November 2018

Dear Takeda Shareholder,

It is my great pleasure to provide you with the latest update on Takeda and the proposed acquisition of Shire. In my June 2018 letter¹, I covered how Takeda is transforming itself to ensure our long-term success in a fast-moving environment and market. To the extent we were able to² at that time, I also detailed how the acquisition of Shire will accelerate Takeda’s transformation to create a global, values-based, R&D-driven biopharmaceutical leader headquartered in Japan.

We just opened our new global headquarters building in Tokyo.³ With an interior created by the renowned Japanese designer, Kashiwa Sato, it is special, modern and distinctively Japanese. It beautifully embodies our mission of contributing to better health and a brighter future for people worldwide, while also paying tribute to our rich history.

The strategic rationale for the acquisition of Shire has not changed, and we have made significant progress. We have now received unconditional clearance for the acquisition from regulatory agencies in several key jurisdictions, including the U.S., Brazil, China and Japan, and we expect a response from the European Commission in November. Considering these developments, we have now called an Extraordinary General Meeting of Shareholders for December 5, 2018 to formally approve the necessary matters relating to the acquisition. Provided the acquisition is approved by both Shire and Takeda shareholders, we continue to be on track for a closing in the first half of calendar year 2019 with an ADS listing on the New York Stock Exchange prior to then.

We see the Shire acquisition as a great opportunity for Takeda and for you, our shareholders, for the following reasons:

1. **The strategic fit is excellent.** The acquisition of Shire accelerates Takeda’s transformation to become a values-based, science-driven, global biopharmaceutical company with a distinctive focus on key therapy areas. It will strengthen Takeda’s presence in gastroenterology (GI) and neuroscience (NS), two of our three core therapeutic areas (i.e. GI, oncology and NS). It will also provide Takeda with a leading position in rare diseases and plasma-derived therapies.

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¹ **Message to Shareholders from Christophe Weber, President & CEO (released in June, 2018).**
² Please note that we must comply with the applicable laws and regulations in various jurisdictions when we provide our shareholders with information, especially forward-looking statements, in connection with the acquisition of Shire. I would greatly appreciate our shareholders’ understanding of our efforts to provide any information regarding the acquisition to the extent reasonably possible under the applicable laws and regulations.
³ **Press Release: Takeda Global Headquarters Grand Opening (released on July 2, 2018).**
We expect that the combined group will derive approximately 75% of its revenue from five areas: GI, oncology, neuroscience and rare diseases, plus plasma-derived therapies. We are fully aware and have also factored in the competitive pressure in these fields, including in hemophilia. At the same time, we are also fully aware that both companies will bring unique growth opportunities in the future. All in all, we are very confident that the assumptions and forecasts we used to value the new combined company remain valid.

2. **We will have the global scale to drive future development.** The acquisition will create a combined group with an attractive geographic footprint and leading positions in Japan and the U.S., respectively the third and first largest pharmaceutical markets globally. China, the second largest market in the world is, and will be, a key priority, and Takeda is planning to launch 7 new medicines there in the next five years. Takeda’s current presence in the U.S., an important and innovation-driven market, will increase significantly, while Shire’s portfolio will benefit from Takeda’s strong international presence in key markets like Russia and Brazil, as well as Japan. We are fully aware that future pricing pressure will increase everywhere including in the U.S., but are confident that the innovative nature of the portfolio and pipeline, as well as the strong margin profile of the combined group, will position Takeda very well.

3. **The Shire acquisition will enhance Takeda’s R&D engine.** Takeda’s R&D engine will be boosted further to deliver innovative medicines in the future. We recently shared our progress during our R&D days\(^4\), which reinforced that our model is unique in the industry and that our R&D productivity will be best-in-class in the long-term. The acquisition will create a highly complementary, robust, modality-diverse pipeline with a greater than 400 billion JPY initial R&D annual budget globally\(^5\), which is highly competitive, especially when considering the budget allocated to pipeline development.

4. **The financial benefits of the acquisition are compelling.** The combined group will be the only pharmaceutical company listed on both the Tokyo (primary listing) and New York stock exchanges. It will have the scale to drive future development as well as the resources to invest in further innovation. It will allow Takeda to deliver substantial synergies and attractive returns to you, our shareholders. We can confirm that we expect recurring pre-tax cost synergies for the combined group to reach at least $1.4 billion each year by the end of the third fiscal year following completion of the acquisition with a one-off cost of $2.4

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\(^4\) Takeda’s R&D Investor Day (Tokyo) [September 27, 2018]; Takeda’s R&D Investor Day (Boston) [October 11, 2018].

\(^5\) The greater than 400 billion JPY initial R&D budget is a reference to the combined historic R&D spend for the period ending March 31, 2017 for Takeda and December 31, 2017 for Shire, less the expected R&D cost synergies.
billion\(^6\). In spite of the new shares issued at closing, the acquisition is expected to be significantly accretive to underlying earnings per Takeda Share\(^7\) from the first full fiscal year following completion. The acquisition is also expected to be earnings accretive per Takeda Share on a reported basis\(^8\) within three years post-acquisition.\(^9\) The return on invested capital (ROIC)\(^10\) is expected to exceed Takeda’s cost of capital\(^11\) within the first full fiscal year following completion. Our intention is therefore to maintain our well-established dividend policy with 180 JPY dividend per share.

