11</sup>	CD19 1XX CAR-T (injection)	Cell and gene therapy	Relapsed/refractory B cell malignancies	-	P-I
TAK-186 <sup>12</sup>	T Cell Engager (Injection)	Biologic and other	EGFR expressing solid tumors		P-I

1. Partnership with Seagen, Inc.

2. Partnership with Exelixis, Inc.

3. Partnership with Chugai Pharmaceutical. Chugai operates Phase 3 development

4. Partnership with Chugai Pharmaceutical. Takeda operates Phase 3 development

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- 5. The U.S. FDA review is being conducted under Project Orbis, an initiative of the FDA Oncology Center of Excellence (OCE), which provides a framework for concurrent submission and review of oncology products among international partners such as the UK, Brazil and Australia.
- 6. The U.K. approval was granted in Mar 2022.
- 7. Partnership with The University of Texas MD Anderson Cancer Center
- 8. Partnership with Noile-Immune Biotech, Inc.
- 9. Partnership with Teva Pharmaceutical Industries Ltd.
- 10. Partnership with Turnstone Biologics
- 11. Partnership with Memorial Sloan Kettering Cancer Center
- 12. Acquired via acquisition of Maverick Therapeutics, Inc.

Additions since FY2021 Q3: TAK-103 for solid tumors (P-I)

TAK-500 for solid tumors (P-I)

Removals since FY2021 Q3: None

#### **Rare Genetics and Hematology Pipeline**

Development code <generic name=""> Brand name (country/region)</generic>	Type of Drug (administration route)	Modality	Indications / additional formulations	Country/ Region	Stage
TAK-743	Plasma kallikrein		Hereditary Angioedema	Japan	Approved (Mar 2022)
<lanadelumab> TAKHZYRO</lanadelumab>	inhibitor	Biologic and other	Pediatric Hereditary Angioedema	Global	P-III
(Global)	(injection)		Bradykinin-Mediated Angioedema	Global	P-III
<b>TAK-577</b> VONVENDI (U.S., Japan),	von Willebrand factor [recombinant]	Dialogia	Adult prophylactic treatment of von Willebrand disease	U.S. Japan EU China	Approved (Jan 2022) Approved (Mar 2022) P-III P-III
VEYVONDI (EU)	(injection)		Pediatric on-demand and surgery treatment of von Willebrand disease	Global	P-III
TAK-620 <sup>1</sup> <maribavir></maribavir>	ir> Benzimidazole riboside	le Small molecule	Post-transplant CMV infection/disease resistant/ refractory to (val) ganciclovir, cidofovir or foscarnet	U.S. EU	Approved (Nov 2021) Filed (Jun 2021)
<i>LIVTENCITY</i> (U.S.)			HSCT Recipients with First CMV Infection	U.S. EU	P-III P-III
TAK-660 ADYNOVATE (U.S., Japan) ADYNOVI (EU)	Antihemophilic factor [recombinant], PEGylated (injection)	Biologic and other	Pediatric Hemophilia A	EU	P-III
			Congenital Thrombotic Thrombocytopenic Purpura	U.S. EU	P-III P-III
TAK-755 <sup>2</sup>	Replacement of the deficient-ADAMTS13	Biologic and other	Immune Thrombotic Thrombocytopenic Purpura	U.S. EU	P-II P-II
	enzyme (injection)		Sickle cell disease	U.S.	P-I
TAK-672 <sup>3</sup> Obizur (US, EU)	Porcine Coagulation Factor VIII (Recombinant) (injection)	Biologic and other	Acquired hemophilia A (AHA)	Japan	P-II/III

TAK-141/JR-141 <sup>4</sup> <pabinafusp alfa=""></pabinafusp>	Recombinant fusion protein of an antibody against the human transferrin receptor and iduronate-2-sulfatase (injection)	Biologic	Hunter syndrome (CNS and somatic symptoms)	EU	P-III
TAK-611	Recombinant human arylsulfatase A for intrathecal administration (injection)	Biologic and other	Metachromatic leukodystrophy	-	P-II
			Myasthenia gravis	-	P-II
TAK-079 <sup>5</sup> <mezagitamab></mezagitamab>	Anti-CD38 monoclonal antibody (injection)	Biologic and other	Immune thrombocytopenic purpura	-	P-II
		5 /	Systemic lupus erythematosus	-	P-I/II
TAK-834 NATPARA (U.S.), NATPAR (EU)	Parathyroid hormone (injection)	Biologic and other	Hypoparathyroidism	Japan	P-I <sup>6</sup>

1. Partnership with GlaxoSmithKline

2. Partnership with KM Biologics for co-exclusive license for commercialization in Japan only

3. Partnership with Ipsen

4. Geographically-focused collaboration and license agreement with JCR Pharma. Takeda will exclusively commercialize TAK-141/JR-141 outside of the United States, including Canada, Europe, and other regions (excluding Japan and certain other Asia-Pacific countries). Takeda receives an option under a separate option agreement, which allows Takeda to acquire an exclusive license to commercialize TAK-141/JR-141 in the U.S. upon completion of the Phase 3 program.

5. Relapsed/refractory Multiple Myeloma will continue until trial completion.

6. P-I study in Japan completed; P-III study start timing under review.

Additions since FY2021 Q3: TAK-141/JR-141 for Hunter syndrome, (CNS and somatic symptoms) (EU, P-III)

TAK-672 for Acquired hemophilia A (AHA) (Japan, P-II/III)

Removals since FY2021 Q3: TAK-609 for Hunter syndrome CNS (U.S., EU, P-II, discontinued)

#### **Neuroscience Pipeline**

Development code <generic name=""> Brand name (country/region)</generic>	Type of Drug (administration route)	Modality	Indications / additional formulations	Country/ Region	Stage
TAK-935	CH24H inhibitor (oral)	Small molecule	Dravet syndrome	Global	P-III
<soticlestat></soticlestat>			Lennox-Gastaut syndrome	Global	P-III
ТАК-994	Orexin 2R agonist (oral)	Small molecule	Narcolepsy	-	P-II <sup>4</sup>
TAK-071	M1 positive allosteric modulator (M1PAM) (oral)	Small molecule	Parkinson's disease	-	P-II
TAK-041 <sup>1</sup>	GPR139 agonist (oral)	Small molecule	Anhedonia in major depressive disorder (MDD)	-	P-II
TAK-653 <sup>1</sup>	AMPA receptor potentiator (oral)	Small molecule	Inadequate response to treatment in major depressive disorder (MDD)	-	P-II

TAK-594/DNL593 <sup>2</sup>	Brain-penetrant progranulin fusion protein (injection)	Biologic and other	Frontotemporal dementia	-	P-I/II
TAK-341/MEDI1341 <sup>3</sup>	Alpha-synuclein antibody (injection)	Biologic and other	Parkinson's disease	-	P-I
TAK-861	Orexin 2R agonist (oral)	Small molecule	Sleep disorders, other disorders	-	P-I
TAK-925	Orexin 2R agonist (injection)	Small molecule	Post-anesthesia recovery, narcolepsy	-	P-I

1. 50:50 co-development and co-commercialization with Neurocrine

2. Partnership with Denali Therapeutics. Denali leads Phase 1 development

3. Partnership with AstraZeneca. AstraZeneca leads Phase 1 development

4. TAK-994 currently on clinical hold.

Additions since FY2021 Q3: TAK-594/DNL593 for Frontotemporal dementia (P-I/II) Removals since FY2021 Q3: None

#### **GI** Pipeline

Development code <generic name=""> Brand name (country/region)</generic>	Type of Drug (administration route)	Modality	Indications / additional formulations	Country/ Region	Stage
			Subcutaneous formulation for ulcerative colitis	U.S.	CompleteResponseLetter(CRL)received(Dec 2019)^7
				Japan	Filed (Aug 2019)
MLN0002			Subcutaneous formulation for Crohn's disease	U.S. Japan	P-III P-III
<pre><vedolizumab> ENTYVIO (Global)</vedolizumab></pre>	Humanized monoclonal antibody against α4β7 integrin (injection)	Biologic and other	Active Chronic Pouchitis	EU	Approved (Jan 2022)
(Global)			Graft-versus-Host Disease prophylaxis in patients undergoing allogeneic hematopoietic stem cell transplantation	EU	P-III
				Japan	P-III
			Pediatrics Study (ulcerative colitis, Crohn's disease*)	Global	P-III
			Acid related diseases (Reflux Esophagitis Maintenance)	China	Approved (Oct 2021)
<vonoprazan> TAKECAB (Japan)</vonoprazan>	• 1	Small molecule	Oral disintegrated tablet formulation	Japan	Approved (Mar 2022)
VOCINTI (China)		Acid related diseases (adjunct to <i>Helicobacter pylori</i> eradication)	China	P-III	
TAK-633 <teduglutide></teduglutide>	eduglutide>	Peptide/	Short bowel syndrome (pediatric indication)	Japan	Approved (Jun 2021)
GATTEA (U.S.) (injection) 0	Oligo- nucleotide	Short bowel syndrome (in adults)	Japan	Approved (Jun 2021)	

Cx601 <darvadstrocel> ALOFISEL (EU, Japan)</darvadstrocel>	A suspension of allogeneic expanded adipose- derived stem cells (injection)	Biologic and other	Refractory complex perianal fistulas in patients with Crohn's disease	U.S. Japan	P-III Approved (Sep 2021)
TAK-954 <sup>1</sup>	5-HT <sub>4</sub> - hydroxytryptamine receptor agonist (injection)	Small molecule	Post-operative gastrointestinal dysfunction	-	P-II (b)
TAK-999 <sup>2</sup>	GalNAc based RNA interference (RNAi) (injection)	Peptide/ Oligo- nucleotide	Alpha-1 antitrypsin-deficiency associated liver disease	U.S. EU	P-II (b) P-II (b)
TAK-101 <sup>3</sup>	Tolerizing Immune Modifying nanoParticle (TIMP) (injection)	Biologic and other	Celiac disease	-	P-II (a)
TAK-018/EB8018 <sup>4</sup> <sibofimloc></sibofimloc>	FimH antagonist (oral)	Small molecule	Crohn's disease (post-operative and ileal-dominant)	-	P-II (a)
TAK-951	Peptide agonist (sub-cutaneous)	Peptide/ Oligo- nucleotide	Nausea and vomiting	-	P-II
TAK-510	Peptide agonist (sub-cutaneous)	Peptide/ Oligo- nucleotide	Nausea and vomiting	-	P-I
TAK-105	Peptide agonist (sub-cutaneous)	Peptide/ Oligo- nucleotide	Nausea and vomiting	-	P-I
TAK-062	Glutenase (oral)	Biologic and other	Celiac disease	-	P-I
TAK-039 <sup>5</sup>	Bacterial consortium (oral)	Microbiome	Clostridium difficile infections <sup>6</sup>	-	P-I

1. Partnership with Theravance Biopharma, Inc.

2. Partnership with Arrowhead Pharmaceuticals, Inc.

3. Acquired development and commercialization license for TAK-101 from COUR Pharmaceuticals. Previously known as TIMP-GLIA.

4. Partnership with Enterome Bioscience SA

5. Partnership with NuBiyota

6. Phase 1 study in clostridium difficile infections completed; strategic intention is to take the program forward in hepatic encephalopathy.

7. In active discussions with the FDA. Timelines under review; potential approval anticipated FY2023.

\* Event occurred after the end of the Q4 reporting period: Update after April 1, 2022

Additions since FY2021 Q3: None

Removals since FY2021 Q3: TAK-906 for Gastroparesis (Ph II (b), discontinued)

### **Plasma-Derived Therapies Pipeline**

Development code <generic name=""> Brand name (country/region)</generic>	Type of Drug (administration route)	Modality	Indications / additional formulations	Country/ Region	Stage							
<b>TAK-664</b> <i>CUVITRU</i> (U.S., EU)	Immunoglobulin 20% [human] (subcutaneous)	Biologic and other	Primary immunodeficiencies	Japan	P-III							
	TAK-771 <sup>1</sup> <ig 10%<br="" infusion="">(Human) w/ Recombinant Human Hyaluronidase&gt; HYQVIA (U.S., EU)</ig>		Pediatric indication for primary immunodeficiency	U.S.	P-III							
<ig 10%<="" infusion="" td=""><td rowspan="3">Biologic and other</td><td>D. 1 .</td><td>Chronic inflammatory demyelinating polyradiculoneuropathy</td><td>U.S. EU</td><td>P-III P-III</td></ig>		Biologic and other	D. 1 .	Chronic inflammatory demyelinating polyradiculoneuropathy	U.S. EU	P-III P-III						
Recombinant Human Hyaluronidase>			Chronic inflammatory demyelinating polyradiculoneuropathy and Multifocal Motor Neuropathy	Japan	P-III							
											Primary Immunodeficiencies,	Japan
TAK-880 <10% IVIG (Low IgA)>	Immunoglobulin (10%) [human] (injection) (Low IgA)	Biologic and other	Primary Immunodeficiencies and Multifocal Motor Neuropathy	U.S. EU	Filing in preparation <sup>2</sup>							
TAK-662 CEPROTIN (U.S., EU)	Protein C concentrate [human] (injection)	Biologic and other	Severe congenital protein C deficiency	Japan	P-I/II							
TAK-881 <facilitated 20%<br="">SCIG&gt;</facilitated>	Immunoglobulin (20%) [human] + recombinant hyaluronidase replacement therapy (injection)	Biologic and other	Immunodeficiencies	-	P-I/II							

1. Partnership with Halozyme

2. Non-interventional study to collect data is in progress

Additions since FY2021 Q3: TAK-771 for Primary Immunodeficiencies (Japan, P-III)

TAK-880 for Primary Immunodeficiencies and Multifocal Motor Neuropathy (U.S., EU, Filing in preparation)

Removals since FY2021 Q3: None

### **Vaccines** Pipeline

Development code Brand name (country/region)	Type of vaccine (administration route)	Modality	Indications / additional formulations	Country/ Region	Stage
TAK-919/ mRNA-1273 <sup>1</sup>	SARS-CoV-2 vaccine	Biologic	Active immunization for the prevention of COVID-19	Japan	Approved (May 2021) <sup>4</sup>
Spikevax Intramuscular Injection (Japan)	(injection)	and other	Active immunization for the prevention of COVID-19 (booster)	Japan	Approved (Dec 2021)
TAK-019/ NVX-CoV2373 <sup>2</sup> Nuvaxovid Intramuscular Injection (Japan)	SARS-CoV-2 vaccine (injection)	Biologic and other	Active immunization for the prevention of COVID-19 (primary and booster)	Japan	Approved (Apr 2022)*
TAK-003	Tetravalent dengue vaccine (injection)	Biologic and other	For the prevention of dengue fever of any severity, due to any serotype, in individuals aged 4 up to 60 years of age	EU and EU- M4all -	Filed (Mar 2021) <sup>5</sup> P-III
TAK-426 <sup>3</sup>	Zika vaccine (injection)	Biologic and other	Active immunization for the prevention of disease caused by Zika virus	-	P-I

1. Partnership with Moderna and MHLW.

2. Partnership with Novavax, Inc.

3. Partnership with The Biomedical Advanced Research and Development Authority (BARDA) of the U.S. Government

4. Change in age indication to expand to 12 years of age and older (July 2021).

5. In addition to filing in the EU and through the EU-M4all (previously Article 58) procedure for countries outside of the EU, filings began in dengue endemic countries

in Latin America and Asia that are not participating in the EU-M4all procedure.

\* Event occurred after the end of the Q4 reporting period: Update after April 1, 2022

Additions since FY2021 Q3: None Removals since FY2021 Q3: None

### II. Recent Progress in stage [Progress in stage since April 1st, 2021]

Development code <generic name=""></generic>	Indications / additional formulations	Country/Region	Progress in stage
SGN-35 <brentuximab vedotin=""></brentuximab>	Cutaneous T cell lymphoma	China	Approved (Apr 2021)
MLN9708 <ixazomib></ixazomib>	Maintenance therapy in patients with newly diagnosed Multiple Myeloma not treated with stem cell transplant	Japan	Approved (May 2021)
TAK-919/mRNA-1273	Active immunization for the prevention of COVID-19	Japan	Approved (May 2021)
TAK-633 <teduglutide></teduglutide>	Short bowel syndrome (pediatric indication and in adults)	Japan	Approved (Jun 2021)
<cabozantinib></cabozantinib>	1L Renal cell carcinoma in combination with nivolumab	Japan	Approved (Aug 2021)
TAK-788 <mobocertinib></mobocertinib>	Previously treated Non-Small Cell Lung Cancer with EGFR exon 20 insertion	U.S.	Approved (Sep 2021)
Cx601 <darvadstrocel></darvadstrocel>	Refractory complex perianal fistulas in patients with Crohn's disease	Japan	Approved (Sep 2021)
TAK-438 <vonoprazan></vonoprazan>	Acid related diseases (Reflux Esophagitis Maintenance)	China	Approved (Oct 2021)
TAK-620 <maribavir></maribavir>	Post-transplant CMV infection/disease resistant/refractory to (val) ganciclovir, cidofovir or foscarnet	U.S.	Approved (Nov 2021)
TAK-919/mRNA-1273	Active immunization for the prevention of COVID-19 (booster)	Japan	Approved (Dec 2021)
TAK-577	Adult prophylactic treatment of von Willebrand disease	U.S.	Approved (Jan 2022)
MLN0002 <vedolizumab></vedolizumab>	Active Chronic Pouchitis	EU	Approved (Jan 2022)
 stinib>	1L & 2L ALK-positive Non Small Cell Lung Cancer	China	Approved (Mar 2022)
TAK-438 <vonoprazan></vonoprazan>	Oral disintegrated tablet formulation	Japan	Approved (Mar 2022)
TAK-743 <lanadelumab></lanadelumab>	Hereditary Angioedema	Japan	Approved (Mar 2022)
TAK-577	Adult prophylactic treatment of von Willebrand disease	Japan	Approved (Mar 2022)
TAK-019/ NVX-CoV2373	Active immunization for the prevention of COVID-19 (primary and booster)	Japan	Approved (Apr 2022)*
TAK-620 <maribavir></maribavir>	Post-transplant CMV infection/disease resistant/refractory to (val) ganciclovir, cidofovir or foscarnet	EU	Filed (Jun 2021)
TAK-788 <mobocertinib></mobocertinib>	Previously treated Non-Small Cell Lung Cancer with EGFR exon 20 insertion	EU, China	Filed (Jul 2021)
TAK-935 <soticlestat></soticlestat>	Dravet Syndrome	Global	P-III
TAK-935 <soticlestat></soticlestat>	Lennox-Gastaut syndrome	Global	P-III
TAK-771 <ig (human)="" 10%="" <br="" infusion="" w="">Recombinant Human Hyaluronidase&gt;</ig>	Chronic inflammatory demyelinating polyradiculoneuropathy and Multifocal Motor Neuropathy	Japan	P-III
TAK-141/JR-141 <pabinafuasp alfa=""></pabinafuasp>	Hunter syndrome, (CNS and somatic symptoms)	EU	P-III
MLN0002 <vedolizumab></vedolizumab>	Pediatrics Study (ulcerative colitis, Crohn's disease*)	Global	P-III

