



Letter to shareholders

MAY 2021



Christophe Weber

President & CEO

Dear Takeda Shareholder,

I hope that this letter finds you and your families well, safe and healthy. We understand the incredible challenges experienced across all corners of the globe, and we are grateful for your trust and commitment to Takeda for serving our patients, especially during these unprecedented times.

On behalf of the Takeda Board of Directors, I would like to invite you to our 2021 Annual Shareholders Meeting on June 29, 2021. To prevent the potential spread of SARS-CoV-2 in Japan, we will provide the option to attend either in person or through an internet livestream. We strongly recommend that you join the internet livestream, if possible, to ensure your health and safety.

As we begin FY2021, we hope an end is in sight to the pandemic. At Takeda, we are privileged to be part of an industry that plays a vital role in the treatment and prevention of COVID-19. The speed of innovation and the unprecedented collaborations across our industry over the past year inspires us.

**TAKEDA'S
RESILIENCE,
UNWAVERING
COMMITMENT TO
PATIENTS DURING
COVID-19**

Throughout FY2020, Takeda has demonstrated resilience, flexibility and strength. Our ability to embrace change and our agility to adapt has once again held us in good stead – this time during the COVID-19 pandemic. I am exceptionally proud of our colleagues who, during many difficult months, maintained business continuity and provided patients with uninterrupted access to our medicines, while simultaneously juggling new ways of working and the many personal and professional challenges presented by the pandemic.

I'm also extremely proud of the leading role Takeda has played in partnering to combat COVID-19, supporting global access to three different COVID-19 vaccines.

In Japan, we are partnering with Novavax to develop and commercialize, based on our manufacturing capacity, more than 250 million doses of Novavax's COVID-19 vaccine candidate. We also plan to import and distribute 50 million doses of Moderna's mRNA COVID-19 vaccine working with Moderna and Japan's Ministry of Health, Labour and Welfare (MHLW). Additionally, with contract manufacturer IDT Biologika GmbH, we are using capacity reserved for our dengue vaccine for three months to manufacture Johnson & Johnson's COVID-19 vaccine.

In addition, early in the pandemic, we joined others in our industry to form the CoVig-19 Plasma Alliance, a one-year plasma collaboration involving organizations from across the world, to pool resources and bring our collective plasma expertise and infrastructure together to contribute to public health. The data results did not meet the clinical trial's primary endpoint. However, the CoVig-19 Plasma Alliance generated new scientific insights about the virus and strengthened relationships within and outside the industry. It advanced pragmatic regulatory frameworks based on scientific evidence and need, including a well-defined, legally compliant framework for future collaborative opportunities to address urgent public health needs.

Exploring new ways of working post COVID-19

The COVID-19 pandemic has drastically impacted and shifted all our lives, causing us to explore future ways of working. We are proactively preparing for the post-COVID-19 environment by taking a holistic and science-driven approach that engages employees across the organization. Our approach is based on:

- embracing hybrid in-person and virtual working models whenever possible
- ensuring frequent in-person interactions that are essential to preserving our culture, organizational efficiency, and career success of our people
- trusting leaders to find the best way to implement these working models locally with their teams

The future of how we work will help us achieve our strategic imperatives and vision of discovering and delivering life-transforming treatments to patients, and will enrich our unique culture and values.

Accelerating digital development

The pandemic has not only impacted the way we work, but also the way patients and health care providers interact. It has accelerated the widespread adoption of telemedicine and digital health solutions that, for a number of reasons, were previously only used by a small percentage of patients and health care providers.

The pandemic has also accelerated Takeda's digital development. We quickly adopted new digital tools and ways of working through our investment in our people and our technology. Our new hybrid work model and upskilling programs build digital capabilities across our workforce and create a future-ready organization.

We are also becoming a cloud-first company that harnesses external partnerships, such as with Amazon Web Services (AWS) and Accenture, establishing an internal engine that accelerates innovation and positions us at the intersection of health, technology and business growth.