As you may know, in May, Takeda entered into a bridge facility agreement of $30.85 billion in connection with the acquisition. It has always been our intention to rapidly reduce or refinance our commitments under the bridge facility prior to completion with a combination of long-term debt, hybrid capital and available cash resources. We have made significant progress to date, already having refinanced $12 billion of the bridge facility with leading financial institutions and we are planning further refinancings prior to completion. We believe that the remaining financing process will be successful at a competitive aggregate interest rate with the right currency balance. Because of the high operating margin and cash flow generation, enhanced by synergies, we are confident that we will remain investment grade as we will return to a target net debt to adjusted EBITDA\(^{12}\) ratio of 2.0x within three to five years following completion, without the need to issue new shares. Furthermore, we will consider disposing of non-core assets to help accelerate the de-leveraging process. Starting with a projected net debt to adjusted EBITDA ratio of 4.8x (as at March 2019), we intend to reduce this to between 2.9x and 3.3x by March 2021, and between 1.7x and 2.1x

\(^6\) This statement includes a quantified financial benefits statement for the purposes of the City Code on Takeovers and Mergers in the UK (the “Takeover Code”). Please see the Notice of Convocation of Extraordinary General Meeting of Shareholders for further information.

\(^7\) Excludes the impacts of divestitures, foreign exchange rates, and other amounts that are unusual, non-recurring items or unrelated to Takeda’s core operations.

\(^8\) Earnings per share as derived from International Financial Reporting Standards (IFRS).

\(^9\) The statement that the acquisition is earnings accretive is not intended as a profit forecast, should not be construed as such and is not subject to the rules on profit forecasts under the Takeover Code. The statement should not be interpreted to mean that the earnings per share in any future fiscal period will necessarily match or be greater than those for the relevant preceding financial period.

\(^10\) Shire’s annual tax-effected core earnings including synergies and excluding cost to achieve synergies and transaction-related costs, as a percentage of the purchase price, or total enterprise value.

\(^11\) Takeda’s weighted average cost of capital representing the company’s blended cost of capital including equity and debt.

\(^12\) “adjusted EBITDA” = EBITDA (net profit before income tax expenses, depreciation and amortization and net interest expense), 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 gains and losses from investments accounted for under the equity method and other items that are unrelated to our core operations such as purchase accounting effects and transaction related costs.
by March 2023 (the lower of such numbers taking into account the potential divestiture of non-core assets of up to approximately $10 billion).

A key consideration has been our ability to integrate the two companies. Both companies leadership teams have a strong track record for executing integrations well. Takeda and Shire have also posted strong results during their respective Q2 and Q3 2018 results.\textsuperscript{13,14} One of the most important milestones to date was when we announced our post-closing operating model to employees. Our aspiration is to create an organization that’s based on three guiding principles. We will be Patient-Centric, developing more innovative medicines supported by world-class services and support capabilities. We will be Agile & Simple, minimizing complexity and empowering local leaders to make local decisions. And we will be Lean & Focused, concentrating our efforts on the four core therapeutic areas of GI, oncology, neuroscience and rare diseases, plus plasma-derived therapies and vaccines.

\textbf{Our R&D effort will primarily be focused on four therapy areas:} GI, oncology, neuroscience and rare diseases. There will also be a focused R&D effort in vaccines and plasma-derived therapies. Our future operating model will be an extension of our existing R&D efforts, which will not be materially disrupted as Takeda’s R&D engine will be expanded to include rare diseases and both companies have R&D hubs in the Boston area.

We will maintain a focus on excelling in Manufacturing & Quality. Our global combined manufacturing network will utilize both in-house and outsourced production, while prioritizing technological and digital innovation. That is how we will make sure the right patients get the right medicines, at the right time, at an affordable price.

We will bring our medicines to patients through our local entities present in approximately 80 countries. Internally, these countries will be grouped into four regions: U.S., Japan, Europe & Canada and a region comprising China, Latin America, Middle East, Asia Pacific, Russia and the Commonwealth of Independent States. We will also create three global Business Units (BUs) for the portfolios that have unique needs and require dedicated focus – oncology, plasma-derived therapies and vaccines.

In addition, we have also selected the future Takeda Executive Team (TET) whose roles will become effective upon closing. It will be comprised of a group of highly experienced and diverse leaders with multiple female leaders and 11 different nationalities. They not only have excellent functional

\begin{footnotesize}
\footnote{Takeda FY2018 Q2 Results (released on October 31, 2018).}
\footnote{Shire Third Quarter 2018 Results (released on November 1, 2018).}
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knowledge, but are truly enterprise leaders who will have a shared commitment to Takeda’s values and our vision for the company’s future once their roles come into effect.