TAK-771 <ig (human)="" 10%="" <br="" infusion="" w="">Recombinant Human Hyaluronidase&gt;</ig>	Primary Immunodeficiencies	Japan	P-III
TAK-672	Acquired hemophilia A (AHA)	Japan	P-II/III
TAK-981	Multiple cancers	-	P-II
TAK-041	Anhedonia in major depressive disorder (MDD)	-	P-II
TAK-653	Inadequate response to treatment in major depressive disorder (MDD)	-	P-II
TAK-662	Severe congenital protein C deficiency	Japan	P-I/II
TAK-594/DNL593	Frontotemporal dementia	-	P-I/II
TAK-861	Sleep disorders, other disorders	-	P-I
TAK-105	Nausea and vomiting	-	P-I
TAK-881 <facilitated 20%="" scig=""></facilitated>	Immunodeficiencies	-	P-I/II
TAK-103	Solid tumors	-	P-I
TAK-500	Solid tumors	-	P-I

 $\ast$  Event occurred after the end of the Q4 reporting period: Update after April 1, 2022

### III. Discontinued projects [Update since April 1st, 2021]

Development code <generic name=""></generic>	Indications (Region/Country, Stage)	Reason
CoVIg-19	Treatment of adult hospitalized patients at onset of clinical progression of COVID-19 (U.S., EU, Japan, P-III)	Phase 3 Inpatient Treatment with Anti-Coronavirus Immunoglobulin (ITAC) clinical trial sponsored and funded by the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health (NIH), did not meet its endpoints.
TAK-169	Relapse/refractory multiple myeloma (P-I)	Takeda has communicated its decision to turn over full rights of TAK-169 to Molecular Templates. Molecular Templates will continue to develop TAK-169.
TAK-831 <luvadaxistat></luvadaxistat>	Negative symptoms and/or cognitive impairment associated with schizophrenia (P-II)	Based on clinical data, our partner Neurocrine announced the discontinuation of development in Schizophrenia Negative Symptoms. Neurocrine will continue developing TAK-831 in Cognitive Impairment Associated with Schizophrenia and Takeda decided not to co-fund a supplemental study with Neurocrine, which resulted in Takeda's maintaining its right to receive milestones and royalties regarding TAK-831.
TAK-671	Acute Pancreatitis (P-I)	Takeda has opted out of further development based on a business decision, and the right to continue developing the asset falls under Samsung Bioepis.
TAK-924 <pevonedistat></pevonedistat>	High-risk Myelodysplastic Syndrome (P-III), Unfit Acute Myelogenous Leukemia (P-III)	Phase 3 PANTHER study did not meet its primary endpoint. The result did not support further development in Phase 3 HR MDS trial and Unfit AML trial. The Phase 1/2 AML trial in combination with venetoclax is ongoing but not recruiting new patients and is not registrational.
TAK-935 <soticlestat></soticlestat>	15q duplication syndrome, CDKL5 deficiency disorder (P-II)	The Phase 2 result did not support further development in these indications.
TAK-252	Solid tumors and lymphomas (P-I)	Shattuck Labs and Takeda mutually agreed to terminate the parties' Collaboration Agreement, resulting in termination of the TAK-252 for Takeda.
TAK-438 <vonoprazan></vonoprazan>	Acid related diseases Duodenal Ulcer (China, Filing withdrawn)	After evaluation of Chinese CDE (Center for Drug Evaluation) assessment, Takeda decided not to pursue this indication further.
TAK-721 <budesonide></budesonide>	Eosinophilic esophagitis (U.S., Filed)	After evaluation of Complete Response Letter (CRL) from U.S. FDA, Takeda decided not to pursue program further.
TAK-906	Gastroparesis (P-II (b))	The Phase 2 (b) study did not support further development in Gastroparesis or other GI indications.
TAK-609	Hunter syndrome CNS (U.S., EU, P-II)	After years of extensive review and regulatory discussions, Takeda has come to the difficult decision to discontinue development. Data is insufficient for filing.

### IV. Main Research & Development collaborations/partnering

[not a comprehensive list of all Takeda R&D collaborations]

#### Oncology

Partner	Country of incorporation	Subject
Adimab	U.S.	Agreement for the discovery, development and commercialization of three mAbs and three CD3 Bi- Specific antibodies for oncology indications.
ASKA Pharmaceutical Co., Ltd*	Japan	Takeda granted exclusive commercialization rights for uterine fibroids and exclusive development and commercialization rights for endometriosis for Japan to maximize the product value of relugolix (TAK-385).
Crescendo Biologics	U.K	Collaboration and licensing agreement for the discovery, development and commercialization of Humabody <sup>®</sup> -based therapeutics for cancer indications.
Egle Therapeutics	France	Identify novel tumor-specific regulatory T cell targets and develop unique anti-suppressor-based immunotherapies.
Exelixis, Inc.	U.S.	Exclusive licensing agreement to commercialize and develop novel cancer therapy cabozantinib and all potential future cabozantinib indications in Japan, including advanced renal cell carcinoma and hepatocellular carcinoma.
GammaDelta Therapeutics <sup>‡</sup>	U.K.	Collaboration agreement to discover and develop new immunotherapies in oncology using GammaDelta Therapeutics' novel T cell platform based on the unique properties of gamma delta T cells derived from human tissues. Takeda exercised its option to acquire GammaDelta Therapeutics in October 2021. Separately, in January 2022, Takeda exercised its option to acquire Adaptate Biotherapeutics, a UK based spin-out company from GammaDelta Therapeutics focused on developing antibody-based therapeutics for the modulation of variable delta 1 (V $\delta$ 1) gamma delta ( $\gamma\delta$ ). Both acquisitions were closed in April 2022.
GlaxoSmithKline	U.K.	Exclusive licensing agreement to develop and commercialize novel cancer therapy niraparib for the treatment of all tumor types in Japan, and all tumor types excluding prostate cancer in South Korea and Taiwan.
Heidelberg Pharma	Germany	Antibody-Drug-Conjugate (ADC) research collaboration on 2 targets and licensing agreement ( $\alpha$ -amanitin payload and proprietary linker).
KSQ Therapeutics	U.S.	Strategic collaboration to research, develop and commercialize novel immune-based therapies for cancer using KSQ's CRISPRomics® technology.
MD Anderson Cancer Center	U.S.	Exclusive license and research agreement to develop cord blood-derived chimeric antigen receptor- directed natural killer (CAR NK) cell therapies, 'armored' with IL-15, for the treatment of B cell malignancies and other cancers.
Memorial Sloan Kettering Cancer Center	U.S.	Strategic research collaboration and license to develop novel chimeric antigen receptor T cell (CAR- T) products for the treatment of multiple myeloma, acute myeloid leukemia and additional solid tumor indications. The collaboration is co-led by Michel Sadelain, who is currently head of the Center for Cell Engineering at Memorial Sloan Kettering
Myovant Sciences <sup>+</sup>	Switzerland	Takeda granted Myovant an exclusive, worldwide license (excluding Japan and certain other Asian countries) to relugolix (TAK-385) and an exclusive, worldwide license to MVT-602 (TAK-448).
National Cancer Center of Japan	Japan	Partnership agreement to develop basic research to clinical development by promoting exchanges among researchers, physicians, and others engaged in anti-cancer drug discovery and cancer biology research.
Noile-Immune Biotech	Japan	Collaboration agreement for the development of next generation CAR-T cell therapy, developed by Professor Koji Tamada at Yamaguchi University. Takeda has exclusive options to obtain licensing rights for the development and commercialization of Noile-Immune Biotech's pipeline and products resulting from this partnership. Due to the success of the collaboration, Takeda licensed NIB-102 and NIB-103.
Presage Biosciences	U.S.	Research collaboration and license for multiple programs using Presage's proprietary platform CIVO to evaluate patients' unique responses to microdoses of cancer drugs.
Seagen	U.S.	Agreement for the joint development of ADCETRIS, an ADC technology which targets CD30 for the treatment of HL. Approved in 67 countries with ongoing clinical trials for additional indications.
Teva	Israel	Agreement for worldwide License to TEV-48573 (TAK-573) (modakafusp alfa, Anti-CD38- Attenukine <sup>TM</sup> ) and multi-target discovery collaboration accessing Teva's Attenukine <sup>TM</sup> platform.
Turnstone Biologics	U.S.	Collaboration to co-develop TAK-605 (RIVAL-01) (novel oncolytic virus expressing aCTLA4, IL12- mb, flt3L) via a worldwide partnership and also conduct collaborative discovery efforts to identify additional novel product candidates based on a Turnstone's vaccinia virus platform.

‡ Executed since April 1, 2021 ♦ Externalized project

# Rare Genetics and Hematology

Partner	Country of incorporation	Subject
Asklepios Biopharmaceuticals	U.S.	Agreement for multiple research and development collaborations using FVIII Gene Therapy for the treatment of Hemophilia A and B.
BioMarin	U.S.	Agreement for the in-license of enabling technology for the exogenous replacement of iduronate-2- sulfatase with Idursulfase-IT in patients via direct delivery to the CNS for the long-term treatment of Hunter Syndrome in patients with cognitive impairment in order to slow progression of cognitive impairment (TAK-609).
Carmine Therapeutics	Singapore	Research collaboration agreement to discover, develop and commercialize transformative non-viral gene therapies for two rare disease targets using Carmine's REGENT(TM) technology, based on red blood cell extracellular vesicles.
Code Bio <sup>‡</sup>	U.S.	Collaboration and license agreement for Takeda and Code Bio to design and develop a targeted gene therapy leveraging Code Bio's 3DNA platform for a liver-directed rare disease program, plus conduct additional studies for central nervous system-directed rare disease programs. Takeda has the right to exercise options for an exclusive license for four programs.
Codexis, Inc.	U.S.	Strategic collaboration and license for the research and development of novel gene therapies for certain disease indications, including the treatment of lysosomal storage disorders and blood factor deficiencies.
Ensoma	U.S.	Research collaboration and license provides Takeda with an exclusive worldwide license to Ensoma's Engenious <sup>™</sup> vectors for up to five rare disease indication.
Evox Therapeutics	U.K.	Collaboration for developing novel protein replacement and mRNA therapies and targeted delivery using Evox's proprietary exosome technology. Partnership for up to five rare disease targets with Takeda assuming responsibility for its clinical development.
Evozyne <sup>‡</sup>	U.S.	Research collaboration and license agreement with Takeda to research and develop proteins that could be incorporated into next-generation gene therapies for up to four rare disease targets.
GlaxoSmithKline	U.K.	In-license agreement between GSK and University of Michigan for TAK-620 (maribavir) in the treatment of human cytomegalovirus.
JCR Pharmaceuticals <sup>‡</sup>	Japan	Exclusive collaboration and license agreement to commercialize TAK-141 (JR-141, pabinafusp alfa), applied with J-Brain Cargo®, JCR's proprietary blood-brain barrier (BBB) penetration technology, for the treatment of Hunter syndrome (MPS II). Takeda will exclusively commercialize TAK-141 outside of the United States, including Canada, Europe, and other regions (excluding Japan and certain other Asia-Pacific countries). Takeda receives an option under a separate option agreement, which allows Takeda to acquire an exclusive license to commercialize TAK-141 in the U.S. upon completion of the Phase 3 program. In March 2022, Takeda and JCR has entered into new exclusive license and collaboration agreement to develop gene therapies that apply J-Brain Cargo® BBB penetration technology for lysosomal storage disorders (LSDs); Takeda has the option to nominate additional rare disease and other disease indications.
Immusoft <sup>‡</sup>	U.S.	Research collaboration and license option agreement to discover, develop and commercialize cell therapies in rare inherited metabolic disorders with central nervous system (CNS) manifestations and complications using Immusoft's Immune System Programming (ISP <sup>TM</sup> ) technology platform.
IPSEN	France	Purchase agreement for the development of Obizur for the treatment of Acquired Hemophilia A including for patients with Congenital Hemophilia A with inhibitors indication in elective or emergency surgery.
KM Biologics	Japan	Agreement for the development collaboration of TAK-755 to overcome the ADAMTS13 deficiency in TTP.
Oak Hill Bio <sup>‡</sup>	UK	Multiple asset and license agreements with Oak Hill Bio, a rare disease therapeutics company. Takeda transfers multiple pre-clinical and clinical programs, including OHB-607 (formerly TAK-607) and OHB-101 (formerly TAK-752), to Oak Hill Bio in exchange for an upfront payment, an ownership stake in Oak Hill Bio and potential milestones and royalty payments.
Poseida Therapeutics <sup>‡</sup>	U.S.	Research collaboration and exclusive license agreement to utilize Poseida's piggyBac, Cas- CLOVER, biodegradable DNA and RNA nanoparticle delivery technology and other proprietary genetic engineering platforms for up to eight gene therapies. The collaboration will focus on developing non-viral in vivo gene therapy programs, including Poseida's Hemophilia A program.
Selecta Biosciences <sup>‡</sup>	U.S.	Research collaboration and license agreement to develop targeted, next-generation gene therapies for two indications within the field of lysosomal storage disorders using Selecta's ImmTOR platform.
Xenetic Biosciences	U.S.	Exclusive R&D license agreement for PolyXen delivery technology for hemophilia factors VII, VIII, IX, X.

‡ Executed since April 1, 2021 ♦ Externalized project

### Neuroscience

Partner	Country of incorporation	Subject
Anima Biotech	U.S.	Strategic collaboration to discover and develop mRNA translation modulators for genetically- defined neurological diseases.
AstraZeneca	UK	Agreement for the joint development and commercialization of MEDI1341, an alpha-synuclein antibody currently in development as a potential treatment for Parkinson's disease.
BridGene Biosciences	U.S.	Research collaboration to discover small molecule drugs for "undruggable" targets using BridGene's chemoproteomics platform.
CNDAP (Cure Network Dolby Acceleration Partners) <sup><math>\ddagger</math></sup>	U.S.	Research collaboration to develop small molecules targeting tau, a protein involved in Alzheimer's disease and other major brain disorders.
Denali Therapeutics	U.S.	Strategic option and collaboration agreement to develop and commercialize up to three specified therapeutic product candidates for neurodegenerative diseases, incorporating Denali's transport vehicle (TV) platform for increased exposure of biotherapeutic products in the brain; options exercised on DNL593/TAK-594 and DNL919/TAK-920 in Q3 FY2021.
Lundbeck	Denmark	Collaboration agreement to develop and commercialize vortioxetine.
Luxna Biotech <sup>‡</sup>	Japan	Exclusive worldwide license agreement for the use of Luxna's breakthrough xeno nucleic acid technology for multiple undisclosed target genes in the area of neurological diseases.
Neurocrine Biosciences	U.S.	Collaboration to develop and commercialize 7 compounds in Takeda's early-to-mid stage neuroscience pipeline, including TAK-041, TAK-653 and TAK-831. Takeda will be entitled to certain development milestones, commercial milestones and royalties on net sales and will, at certain development events, be able opt in or out of a 50:50 profit share on all clinical programs on an asset-by-asset basis.
PeptiDream <sup>‡</sup>	Japan	Collaborative research and exclusive license agreement to create peptide-drug conjugates (PDCs) for neuromuscular and neurodegenerative diseases.
Skyhawk Therapeutics	U.S.	Collaboration and licensing agreement to develop and commercialize RNA modulation therapies targeting neurodegenerative diseases.
StrideBio	U.S.	Collaboration and license agreement to develop <i>in vivo</i> adeno-associated viruses (AAV) based therapies for Friedreich's Ataxia (FA) and two additional undisclosed targets.
Wave Life Sciences	Singapore	Multi-program option agreement to co-develop and co-commercialize antisense oligonucleotides for a range of neurological diseases.

‡ Executed since April 1, 2021

# Gastroenterology

Partner	Country of incorporation	Subject
Ambys Medicines	U.S.	Collaboration agreement for the application of novel modalities, including cell and gene therapy and gain-of-function drug therapy, to meet the urgent need for treatments that restore liver function and prevent the progression to liver failure across multiple liver diseases. Under the terms of the agreement, Takeda has an option to ex-U.S. commercialization rights for the first 4 products that reach an investigational new drug application.
Arcturus	U.S.	Collaboration agreement to develop RNA-based therapeutics for the treatment of non-alcoholic steatohepatitis and other gastrointestinal related disorders using Arcturus' wholly-owned LUNAR <sup>™</sup> lipid-mediated delivery systems and UNA Oligomer chemistry.
Arrowhead Pharmaceuticals	U.S.	Collaboration and licensing agreement to develop TAK-999 (ARO-AAT), a Phase 2 investigational RNA interference (RNAi) therapy in development to treat alpha-1 antitrypsin- associated liver disease (AATLD). ARO-AAT is a potential first-in-class therapy designed to reduce the production of mutant alpha-1 antitrypsin protein, the cause of AATLD progression.
Beacon Discovery	U.S.	Collaboration agreement for the G-protein coupled receptor drug discovery and development program to identify drug candidates for a range of gastrointestinal disorders. The agreement grants Takeda worldwide rights to develop, manufacture and commercialize products resulting from the collaboration.
Cerevance	U.S.	Multi-year research alliance to identify novel target proteins expressed in the central nervous system and to develop new therapies against them for certain GI disorders. Goal of the collaboration is to select, confirm and validate targets from gene expression data sets generated by Cerevance's NETSseq technology.
COUR Pharmaceuticals	U.S.	Takeda has acquired an exclusive global license to develop and commercialize the investigational medicine TIMP-GLIA (TAK-101), an immune modifying nanoparticle containing gliadin proteins.

Engitix	U.K.	Collaboration and licensing agreement to utilize Engitix's unique extracellular matrix discovery platform to identify and develop novel therapeutics for liver fibrosis and fibrostenotic inflammatory bowel disease, including Crohn's disease and ulcerative colitis.
Enterome	France	Collaboration agreement to research and develop microbiome targets thought to play crucial roles in gastrointestinal disorders, including inflammatory bowel diseases (e.g. ulcerative colitis). The agreement includes a global license and co-development of EB8018/TAK-018 in Crohn's disease.
Finch Therapeutics	U.S.	Global agreement to develop TAK-524, a live biotherapeutic product composed of cultured bacterial strains linked to favorable clinical outcomes in studies of microbiota transplantations in inflammatory bowel disease. Under the terms of the agreement, Takeda has the exclusive worldwide rights to develop and commercialize TAK-524 and rights to follow-on products in inflammatory bowel diseases. Following a contract amendment in Aug 2021, Takeda assumed sole responsibility for development of TAK-524, prior to the start of clinical development.
Genevant Sciences Corporation <sup>‡</sup>	U.S.	Collaboration and License Agreements to leverage Genevant's hepatic stellate cell-partitioning LNP platform to deliver Takeda-designed RNAi oligonucleotides intended to halt or reverse the progression of liver fibrosis, and to deliver Takeda-designed non-viral gene therapies for the treatment of specified rare liver diseases.
NuBiyota	Canada	Collaboration and License Agreement for the development and commercialization of Microbial Ecosystem Therapeutic (MET) products for gastroenterology indications.
Mirum Pharmaceuticals <sup>‡</sup>	U.S.	Exclusive licensing agreement for the development and commercialization of maralixibat in Japan for Alagille syndrome (ALGS), progressive familial intrahepatic cholestasis (PFIC), and biliary atresia (BA).
Phathom Pharmaceuticals*	U.S.	Takeda has granted a license to Phathom Pharmaceuticals for the development and exclusive commercialization rights to vonoprazan in the U.S., Europe and Canada in exchange for upfront cash and equity, as well as future cash milestones and royalties on net sales.
Sosei Heptares	UK	Collaboration and License agreement to leverage Sosei Heptares's StaR® technology and structural biology expertise with GPCRs to enable structure based drug discovery to advance novel therapeutics for gastroenterology diseases.
Theravance Biopharma	U.S.	Global license, development and commercialization agreement for TAK-954, a selective 5-HT4 receptor agonist for motility disorders.
UCSD/Fortis Advisors	U.S.	Technology license for the development of oral budesonide formulation (TAK-721) for treatment of eosinophilic esophagitis.