With innovative partners like the Massachusetts Institute of Technology (MIT), we are expanding the use of Artificial Intelligence-augmented algorithms across Takeda to improve our clinical development processes to get medicines to patients faster.

Through investment in technologies, be it clinical trial data, biomarker data or real-world data, we can better translate science into highly innovative, life-transforming medicines that address unmet needs and measurably impact patient outcomes.

ANTICIPATING THE NEXT PANDEMIC AND PROTECTING RESEARCH

COVID-19 has demonstrated that we must do more to prepare for future pandemics. We must globally commit to sustain and build over the long term from our lessons learned over the past 12 months. We believe that the following steps are necessary to prepare for the next pandemic:

1. Establish a worldwide inventory and revolving stock of protective equipment, medical devices, testing kits, vaccines and treatments, which we can use early and rapidly
2. Create a transparent global detection system
3. Fund research to better understand zoonotic diseases and how to prevent them
4. Fund research into diagnostic kits, vaccines and treatments against possible emerging pathogens and diseases, starting with coronaviruses

Establishing a worldwide revolving stock of protective equipment, medical devices, testing kits, vaccines and treatments is necessary to fight against the pandemic in the early weeks of its detection. Maintaining such a ready-to-use stock is not an easy task given the need to constantly manage expiration dates. A supranational organization, for example the World Health Organization, mandated by all countries, could organize such a task, even if it means delegating the day-to-day operations to private entities. The management of such a stock would provide an excellent and dynamic overview of supply chains, a key insight to better manage limited supply when a pandemic strikes again and could trigger the necessary technology transfers to quickly increase capacity.

Research funding of vaccines is happening through organizations like the Coalition for Epidemic Preparedness Innovations (CEPI). However, no similar mechanism exists to spur research and development of new antivirals. Takeda, along with other companies, is working at setting up such an initiative in 2021.

Recently, a number of governments have expressed their support for a proposal to waive patent protections for COVID-19 vaccines and medicines. While Takeda agrees that extraordinary measures are necessary to support equitable access to COVID-19 vaccines and medicines worldwide, we also believe that patent protection is not a significant barrier to expand capacity. As the world prepares for possible emerging pathogens and diseases, we must continue to reward research to protect future innovation.

Protecting health care financing and research

For the last decade, increasing life expectancy, lifestyle changes, and the availability of more advanced solutions for complex diseases have driven investment in health care to rise faster than gross domestic product (GDP) and incomes. In most developed economies, government funds the majority of health care spending.

The government response to the economic crisis due to the COVID-19 pandemic will certainly bring long-term financing challenges. Governments across the world have responded with unprecedented degrees of fiscal spending even as the economic fallout has impacted tax receipts. For example, in the U.S. total public debt to GDP now stands at over 125%, and the Federal deficit is the largest it has been in decades. To pay for this spending, taxes may need to be raised while health care budgets may be restrained. This could accelerate downward pressure on drug pricing.

Recent innovation has led to changes in many areas of medicine. Without due care from governments, untargeted reductions in drug prices could impede this trend. We believe rewarding innovation is fundamental to spurring research. We advocate improving health care system efficiency through value-based health care that correlates health care costs to patient outcomes instead of the cost of the intervention. Specific to the pharmaceutical market, we favor the development of generics and biosimilars once the patent covering the innovation has expired.

TRANSFORMATION OF TAKEDA – OUR PROGRESS

Since 2014, Takeda has been on a transformation journey, becoming a truly global, values-based, R&D driven biopharmaceutical leader. As we celebrate Takeda's 240th anniversary this year, we are well-positioned to deliver highly-innovative medicines and transformative care to patients around the world.

Transforming our R&D strategy

In 2015, we initiated a fundamental R&D transformation based on the following principles: only invest in potentially life transforming medicines, focus on a few select therapy areas, actively seek external partnerships to complement our in-house research, and diversify our technology from small molecules to multi modalities. This strategy is starting to yield results with a diverse and dynamic pipeline in areas of high unmet need across our four innovative biopharma core therapeutic areas - Oncology, Rare Genetic & Hematology, Neuroscience and Gastroenterology.