Twenty functional integration teams, comprised of representatives from both Takeda and Shire, are working on plans to bring the two companies together in their respective business areas post-closing. The integration plan will be developed further and, following closing, Takeda will warmly and respectfully welcome Shire employees into a new Takeda, which will maintain our Mission, Vision 2025 and the values that drive everything we do. By doing so, we will become a global, values-based, R&D-driven biopharmaceutical leader with a stronger and more innovative portfolio supported by a lean and focused organization. All of which will allow us to improve the lives of many more patients and deliver more value to shareholders.

As for our Corporate Governance, Takeda’s Board is today composed of eight external independent directors and four internal directors with an Audit & Supervisory Committee as defined by law, as well as a Nomination Committee and a Compensation Committee, all three committees being chaired by an external director. The Board meetings are also chaired by an independent director.¹⁵

Needless to say, the Takeda Board has been fully involved early on in the project of acquiring Shire, with the key decision on March 22, 2018 to pursue this acquisition. On this date, after many reviews starting in 2017, all directors present at the Board meeting¹⁶ unanimously agreed to reach out to the Shire Board in a friendly manner in order to negotiate a recommended acquisition within specific parameters. Subsequently, the Board held an Extraordinary Board meeting on May 7, 2018 and all directors present at the Board meeting¹⁷ unanimously approved the final agreement between Takeda and Shire.

During our multiple reviews with both the Takeda Executive Team as well as the Board, we extensively discussed the opportunity, but also the risks associated with this acquisition. We discussed, in detail, the financial market risk, the business risk and the integration risk.

¹⁵ Presentation: 142nd Ordinary General Meeting of Shareholders (released on June 28, 2018). Board of Directors on slide 4.
¹⁶ There was one director absent from the Takeda Board. Mr. Jean-Luc Butel recused himself from the Takeda Board’s consideration and approval of the acquisition of Shire as a result of his interest in Shire shares, pursuant to Article 369 of the Japanese Companies Act (Act No. 86 2005) (the “Japanese Companies Act”).
¹⁷ There were two directors absent from the Takeda Board. Mr. Jean-Luc Butel recused himself from the Takeda Board’s consideration and approval of the acquisition of Shire in light of his previously announced resignation from his position as Takeda’s Chief Financial Officer (effective March 31, 2018) and as a Takeda Director (effective on May 31, 2018).
1. The financial market risk is being managed by ensuring that we will remain investment grade credit-rated, which was a key criteria when defining the share and cash split of the transaction. It was also mitigated by denominating the debt in an appropriate mix of currencies to reduce currency risk and hedging costs. As previously mentioned, we will consider disposing of non-core assets to help accelerate the de-leveraging process.

2. The business risk was assessed as fully as possible and taken into consideration, especially in segments with high competitive pressures (e.g. hemophilia). We have taken a prudent approach to our forecasts compared to external analysts and we pressure tested our scenarios with sensitivity analyses. As a result of the prudent forecasts applied to its in-market product and pipeline to determine our purchase price, we believe there is a low risk of impairments to goodwill and intangible assets in the future.

3. We are planning for and will adopt an integration method which we believe will mitigate the risks associated with such a large acquisition. The company name, values and purpose will remain Takeda’s. Takeda and Shire share the same intent to be an R&D-driven company post-closing and, following completion of the acquisition, Takeda’s R&D engine will be expanded to include rare diseases. The post-closing business integration will ensure Takeda and Shire know-how is leveraged, as described in the future operating model above.

All in all, when considering the risks and opportunities of a Takeda standalone scenario compared to the acquisition scenario, the Board concluded that the acquisition is a unique opportunity.

Upon closing, and subject to your approval at the upcoming Extraordinary General Meeting of Shareholders, three new external board members from the Shire Board will join the Takeda Board further reinforcing the diversity and strength of the Takeda Board.

In summary, I want to emphasize that Takeda’s current strategy is working, and that the Takeda Board, Takeda Executive Team and I are confident that the acquisition of Shire will enable Takeda to significantly accelerate its transformational journey to become a global, values-based, R&D-driven, biopharmaceutical leader headquartered in Japan. We will be a company that delivers highly innovative medicines and transformative care to patients around the world.

What will remain constant on this journey is our commitment to Takeda’s values of integrity, fairness, honesty and perseverance. We will always put the patient at the center, build trust with society, reinforce our reputation and deliver superior business performance, in that order. These are not only the right values for a company committed to healthcare, they are also fundamental to the success of Takeda in the long-term.
We hope that you will support this vision and we look forward to sharing with you our further progress in the near future.

With my best regards,

Christophe Weber  
President & CEO  
Takeda Pharmaceutical Company Limited

More information in relation to the offer for Shire including this letter and related presentations are available at: https://www.takeda.com/investors/offer-for-shire/

Please note that all factual matters stated here are those as of November 1, 2018. Any material updates thereafter are also announced at https://www.takeda.com/investors/offer-for-shire/.

In accordance with the Takeover Code, the directors of Takeda accept responsibility for the information contained in this document, including any expressions of opinion, and confirm that to the best of the knowledge and belief of the directors of Takeda (each of whom has taken all reasonable care to ensure that such is the case), the information contained in this document is in accordance with the facts and does not omit anything likely to affect the import of such information.