‡ Executed since April 1, 2021 ♦ Externalized project

### **Plasma Derived Therapies**

Partner	Country of incorporation	Subject
Halozyme	U.S.	Agreement for the in-license of Halozyme's proprietary ENHANZE <sup>TM</sup> platform technology to increase dispersion and absorption of HyQvia. Ongoing development work for a U.S. pediatric indication to treat primary immunodeficiencies and a Phase 3 indication in Chronic Inflammatory Demyelinating Polyradiculoneuropathy.
Kamada	Israel	In-license agreement to develop and commercialize IV Alpha-1 proteinase inhibitor (Glassia); Exclusive supply and distribution of Glassia in the U.S., Canada, Australia and New Zealand; work on post market commitments ongoing.
ProThera Biologics	U.S.	Global licensing agreement to develop a novel plasma-derived Inter-alpha Inhibitor Proteins (IAIP) therapy for the treatment of acute inflammatory conditions.
PreviPharma <sup>‡</sup>	EU	Research collaboration and option agreement to develop new targeted proteins

‡ Executed since April 1, 2021

### Vaccines

Partner	Country of incorporation	Subject
U.S. Government - The Biomedical Advanced Research and Development Authority (BARDA)	U.S.	Partnership to develop TAK-426, a Zika vaccine candidate, for the U.S. with the option to use data generated for filing also in affected regions around the world.
HilleVax, Inc. <sup>‡•</sup>	U.S.	Collaboration with Frazier Healthcare Partners to launch HilleVax, Inc., a biopharmaceutical company to advance the development and commercialization of norovirus vaccine candidate HIL-214 (formerly TAK-214). HilleVax has exclusive global development rights and commercialization rights worldwide outside of Japan in exchange for upfront consideration, as well as future cash milestones and royalties on net sales (Takeda retains commercialization rights in Japan).
Novavax	U.S.	Partnership for the development, manufacturing and commercialization of Nuvaxovid Intramuscular Injection,Novavax' COVID-19 vaccine in Japan, which is being funded by the Government of Japan's Ministry of Health, Labour and Welfare.(MHLW) and Agency for Medical Research and Development (AMED). Takeda finalized an agreement with the MHLW to supply 150 million doses of Nuvaxovid, the supply of which will be dependent on many factors, including need.
Moderna	U.S.	Three-way agreement with Moderna and the Government of Japan's Ministry of Health Labour & Welfare (MHLW) to import and distribute Moderna's COVID-19 vaccine, known as Spikevax Intermuscular Injection in Japan. The MHLW granted special approval for the primary series in May 2021 and regulatory approval for a 50 µg booster dose in December 2021. Takeda started importation of 93 million doses (50 µg booster dose) to Japan in 2022, in addition to the 50 million doses (100 µg) delivered in 2021.

‡ Executed since April 1, 2021 ♦ Externalized project

### Other / Multiple Therapeutic Area

Partner	Country of incorporation	Subject
Bridge Medicines	U.S.	Partnership with Tri-Institutional Therapeutics Discovery Institute, Bay City Capital and Deerfield Management in the establishment of Bridge Medicines. Bridge Medicines will give financial, operational and managerial support to move projects seamlessly from a validating, proof-of-concept study to an in-human clinical trial.
Center for iPS Cell Research Application, Kyoto University (CiRA)	Japan	Collaboration agreement for clinical applications of iPS cells in Takeda strategic areas including applications in neurosciences, oncology and GI as well as discovery efforts in additional areas of compelling iPSC translational science.
Charles River Laboratories	U.S.	Collaboration on multiple integrated programs across Takeda's core therapeutic areas using Charles River Laboratories' end-to-end drug discovery and safety assessment platform to progress these programs towards candidate status.
Evotec SE	Germany	Research alliance to support Takeda's growing number of research stage gene therapy discovery programs. Evotec and Takeda have also entered into a multi-RNA target alliance to discover and develop RNA targeting small molecule therapeutics for targets that are difficult to address via more conventional approaches.
Massachusetts Institute of Technology	U.S.	MIT-Takeda Program to fuel the development and application of artificial intelligence (AI) capabilities to benefit human health and drug development. Centered within the Abdul Latif Jameel Clinic for Machine Learning in Health (J-Clinic), the new program will leverage the combined expertise of both organizations, and is supported by Takeda's three-year investment (with the potential for a two-year extension).
Portal Instruments	U.S.	Agreement for the development and commercialization of Portal's jet injector drug delivery device for potential use with Takeda's investigational or approved biologic medicines.
Schrödinger	U.S.	Agreement for the multi-target research collaboration combining Schrödinger's in silico platform- driven drug discovery capabilities with Takeda's deep therapeutic area knowledge and expertise in structural biology.
Stanford University	U.S.	Collaboration agreement with Stanford University to form the Stanford Alliance for Innovative Medicines to more effectively develop innovative treatments and therapies.

Tri-Institutional Therapeutics Discovery Institute (Tri-I TDI)	U.S.	Agreement for the collaboration of academic institutions and industry to more effectively develop innovative treatments and therapies.
Twist Bioscience	U.S.	Agreement and license for Takeda to access Twist's "Library of Libraries," a panel of synthetic antibody phage display libraries derived only from sequences that exist in the human body. Together, the companies will work to discover, validate and optimize new antibody candidates.

### Completed Partnerships [Update since April 1st, 2021]

Partner	Country of incorporation	Subject
CoVIg-19 Plasma Alliance	-	Alliance formed by Takeda and CSL Behring to develop a potential plasma-derived therapy for treating COVID-19. The alliance goal is the development of a non-branded hyperimmune globulin medicine (CoVIg-19) with the potential to treat hospitalized adult patients with COVID-19.
Maverick Therapeutics	U.S.	Collaboration agreement for the development of Maverick Therapeutics' T-cell engagement platform created specifically to improve the utility of T-cell redirection therapy for the treatment of cancer. Under the agreement, Takeda has the exclusive option to acquire Maverick Therapeutics 5 years after partnership initiation in 2017 which was exercised April 2021.
Samsung Bioepis	Korea	Strategic collaboration agreement to jointly fund and co-develop multiple novel biologic therapies in unmet disease areas. The program's first therapeutic candidate is TAK-671, which is intended to treat severe acute pancreatitis.
Silence Therapeutics	U.K.	Technology Evaluation Agreement with Silence Therapeutics to access their GalNAc-siRNA technology platform. The objective of the evaluation is to identify a GalNAc-conjugated siRNA that inhibits expression of a proprietary Takeda target.
Centre d'Immunologie de Marseille-Luminy	France	Collaboration agreement to bring together expertise and knowledge in innate biology with Takeda's BacTrap capabilities to identify novel targets and pathways in myeloid cells.
Shattuck Labs	U.S.	Collaboration agreement to explore and develop checkpoint fusion proteins utilizing Shattuck's unique Agonist Redirected Checkpoint (ARC) <sup>TM</sup> platform which enables combination immunotherapy with a single product . Takeda will have the option to take an exclusive license to further develop and commercialize TAK-252/SL-279252). Takeda and Shattuck Labs mutually agree to terminate Collaboration Agreement in November 2021.
Rani Therapeutics	U.S.	Research collaboration agreement to evaluate a micro tablet pill technology for oral delivery of FVIII therapy in hemophilia.
Biological E. Limited	India	Takeda agreed to transfer existing measles and acellular pertussis vaccine bulk production technology to develop low-cost combination vaccines for India, China and low- and middle-income countries.
Seattle Collaboration	U.S.	Agreement for SPRInT (Seattle Partnership for Research on Innovative Therapies) to accelerate the translation of Fred Hutchinson Cancer Research Center's and University of Washington's cutting-edge discoveries into treatments for human disease (focusing on Oncology, GI and Neuroscience).
Molecular Templates	U.S.	Research collaboration to apply Molecular Templates' engineered toxin bodies (ETB) technology platform to potential therapeutic targets provided by Takeda, which has rights to exercise exclusive options to obtain license rights to products resulting from the collaboration.
Hemoshear Therapeutics	U.S.	Collaboration agreement for novel target and therapeutic development for liver diseases, using Hemoshear's proprietary REVEAL-Tx drug discovery platform.
HiFiBio	U.S.	Collaboration agreement for functional therapeutics high-throughput antibody discovery platform that enables identification of antibodies for rare events for discovery of therapeutic antibodies for GI therapeutic areas.

#### Clinical study protocol summaries

Clinical study protocol summaries are disclosed on the English-language web-site (<u>https://clinicaltrials.takeda.com/</u>) and clinical study protocol information in the Japanese-language is disclosed on the Japanese-language web-site (<u>https://www.takeda.com/what-we-do/research-and-development/takeda-clinical-trial-transparency/</u>).

We anticipate that this disclosure will assure transparency of information on Takeda's clinical trials for the benefit of healthcare professionals, their patients and other stakeholders, which we believe will contribute to the appropriate use of Takeda's products worldwide.

### 2. Supplementary Financial Information

#### Revenue by region

Year to date

		Reported *1							
Bn JPY)	FY20Q4 YTD	FY21Q4 YTD	YOY	<i>I</i>	YOY				
Total revenue	3,197.8	3,569.0	371.2	11.6 %	7.4 %				
Japan *2	559.7	659.0	99.2	17.7 %	8.1 %				
% of revenue	17.5%	18.5%	1.0pt						
United States	1,567.9	1,714.4	146.5	9.3 %	3.5 %				
% of revenue	49.0%	48.0%	(1.0)pt						
Europe and Canada	666.2	739.2	73.0	11.0 %	12.5 %				
% of revenue	20.8%	20.7%	(0.1)pt						
Growth and Emerging Markets *3	404.0	456.4	52.5	13.0 %	14.8 %				
% of revenue	12.6%	12.8%	0.2pt						
Asia (excluding Japan)	156.2	197.0	40.7	26.1 %	24.9 9				
% of revenue	4.9%	5.5%	0.6pt						
Latin America	121.6	128.5	6.8	5.6 %	14.5 %				
% of revenue	3.8%	3.6%	(0.2)pt						
Russia/CIS	57.6	62.1	4.5	7.8 %	4.9 %				
% of revenue	1.8%	1.7%	(0.1)pt						
Other *4	68.5	68.9	0.4	0.6 %	2.3 %				
% of revenue	2.1%	1.9%	(0.2)pt						

 Of which royalty / service income \*2
 92.4
 273.3
 180.8
 195.6 %

\*1 Revenue amount is classified into countries or regions based on the customer location.

\*2 The 133.0 billion JPY selling price of the sale of diabetes portfolio in Japan is included in FY21Q4YTD.

\*3 GEM: Growth and Emerging Markets, which include Asia (excluding Japan), Latin America, Russia/CIS, Middle East, Oceania and Africa.

\*4 Other region includes Middle East, Oceania and Africa.

#### Quarterly

		Reported *1											
		FY20				FY21							
(Bn JPY)	Q1	Q2	Q3	Q4	Q1	YOY	Q2	YOY	Q3	YOY	Q4	YOY	
Total revenue	801.9	788.9	836.8	770.3	949.6	18.4%	844.8	7.1%	901.3	7.7%	873.3	13.4 %	
Japan *2	144.0	138.3	152.7	124.6	259.0	79.8%	131.9	(4.6%)	139.4	(8.7%)	128.7	3.3 %	
% of revenue	18.0%	17.5%	18.3%	16.2%	27.3%		15.6%		15.5%		14.7 %		
United States	402.6	383.5	402.8	379.0	412.2	2.4%	426.2	11.1%	458.6	13.9%	417.4	10.1 %	
% of revenue	50.2%	48.6%	48.1%	49.2%	43.4%		50.4 %		50.9 %		47.8 %		
Europe and Canada	157.6	169.6	172.8	166.2	178.7	13.4%	175.2	3.3%	187.0	8.2%	198.2	19.2 %	
% of revenue	19.6%	21.5%	20.7%	21.6%	18.8%		20.7 %		20.7 %		22.7 %		
Growth and Emerging Markets *3	97.6	97.5	108.4	100.5	99.7	2.1%	111.5	14.4%	116.3	7.3%	129.0	28.4 %	
% of revenue	12.2%	12.4%	13.0%	13.0%	10.5%		13.2 %		12.9 %		14.8 %		
Asia (excluding Japan)	36.9	41.4	40.9	37.1	40.3	9.3%	49.4	19.3%	50.1	22.4%	57.2	54.3 %	
% of revenue	4.6%	5.2%	4.9%	4.8%	4.2%		5.8 %		5.6 %		6.5 %		
Latin America	30.8	28.2	36.4	26.2	30.1	(2.3%)	31.3	11.1%	32.2	(11.7%)	34.9	33.2 %	
% of revenue	3.8%	3.6%	4.4%	3.4%	3.2%		3.7 %		3.6 %		4.0 %		
Russia/CIS	13.0	8.6	17.1	18.8	12.3	(5.4%)	12.8	48.0%	18.5	8.4%	18.5	(1.9)%	
% of revenue	1.6%	1.1%	2.0%	2.4%	1.3%		1.5 %		2.1 %		2.1 %		
Other *4	16.9	19.3	14.0	18.3	17.0	0.3%	18.0	(6.3%)	15.5	11.1%	18.4	0.2 %	
% of revenue	2.1%	2.4%	1.7%	2.4%	1.8%		2.1 %		1.7 %		2.1 %		
Of which royalty / service income *2	18.1	28.2	22.8	23.4	157.7	773.2%	25.4	(9.8%)	27.4	20.5%	62.7	168.1 %	

 $\ast 1$  Revenue amount is classified into countries or regions based on the customer location.

\*2 The 133.0 billion JPY selling price of the sale of diabetes portfolio in Japan is included in FY21Q1.

\*3 GEM: Growth and Emerging Markets, which include Asia (excluding Japan), Latin America, Russia/CIS, Middle East, Oceania and Africa.

\*4 Other region includes Middle East, Oceania and Africa.

#### Product Sales Analysis (vs PY Reported Actual) (Sales amount includes royalty income and service income)

• Year to date

						R	eported						
(Bn JPY)	FY20Q4 YTD	FY21Q4 YTD	YOY	US	YOY	Japan	YOY	EUCAN	YOY	GEM*5	YOY	Ex-US	YOY
GI	777.8	875.7	12.6 %	487.9	8.0 %	108.2	16.3 %	194.5	22.2 %	67.4	15.4 %	17.7	15.4 %
ENTYVIO	429.3	521.8	21.5 %	349.5	18.8 %	11.3	27.0 %	136.0	24.8 %	25.0	45.7 %		
TAKECAB-F *1	84.8	102.4	20.7 %	0.1	-	94.6	13.6 %	—	-	7.7	398.4 %		
GATTEX/REVESTIVE	64.6	75.8	17.3 %	61.1	11.4 %	1.6	-	11.0	25.7 %	2.1	117.3 %		
DEXILANT	55.6	50.8	(8.7)%	28.4	(16.7)%		-	10.4	18.9 %	12.0	(6.0)%		
PANTOLOC/CONTROLOC*2	43.1	40.3	(6.6)%	2.1	0.8 %		-	26.4	12.8 %	11.7	(33.3)%		
LIALDA/MEZAVANT *3	25.5	26.5	3.9 %	8.8	(13.5)%							17.7	15.4 %
PENTASA	23.1	20.2	(12.7)%	20.2	(12.7)%								
AMITIZA	21.2	6.5	(69.6)%	5.8	(72.1)%			—	-	0.7	50.3 %		
RESOLOR/MOTEGRITY	11.2	13.0	15.6 %	9.8	24.5 %		-	3.1	(5.5)%		(100.0)%		
ALOFISEL	0.8	1.8	135.1 %	_	-	_	-	1.6	155.1 %	0.3	63.8 %		
Others	18.6	16.8	(9.8)%	2.2	(53.1)%	0.7	(17.3)%	6.0	11.3 %	7.9	2.0 %		
Rare Diseases	591.7	611.2	3.3 %	269.6	2.3 %	28.9	(2.6)%	150.8	8.3 %	110.3	2.4 %	51.7	(0.1)%
Rare Metabolic	162.6	172.6	6.1 %	37.8	8.7 %	2.3	(14.7)%	48.2	11.3 %	32.5	8.4 %	51.7	(0.1)%
ELAPRASE	68.8	73.1	6.3 %	20.3	4.8 %	1.0	(35.9)%	27.3	9.0 %	24.5	7.5 %		
REPLAGAL *3	51.8	51.7	(0.1)%	—	-							51.7	(0.1)%
VPRIV	38.5	42.4	10.1 %	17.5	11.7 %	1.3	13.8 %	15.6	7.5 %	8.0	11.4 %		
NATPARA/NATPAR	3.6	5.4	50.7 %	0.0	-	—	-	5.3	42.1 %	0.1	(26.5)%		
Rare Hematology	289.8	283.7	(2.1)%	120.0	(0.9)%	24.8	(3.0)%	67.1	(4.1)%	71.8	(1.8)%		
ADVATE	128.5	118.5	(7.8)%	55.1	(8.1)%	5.7	(11.4)%	25.6	(17.2)%	32.1	2.7 %		
ADYNOVATE/ADYNOVI	58.1	60.7	4.6 %	26.1	1.1 %	14.8	(1.3)%	14.4	9.4 %	5.4	33.0 %		
FEIBA *4	44.5	39.2	(12.0)%	12.6	24.6 %	0.7	(25.4)%	9.8	(10.1)%	16.1	(28.8)%		
RECOMBINATE	13.4	12.3	(8.2)%	11.4	(5.2)%	—	-	0.8	(4.7)%	0.1	(81.9)%		
HEMOFIL/IMMUNATE/IMMUNINE*4	18.7	17.7	(5.0)%	3.4	(0.4)%	—	-	4.2	(7.6)%	10.1	(5.4)%		
Other PDT Products *4 *6	3.5	3.9	13.2 %	0.0	-	—	-	3.5	20.1 %	0.4	(25.8)%		
Others *7	23.2	31.4	35.3 %	11.3	16.1 %	3.6	12.1 %	8.8	31.1 %	7.7	117.9 %		
Hereditary Angioedema	139.3	153.6	10.2 %	110.4	2.7 %	1.7	29.2 %	35.5	36.7 %	5.9	30.5 %		
TAKHZYRO	86.7	103.2	19.1 %	79.1	8.2 %	_	-	21.0	70.9 %	3.1	139.0 %		
FIRAZYR	26.8	26.7	(0.5)%	13.5	(6.8)%	1.7	29.2 %	9.2	12.9 %	2.3	(20.8)%		
CINRYZE *4	21.9	19.3	(11.8)%	13.5	(15.7)%	_	-	5.3	(4.4)%	0.6	47.4 %		
KALBITOR	3.9	4.4	11.3 %	4.4	11.3 %	_	-		-		(100.0)%		
Others	_	1.3	-	1.3	-	—	-	—	-	0.0	-		
*1751 6 1 1 1 1 4 6 6 1													

\*1 The figures include the amounts of fixed dose combinations and blister packs.

\*2 generic name: pantoprazole

\*3 License-out product : Regional breakdown is not available due to contract.

\*4 PDT products

\*5 GEM: Growth and Emerging Markets, which include Asia (excluding Japan), Latin America, Russia/CIS, Middle East, Oceania and Africa

\*6 Other PDT products in Rare Hematology include BEBULIN, PROTHROMPLEX and Factor VII.