We have integrated Takeda's world class laboratories with a network of over 200 partners, including Maverick, a pioneer in T-cell therapy, which we acquired early this year. These partnerships contributed to the transformation of our research pipeline. Today, 80% of our programs leverage modalities beyond small molecules, ranging from biologics and peptides/ oligonucleotides, to cell and gene therapy. This is a significant change from 2014 when ~80% of our pipeline assets were small molecules.

Globalizing and upscaling our business

Our transformation journey has resulted in our revenues increasing from 1.78 trillion yen in FY2014 to 3.2 trillion yen in FY2020. This is mainly due to the commercialization and growth of Takeda's new global products, the first being Entyvio for Inflammatory Bowel Disease (IBD), and also the contribution from the acquisition of Shire. Scale has allowed us to more than double our core operating profit over the last five years, and we reached a 30% margin in FY2020. We expect to maintain the same level into FY2021 even while ramping up our R&D investment to JPY 522 billion, up approximately 40% from FY2014. Takeda's successful transformation journey has given the company continued growth momentum, driven by demand for critical medicines, new pipeline launches, new indications and sales growth in key geographies. The combination of solid performance across our 14 global brands, continued operational discipline and accelerated realization of cost synergies ahead of plan, has resulted in strong margins and cash flow, and a robust financial position at the end of FY2020.

Demonstrating growth acceleration and execution capability in FY2020

Strong business performance is fundamental to how we create value. Despite many challenges and uncertainties, our fiscal year 2020 results demonstrate the resilience of our portfolio, which drove 3.2 trillion yen in revenues and underlying revenue growth of 2.2%. Five key business areas, which had 4.7% underlying revenue growth, and our 14 global brands, which had 16% underlying revenue growth, have driven our strong performance. Our employees' tremendous commitment and focus to deliver treatments to patients in need and advance our clinical programs through the current pandemic will continue our momentum.

Equally important in our commitment to patients is our responsibility to ensure quality across our operations. We have more than 30 manufacturing sites which will continue to strive for strong quality track records to meet the expectations of regulatory agency across the world. Following the U.S. Food and Drug Administration's (FDA) Warning Letter related to a November 2019 inspection of Takeda's Hikari Plant in Japan, we have put in place a comprehensive corrective and preventative action plan and have recently confirmed a re-inspection of the facility with the FDA in July of this year.

Takeda's fiscal year 2020 underlying core operating profit margin¹ was 30.2%, due to our continued cost discipline and accelerated realization of synergies, with adjusted EBITDA² of JPY 1,083.5 billion yen. We are pleased to share that integration and synergy capture from our acquisition of Shire is essentially complete. In fact, we were able to operate as One Takeda one year after closing the Shire acquisition and to deliver our 2.3 billion USD synergy target two years after closing. We also generated robust operating cash flow of 1,010.9 billion yen, which when combined with this year's divestitures and capital expenditures, results in free cash flow³ of 1,237.8 billion yen, representing a year-on-year increase of 27.9%.

We also remain on course against our net debt to adjusted EBITDA ratio⁴ target of 2x (i.e. "low twos") within FY2021-FY2023. Over the past two fiscal years, we have reduced this debt ratio significantly from 4.7x in March 2019 after the acquisition of Shire to 3.2x as of March 2021. In FY2020 we also exceeded our \$10 billion non-core asset divestiture target, announcing 12 deals since January 2019 to date for a total aggregate value of up to approximately 12.9 billion USD⁵. These non-core divestments are strategic not only because they allow us to deleverage more rapidly but also because they allow us to focus our resources on highly innovative therapies within our key business areas. Takeda's Return on Equity (ROE) was 7.6% in FY2020, which was a significant increase from last year.