\*7 Others in Rare Hematology include VONVENDI, OBIZUR, RIXUBIS, AGRYLIN/XAGRID, OCTOFACTOR, COAGIL-VII, INNONAFACTOR, and Other Hemophilia.

ĺ							Reported						
(Bn JPY)	FY20Q4 YTD	FY21Q4 YTD	YOY	US	YOY	Japan	YOY	EUCAN	YOY	GEM*5	YOY	Ex-US	YOY
PDT Immunology	420.4	507.0	20.6 %	329.9	13.9 %							177.1	35.4 %
immunoglobulin *1	334.9	385.9	15.2 %	288.3	13.6 %							97.6	20.4 %
albumin *1	57.6	90.0	56.4 %	17.4	21.8 %							72.6	67.8 %
Others *1 *6	27.9	31.1	11.2 %	24.2	12.6 %							6.8	6.3 %
Oncology	416.5	468.7	12.5 %	222.1	10.4 %	84.3	6.6 %	79.1	8.5 %	74.3	38.9 %	9.0	(8.3)%
VELCADE *2	101.1	110.0	8.8 %	106.7	10.8 %							3.4	(30.2)%
LEUPLIN/ENANTONE	95.4	106.5	11.6 %	24.0	85.7 %	27.3	(22.1)%	32.2	5.5 %	23.0	36.0 %		
NINLARO	87.4	91.2	4.4 %	53.7	(5.7)%	6.1	20.3 %	13.6	0.9 %	17.8	50.0 %		
ADCETRIS	59.4	69.2	16.4 %			11.5	4.4 %	28.2	10.1 %	29.5	29.4 %		
ICLUSIG *2	34.2	34.9	1.9 %	29.2	0.1 %							5.6	12.9 %
VECTIBIX	23.8	24.7	3.7 %			24.7	3.7 %						
ALUNBRIG	8.8	13.6	54.9 %	6.7	14.9 %	1.0	-	3.9	82.1 %	2.0	145.3 %		
Others	6.4	18.6	191.7 %	1.8	5,769.1 %	13.6	231.7 %	1.2	5.3 %	1.9	83.4 %		
Neuroscience	417.3	482.3	15.6 %	371.6	15.7 %	34.8	(9.1)%	65.7	29.5 %	10.2	41.7 %		
VYVANSE/ELVANSE	271.5	327.1	20.4 %	268.6	17.0 %	0.5	7,099.7 %	48.7	37.7 %	9.3	42.3 %		
TRINTELLIX	68.9	82.3	19.5 %	76.9	15.1 %	5.4	167.2 %			_	(100.0)%		
INTUNIV	20.4	18.9	(7.2)%	0.1	(83.1)%	7.1	(33.0)%	10.9	29.8 %	0.8	32.5 %		
ADDERALL XR	17.8	20.9	17.5 %	18.9	16.4 %	—	-	2.0	29.0 %	_	-		
ROZEREM	12.0	11.7	(2.9)%	(0.2)	-	11.8	0.8 %	0.0	-	0.1	126.3 %		
Others *7	26.7	21.4	(19.7)%	7.4	0.2 %	10.0	(28.3)%	4.1	(24.6)%	0.0	(56.2)%		
Others *3	574.1	624.1	8.7 %										
AZILVA-F *4	82.2	76.3	(7.2)%	_	-	76.3	(7.2)%	—	-	_	-		
LOTRIGA	31.8	32.7	2.9 %			32.7	2.9 %						
AIPHAGAN	15.9	14.9	(6.4)%	_	-	14.9	(6.4)%	_	-	_	-		
FOSRENOL *2	13.5	13.6	1.0 %	1.7	(10.2)%							11.9	2.8 %
ACTOVEGIN	10.7	13.4	25.4 %	_	-	—	-	0.7	23.0 %	12.7	25.6 %		

\*1 PDT products

\*2 License-out product : Regional breakdown is not available due to contract.

\*3 The 133.0 billion JPY selling price of the sale of diabetes portfolio in Japan is included in FY21Q4YTD.

\*4 The figures include the amounts of fixed dose combinations.

\*5 GEM: Growth and Emerging Markets, which include Asia (excluding Japan), Latin America, Russia/CIS, Middle East, Oceania and Africa

\*6 Other in PDT Immunology include ARALAST, GLASSIA, CEPROTIN, ANTITHROMBIN III, KENKTSU-NONTHRON and others

\*7 Others in Neuroscience include REMINYL, COPAXONE, AZILECT, MYDAYIS, BUCCOLAM, EQUASYM and CARBATROL

- Quarterly
- Q1

	Reported												
(Bn JPY)	FY20 Q1	FY21 Q1	YOY	US	YOY	Japan	YOY	EUCAN	YOY	GEM*5	YOY	Ex-US	YOY
GI	186.9	210.5	12.6 %	117.6	3.3 %	25.6	15.9 %	47.1	36.1 %	16.0	23.6 %	4.2	20.5 %
ENTYVIO	101.2	125.4	23.9 %	83.7	17.1 %	2.5	26.6 %	32.7	35.6 %	6.4	78.9 %		
TAKECAB-F *1	20.2	24.3	20.1 %		-	22.9	15.0 %	—	-	1.4	346.2 %		
GATTEX/REVESTIVE	17.5	18.1	3.7 %	15.2	(1.1)%	—	-	2.7	43.5 %	0.2	3.6 %		
DEXILANT	13.6	10.8	(20.7)%	6.0	(31.3)%	_	-	2.2	18.3 %	2.5	(14.3)%		
PANTOLOC/CONTROLOC*2	9.2	10.4	13.8 %	0.7	39.8 %	—	-	6.7	37.4 %	3.1	(19.1)%		
LIALDA/MEZAVANT *3	5.5	6.4	16.2 %	2.2	8.6 %							4.2	20.5 %
PENTASA	6.2	4.8	(21.6)%	4.8	(21.6)%								
AMITIZA	6.3	2.1	(65.8)%	2.0	(67.8)%			—	-	0.1	133.0 %		
RESOLOR/MOTEGRITY	2.7	3.2	16.9 %	2.2	10.2 %	—	-	1.0	43.4 %	_	(100.0)%		
ALOFISEL	0.0	0.4	3,556.0 %	—	-	—	-	0.3	4,796.0 %	0.1	1,513.3 %		
Others	4.5	4.5	0.0 %	0.7	(41.8)%	0.2	(7.1)%	1.5	26.6 %	2.1	10.8 %		
Rare Diseases	155.0	155.5	0.3 %	71.2	(3.9)%	7.5	(2.4)%	38.6	11.8 %	24.1	(9.0)%	14.1	15.2 %
Rare Metabolic	39.9	44.3	10.9 %	9.4	5.5 %	0.7	(2.6)%	11.8	17.1 %	8.3	3.7 %	14.1	15.2 %
ELAPRASE	17.6	18.6	5.5 %	5.0	0.1 %	0.4	(5.1)%	6.7	13.9 %	6.4	2.5 %		
REPLAGAL *3	12.2	14.1	15.2 %	_	-							14.1	15.2 %
VPRIV	9.3	10.5	11.9 %	4.4	13.8 %	0.3	0.8 %	3.9	12.7 %	1.8	7.9 %		
NATPARA/NATPAR	0.7	1.2	56.8 %	(0.0)	-	_	-	1.2	64.6 %	0.0	45.1 %		
Rare Hematology	76.8	72.2	(5.9)%	33.3	(0.4)%	6.4	(2.6)%	18.0	(6.0)%	14.6	(17.6)%		
ADVATE	33.7	30.7	(8.9)%	15.1	(11.1)%	1.6	(5.4)%	7.1	(13.0)%	6.9	0.6 %		
ADYNOVATE/ADYNOVI	15.3	15.4	0.6 %	6.8	(5.5)%	3.7	(3.4)%	3.6	6.1 %	1.2	50.6 %		
FEIBA *4	12.9	11.4	(11.3)%	3.9	60.3 %	0.2	(8.8)%	3.2	(2.3)%	4.1	(40.7)%		
RECOMBINATE	3.7	3.7	(0.9)%	3.5	4.9 %	—	-	0.2	(8.0)%	0.0	(91.1)%		
HEMOFIL/IMMUNATE/IMMUNINE*4	4.4	3.3	(25.6)%	0.9	12.8 %	—	-	1.0	(36.7)%	1.4	(31.4)%		
Other PDT Products *4 *6	0.9	0.9	(1.1)%	0.0	-	—	-	0.8	15.6 %	0.0	(81.4)%		
Others *7	5.9	6.9	16.4 %	3.1	15.1 %	0.9	8.5 %	2.1	16.3 %	0.8	32.8 %		
Hereditary Angioedema	38.3	39.0	1.8 %	28.5	(10.1)%	0.4	2.9 %	8.9	64.8 %	1.3	48.2 %		
TAKHZYRO	23.2	25.5	9.6 %	19.9	(5.7)%	—	-	4.9	140.6 %	0.6	572.2 %		
FIRAZYR	8.1	6.9	(15.1)%	3.4	(34.7)%	0.4	2.9 %	2.6	36.1 %	0.5	(15.7)%		
CINRYZE *4	5.9	5.6	(5.7)%	4.1	(4.9)%	_	-	1.3	(5.8)%	0.1	(26.9)%		
KALBITOR	1.1	1.1	2.8 %	1.1	2.8 %	_	-	_	-	_	-		
Others	_	—	-	—	-	_	-	_	-	_	-		

\*1 The figures include the amounts of fixed dose combinations and blister packs.

\*2 generic name: pantoprazole

\*3 License-out product : Regional breakdown is not available due to contract.

\*4 PDT products

\*5 GEM: Growth and Emerging Markets, which include Asia (excluding Japan), Latin America, Russia/CIS, Middle East, Oceania and Africa

\*6 Other PDT products in Rare Hematology include BEBULIN, PROTHROMPLEX and Factor VII.

\*7 Others in Rare Hematology include VONVENDI, OBIZUR, RIXUBIS, AGRYLIN/XAGRID and Other Hemophilia.

#### ■ Q1

		Reported												
(Bn JPY)	FY20 Q1	FY21 Q1	YOY	US	YOY	Japan	YOY	EUCAN	YOY	GEM*5	YOY	Ex-US	YOY	
PDT Immunology	105.3	107.2	1.8 %	70.3	(5.4)%							36.9	19.2 %	
immunoglobulin *1	85.1	81.6	(4.1)%	59.0	(10.7)%							22.6	19.0 %	
albumin *1	13.0	17.8	36.8 %	5.3	100.9 %							12.5	20.6 %	
Others *1 *6	7.2	7.8	9.1 %	6.0	7.8 %							1.8	13.5 %	
Oncology	108.0	121.4	12.4 %	60.4	20.7 %	21.0	(11.0)%	21.2	15.4 %	16.6	23.7 %	2.1	(15.9)%	
VELCADE *2	24.2	30.1	24.6 %	29.4	27.3 %							0.8	(30.8)%	
LEUPLIN/ENANTONE	27.4	26.2	(4.3)%	4.8	128.5 %	7.5	(41.4)%	9.7	17.7 %	4.2	(1.7)%			
NINLARO	22.9	24.4	6.3 %	15.4	(1.3)%	1.5	19.3 %	3.5	3.5 %	4.1	46.0 %			
ADCETRIS	15.1	17.2	14.2 %			2.8	(2.4)%	7.0	13.2 %	7.5	22.9 %			
ICLUSIG *2	9.2	10.4	12.3 %	9.1	15.0 %							1.3	(3.6)%	
VECTIBIX	6.2	6.2	0.1 %			6.2	0.1 %							
ALUNBRIG	2.0	3.1	54.4 %	1.7	18.0 %	0.2	-	0.8	89.6 %	0.4	160.4 %			
Others	0.9	3.8	300.0 %	0.1	-	2.8	418.7 %	0.3	25.9 %	0.5	231.1 %			
Neuroscience	106.9	113.4	6.1 %	87.3	8.7 %	7.5	(39.9)%	15.9	37.0 %	2.8	10.1 %			
VYVANSE/ELVANSE	66.0	79.2	20.0 %	65.2	16.6 %	0.0	-	11.5	48.3 %	2.5	7.8 %			
TRINTELLIX	16.9	17.9	5.9 %	16.7	0.9 %	1.1	273.0 %			_	-			
INTUNIV	5.6	3.3	(42.5)%	(0.0)	-	0.4	(89.1)%	2.7	44.6 %	0.2	59.1 %			
ADDERALL XR	5.3	3.9	(24.9)%	3.5	(27.5)%	_	-	0.4	4.0 %	_	-			
ROZEREM	3.0	3.2	6.9 %	0.1	485.1 %	3.1	4.1 %	_	-	0.0	8.5 %			
Others *7	10.0	5.9	(41.2)%	1.8	(29.7)%	2.9	(51.1)%	1.2	(21.7)%	0.0	(51.2)%			
Others *3	139.8	241.6	72.8 %											
AZILVA-F *4	20.9	22.6	8.6 %	_	-	22.6	8.6 %	_	-	_	-			
LOTRIGA	8.1	7.8	(3.0)%			7.8	(3.0)%							
AIPHAGAN	4.0	4.6	15.0 %	_	-	4.6	15.0 %	_	-	_	-			
FOSRENOL *2	3.2	3.4	4.7 %	0.5	(30.2)%							2.8	15.9 %	
ACTOVEGIN	1.7	3.2	87.2 %		-	_	-	0.2	222.9 %	3.0	81.8 %			

\*1 PDT products

\*2 License-out product : Regional breakdown is not available due to contract.

\*3 The 133.0 billion JPY selling price of the sale of diabetes portfolio in Japan is included in FY21Q1.

\*4 The figures include the amounts of fixed dose combinations.

\*5 GEM: Growth and Emerging Markets, which include Asia (excluding Japan), Latin America, Russia/CIS, Middle East, Oceania and Africa

\*6 Other in PDT Immunology include ARALAST, GLASSIA, CEPROTIN, ANTITHROMBIN III, KENKTSU-NONTHRON and others

\*7 Others in Neuroscience include REMINYL, COPAXONE, AZILECT, MYDAYIS, BUCCOLAM, EQUASYM and CARBATROL

■ Q2

						l	Reported						
(Bn JPY)	FY20 Q2	FY21 Q2	YOY	US	YOY	Japan	YOY	EUCAN	YOY	GEM*5	YOY	Ex-US	YOY
GI	192.9	218.6	13.3 %	123.2	11.3 %	26.3	21.9 %	48.0	16.7 %	17.2	8.3 %	3.9	6.5 %
ENTYVIO	105.7	130.5	23.4 %	87.6	22.3 %	2.9	42.1 %	33.9	23.7 %	6.2	31.5 %		
TAKECAB-F *1	19.7	24.8	25.9 %	_	-	23.1	19.2 %	—	-	1.7	413.4 %		
GATTEX/REVESTIVE	15.7	18.7	18.8 %	15.4	16.1 %	0.1	-	2.6	14.3 %	0.6	176.0 %		
DEXILANT	14.8	14.9	0.8 %	8.7	(4.1)%	—	-	2.6	11.7 %	3.6	6.6 %		
PANTOLOC/CONTROLOC*2	12.3	9.4	(23.4)%	0.4	(22.4)%	_	-	6.1	(5.9)%	2.9	(45.2)%		
LIALDA/MEZAVANT *3	6.1	5.3	(13.1)%	1.4	(42.9)%							3.9	6.5 %
PENTASA	5.5	5.2	(5.6)%	5.2	(5.6)%								
AMITIZA	6.2	1.8	(71.6)%	1.5	(75.5)%			_	-	0.3	92.2 %		
RESOLOR/MOTEGRITY	2.2	3.2	43.3 %	2.4	68.4 %	—	-	0.8	1.8 %	—	(100.0)%		
ALOFISEL	0.3	0.4	52.2 %	_	-	—	-	0.3	43.9 %	0.1	93.5 %		
Others	4.3	4.3	(0.0)%	0.7	(13.9)%	0.2	(0.4)%	1.6	1.9 %	1.9	4.4 %		
Rare Diseases	140.4	144.6	3.0 %	62.1	(2.1)%	6.6	(17.3)%	37.8	9.2 %	26.2	21.4 %	11.9	(7.0)%
Rare Metabolic	39.7	40.0	0.6 %	9.1	1.6 %	0.3	(62.8)%	12.0	12.1 %	6.7	1.9 %	11.9	(7.0)%
ELAPRASE	16.7	16.2	(2.8)%	4.9	(6.0)%	(0.1)	-	6.7	7.4 %	4.6	(4.5)%		
REPLAGAL *3	12.8	11.9	(7.0)%	—	-							11.9	(7.0)%
VPRIV	9.5	10.5	11.0 %	4.2	6.7 %	0.3	(9.8)%	4.0	13.5 %	2.1	19.7 %		
NATPARA/NATPAR	0.8	1.3	72.1 %	0.0	-		-	1.3	39.0 %	0.0	7.6 %		
Rare Hematology	66.1	69.4	5.0 %	28.1	(0.1)%	6.0	(13.0)%	17.1	(0.9)%	18.2	31.9 %		
ADVATE	29.8	30.6	2.9 %	13.3	(4.0)%	1.4	(13.7)%	7.1	(13.9)%	8.8	46.9 %		
ADYNOVATE/ADYNOVI	14.2	14.6	2.6 %	6.5	11.4 %	3.6	(12.5)%	3.2	(5.3)%	1.4	41.0 %		
FEIBA *4	7.7	8.8	13.7 %	2.2	(13.5)%	0.2	(23.3)%	2.8	39.2 %	3.6	22.7 %		
RECOMBINATE	3.2	2.6	(18.5)%	2.4	(13.2)%	—	-	0.2	(39.5)%	0.0	(76.2)%		
HEMOFIL/IMMUNATE/IMMUNINE*4	4.9	5.1	3.0 %	0.8	(19.5)%	—	-	1.3	32.8 %	3.0	1.2 %		
Other PDT Products *4 *6	0.8	1.1	31.3 %	0.0	-	—	-	0.9	19.5 %	0.2	124.3 %		
Others *7	5.4	6.6	22.5 %	2.8	38.2 %	0.8	(11.7)%	1.7	2.3 %	1.3	62.7 %		
Hereditary Angioedema	34.6	35.2	1.8 %	24.9	(5.4)%	0.4	(12.9)%	8.7	30.3 %	1.3	7.2 %		
TAKHZYRO	20.5	22.1	7.6 %	16.6	(2.2)%	_	-	5.0	56.7 %	0.4	36.7 %		
FIRAZYR	7.1	7.5	5.9 %	4.1	7.1 %	0.4	(12.9)%	2.4	14.7 %	0.6	(13.8)%		
CINRYZE *4	6.1	4.6	(24.3)%	3.1	(31.9)%	—	-	1.3	(6.5)%	0.2	54.2 %		
KALBITOR	0.9	1.1	14.0 %	1.1	14.0 %	—	-	_	-		-		
Others	-	_	-	_	-	—	-		-		-		

\*1 The figures include the amounts of fixed dose combinations and blister packs.

\*2 generic name: pantoprazole

\*3 License-out product : Regional breakdown is not available due to contract.

\*4 PDT products

\*5 GEM: Growth and Emerging Markets, which include Asia (excluding Japan), Latin America, Russia/CIS, Middle East, Oceania and Africa

\*6 Other PDT products in Rare Hematology include BEBULIN, PROTHROMPLEX and Factor VII. \*7 Others in Rare Hematology include VONVENDI, OBIZUR, RIXUBIS, AGRYLIN/XAGRID and Other Hemophilia.