¹ Please refer to slide 48 for definition and slide 63 for reconciliation of the FY2020 Full Year earnings presentation for reconciliation to IFRS measures.

² Please refer to slide 50 for definition and slides 69-70 for reconciliation of the FY2020 Full Year earnings presentation for reconciliation to IFRS measures.

³ Please refer to slide 49 for definition and slide 68 for reconciliation of the FY2020 Full Year earnings presentation

⁴ Please refer to slide 50 for definition and slides 69-70 for reconciliation of the FY2020 Full Year earnings presentation

⁵ Includes transactions yet to close and the full value of milestones and other contingent payments not guaranteed to be made
https://www.takeda.com/499b90/siteassets/system/investors/quarterly-announcements/fy2020/qr2020_q4_p01_en.pdf

**OUR PURPOSE:
BETTER HEALTH FOR
PEOPLE, BRIGHTER
FUTURE FOR THE
WORLD**

Takeda's purpose – “better health for people, brighter future for the world” – defines why we exist and guides us in our daily work. As a value based company, everything we do and every business decision we make must align with our values of Takeda-ism (Integrity, Fairness, Honesty, and Perseverance), brought to life through actions based on Patient-Trust-Reputation-Business, in that order. Our vision “to discover and deliver life-transforming treatments, guided by our commitment to patients, our people and the planet,” encompasses what we want to achieve and how we want to contribute to society.

Our commitment to patients: FY2021 will be an inflection year for our promising R&D pipeline

Since we initiated our R&D transformation in 2015, we have built a world-class R&D engine, leveraging internal research capabilities while also actively engaging with innovative ecosystems around the world.

FY2021 in particular will be an inflection year for the pipeline as we anticipate having an unprecedented five to six regulatory submissions under review by the FDA and other major global regulatory agencies by year-end FY2021, with the potential for up to four approvals. In addition, we expect continued late-stage pipeline momentum with seven programs in pivotal studies across 10 indications by year-end FY2021. Our dynamic pipeline reflects our recent decision to significantly increase our investment in R&D to JPY 522 billion in FY2021 to accelerate its continued evolution.

We now have a diverse and dynamic pipeline, across our core therapeutic areas, with approximately 40 current new molecular entities (NMEs), which includes 11 NMEs with potential for 15 launches through FY2024, what we refer to as “Wave 1” of our R&D transformation.

WAVE 1 PIPELINE ASSETS HAVE SIGNIFICANT MARKET POTENTIAL

	PRODUCT	INDICATION	FULL MARKET OPPORTUNITY ²	TAKEDA'S PEAK REVENUE POTENTIAL ⁵
ONCOLOGY	mobocertinib (TAK-788)	Exon 20 non-small cell lung cancer 1L		\$300 – 600MN
		Exon 20 non-small cell lung cancer 2L		
	pevonedistat (TAK-924)	Higher risk-Myelodysplastic syndromes Unfit Acute myeloid leukemia		\$400 – 800MN
RARE GENETIC & HEMATOLOGY	TAK-007	3L+ Diffuse Large B-Cell Lymphoma 3L+ Chronic Lymphocytic Leukemia 3L+ Follicular Lymphoma		\$700 – 1,500MN
	TAK-609	Hunter CNS (intrathecal) ¹		<\$100MN
	maribavir (TAK-620)	CMV infection in transplant patients (R/R & 1L)		\$700 – 800MN
	TAK-611	Metachromatic leukodystrophy (intrathecal)		\$300 – 450MN
NEUROSCIENCE	Orexin programs ³	Narcolepsy type 1 (NT1)		\$3,000 – 4,000MN (NT1)
		Narcolepsy type 2 (NT2)		\$1,000 – 2,000MN (NT2 + IH)
		Idiopathic hypersomnia		
	soticlestat (TAK-935)	Dravet syndrome, Lennox-Gastaut syndrome		\$400-500MN
GASTROENTEROLOGY (GI)	Eohilia ⁴ (TAK-721)	Eosinophilic Esophagitis		\$300 – 500MN
VACCINES	TAK-003	Prevention of dengue		\$700 – 1,600MN

KEY	≤ \$0.5BN	\$0.5BN - \$1.0BN	\$1.0BN - \$3.0BN	≥ \$3.0BN

1. MPSII market in total (somatic + CNS)

2. Market potential indicates Takeda's best estimate about addressable market size, based on available data and estimates.

3. Other rare indications than NT1, NT2 and IH are not included in the calculation.

4. Eohilia is the proposed brand name for TAK-721. TAK-721 is an investigational treatment and has not been approved for use by the FDA or other regulatory authorities. In active discussions with the FDA. Projected approval subject to outcome of discussions

5. Includes incremental revenue not adjusted for Probability of Technical Success (PTS) and is not a "forecast" or "target" figure. PTS applies to the probability that a given clinical trial/study will be successful based on pre-defined endpoints, feasibility and other factors and regulatory bodies will grant approval. Actual future net sales achieved by our commercialized products and pipelines will be different, perhaps materially so, as there is a range of possible outcomes from clinical development, driven by a number of variables, including safety, efficacy and product labelling. If a product is approved, the effect of commercial factors including the patient population, the competitive environment, pricing and reimbursement is also uncertain

Source: Wave 1 Pipeline Market Opportunity Call Part 2

https://www.takeda.com/4961c7/siteassets/system/investors/investor--events/wave1marketeventpart2_en.pdf

April 6, 2021

Highlighting a few:

- Our promising orexin 2 receptor agonist franchise has the potential to transform treatment of narcolepsy type 1, a rare chronic and debilitating sleep disorder, by addressing the underlying disease pathophysiology. Early clinical trial results have suggested unprecedented efficacy in both Narcolepsy Type 1 and other rare and more common disorders characterized by altered sleep-wake cycles.
- Takeda's industry-leading oncology cell therapy capabilities focusing on the innate immune system have seen significant progress including initial clinical proof-of-concept for TAK-007, demonstrating the potential combination of efficacy, safety and allogeneic or "off-the shelf" supply chains.
- TAK-755 is a potential first-in-class/best-in-class therapy for thrombotic thrombocytopenic purpura (TTP), a rare blood disorder that is also associated with long-term organ damage, including increased risk for stroke, heart attack or kidney failure. A pivotal Phase 3 study is underway with a planned readout for early FY2022.
- We're on the cusp of a potential vaccine for dengue that would provide a solution to one of the World Health Organization's 2019 top 10 threats to global health.

Our pipeline is poised to deliver life-transforming treatments to patients now and in the future. Our Wave 2 pipeline contains approximately 30 modality diverse NMEs across our core therapeutic areas, each with the potential to become transformative, lifesaving and even curative treatments in the next decade. Two examples of our exciting Wave 2 pipeline assets are TAK-981 and TAK-999. With the small molecule TAK-981, a first-in-class inhibitor of SUMOylation that is being studied across both hematologic and solid cancers, we are leveraging the power of innate immunity to treat cancer, a building theme in our advancing oncology portfolio. With the anti-sense oligonucleotide therapy, TAK-999, we are advancing with our partners at Arrowhead Pharmaceuticals, the most advanced experimental therapy to treat a severe rare liver disease caused by alpha 1-antitrypsin deficiency.

Our commitment to people

At Takeda, we're committed to creating an exceptional people experience. For the fourth consecutive year, the Top Employer Institute has named Takeda a Global Top Employer. Our people are the cornerstone of Takeda's success, and we recognize that creating diverse, inclusive, and equitable work environments are critical to building a healthy company culture that empowers our employees to live our purpose every day. Globally, Takeda comprises of 52% female and 48% male employees. We continue to strive to have a workforce as diverse as the communities where we operate and the patients we serve. We're also focused on creating an environment that fosters lifelong learning and a growth mindset, enabling employees to grow and thrive.