■ Q2

						I	Reported						
(Bn JPY)	FY20 Q2	FY21 Q2	YOY	US	YOY	Japan	YOY	EUCAN	YOY	GEM*4	YOY	Ex-US	үөү
PDT Immunology	100.6	130.8	30.0 %	86.8	28.9 %							44.0	32.3 %
immunoglobulin *1	77.6	99.7	28.6 %	76.5	32.1 %							23.2	18.1 %
albumin *1	15.6	24.0	53.8 %	4.7	28.0 %							19.3	61.7 %
Others *1 *5	7.5	7.1	(4.6)%	5.7	(2.8)%							1.5	(11.2)%
Oncology	102.1	112.3	10.0 %	51.0	0.8 %	21.7	21.8 %	19.1	4.6 %	18.2	40.2 %	2.2	(4.4)%
VELCADE *2	25.8	25.0	(3.3)%	24.1	(1.8)%							0.9	(31.7)%
LEUPLIN/ENANTONE	22.5	27.6	23.0 %	7.0	85.4 %	7.6	1.5 %	7.2	(0.9)%	5.9	47.5 %		
NINLARO	21.4	21.4	0.0 %	12.0	(15.4)%	1.5	25.6 %	3.5	11.1 %	4.5	53.4 %		
ADCETRIS	15.5	16.9	9.3 %			2.9	3.5 %	7.2	1.9 %	6.8	21.5 %		
ICLUSIG *2	7.6	7.5	(1.6)%	6.2	(6.6)%							1.3	30.9 %
VECTIBIX	5.7	6.6	15.0 %			6.6	15.0 %						
ALUNBRIG	2.3	3.1	38.8 %	1.4	(8.0)%	0.3	-	0.9	72.7 %	0.5	162.1 %		
Others	1.3	4.1	225.6 %	0.4	-	2.9	315.5 %	0.4	11.4 %	0.5	95.0 %		
Neuroscience	100.9	120.3	19.2 %	94.6	18.4 %	8.5	21.1 %	14.9	14.6 %	2.3	117.6 %		
VYVANSE/ELVANSE	66.6	80.1	20.2 %	66.7	16.8 %	0.2	-	11.0	29.0 %	2.1	126.2 %		
TRINTELLIX	18.1	22.2	22.7 %	20.9	17.7 %	1.3	289.6 %			_	(100.0)%		
INTUNIV	3.3	4.2	26.6 %	0.0	(78.6)%	1.4	44.8 %	2.6	23.0 %	0.2	66.1 %		
ADDERALL XR	3.7	5.7	52.9 %	5.2	54.8 %	—	-	0.5	35.9 %	—	-		
ROZEREM	2.9	3.1	5.7 %	0.1	(13.4)%	3.0	5.8 %	0.0	-	0.0	91.5 %		
Others *6	6.3	5.1	(19.3)%	1.7	21.4 %	2.6	(11.0)%	0.8	(60.7)%	_	(100.0)%		
Others	152.0	118.2	(22.3)%										
AZILVA-F *3	19.1	17.7	(7.2)%	—	-	17.7	(7.2)%	—	-	_	-		
LOTRIGA	7.6	8.2	8.5 %			8.2	8.5 %						
AIPHAGAN	3.7	3.8	3.3 %	_	-	3.8	3.3 %	_	-	_	-		
FOSRENOL *2	3.3	3.6	9.9 %	0.7	479.3 %							2.9	(9.1)%
ACTOVEGIN	3.2	3.5	8.8 %	_	-	_	-	0.2	20.0 %	3.3	8.1 %		

\*1 PDT products

\*2 License-out product : Regional breakdown is not available due to contract.

\*3 The figures include the amounts of fixed dose combinations.

\*4 GEM: Growth and Emerging Markets, which include Asia (excluding Japan), Latin America, Russia/CIS, Middle East, Oceania and Africa

\*5 Other in PDT Immunology include ARALAST, GLASSIA, CEPROTIN, ANTITHROMBIN III, KENKTSU-NONTHRON and others

\*6 Others in Neuroscience include REMINYL, COPAXONE, AZILECT, MYDAYIS, BUCCOLAM, EQUASYM and CARBATROL

■ Q3

- 23						]	Reported						
(Bn JPY)	FY20 Q3	FY21 Q3	YOY	US	YOY	Japan	YOY	EUCAN	YOY	GEM*5	YOY	Ex-US	YOY
GI	209.0	236.6	13.2 %	132.8	9.3 %	31.2	17.8 %	51.0	22.3 %	16.3	5.0 %	5.3	41.0 %
ENTYVIO	112.3	139.5	24.2 %	94.7	24.4 %	3.1	24.6 %	35.6	22.8 %	6.0	28.0 %		
TAKECAB-F *1	24.2	29.3	21.0 %	—	-	27.3	15.0 %	—	-	1.9	367.7 %		
GATTEX/REVESTIVE	16.9	19.8	17.0 %	15.8	10.6 %	0.6	-	2.9	24.8 %	0.5	53.0 %		
DEXILANT	15.1	14.4	(4.1)%	8.5	(10.7)%	—	-	2.9	42.2 %	3.1	(12.8)%		
PANTOLOC/CONTROLOC*2	10.9	10.2	(6.5)%	0.6	11.4 %		-	6.9	18.0 %	2.7	(40.7)%		
LIALDA/MEZAVANT *3	7.1	7.3	3.1 %	2.0	(40.3)%							5.3	41.0 %
PENTASA	6.2	5.7	(6.9)%	5.7	(6.9)%								
AMITIZA	6.4	2.0	(69.2)%	1.8	(70.8)%			—	-	0.1	22.6 %		
RESOLOR/MOTEGRITY	3.6	3.7	4.5 %	3.0	13.7 %	_	-	0.7	(27.5)%		(100.0)%		
ALOFISEL	0.3	0.6	94.9 %	_	-	—	-	0.5	121.3 %	0.1	5.6 %		
Others	6.1	4.1	(32.0)%	0.6	(77.0)%	0.2	(31.3)%	1.5	16.6 %	1.9	(2.1)%		
Rare Diseases	151.3	162.8	7.6 %	71.2	10.9 %	9.0	24.0 %	39.3	14.5 %	29.7	(6.1)%	13.6	(2.0)%
Rare Metabolic	42.2	49.2	16.6 %	9.8	15.0 %	1.1	264.6 %	12.2	9.6 %	12.5	49.5 %	13.6	(2.0)%
ELAPRASE	17.2	22.9	33.0 %	5.2	16.3 %	0.7	774.6 %	6.9	8.6 %	10.1	60.9 %		
REPLAGAL *3	13.9	13.6	(2.0)%	—	-							13.6	(2.0)%
VPRIV	10.0	11.2	11.4 %	4.5	12.6 %	0.4	96.7 %	3.9	2.8 %	2.4	15.7 %		
NATPARA/NATPAR	1.0	1.4	45.1 %	0.0	-	—	-	1.4	41.5 %	0.0	(45.6)%		
Rare Hematology	75.8	70.0	(7.6)%	29.8	(3.2)%	7.1	7.1 %	17.3	6.7 %	15.8	(28.7)%		
ADVATE	33.7	28.0	(16.8)%	14.1	(4.8)%	1.6	(9.4)%	6.1	(17.7)%	6.3	(35.6)%		
ADYNOVATE/ADYNOVI	14.3	15.9	11.5 %	6.4	(2.1)%	4.2	10.6 %	3.9	41.7 %	1.5	19.0 %		
FEIBA *4	13.7	8.8	(35.6)%	2.8	(8.1)%	0.2	(27.9)%	1.9	(29.0)%	3.9	(49.2)%		
RECOMBINATE	3.5	3.3	(7.0)%	3.1	(4.1)%	_	-	0.2	2.4 %	0.0	(83.0)%		
HEMOFIL/IMMUNATE/IMMUNINE*4	3.9	5.2	33.5 %	1.0	26.5 %	—	-	1.2	27.6 %	3.0	38.7 %		
Other PDT Products *4 *6	0.9	1.1	23.0 %	(0.0)	(4,573.1) %	_	-	1.0	31.8 %	0.1	(24.2)%		
Others *7	5.8	7.7	32.2 %	2.5	2.0 %	1.2	35.8 %	3.0	106.2 %	1.0	(1.5)%		
Hereditary Angioedema	33.4	43.5	30.1 %	31.4	26.0 %	0.8	140.1 %	9.8	40.2 %	1.4	25.0 %		
TAKHZYRO	22.1	30.9	39.5 %	24.2	32.5 %	—	-	5.9	68.7 %	0.8	110.8 %		
FIRAZYR	5.0	7.1	43.9 %	3.2	74.9 %	0.8	140.1 %	2.5	20.5 %	0.6	(11.3)%		
CINRYZE *4	5.2	4.5	(14.2)%	3.1	(17.8)%	_	-	1.4	(2.1)%	0.0	(54.7)%		
KALBITOR	1.1	1.0	(11.5)%	1.0	(11.4)%	_	-	—	-	—	(100.0)%		
Others	-	0.2	-	0.2	-	—	-	—	-	—	-		

\*1 The figures include the amounts of fixed dose combinations and blister packs.

\*2 generic name: pantoprazole

\*3 License-out product : Regional breakdown is not available due to contract.

\*4 PDT products

\*5 GEM: Growth and Emerging Markets, which include Asia (excluding Japan), Latin America, Russia/CIS, Middle East, Oceania and Africa

\*6 Other PDT products in Rare Hematology include BEBULIN, PROTHROMPLEX and Factor VII.

\*7 Others in Rare Hematology include VONVENDI, OBIZUR, RIXUBIS, AGRYLIN/XAGRID, OCTOFACTOR, COAGIL-VII, and Other Hemophilia.

■ Q3

						]	Reported						
(Bn JPY)	FY20 Q3	FY21 Q3	YOY	US	YOY	Japan	YOY	EUCAN	YOY	GEM*4	YOY	Ex-US	YOY
PDT Immunology	107.1	125.2	16.9 %	81.8	11.6 %							43.4	28.4 %
immunoglobulin *1	85.4	97.0	13.6 %	71.9	11.8 %							25.1	19.2 %
albumin *1	15.0	19.7	31.4 %	3.5	(13.3)%							16.3	47.5 %
Others *1 *5	6.7	8.5	25.7 %	6.4	28.3 %							2.1	18.1 %
Oncology	108.4	125.4	15.7 %	60.0	13.8 %	24.3	17.7 %	19.4	4.7 %	18.9	38.0 %	2.6	(3.3)%
VELCADE *2	25.9	29.3	13.4 %	28.3	15.2 %							1.0	(20.8)%
LEUPLIN/ENANTONE	25.4	28.4	11.7 %	6.3	67.7 %	8.2	(7.6)%	7.8	(6.9)%	6.1	38.3 %		
NINLARO	23.5	24.9	6.1 %	15.6	3.9 %	1.7	19.2 %	3.5	(6.4)%	4.2	23.8 %		
ADCETRIS	13.8	17.6	27.7 %			3.1	9.4 %	6.9	21.9 %	7.7	43.5 %		
ICLUSIG *2	9.4	8.8	(6.2)%	7.2	(9.6)%							1.6	13.0 %
VECTIBIX	6.5	6.6	1.7 %			6.6	1.7 %						
ALUNBRIG	2.2	3.9	75.6 %	2.0	44.5 %	0.3	-	1.0	81.6 %	0.5	118.9 %		
Others	1.7	5.8	234.8 %	0.6	-	4.5	317.8 %	0.3	2.5 %	0.5	33.1 %		
Neuroscience	107.3	128.9	20.1 %	99.5	20.9 %	9.3	(11.3)%	17.6	36.7 %	2.5	51.8 %		
VYVANSE/ELVANSE	69.8	85.7	22.8 %	70.3	19.6 %	0.0	84.3 %	13.1	38.4 %	2.3	46.9 %		
TRINTELLIX	17.7	23.0	29.6 %	21.4	25.1 %	1.6	151.5 %			—	-		
INTUNIV	5.9	5.0	(13.9)%	0.1	39.2 %	1.7	(52.3)%	3.0	42.9 %	0.2	122.1 %		
ADDERALL XR	4.4	6.3	44.4 %	5.7	44.3 %	_	-	0.6	45.7 %	—	-		
ROZEREM	3.6	3.1	(12.6)%	(0.1)	-	3.2	(2.0)%	—	-	0.0	184.0 %		
Others *6	6.0	5.7	(4.0)%	2.0	(1.8)%	2.8	(7.3)%	0.9	1.9 %	—	(100.0)%		
Others	153.5	122.3	(20.3)%										
AZILVA-F *3	22.9	19.7	(13.8)%	—	-	19.7	(13.8)%	_	-	_	-		
LOTRIGA	8.8	8.7	(1.3)%			8.7	(1.3)%						
AIPHAGAN	4.6	3.6	(20.7)%	—	-	3.6	(20.7)%	_	-	_	-		
FOSRENOL *2	3.7	3.2	(13.6)%	(0.0)	-							3.2	2.4 %
ACTOVEGIN	3.4	4.3	29.4 %	—	-	_	-	0.2	11.3 %	4.2	30.3 %		

\*1 PDT products

\*2 License-out product : Regional breakdown is not available due to contract.

\*3 The figures include the amounts of fixed dose combinations.

\*4 GEM: Growth and Emerging Markets, which include Asia (excluding Japan), Latin America, Russia/CIS, Middle East, Oceania and Africa

\*5 Other in PDT Immunology include ARALAST, GLASSIA, CEPROTIN, ANTITHROMBIN III, KENKTSU-NONTHRON and others

\*6 Others in Neuroscience include REMINYL, COPAXONE, AZILECT, MYDAYIS, BUCCOLAM, EQUASYM and CARBATROL

■ Q4

• <b>Y</b> <sup>+</sup>						]	Reported						
(Bn JPY)	FY20 Q4	FY21 Q4	YOY	US	YOY	Japan	YOY	EUCAN	YOY	GEM*5	YOY	Ex-US	YOY
GI	189.0	210.0	11.1 %	114.4	8.0 %	25.0	9.6 %	48.5	15.8 %	17.9	27.4 %	4.2	(3.5)%
ENTYVIO	110.0	126.4	14.9 %	83.5	11.3 %	2.8	16.8 %	33.7	18.7 %	6.4	53.3 %		
TAKECAB-F *1	20.7	24.0	16.1 %	0.1	-	21.2	5.1 %	—	-	2.7	446.6 %		
GATTEX/REVESTIVE	14.4	19.1	32.6 %	14.7	23.1 %	0.8	-	2.8	23.6 %	0.8	285.2 %		
DEXILANT	12.1	10.6	(12.3)%	5.2	(23.1)%	—	-	2.7	7.2 %	2.8	(4.0)%		
PANTOLOC/CONTROLOC*2	10.7	10.2	(4.9)%	0.4	(20.0)%	_	-	6.7	8.1 %	3.1	(23.2)%		
LIALDA/MEZAVANT *3	6.8	7.4	10.1 %	3.2	34.6 %							4.2	(3.5)%
PENTASA	5.3	4.4	(16.6)%	4.4	(16.6)%								
AMITIZA	2.4	0.6	(75.5)%	0.5	(78.7)%			_	-	0.1	(16.0)%		
RESOLOR/MOTEGRITY	2.7	2.9	6.2 %	2.2	21.9 %	_	-	0.7	(24.7)%	_	-		
ALOFISEL	0.2	0.5	124.0 %	_	-	—	-	0.4	166.3 %	0.1	5.3 %		
Others	3.7	3.8	3.5 %	0.2	-	0.2	(21.9)%	1.4	3.7 %	2.0	(4.4)%		
Rare Diseases	145.0	148.3	2.2 %	65.1	5.4 %	5.8	(14.3)%	35.1	(1.8)%	30.2	8.1 %	12.1	(5.8)%
Rare Metabolic	40.8	39.2	(4.0)%	9.6	13.0 %	0.3	(74.7)%	12.2	7.2 %	5.0	(29.1)%	12.1	(5.8)%
ELAPRASE	17.3	15.4	(10.7)%	5.2	10.9 %	-0.0	-	7.0	6.4 %	3.3	(38.6)%		
REPLAGAL *3	12.9	12.1	(5.8)%	—	-							12.1	(5.8)%
VPRIV	9.7	10.2	6.1 %	4.4	13.7 %	0.3	(9.4)%	3.8	1.7 %	1.7	1.2 %		
NATPARA/NATPAR	1.0	1.4	36.1 %	0.0	-	—	-	1.4	30.5 %	0.0	(93.6)%		
Rare Hematology	71.2	72.1	1.2 %	28.9	0.0 %	5.3	(3.2)%	14.7	(15.4)%	23.3	19.0 %		
ADVATE	31.4	29.2	(7.2)%	12.6	(11.9)%	1.1	(18.4)%	5.3	(25.2)%	10.1	17.2 %		
ADYNOVATE/ADYNOVI	14.3	14.9	3.8 %	6.4	2.4 %	3.3	1.3 %	3.8	1.9 %	1.3	27.8 %		
FEIBA *4	10.3	10.2	(0.7)%	3.7	78.5 %	0.1	(48.4)%	1.9	(35.6)%	4.5	(11.5)%		
RECOMBINATE	2.9	2.7	(7.5)%	2.5	(10.4)%	—	-	0.2	95.7 %	0.0	(54.7)%		
HEMOFIL/IMMUNATE/IMMUNINE*4	5.4	4.2	(23.0)%	0.7	(13.5)%	_	-	0.7	(32.6)%	2.7	(22.5)%		
Other PDT Products *4 *6	0.9	0.9	0.4 %	-0.0	99.6 %	—	-	0.8	13.2 %	0.1	(62.0)%		
Others *7	6.0	10.1	68.7 %	2.9	13.2 %	0.8	18.6 %	2.0	11.4 %	4.5	336.8 %		
Hereditary Angioedema	33.0	35.8	8.7 %	25.5	4.5 %	0.2	(12.4)%	8.2	17.6 %	2.0	44.2 %		
TAKHZYRO	20.8	24.8	19.2 %	18.4	9.8 %	—	-	5.2	45.7 %	1.2	143.4 %		
FIRAZYR	6.7	5.2	(22.4)%	2.8	(22.2)%	0.2	(12.4)%	1.7	(17.4)%	0.5	(39.4)%		
CINRYZE *4	4.6	4.6	(0.2)%	3.1	(5.1)%	_	-	1.3	(3.0)%	0.2	419.0 %		
KALBITOR	0.8	1.2	50.0 %	1.2	50.0 %		-	_	-		-		
Others	_	1.1	-	1.1	-	_	-	—	-	0.0	-		

\*1 The figures include the amounts of fixed dose combinations and blister packs.

\*2 generic name: pantoprazole

\*3 License-out product : Regional breakdown is not available due to contract.

\*4 PDT products

\*5 GEM: Growth and Emerging Markets, which include Asia (excluding Japan), Latin America, Russia/CIS, Middle East, Oceania and Africa

\*6 Other PDT products in Rare Hematology include BEBULIN, PROTHROMPLEX and Factor VII.

\*7 Others in Rare Hematology include VONVENDI, OBIZUR, RIXUBIS, AGRYLIN/XAGRID, OCTOFACTOR, COAGIL-VII, INNONAFACTOR, and Other Hemophilia.

#### ■ Q4

							Reported						
(Bn JPY)	FY20 Q4	FY21 Q4	YOY	US	YOY	Japan	YOY	EUCAN	YOY	GEM*4	YOY	Ex-US	YOY
PDT Immunology	107.3	143.7	33.9 %	91.0	21.9 %							52.7	61.2 %
immunoglobulin *1	86.8	107.6	23.9 %	80.9	23.5 %							26.7	25.0 %
albumin *1	14.0	28.5	104.2 %	4.0	(1.0)%							24.6	146.5 %
Others *1 *5	6.5	7.6	16.5 %	6.1	20.0 %							1.5	4.2 %
Oncology	98.0	109.6	11.8 %	50.6	5.8 %	17.2	1.5 %	19.2	9.2 %	20.5	53.8 %	2.1	(10.1)%
VELCADE *2	25.2	25.6	1.5 %	24.9	3.3 %							0.7	(39.2)%
LEUPLIN/ENANTONE	20.1	24.2	20.6 %	5.8	79.1 %	4.1	(31.8)%	7.5	13.1 %	6.8	61.0 %		
NINLARO	19.5	20.5	4.7 %	10.8	(12.0)%	1.4	17.3 %	3.2	(3.1)%	5.1	82.2 %		
ADCETRIS	15.0	17.4	15.7 %			2.7	7.4 %	7.1	5.9 %	7.5	30.8 %		
ICLUSIG *2	7.9	8.2	3.0 %	6.7	0.7 %							1.4	15.7 %
VECTIBIX	5.4	5.3	(1.8)%			5.3	(1.8)%						
ALUNBRIG	2.3	3.5	51.4 %	1.6	7.3 %	0.2	-	1.1	85.5 %	0.6	148.8 %		
Others	2.4	4.9	101.5 %	0.7	2,318.7 %	3.4	90.4 %	0.2	(15.7)%	0.5	58.5 %		
Neuroscience	102.2	119.7	17.1 %	90.3	14.8 %	9.6	14.3 %	17.3	30.5 %	2.6	32.1 %		
VYVANSE/ELVANSE	69.1	82.1	18.8 %	66.4	14.8 %	0.2	6,317.8 %	13.1	36.2 %	2.4	40.2 %		
TRINTELLIX	16.2	19.3	19.1 %	17.9	16.1 %	1.4	82.3 %			_	-		
INTUNIV	5.6	6.4	15.4 %	0.0	(87.1)%	3.7	28.9 %	2.5	11.3 %	0.2	(27.7)%		
ADDERALL XR	4.4	4.9	11.5 %	4.4	9.6 %	_	-	0.5	32.7 %	_	-		
ROZEREM	2.5	2.2	(10.9)%	(0.3)	(130.4)%	2.5	(4.6)%	0.0	-	0.0	-		
Others *6	4.4	4.7	7.3 %	1.8	39.4 %	1.7	(17.4)%	1.2	17.3 %	_	-		
Others	128.7	142.0	10.4 %										
AZILVA-F *3	19.4	16.2	(16.3)%	—	-	16.2	(16.3)%	_	-	_	-		
LOTRIGA	7.3	7.9	8.7 %			7.9	8.7 %						
AIPHAGAN	3.7	2.9	(21.3)%	—	-	2.9	(21.3)%	_	-	_	-		
FOSRENOL *2	3.3	3.4	4.8 %	0.4	1.8 %							3.0	5.2 %
ACTOVEGIN	2.4	2.4	(1.9)%	—	-	_	-	0.1	(32.7)%	2.3	0.7 %		

\*1 PDT products

\*2 License-out product : Regional breakdown is not available due to contract.

\*3 The figures include the amounts of fixed dose combinations.

\*4 GEM: Growth and Emerging Markets, which include Asia (excluding Japan), Latin America, Russia/CIS, Middle East, Oceania and Africa

\*5 Other in PDT Immunology include ARALAST, GLASSIA, CEPROTIN, ANTITHROMBIN III, KENKTSU-NONTHRON and others

\*6 Others in Neuroscience include REMINYL, COPAXONE, AZILECT, MYDAYIS, BUCCOLAM, EQUASYM and CARBATROL

#### Product Sales Analysis (Reported & Underlying Growth)

		FY20 R	eported	FY21 Reported & Underlying Growth															
						YC	DY			YOY				YOY				YOY	
(Bn JPY)	Q1	Q2	Q3	Q4	Q1	Reported	Underlying	Q2	Reported	Underlying	YTD Underlying	Q3	Reported	Underlying	YTD Underlying	Q4	Reported	Underlying	YTD Underlying
GI	186.9	192.9	209.0	189.0	210.5	12.6 %	7.9 %	218.6	13.3 %	8.7 %	8.3 %	236.6	13.2 %	6.2 %	7.6 %	210.0	11.1 %	4.2 %	6.8 %
ENTYVIO	101.2	105.7	112.3	110.0	125.4	23.9 %	18.2 %	130.5	23.4 %	18.1 %	18.1 %	139.5	24.2 %	15.5 %	17.2 %	126.4	14.9 %	6.7 %	14.5 %
TAKECAB-F *1	20.2	19.7	24.2	20.7	24.3	20.1 %	19.5 %	24.8	25.9 %	25.2 %	22.3 %	29.3	21.0 %	20.2 %	21.5 %	24.0	16.1 %	14.5 %	19.8 %
GATTEX/REVESTIVE	17.5	15.7	16.9	14.4	18.1	3.7 %	0.3 %	18.7	18.8 %	14.1 %	6.9 %	19.8	17.0 %	9.0 %	7.6 %	19.1	32.6 %	22.8 %	11.0 %
DEXILANT	13.6	14.8	15.1	12.1	10.8	(20.7)%	(24.6)%	14.9	0.8 %	(4.8)%	(14.3)%	14.4	(4.1)%	(11.4)%	(13.3)%	10.6	(12.3)%	(19.3)%	(14.6)%
PANTOLOC/CONTROLOC*2	9.2	12.3	10.9	10.7	10.4	13.8 %	4.5 %	9.4	(23.4)%	(28.2)%	(14.1)%	10.2	(6.5)%	(12.3)%	(13.5)%	10.2	(4.9)%	(6.4)%	(11.8)%
LIALDA/MEZAVANT	5.5	6.1	7.1	6.8	6.4	16.2 %	7.0 %	5.3	(13.1)%	(18.5)%	(6.3)%	7.3	3.1 %	(5.3)%	(5.9)%	7.4	10.1 %	3.0 %	(3.6)%
PENTASA	6.2	5.5	6.2	5.3	4.8	(21.6)%	(23.2)%	5.2	(5.6)%	(9.0)%	(16.4)%	5.7	(6.9)%	(13.6)%	(15.4)%	4.4	(16.6)%	(24.3)%	(17.5)%
AMITIZA	6.3	6.2	6.4	2.4	2.1	(65.8)%	(66.5)%	1.8	(71.6)%	(72.7)%	(69.6)%	2.0	(69.2)%	(71.5)%	(70.3)%	0.6	(75.5)%	(78.0)%	(71.2)%
RESOLOR/MOTEGRITY	2.7	2.2	3.6	2.7	3.2	16.9 %	11.4 %	3.2	43.3 %	37.0 %	22.8 %	3.7	4.5 %	(3.0)%	12.0 %	2.9	6.2 %	(1.4)%	8.7 %
ALOFISEL	0.0	0.3	0.3	0.2	0.4	3,556.0 %	3,222.0 %	0.4	52.2 %	42.8 %	166.8 %	0.6	94.9 %	80.9 %	123.3 %	0.5	124.0 %	117.3 %	121.7 %
Others	4.5	4.3	6.1	3.7	4.5	0.0 %	(6.2)%	4.3	(0.0)%	(4.2)%	(5.2)%	4.1	(32.0)%	(35.5)%	(17.6)%	3.8	3.5 %	(0.0)%	(14.2)%
Rare Diseases	155.0	140.4	151.3	145.0	155.5	0.3 %	(3.5)%	144.6	3.0 %	(0.7)%	(2.2)%	162.8	7.6 %	1.3 %	(1.0)%	148.3	2.2 %	(2.6)%	(1.4)%
Rare Metabolic	39.9	39.7	42.2	40.8	44.3	10.9 %	6.6 %	40.0	0.6 %	(2.5)%	2.1 %	49.2	16.6 %	11.1 %	5.2 %	39.2	(4.0)%	(6.1)%	2.4 %
ELAPRASE	17.6	16.7	17.2	17.3	18.6	5.5 %	2.5 %	16.2	(2.8)%	(5.8)%	(1.5)%	22.9	33.0 %	26.2 %	7.8 %	15.4	(10.7)%	(12.4)%	2.7 %
REPLAGAL	12.2	12.8	13.9	12.9	14.1	15.2 %	10.2 %	11.9	(7.0)%	(9.6)%	0.2 %	13.6	(2.0)%	(5.2)%	(1.8)%	12.1	(5.8)%	(6.0)%	(2.8)%
VPRIV	9.3	9.5	10.0	9.7	10.5	11.9 %	6.9 %	10.5	11.0 %	7.6 %	7.2 %	11.2	11.4 %	5.6 %	6.7 %	10.2	6.1 %	0.9 %	5.2 %
NATPARA/NATPAR	0.7	0.8	1.0	1.0	1.2	56.8 %	39.1 %	1.3	72.1 %	61.5 %	50.4 %	1.4	45.1 %	37.1 %	45.2 %	1.4	36.1 %	33.8 %	41.9 %
Rare Hematology	76.8	66.1	75.8	71.2	72.2	(5.9)%	(9.6)%	69.4	5.0 %	1.1 %	(4.6)%	70.0	(7.6)%	(13.2)%	(7.6)%	72.1	1.2 %	(3.6)%	(6.7)%
ADVATE	33.7	29.8	33.7	31.4	30.7	(8.9)%	(12.9)%	30.6	2.9 %	(1.5)%	(7.6)%	28.0	(16.8)%	(22.2)%	(12.7)%	29.2	(7.2)%	(12.6)%	(12.7)%
ADYNOVATE/ADYNOVI	15.3	14.2	14.3	14.3	15.4	0.6 %	(3.3)%	14.6	2.6 %	(0.9)%	(2.1)%	15.9	11.5 %	6.1 %	0.6 %	14.9	3.8 %	(1.2)%	0.1 %
FEIBA *3	12.9	7.7	13.7	10.3	11.4	(11.3)%	(12.6)%	8.8	13.7 %	10.1 %	(4.0)%	8.8	(35.6)%	(38.8)%	(18.2)%	10.2	(0.7)%	(4.5)%	(15.1)%
RECOMBINATE	3.7	3.2	3.5	2.9	3.7	(0.9)%	(3.7)%	2.6	(18.5)%	(21.6)%	(12.0)%	3.3	(7.0)%	(13.6)%	(12.6)%	2.7	(7.5)%	(15.5)%	(13.2)%
HEMOFIL/IMMUNATE/ IMMUNINE*3	4.4	4.9	3.9	5.4	3.3	(25.6)%	(29.4)%	5.1	3.0 %	2.4 %	(13.1)%	5.2	33.5 %	22.1 %	(2.4)%	4.2	(23.0)%	(20.1)%	(7.2)%
Other PDT Products *3 *4	0.9	0.8	0.9	0.9	0.9	(1.1)%	(10.2)%	1.1	31.3 %	24.6 %	6.4 %	1.1	23.0 %	15.8 %	9.6 %	0.9	0.4 %	(1.5)%	6.9 %
Others *5	5.9	5.4	5.8	6.0	6.9	16.4 %	10.4 %	6.6	22.5 %	17.1 %	13.6 %	7.7	32.2 %	24.7 %	17.4 %	10.1	68.7 %	58.4 %	27.9 %
Hereditary Angioedema	38.3	34.6	33.4	33.0	39.0	1.8 %	(1.7)%	35.2	1.8 %	(2.2)%	(1.9)%	43.5	30.1 %	21.1 %	5.4 %	35.8	8.7 %	0.8 %	4.3 %
TAKHZYRO	23.2	20.5	22.1	20.8	25.5	9.6 %	6.0 %	22.1	7.6 %	3.2 %	4.7 %	30.9	39.5 %	29.6 %	13.2 %	24.8	19.2 %	9.9 %	12.4 %
FIRAZYR	8.1	7.1	5.0	6.7	6.9	(15.1)%	(18.3)%	7.5	5.9 %	2.1 %	(8.8)%	7.1	43.9 %	35.0 %	2.2 %	5.2	(22.4)%	(26.5)%	(5.0)%
CINRYZE *3	5.9	6.1	5.2	4.6	5.6	(5.7)%	(9.2)%	4.6	(24.3)%	(27.3)%	(18.4)%	4.5	(14.2)%	(19.8)%	(18.8)%	4.6	(0.2)%	(7.2)%	(16.4)%
KALBITOR	1.1	0.9	1.1	0.8	1.1	2.8 %	0.8 %	1.1	14.0 %	9.9 %	5.1 %	1.0	(11.5)%	(17.9)%	(3.1)%	1.2	50.0 %	36.3 %	5.1 %
Others	—	_	—	—	—	—	-	_	_	-	-	0.2	-	-	-	1.1	-	-	-

\*1 The figures include the amounts of fixed dose combinations and blister packs.

\*2 Generic name: pantoprazole

\*3 PDT products

\*4 Other PDT products in Rare Hematology include BEBULIN, PROTHROMPLEX and Factor VII.

\*5 Other in Rare Hematology include VONVENDI, OBIZUR, RIXUBIS, AGRYLIN/XAGRI, OCTOFACTOR, COAGIL-VII, INNONAFACTOR, and Other Hemophilia.

		FY20 R	eported								FY21 Repor	ted & Ui	nderlying Gr	owth					
						YO	)Y			YOY				YOY				YOY	
(Bn JPY)	Q1	Q2	Q3	Q4	Q1	Reported	Underlying	Q2	Reported	Underlying	YTD Underlying	Q3	Reported	Underlying	YTD Underlying	Q4	Reported	Underlying	YTD Underlying
PDT Immunology	105.3	100.6	107.1	107.3	107.2	1.8 %	(1.8)%	130.8	30.0 %	24.6 %	11.1 %	125.2	16.9 %	8.7 %	10.3 %	143.7	33.9 %	23.5 %	13.6 %
immunoglobulin *1	85.1	77.6	85.4	86.8	81.6	(4.1)%	(6.9)%	99.7	28.6 %	24.2 %	8.0 %	97.0	13.6 %	6.1 %	7.3 %	107.6	23.9 %	15.4 %	9.4 %
albumin *1	13.0	15.6	15.0	14.0	17.8	36.8 %	26.4 %	24.0	53.8 %	42.2 %	35.0 %	19.7	31.4 %	19.4 %	29.7 %	28.5	104.2 %	82.7 %	42.3 %
Others *1 *4	7.2	7.5	6.7	6.5	7.8	9.1 %	6.0 %	7.1	(4.6)%	(8.1)%	(1.2)%	8.5	25.7 %	17.6 %	4.8 %	7.6	16.5 %	7.6 %	5.4 %
Oncology	108.0	102.1	108.4	98.0	121.4	12.4 %	8.7 %	112.3	10.0 %	6.6 %	7.7 %	125.4	15.7 %	9.2 %	8.2 %	109.6	11.8 %	5.6 %	7.6 %
VELCADE	24.2	25.8	25.9	25.2	30.1	24.6 %	22.1 %	25.0	(3.3)%	(6.7)%	7.1 %	29.3	13.4 %	5.3 %	6.5 %	25.6	1.5 %	(7.8)%	2.9 %
LEUPLIN/ENANTONE	27.4	22.5	25.4	20.1	26.2	(4.3)%	(8.8)%	27.6	23.0 %	18.8 %	3.6 %	28.4	11.7 %	7.7 %	5.0 %	24.2	20.6 %	15.8 %	7.2 %
NINLARO	22.9	21.4	23.5	19.5	24.4	6.3 %	2.0 %	21.4	0.0 %	(4.4)%	(1.1)%	24.9	6.1 %	(1.1)%	(1.1)%	20.5	4.7 %	(2.9)%	(1.5)%
ADCETRIS	15.1	15.5	13.8	15.0	17.2	14.2 %	8.8 %	16.9	9.3 %	5.7 %	7.2 %	17.6	27.7 %	22.2 %	11.9 %	17.4	15.7 %	14.0 %	12.4 %
ICLUSIG	9.2	7.6	9.4	7.9	10.4	12.3 %	10.0 %	7.5	(1.6)%	(5.0)%	3.2 %	8.8	(6.2)%	(13.0)%	(2.7)%	8.2	3.0 %	(6.2)%	(3.5)%
VECTIBIX	6.2	5.7	6.5	5.4	6.2	0.1 %	0.1 %	6.6	15.0 %	15.0 %	7.3 %	6.6	1.7 %	1.7 %	5.3 %	5.3	(1.8)%	(1.8)%	3.7 %
ALUNBRIG	2.0	2.3	2.2	2.3	3.1	54.4 %	47.3 %	3.1	38.8 %	33.0 %	39.7 %	3.9	75.6 %	64.9 %	48.4 %	3.5	51.4 %	42.9 %	46.9 %
Others	0.9	1.3	1.7	2.4	3.8	300.0 %	307.2 %	4.1	225.6 %	242.2 %	270.0 %	5.8	234.8 %	205.3 %	241.7 %	4.9	101.5 %	99.1 %	187.7 %
Neuroscience	106.9	100.9	107.3	102.2	113.4	6.1 %	2.9 %	120.3	19.2 %	15.7 %	9.1 %	128.9	20.1 %	11.7 %	10.0 %	119.7	17.1 %	8.1 %	9.5 %
VYVANSE/ELVANSE	66.0	66.6	69.8	69.1	79.2	20.0 %	15.6 %	80.1	20.2 %	14.9 %	15.2 %	85.7	22.8 %	13.5 %	14.6 %	82.1	18.8 %	8.6 %	13.1 %
TRINTELLIX	16.9	18.1	17.7	16.2	17.9	5.9 %	4.0 %	22.2	22.7 %	18.7 %	11.6 %	23.0	29.6 %	21.0 %	14.8 %	19.3	19.1 %	8.9 %	13.4 %
INTUNIV	5.6	3.3	5.9	5.6	3.3	(42.5)%	(49.5)%	4.2	26.6 %	17.8 %	(25.1)%	5.0	(13.9)%	(19.5)%	(22.9)%	6.4	15.4 %	15.0 %	(13.0)%
ADDERALL XR	5.3	3.7	4.4	4.4	3.9	(24.9)%	(27.4)%	5.7	52.9 %	46.8 %	3.5 %	6.3	44.4 %	33.5 %	13.5 %	4.9	11.5 %	1.9 %	10.6 %
ROZEREM	3.0	2.9	3.6	2.5	3.2	6.9 %	7.1 %	3.1	5.7 %	5.9 %	6.5 %	3.1	(12.6)%	(12.4)%	(0.6)%	2.2	(10.9)%	(10.0)%	(2.6)%
Others *5	10.0	6.3	6.0	4.4	5.9	(41.2)%	(41.1)%	5.1	(19.3)%	(3.5)%	(27.7)%	5.7	(4.0)%	(8.0)%	(21.8)%	4.7	7.3 %	6.5 %	(16.9)%
Others *2	139.8	152.0	153.5	128.7	241.6	72.8 %	8.7 %	118.2	(22.3)%	9.1 %	8.9 %	122.3	(20.3)%	10.9 %	9.6 %	142.0	10.4 %	22.6 %	12.8 %
AZILVA-F *3	20.9	19.1	22.9	19.4	22.6	8.6 %	8.6 %	17.7	(7.2)%	(7.2)%	1.1 %	19.7	(13.8)%	(13.8)%	(4.4)%	16.2	(16.3)%	(16.3)%	(7.2)%
LOTRIGA	8.1	7.6	8.8	7.3	7.8	(3.0)%	(3.0)%	8.2	8.5 %	8.2 %	2.4 %	8.7	(1.3)%	(1.6)%	1.0 %	7.9	8.7 %	7.3 %	2.4 %
AIPHAGAN	4.0	3.7	4.6	3.7	4.6	15.0 %	15.0 %	3.8	3.3 %	3.3 %	9.4 %	3.6	(20.7)%	(20.7)%	(1.9)%	2.9	(21.3)%	(21.3)%	(6.4)%
FOSRENOL	3.2	3.3	3.7	3.3	3.4	4.7 %	(3.2)%	3.6	9.9 %	4.5 %	0.7 %	3.2	(13.6)%	(19.4)%	(6.6)%	3.4	4.8 %	0.0 %	(5.0)%
ACTOVEGIN	1.7	3.2	3.4	2.4	3.2	87.2 %	83.3 %	3.5	8.8 %	3.8 %	31.8 %	4.3	29.4 %	14.9 %	24.7 %	2.4	(1.9)%	(3.4)%	18.4 %

\*1 PDT products

\*2 The 133.0 billion JPY selling price of the sale of diabetes portfolio in Japan is included in FY21Q1 Reported.