Our commitment to planet

Today, pressure on environmental health, as evidenced by degrading air quality, increasing scarcity of clean water and other natural resources, waning biodiversity and the impacts of climate change, increasingly poses threats to human health. As a responsible corporate citizen, we must do our part to continually reduce our environmental footprint. In 2020, we achieved carbon neutrality in our value chain, so we will now turn to our longer-term targets – a 40% reduction in greenhouse emissions from our internal operations and a 15% reduction in supplier emissions by 2025.

Robust corporate governance structure

Our corporate governance structure is designed to make rapid, deliberate decisions on a global scale, keeping Takeda's purpose, values and vision intact. Our Board has 16 Directors with diverse backgrounds, skills and experiences. Eleven of these members are independent External Directors. Takeda operates under a governance with an Audit and Supervisory Committee, chaired by an External Director. The Nomination Committee and Compensation Committee, chaired and composed of External Directors, serve as advisory bodies to the Board to ensure transparency and objectivity in decision-making processes, including on personnel matters related to Directors. The Takeda Executive Team (TET) of 19 is also diverse with 10 nationalities and six women, and considers the perspectives of many other stakeholders in their discussions and decision-making. We recognize the benefits of strengthening gender diversity and inclusion in our Board, and we will continue to take steps to address this in the future.

DELIVERING VALUE TO PATIENTS, SOCIETY & SHAREHOLDERS

As we communicated at our Wave 1 Pipeline Market Opportunity Call Part 2 in April 2021, our pipeline has the potential to contribute significantly to revenue growth, and to help us deliver on our goal to reach JPY5 trillion (\$47 billion) revenue by FY2030⁶, representing 50% growth from FY2019.

I am confident that this growth outlook will support our Total Shareholder Returns (TSR), and we look forward to a new phase of creating significant shareholder value in the mid-to-long term as we continue to execute on our strategy. Shareholder returns are a key element of our capital allocation policy, and we remain committed to our well-established dividend policy of 180 yen per share annually.

⁶ Includes incremental revenue not adjusted for probability of technical success (PTS) and is not a "forecast" or "target" figure. PTS applies to the probability that a given clinical trial/study will be successful based on pre-defined endpoints, feasibility and other factors and regulatory bodies will grant approval. Actual future net sales achieved by our commercialized products and pipelines will be different, perhaps materially so, as there is a range of possible outcomes from clinical development, driven by a number of variables, including safety, efficacy and product labelling. If a product is approved, the effect of commercial factors including the patient population, the competitive environment, pricing and reimbursement is also uncertain.

As a global biopharmaceutical company, we understand our responsibilities to all of our stakeholders: patients, health care professionals, payors, regulators, governments, colleagues and shareholders, as well as the communities where we operate and which we serve.

To better align our interests with our stakeholders, in January 2021, Takeda, along with more than 60 leading global companies, committed to reporting on the World Economic Forum International Business Council's (IBC) Stakeholder Capitalism Metrics. The metrics align closely to our own corporate philosophy and focus on the most pressing societal priorities based on four pillars; people, planet, prosperity and governance. As a values-based company, we recognize and embrace the opportunity for greater transparency on our non-financial material data across our corporate stakeholders. In doing so, we hold ourselves accountable to creating more prosperous societies, reducing health inequities, supporting a diverse, equitable and inclusive workplace culture and fulfilling our obligation to protect the planet. We will further report on our progress in the annual integrated report to be issued later this year.

We are proud of the recent accomplishments that Takeda has made, and of all the achievements over the past 240 years of the company's history. We are also confident in our outlook for the future and believe our strengths will continue to drive us as a purpose-led and sustainable company for many years to come.

As a valued shareholder, I would like to sincerely thank you for believing in Takeda's purpose. You are integral to our ability to deliver life-saving treatments for patients around the world, and we are grateful for your support. We look forward to sharing more accomplishments and details on the strength of our business with you at the Annual Shareholder Meeting next month.

With my best regards,



Christophe Weber
President & CEO