\*3 The figures include the amounts of fixed dose combinations.

\*4 Other in PDT Immunology include ARALAST, GLASSIA, CEPROTIN, ANTITHROMBIN III, KENKTSU-NONTHRON and others

\*5 Other in Neuroscience include REMINYL, COPAXONE, AZILECT, MYDAYIS, BUCCOLAM, EQUASYM and CARBATROL

#### **Product Forecasts**

	FY21 Reported	FY22	<b>Reported Fore</b>	FY22 CER Growth	
(Bn JPY)	Annual	Annual	YC	γ	Forecasts
GI	875.7		]	Mid-teen growth	Low-teen growth
ENTYVIO	521.8	659.0	137.2	26 %	20 %
TAKECAB-F *1	102.4	112.0	9.6	9 %	9 %
GATTEX/REVESTIVE	75.8	91.0	15.2	20 %	15 %
DEXILANT	50.8	40.0	(10.8)	(21)%	(26)%
PANTOLOC/CONTROLOC*2	40.3	40.0	(0.3)	(1)%	(3)%
LIALDA/MEZAVANT	26.5	23.0	(3.5)	(13)%	(15)%
PENTASA	20.2	17.0	(3.2)	(16)%	(21)%
RESOLOR/MOTEGRITY	13.0	14.0	1.0	8 %	4 %
ALOFISEL	1.8	4.0	2.2	117 %	102 %
Others *3	23.2			-25% to -20%	-30% to -25%
Rare Diseases	611.2				
Rare Hematology	283.7		Low-sir	gle-digit growth	Low-single-digit decrease
ADVATE	118.5	173.0	(6.2)	(3)%	(8)%
ADYNOVATE/ADYNOVI	60.7	175.0	(0.2)	(3)/0	(8)/8
FEIBA *4	39.2	38.0	(1.2)	(3)%	(7)%
RECOMBINATE	12.3	13.0	0.7	6 %	4 %
HEMOFIL/IMMUNATE/IMMUNINE*4	17.7	19.0	1.3	7 %	4 %
Other PDT Products *4 *5	3.9	4.0	0.1	2 %	4 %
Others *6	31.4			+25% to +30%	+20% to +25%
Rare Genetics and Other	327.5			Low-teen growth	High-single-digit growth
TAKHZYRO	103.2	125.0	21.8	21 %	15 %
ELAPRASE	73.1	77.0	3.9	5 %	4 %
REPLAGAL	51.7	68.0	16.3	31 %	30 %
VPRIV	42.4	46.0	3.6	8 %	6 %
FIRAZYR	26.7	21.0	(5.7)	(21)%	(25)%
CINRYZE *4	19.3	13.0	(6.3)	(33)%	(37)%
LIVTENCITY	1.3			+>200%	+>200%
Others *7	9.7			-20% to -10%	-30% to -20%

\*1 The figures include the amounts of fixed dose combinations and blister packs.

\*2 Generic name: pantoprazole

\*3 Others in GI include PREVACID/TAKEPRON, AMITIZA

\*4 PDT products

\*5 Other PDT products in Rare Hematology include BEBULIN, PROTHROMPLEX and Factor VII.

\*6 Others in Rare Hematology include VONVENDI, OBIZUR, RIXUBIS, AGRYLIN/XAGRID, OCTOFACTOR, COAGIL-VII, INNONAFACTOR, and Other Hemophilia.

\*7 Others in Rare Genetics and Other includes NATPARA/NATPAR, KALBITOR

Average FX rates for FY21: 1 USD = 112 JPY, 1 Euro = 131 JPY, 1 RUB = 1.5 JPY, 1 BRL = 20.9 JPY, 1 CNY = 17.4 JPY

Assumption of FX rates for FY22 Reported Forecasts : 1 USD = 119 JPY, 1 Euro = 133 JPY, 1 RUB = 1.3 JPY, 1 BRL = 24.0 JPY, 1 CNY = 18.8 JPY

CER (Constant Exchange Rate) eliminates the effect of foreign exchange rates by translating results of operations using corresponding exchange rates in the same period of the previous fiscal year.

	FY21 Reported	FY22	Reported Forecas	ts	FY22 CER Growth
(Bn JPY)	Annual	Annual	YOY	7	Forecasts
PDT Immunology	507.0			+20% to +30%	+10% to +20%
immunoglobulin *1	385.9			+20% to +30%	+10% to +20%
albumin *1	90.0			+20% to +30%	+10% to +20%
Others *1 *2	31.1			0% to +10%	0% to +10%
Oncology	468.7		Low-sing	e-digit decrease	Mid-single-digit decrease
VELCADE	110.0	47.0	(63.0)	(57)%	(61)%
LEUPLIN/ENANTONE	106.5	106.0	(0.5)	(0)%	(3)%
NINLARO	91.2	103.0	11.8	13 %	8 %
ADCETRIS	69.2	75.0	5.8	8 %	7 %
ICLUSIG	34.9	41.0	6.1	18 %	10 %
VECTIBIX	24.7	24.0	(0.7)	(3)%	(3)%
ALUNBRIG	13.6	26.0	12.4	91 %	85 %
ZEJULA	8.0	12.0	4.0	50 %	50 %
CABOMETYX	6.4	8.0	1.6	26 %	26 %
EXKIVITY	1.0			+>300%	+>300%
Others	3.3			+>30%	+>30%
Neuroscience	482.3		High-sin	gle-digit growth	Low-single-digit growth
VYVANSE/ELVANSE	327.1	372.0	44.9	14 %	7 %
TRINTELLIX	82.3	95.0	12.7	15 %	9 %
INTUNIV	18.9	19.0	0.1	0 %	(4)%
ADDERALL XR	20.9	9.0	(11.9)	(57)%	(59)%
ROZEREM	11.7	8.0	(3.7)	(31)%	(30)%
Others *3	21.4			-10% to -5%	-10% to -5%
Others	624.2			->30%	-20% to -10%
AZILVA-F *4	76.3	73.0	(3.3)	(4)%	(4)%
LOTRIGA	32.7	13.0	(19.7)	(60)%	(60)%
FOSRENOL	13.6	11.0	(2.6)	(19)%	(20)%
ACTOVEGIN	13.4	12.0	(1.4)	(11)%	(3)%

\*1 PDT products

\*2 Others in PDT Immunology include ARALAST, GLASSIA, CEPROTIN, ANTITHROMBIN III, KENKTSU-NONTHRON and others

\*3 Others in Neuroscience include REMINYL, COPAXONE, AZILECT, MYDAYIS, BUCCOLAM, EQUASYM and CARBATROL

\*4 The figures include the amounts of fixed dose combinations.

Average FX rates for FY21: 1 USD = 112 JPY, 1 Euro = 131 JPY, 1 RUB = 1.5 JPY, 1 BRL = 20.9 JPY, 1 CNY = 17.4 JPY

Assumption of FX rates for FY22 Reported Forecasts : 1 USD = 119 JPY, 1 Euro = 133 JPY, 1 RUB = 1.3 JPY, 1 BRL = 24.0 JPY, 1 CNY = 18.8 JPY

CER (Constant Exchange Rate) eliminates the effect of foreign exchange rates by translating results of operations using corresponding exchange rates in the same period of the previous fiscal year.

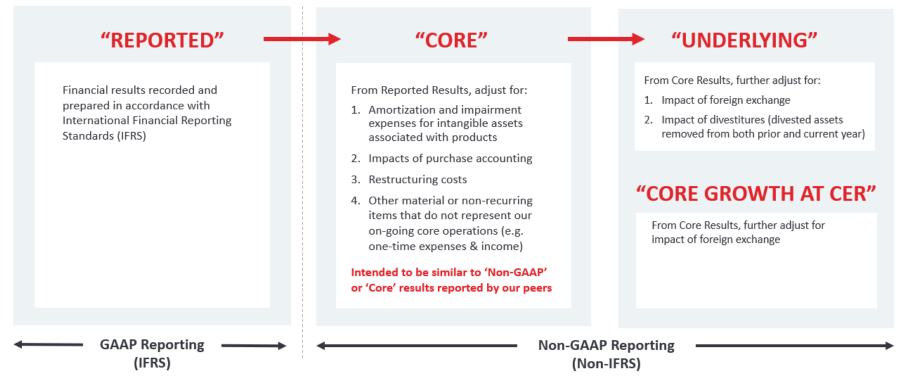
## **Exchange Rate**

			(yen)					(100 million yen)
	Average Excl	nange Rates vs. J	PY	J	Impact of depreciation of	of yen from April 202	22 to March 2023	
CURRENCY	FY20Q4 YTD FY21Q4 YTD FY22 Assumption (Apr-Mar) (Apr-Mar) (Apr-Mar)			Revenue (IFRS)	Core Operating Profit (non-IFRS)	Operating Profit (IFRS)	Net Profit (IFRS)	
				1% depreciation	+192.2	+75.1	+34.7	+29.8
USD	106	112	119	1 yen depreciation	+161.7	+63.2	+29.2	+25.1
				1% depreciation	+49.6	(21.8)	(31.6)	(33.5)
EUR	123	131	133	1 yen depreciation	+37.4	(16.5)	(23.8)	(25.3)
RUB	1.4	1.5	1.3		+4.0	+2.5	+2.1	+2.1
CNY	15.5	17.4	18.8	1% depreciation	+15.6	+8.6	+8.6	+8.6
BRL	19.6	20.9	24.0		+8.8	+5.6	+5.5	+5.5

## CAPEX, depreciation and amortization and impairment losses

(Bn JPY)	FY20Q4 YTD	FY21Q4 YTD	YOY		FY22 Forecasts
Capital expenditures*	236.5	186.0	(50.4)	(21.3)%	260.0 - 310.0
Tangible assets	111.2	123.3	12.0	10.8 %	
Intangible assets	125.3	62.8	(62.5)	(49.9)%	
* Cash flow base					
Depreciation and amortization	558.0	579.8	21.8	3.9 %	588.0
Depreciation of tangible assets* (A)	124.4	132.4	8.0	6.4 %	
Amortization of intangible assets (B)	433.6	447.4	13.8	3.2 %	
Of which Amortization associated with products (C)	405.3	418.8	13.5	3.3 %	438.0
Of which Amortization excluding intangible assets associated with products (D)	28.3	28.6	0.3	0.9 %	
* Excluding depreciation from investment properties					
Depreciation and amortization (excluding intangible assets associated with products) (A)+(D)	152.7	161.0	8.3	5.4 %	150.0
Impairment losses	25.5	54.5	29.1	114.2 %	
Impairment losses associated with products	16.6	54.1	37.5	226.1 %	50.0
Amortization and impairment losses on intangible assets associated with products	421.9	472.9	51.1	12.1 %	488.0

# **3. Definition of Non-IFRS Measures** TAKEDA'S DISCLOSURE METRICS



Beginning with FY2022, Takeda will now use growth in its Core financial measures on a Constant Exchange Rate basis ("Core Growth at CER") to provide its Management Guidance. Previously, Takeda used Underlying financial measures for its Management Guidance, which also adjusted for the impact of divestitures. Because Takeda now anticipates that all the major divestitures following its acquisition of Shire have been completed, we will no longer use Underlying financial measures in our financial reporting going forward.

## DEFINITION OF CORE, UNDERLYING GROWTH AND CONSTANT EXCHANGE RATE

Takeda uses the concept of Underlying Growth for internal planning and performance evaluation purposes. Underlying Growth compares two periods (fiscal quarters or years) of financial results under a common basis and is used by management to assess the business. These financial results are calculated on a constant currency basis using a full year plan rate and exclude the impacts of divestitures and other amounts that are unusual, non-recurring items or unrelated to our ongoing operations. Although these are not measures defined by IFRS, Takeda believes Underlying Growth is useful to investors as it provides a consistent measure of our performance.

Takeda uses "Underlying Revenue Growth", "Underlying Core Operating Profit Growth", and "Underlying Core EPS Growth" as key financial metrics.

**Underlying Revenue** represents revenue on a constant currency basis and excluding non-recurring items and the impact of divestitures that occurred during the reporting periods presented.

**Underlying Core Operating Profit** represents Core Operating Profit (as defined to the right) on a constant currency basis and further adjusted to exclude the impacts of divestitures that occurred during the reporting periods presented.

**Underlying Core EPS** represents net profit based on a constant currency basis, adjusted to exclude the impact of divestitures and items excluded in the calculation of Core EPS (as defined to the right), divided by the outstanding shares (excluding treasury shares) as of the end of the comparative period.

Core Revenue represents revenue adjusted to exclude significant items unrelated to Takeda's core operations.

**Core Operating Profit** represents net profit adjusted to exclude income tax expenses, the share of profit or loss of investments accounted for using the equity method, finance expenses and income, other operating expenses and income, amortization and impairment losses on acquired intangible assets and other items unrelated to Takeda's core operations, such as non-recurring items, purchase accounting effects and transaction related costs.

**Core EPS** represents net profit adjusted to exclude the impact of items excluded in the calculation of Core Operating Profit, and other non-operating items (e.g. amongst other items, fair value adjustments and the imputed financial charge related to contingent consideration) that are unusual, non-recurring in nature or unrelated to Takeda's ongoing operations and the tax effect of each of the adjustments, divided by the average outstanding shares (excluding treasury shares) of the reporting periods presented.

**CER (Constant Exchange Rate)** eliminates the effect of foreign exchange rates by translating results of operations using corresponding exchange rates in the same period of the previous fiscal year.

## **DEFINITION OF FREE CASH FLOW**

We present Free Cash Flow because we believe that this measure is useful to investors as similar measures of liquidity are frequently used by securities analysts, investors and other interested parties in the evaluation of companies in our industry. Free Cash Flow is also used by our management to evaluate our liquidity and our cash flows, particularly as they relate to our ability to meet our liquidity requirements and to support our capital allocation policies. We also believe that Free Cash Flow is helpful to investors in understanding how our strategic divestitures of non-core businesses and of portions of our investment portfolio contribute to the cash flows and liquidity available to us.

We define Free Cash Flow as cash flows from operating activities, subtracting acquisition of property, plant and equipment ("PP&E"), intangible assets and investments as well as any other cash that is not available to Takeda's immediate or general business use, and adding proceeds from sales of PP&E, as well as from sales of investments and businesses, net of cash and cash equivalents divested.

The usefulness of Free Cash Flow to investors has significant limitations including, but not limited to, (i) it may not be comparable to similarly titled measures used by other companies, including those in our industry, (ii) it does not reflect the effect of our current and future contractual and other commitments requiring the use or allocation of capital and (iii) the addition of proceeds from sales and redemption of investments and the proceeds from sales of business, net of cash and cash equivalents divested do not reflect cash received from our core ongoing operations. Free Cash Flow should not be considered in isolation and is not, and should not be viewed as, a substitute for cash flows from operating activities or any other measure of liquidity presented in accordance with IFRS. The most directly comparable measure under IFRS for Free Cash Flow is net cash from operating activities.

## DEFINITION OF EBITDA/ADJUSTED EBITDA AND NET DEBT

#### **EBITDA and Adjusted EBITDA**

We present EBITDA and Adjusted EBITDA because we believe that these measures are useful to investors as they are frequently used by securities analysts, investors and other interested parties in the evaluation of companies in our industry. We further believe that Adjusted EBITDA is helpful to investors in identifying trends in its business that could otherwise be obscured by certain items unrelated to ongoing operations because they are highly variable, difficult to predict, may substantially impact our results of operations and may limit the ability to evaluate our performance from one period to another on a consistent basis.

EBITDA and Adjusted EBITDA should not be considered in isolation or construed as alternatives to operating income, net profit for the year or any other measure of performance presented in accordance with IFRS. These non-IFRS measures may not be comparable to similarly-titled measures presented by other companies.

The usefulness of EBITDA and Adjusted EBITDA to investors has limitations including, but not limited to, (i) they may not be comparable to similarly titled measures used by other companies, including those in our industry, (ii) they exclude financial information and events, such as the effects of an acquisition or amortization of intangible assets, that some may consider important in evaluating our performance, value or prospects for the future, (iii) they exclude items or types of items that may continue to occur from period to period in the future and (iv) they may not exclude all items which investors may consider to be unrelated to our long-term operations, such as the results of businesses divested during a period. These non-IFRS measures are not, and should not be viewed as, substitutes for IFRS reported net income (loss). We encourage investors to review our historical financial statements in their entirety and caution investors to IFRS measures as the primary means of evaluating our performance, value and prospects for the future, and EBITDA and Adjusted EBITDA as supplemental measures.

We define EBITDA as net profit before income tax expenses, depreciation and amortization and net interest expense. We define Adjusted EBITDA as EBITDA further adjusted to exclude impairment losses, other operating expenses and income (excluding depreciation and amortization), finance expenses and income (excluding net interest expense), our share of loss from investments accounted for under the equity method and other items that management believes are unrelated to our core operations such as purchase accounting effects and transaction related costs.

The most closely comparable measure presented in accordance with IFRS is net profit for the year. Please refer to "<u>NET PROFIT TO</u> <u>ADJUSTED EBITDA BRIDGE</u>" for a reconciliation to the respective most closely comparable measures presented in accordance with IFRS.

#### Net Debt

We present Net Debt because we believe that it is useful to investors in that our management uses it to monitor and evaluate our indebtedness, net of cash and cash equivalents, and, in conjunction with Adjusted EBITDA, to monitor our leverage. We also believe that similar measures of indebtedness are frequently used by securities analysts, investors and other interested parties in the evaluation of companies in our industry.

We define Net Debt first by calculating the sum of the current and non-current portions of bonds and loans as shown on our consolidated statement of financial position, which is then adjusted to reflect (i) the use of prior 12-month average exchange rates for non-JPY debt outstanding at the beginning of the period and the use of relevant spot rates for new non-JPY debt incurred and existing non-JPY debt redeemed during the reporting period, which reflects the methodology our management uses to monitor our leverage, and (ii) a 50% equity credit applied to our aggregate principal amount of 500.0 billion hybrid (subordinated) bonds issued in June 2019 by S&P Global Rating Japan in recognition of the equity-like features of those bonds pursuant to such agency's ratings methodology. From this figure, we deduct cash and cash equivalents, excluding cash that is temporarily held by Takeda on behalf of third parties related to vaccine operations and the trade receivables sales program, to calculate Net Debt.

The usefulness of Net Debt to investors has significant limitations including, but not limited to, (i) it may not be comparable to similarly titled measures used by other companies, including those in our industry, (ii) it does not reflect the amounts of interest payments to be paid on our indebtedness, (iii) it does not reflect any restrictions on our ability to prepay or redeem any of our indebtedness, (iv) it does not reflect any fees, costs or other expenses that we may incur in converting cash equivalents to cash, in converting cash from one currency into another or in moving cash within our consolidated group, (v) it applies to gross debt an adjustment for average foreign exchange rates which, although consistent with our financing agreements, does not reflect the actual rates at which we would be able to convert one currency into another and (vi) it reflects an equity credit due to the fact that the amounts of our subordinated bonds, although we believe it to be reasonable, do not affect the status of those instruments as indebtedness. Net Debt should not be considered in isolation and are not, and should not be viewed as, a substitute for bonds and loans or any other measure of indebtedness presented in accordance with IFRS.

The most directly comparable measures under IFRS for Net Debt is bonds and loans. Please refer to "<u>Net Debt to Adjusted EBITDA</u>" for a reconciliation to this measure.

# 4. Reconciliation

## FY2021 Full Year Reconciliation from Reported Revenue to Core/Underlying Revenue

(Billion JPY)	FY2020	FY2021	Change versus the prev	vious year
Revenue	3,197.8	3,569.0	+371.2	+ 11.6%
Sales of Japan diabetes portfolio <sup>1</sup> and other non-core product divestitures	_	(148.5)	(148.5)	-4.6pp
Core Revenue	3,197.8	3,420.5	222.7	+ 7.0%
FX effects <sup>2</sup>				-5.2pp
Divestitures <sup>3</sup>				+5.6pp
Regional portfolio				+4.1pp
Japan diabetes portfolio				+1.0pp
TACHOSIL				+0.4pp
Others				+0.1pp
Underlying Revenue Growth				+ 7.4%

\*1 The non-recurring item of the 133.0 billion JPY selling price as the result of the completion of the divestiture is excluded from FY2021.

<sup>2</sup> FX adjustment applies plan rate to both periods.

\*3 Major adjustments are as follows:

• Revenue of select over-the-counter and non-core products in Asia Pacific is excluded from FY2020 as the divestiture was completed in November 2020.

• Revenue of select non-core prescription pharmaceutical products predominantly in Europe is excluded from FY2020 as the divestiture was completed in December 2020.

• Revenue of select over-the-counter and non-core products in Latin America is excluded from FY2020 as the divestiture was completed in January 2021.

• Net sales from TACHOSIL, a surgical patch, are excluded from FY2020 as the divestiture was completed in January 2021.

• Revenue of select over-the-counter and non-core products predominantly in Europe is excluded from FY2020 as the divestiture was completed in March 2021.

• Revenue of the former subsidiary, Takeda Consumer Healthcare Company Limited, is excluded from FY2020 as the divestiture was completed in March 2021.

• Net sales from a portfolio of diabetes products in Japan (NESINA, LIOVEL, INISYNC and ZAFATEK) are excluded from FY2020 as the divestiture was completed at the beginning of April 2021.

• Revenue of select non-core prescription pharmaceutical products in China had been excluded from both the current fiscal year and the previous fiscal year until the third quarter of the fiscal year ended March

31, 2022. However, as the divestiture was completed at the end of March 2022, the current fiscal year and the previous fiscal year are comparable, thus, in this quarter, no exclusion of its divestiture impact has been made for either fiscal year.

# FY2021 Full Year Reconciliation from Reported to Core/Underlying Core

FY2021

FY2021		REPORTED TO CORE ADJUSTMENTS								CORE TO UNDERLYING CORE ADJ.			
(Billion JPY)	REPORTED	Amortization of intangible assets	Impairment of intangible assets	Other operating income/ expenses	Sale of Japan diabetes portfolio	Irish Tax Assessment *1	TEVA JV related accounting adjustments	Others	CORE	FX	Divestitures	UNDERLYING GROWTH	
Revenue	3,569.0				(133.0)		(0.8)	(14.6)	3,420.5	(166.9)	(6.9)	+7.4%	
Cost of sales	(1,106.8)				0.6			45.6	(1,060.6)	52.0	3.6		
Gross profit	2,462.2				(132.4)		(0.8)	31.0	2,359.9	(114.9)	(3.2)		
SG&A expenses	(886.4)				1.0			5.1	(880.2)	46.1	0.0		
R&D expenses	(526.1)							1.6	(524.5)	25.6	(0.0)		
Amortization of intangible assets	(418.8)	418.8											
Impairment losses on intangible assets	(54.1)		54.1						_				
Other operating income	43.1			(41.7)			(1.4)		—				
Other operating expenses	(159.1)			159.1					—				
Operating profit	460.8	418.8	54.1	117.4	(131.4)		(2.2)	37.7	955.2	(43.2)	(3.2)	+5.4%	
Margin	12.9 %								27.9%			28.0%*2	
Financial income/expenses	(142.9)							21.0	(121.9)	13.5			
Equity income/loss	(15.4)						7.3	11.8	3.7	0.3			
Profit before tax	302.6	418.8	54.1	117.4	(131.4)		5.1	70.5	837.0	(29.4)	(3.2)		
Tax expenses	(72.4)	(89.7)	(15.2)	(26.1)	40.2	65.4	(1.6)	(73.8)	(173.2)	6.1	1.0		
Non-controlling interests	(0.1)								(0.1)	(0.0)	0.0		
Net profit	230.1	329.1	38.9	91.2	(91.2)	65.4	3.5	(3.2)	663.7	(23.3)	(2.2)		
EPS (yen)	147								425	(15)	(1)	+9.4%	
Number of shares (millions)	1,564								1,564			1,563	

\*1 A tax charge of 65.4 billion JPY for tax and interest, net of 0.5 billion JPY of associated tax benefit, arising from tax assessment involving Irish taxation of the break fee Shire received from AbbVie in connection with the terminated offer to acquire Shire made by AbbVie in 2014.

\*2 Underlying Core Operating Profit Margin.

## FY2020 Full Year Reconciliation from Reported to Core/ Underlying Core

FY2020

F Y 2020			REPORT	ED TO COF	RE ADJUSTM			CORE TO UNDERLYING CORE ADJ.			
(Billion JPY)	REPORTED	Amortization of intangible assets	Impairme nt of intangible assets	Other operating income/ expenses	TEVA JV related accounting adjustments	TCHC Divestiture *1	Others	CORE	FX	Divestitures	UNDERLYING GROWTH
Revenue	3,197.8							3,197.8	(1.4)	(174.4)	+2.2%
Cost of sales	(994.3)						87.4	(906.9)	(2.6)	52.7	
Gross profit	2,203.5						87.4	2,290.9	(4.0)	(121.7)	
SG&A expenses	(875.7)			1.9			1.2	(872.6)	2.2	16.7	
R&D expenses	(455.8)			(0.3)			5.8	(450.4)	0.0	0.8	
Amortization of intangible assets	(405.3)	405.3						_			
Impairment losses on intangible assets	(16.6)		16.6					_			
Other operating income	318.0			(116.9)	(1.5)	) (139.5)	(60.2)	—			
Other operating expenses	(258.9)			185.3			73.6				
Operating profit	509.3	405.3	16.6	70.0	(1.5)	) (139.5)	107.7	967.9	(1.8)	(104.2)	+13.0%
Margin	15.9 %							30.3%			28.5%*2
Financial income/expenses	(143.1)						16.8	(126.3)	6.0	(0.0)	
Equity income/loss	0.1				16.6		(13.1)	3.5	(0.2)	(0.0)	
Profit before tax	366.2	405.3	16.6	70.0	15.1	(139.5)	111.4	845.1	4.0	(104.2)	
Tax expenses	9.9	(90.5)	(3.8)	(9.5)	(4.6)	)	(91.0)	(189.4)	(0.9)	29.1	
Non-controlling interests	(0.2)							(0.2)	0.0	0.0	
Net profit	376.0	314.8	12.8	60.5	10.5	(139.5)	20.4	655.5	3.1	(75.1)	
EPS (yen)	241							420	3	(48)	+24.6%
Number of shares (millions)	1,562							1,562			1,558

\*1 On March 31, 2021, Takeda completed the sale of Takeda Consumer Healthcare Company Limited ("TCHC"), a wholly-owned subsidiary of Takeda primarily focused on the consumer healthcare market in Japan, to The Blackstone Group Inc.

\*2 Underlying Core Operating Profit Margin.

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# Free Cash Flow

(BN JPY)	FY2020	FY2021	vs. P'	Y
Net profit	376.2	230.2	(146.0)	-38.8 %
Depreciation, amortization and impairment loss	585.1	637.7	52.5	
Decrease (increase) in trade working capital	53.3	206.3	153.0	
Income taxes paid	(235.8)	(147.7)	88.1	
Tax refunds and interest on tax refunds received	34.1	7.3	(26.8)	
Other	198.0	189.4	(8.6)	
Net cash from operating activities	1,010.9	1,123.1	112.2	+11.1 %
Adjustment for cash temporarily held by Takeda on behalf of third parties <sup>1</sup>	(175.5)	(32.0)	143.5	
Acquisition of PP&E	(111.2)	(123.3)	(12.0)	
Proceeds from sales of PP&E	46.5	1.8	(44.6)	
Acquisition of intangible assets	(125.3)	(62.8)	62.5	
Acquisition of investments	(12.6)	(8.3)	4.3	
Proceeds from sales and redemption of investments	74.6	16.9	(57.7)	
Proceeds from sales of business, net of cash and cash equivalents divested	530.4	28.2	(502.2)	
Free Cash Flow	1,237.8	943.7	(294.2)	(23.8)%

1 Adjustment refers to cash temporarily held by Takeda on behalf of third parties related to vaccine operations and the trade receivables sales program.

# NET PROFIT TO ADJUSTED EBITDA BRIDGE

(BN JPY)	FY2020	FY2021	vs. P	Υ
Net profit	376.2	230.2	(146.0)	(38.8)%
Income tax expenses	(9.9)	72.4		
Depreciation and amortization	559.7	583.2		
Interest expense, net	129.0	117.8		
EBITDA	1,054.9	1,003.6	(51.4)	(4.9)%
Impairment losses	25.5	54.5		
Other operating expense (income), net, excluding depreciation and amortization and other miscellaneous expenses (non-cash item)	(74.5)	106.3		
Finance expense (income), net, excluding interest income and expense, net	14.1	25.1		
Share of loss on investments accounted for under the equity method	(0.1)	15.4		
Other adjustments:	131.4	(30.2)		
Non-core expense related to COVID-19	14.0	10.4		
Sales of Japan diabetes portfolio and other non-core product divestitures	_	(144.8)		
Impact on profit related to fair value step up of inventory in Shire acquisition	79.4	31.9		
Acquisition costs related to Shire	1.9	_		
Other costs <sup>*1</sup>	36.1	72.4		
EBITDA from divested products <sup>*2</sup>	(67.8)	(6.6)		
Adjusted EBITDA	1,083.5	1,168.0	84.5	+7.8%

\*1 Includes adjustments for non-cash equity-based compensation expense and other one time non-cash expense.

\*2 Represents adjustments for EBITDA from divested products which are removed as part of Adjusted EBITDA

## Net Debt to Adjusted EBITDA

#### FY2021 Q4 (Full Year)

NET DEBT/ADJUSTED EBITDA RAT	10	NET INCREASE (DECREASE) IN CASH				
(BN JPY)	FY2021	(BN JPY)	FY2020	FY2021	vs. P	Y
Cash and cash equivalents*1	642.2	Net cash from operating activities	1,010.9	1,123.1	112.2	+11.1 %
Book value debt on the balance sheet	(4,345.4)	Acquisition of PP&E	(111.2)	(123.3)		
Hybrid bond 50% equity credit	250.0	Proceeds from sales of PP&E	46.5	1.8		
FX adjustment*2	219.4	Acquisition of intangible assets	(125.3)	(62.8)		
Gross debt*3	(3,876.0)	Acquisition of investments	(12.6)	(8.3)		
Net cash (debt)	(3,233.8)	Proceeds from sales and redemption of investments	74.6	16.9		
		Acquisition of business, net of cash and cash equivalents acquired	_	(49.7)		
Net debt/Adjusted EBITDA ratio	<b>2.8</b> x	Proceeds from sales of business, net of cash and cash equivalents divested	530.4	28.2		
		Net increase (decrease) in short-term loans and commercial papers	(149.0)	(0.0)		
Adjusted EBITDA	1,168.0	Repayment of long-term loans	(792.5)	(414.1)		
		Proceeds from issuance of bonds	1,179.5	249.3		
		Repayment of bonds	(859.2)	(396.0)		
		Purchase of treasury shares	(2.1)	(77.5)		
		Interest paid	(107.3)	(108.2)		
		Dividends paid	(283.4)	(283.7)		
		Others	(83.1)	(41.1)		
	Net increase (decrease) in cash	316.1	(145.3)	(461.4)	-	

\*1 Includes short-term investments which mature or become due within one year from the reporting date and excludes cash temporarily held by Takeda on behalf of third parties related to vaccine operations and the trade receivables sales program.

<sup>\*2</sup> FX adjustment refers to change from month-end rate to average rate used for non-JPY debt calculation outstanding at the beginning of the period to match with adjusted EBITDA (which is calculated based on average rates). New non-JPY debt incurred and existing non-JPY debt redeemed during the reporting period are translated to JPY at relevant spot rates as of the relevant date.

<sup>\*3</sup> Bonds and loans of current and non-current liabilities. 250Bn yen reduction in debt due to 500Bn yen hybrid bond issuance in June 2019, given that the hybrid bond qualifies for 50% equity credit for leverage purposes. Includes non-cash adjustments related to debt amortization and FX impact.

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### FY2020 Q4 (Full Year)

NET DEBT/ADJUSTED EBITDA RATIO		NET INCREASE (DECREASE) IN CASH						
(BN JPY)	FY2020	(BN JPY) FY2019 FY20		FY2020	vs. PY			
Cash and cash equivalents*1	790.7	Net cash from operating activities	669.8	1,010.9	+341.2	+50.9%		
Book value debt on the balance sheet	(4,635.4)	Acquisition of PP&E	(127.1)	(111.2)				
Hybrid bond 50% equity credit	250.0	Proceeds from sales of PP&E	12.6	46.5				
FX adjustment*2	165.2	Acquisition of intangible assets	(90.6)	(125.3)				
Gross debt*3	(4,220.2)	Acquisition of investments	(7.6)	(12.6)				
Net cash (debt)	(3,429.4)	Proceeds from sales and redemption of investments	49.4	74.6				
		Acquisition of business, net of cash and cash equivalents acquired	(4.9)	_				
Net debt/Adjusted EBITDA ratio	3.2 x	Proceeds from sales of business, net of cash and cash equivalents divested	461.5	530.4				
		Net increase (decrease) in short-term loans and commercial papers	(351.2)	(149.0)				
Adjusted EBITDA	1,083.5	Repayment of long-term loans	(137.4)	(792.5)				
		Proceeds from issuance of bonds	496.2	1,179.5				
		Repayment of bonds	(563.6)	(859.2)				
		Interest paid	(127.2)	(107.3)				
		Dividends paid	(282.6)	(283.4)				
		Others	(40.6)	(85.3)				
		Net increase (decrease) in cash	(43.3)	316.1	+359.4	_		

\*1 Includes short-term investments which mature or become due within one year from the reporting date and excludes deposits restricted to certain vaccines operations.

\*2 FX adjustment refers to change from month-end rate to average rate used for non-JPY debt calculation, to match with adjusted EBITDA calculation.

<sup>\*3</sup> Bonds and loans of current and non-current liabilities. 250Bn yen reduction in debt due to 500Bn yen hybrid bond issuance in June 2019, given that the hybrid bond qualifies for 50% equity credit for leverage purposes. Includes cash and non cash adjustments to debt book-value. Non cash adjustments include changes dues to debt amortization and FX impact.

# **Reconciliation from Reported Operating Profit to Core Operating Profit - FY2022 Forecast**

		REPORTED TO CORE ADJUSTMENTS					
(BN JPY)	REPORTED	Amortization of intangible assets	Impairment of intangible assets	Other operating income/ expenses	Others	CORE	
Revenue	3,690.0					3,690.0	
Cost of sales					24.0		
Gross Profit					24.0		
SG&A and R&D expenses					7.0		
Amortization of intangible assets	(438.0)	438.0				—	
Impairment losses on intangible assets	(50.0)		50.0			—	
Other operating income	12.0			(12.0)		—	
Other operating expenses	(73.0)			73.0		—	
Operating profit	520.0	438.0	50.0	61.0	31.0	1,100.0	

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This report and any materials distributed in connection with this report may contain forward-looking statements, beliefs or opinions regarding Takeda's future business, future position and results of operations, including estimates, forecasts, targets and plans for Takeda. Without limitation, forward-looking statements often include words such as "targets", "plans", "believes", "hopes", "continues", "expects", "aims", "intends", "ensures", "will", "may", "should", "would", "could" "anticipates", "estimates", "projects" or similar expressions or the negative thereof. These forward-looking statements are based on assumptions about many important factors, including the following, which could cause actual results to differ materially from those expressed or implied by the forward-looking statements: the economic circumstances surrounding Takeda's global business, including general economic conditions in Japan and the United States; competitive pressures and developments; changes to applicable laws and regulations, including global health care reforms; challenges inherent in new product development, including uncertainty of clinical success and decisions of regulatory authorities and the timing thereof; uncertainty of commercial success for new and existing products; manufacturing difficulties or delays; fluctuations in interest and currency exchange rates; claims or concerns regarding the safety or efficacy of marketed products or product candidates; the impact of health crises, like the novel coronavirus pandemic, on Takeda and its customers and suppliers, including foreign governments in countries in which Takeda operates, or on other facets of its business; the timing and impact of post-merger integration efforts with acquired companies; the ability to divest assets that are not core to Takeda's operations and the timing of any such divestment(s); and other factors identified in Takeda's most recent Annual Report on Form 20-F and Takeda's other reports filed with the U.S. Securities and Exchange Commission, available on Takeda's website at: https:// www.takeda.com/investors/sec-filings/ or at www.sec.gov. Takeda does not undertake to update any of the forward-looking statements contained in this report or any other forward-looking statements it may make, except as required by law or stock exchange rule. Past performance is not an indicator of future results and the results or statements of Takeda in this report may not be indicative of, and are not an estimate, forecast, guarantee or projection of Takeda's future results.

#### **Certain Non-IFRS Financial Measures**

This report includes certain non-IFRS financial measures and targets. Takeda's management evaluates results and makes operating and investment decisions using both IFRS and non-IFRS measures included in this report. Non-IFRS results exclude certain income and cost items which are included in IFRS results. By including these non-IFRS measures, management intends to provide investors with additional information to further analyze Takeda's performance, core results and underlying trends. Non-IFRS results are not prepared in accordance with IFRS and non-IFRS information should be considered a supplement to, and not a substitute for, financial statements prepared in accordance with IFRS. Investors are encouraged to review the reconciliations of non-IFRS financial measures to their most directly comparable IFRS measures, which are on "*Supplementary Information - 3. Reconciliation.*"

#### **Medical information**

This report contains information about products that may not be available in all countries, or may be available under different trademarks, for different indications, in different dosages, or in different strengths. Nothing contained herein should be considered a solicitation, promotion or advertisement for any prescription drugs including the ones under development.

#### **Financial information**

Takeda's financial statements are prepared in accordance with International Financial Reporting Standards ("IFRS").