June 2018

Dear Fellow Takeda Shareholder,

Since joining Takeda in April 2014, my mission has been to continue the transformation of Takeda in order to ensure that Takeda will be a successful company in the long term. I promised to respect the interests of, and create value for, all stakeholders, including patients, employees, society and, of course, Takeda's shareholders. I also promised to develop the company without taking so much risk that it could possibly jeopardize the existence of the company.

Fully in line with this context, we decided to accelerate the Takeda transformation, initiated by my predecessors, to become an R&D driven, global company, always keeping in mind the strong values Takeda has held since our establishment in 1781. These include Takeda-ism (Integrity, Fairness, Honesty and Perseverance) and our four principles of always putting the patient at the center, building trust with society, reinforcing the reputation of the company and delivering superior business performance, in that order.

Over the past four years, Takeda has been on a transformation journey, focused on becoming an agile, R&D-driven, global pharmaceutical company that is well-positioned to deliver highly-innovative medicines and transformative care to patients around the world. To achieve our transformation goals, Takeda has continued to develop innovative therapies and actively engage in R&D collaborations, while always remaining true to our values. Through our research efforts in gastroenterology (GI), oncology and neuroscience, plus vaccines, Takeda has focused on developing and commercializing innovative therapies that address unmet clinical needs.

This transformation is necessary and inevitable as pharmaceutical market growth relies on different components than in the past. Countries around the world are struggling to finance healthcare, resulting in a stringent selection of drugs to be reimbursed and significant price pressures. Despite these pressures, science and innovation has never been so dynamic and productive, driving worldwide market growth to 3-5% per annum. The market dynamic has changed immensely and Japan is a good representation of these changes. In 1994, the Japanese pharmaceutical market represented 20% of the worldwide market. Today, it represents less than 8% and in 2018, the average market price reduction will be about 7%, which means that the overall market will decline.

Takeda’s strategic response to such changing circumstances has been comprehensive and decisive:

- To improve our R&D productivity by reinventing our R&D engine. We aspire to deliver innovation to patients, and by design are focusing on three therapy areas (Gastroenterology, Neuroscience, Oncology) plus vaccines, aiming to be the best partner

with external research groups, only investing in transformative medicines. Our pipeline addresses medical need across the spectrum, focusing on treatment (of both common and rare diseases, which affect hundreds of thousands of patients), and prevention (vaccine-based programs aimed at preventing disease in hundreds of millions of people, often in under-served regions of the world).
- To actively globalize the company and its talent in order to be competitive and grow in key markets like the United States, Europe, China and Brazil (as examples). The Takeda Executive Team is also highly experienced and diverse.
- To progressively improve our margin following a deterioration since the patent expiry of Actos back in 2008.

Our strategy is working, as demonstrated in our 2017 results. Our FY2017 results demonstrate our success, as underlying revenue grew by 5.5%, with Takeda's global Growth Drivers (GI, oncology, neuroscience and emerging markets) posting strong underlying revenue growth of 12.8%, and our core earnings margin increased by 420bps due to product mix improvement and strong cost discipline. Takeda’s pipeline also progressed well with 17 stage-ups in FY2017. We continued to successfully partner with 180 partnerships now on-going and around 36% of our pipeline being partnered.

Overall, this transformation has created value for all our stakeholders including our shareholders, with Takeda’s well- established dividend policy remaining a key component of our shareholder return.

If our strategy is working, why are we considering acquiring Shire Plc?

The acquisition of Shire will accelerate Takeda’s transformation, building on our success and creating a global, values-based, R&D-driven biopharmaceutical company, headquartered in Japan.

We see this transaction as a great opportunity for Takeda and for our shareholders.

1. **The strategic fit is excellent.** The acquisition of Shire will strengthen Takeda’s presence in two (GI and neuroscience) of our three core therapeutic areas. It will also give us leading positions in rare diseases and plasma-derived therapies to complement our strength in oncology and focused efforts in vaccines. We expect to derive approximately 75% of sales from five areas: GI, neuroscience, oncology and rare diseases, plus plasma-derived therapies.
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., two of the largest drug markets geographically. Takeda's exposure in the U.S., an important and growing market, would increase significantly, while Shire's portfolio will benefit from Takeda's strong international presence in emerging markets and Japan.

3. **Takeda's and Shire's pipelines are highly complementary.** The acquisition will create a highly complementary, robust, modality-diverse pipeline (e.g. 10 assets in Phase III) and a strengthened R&D engine focused on breakthrough innovation. Takeda has transformed our R&D engine to drive productivity and we have begun to realize the value of the therapeutic area focus and increased external partnerships as evidenced by the enrichment of our early stage pipeline. The acquisition will accelerate this transformation and will provide additional cash flow to continue to invest in our R&D engine to benefit to patients.
4. **There are compelling financial benefits.** The acquisition will enhance Takeda's scale and financial strength. On an historical pro-forma basis, the combined group had annual revenues in excess of 3.4tY/30bUSD and EBITDA greater than 1tY/9bUSD. The new combined group will have the scale to drive future development and financial strength that will enable Takeda to further invest in innovation – all of which will allow us to better deliver value for our stakeholders.

Let's now analyze the financing of this acquisition and its implications for the shareholders. We intend to acquire Shire through a combination of new Takeda shares listed on the Tokyo Stock Exchange and the New York Stock Exchange (i.e. Shire shareholders can elect to receive either 0.839 new Takeda shares in Japan or 1.678 Takeda ADSs in the U.S.) and cash (i.e. $30.33 in cash), per share of Shire.

After the successful acquisition, the number of issued Takeda shares will essentially double but the acquisition will be significantly accretive to underlying earnings per Takeda share from the first full fiscal year following completion even though there will be share dilution. This is because we expect that the new combined group will be much bigger and much more profitable than Takeda (as demonstrated by the historical pro-forma EBITDA which is approximately three times larger than Takeda's). Thus, we do not think it appropriate that 'dilution' is discussed or concerned only in the context of dilution of 'voting rights' per share. Rather, we believe it needs to be understood within the entire context of 'value', including earnings per Takeda share (EPS). We also plan to maintain our well-established dividend policy. The transaction's Return on Invested Capital (ROIC) is expected to exceed Takeda's weighted average cost of capital (WACC) within the first full fiscal year following completion.

EPS is expected to increase in spite of the dilution and the dividend policy is secure – but is the debt level sustainable?

The cash portion is funded by a $30.85Bn loan through a fully underwritten bridge facility, arranged by J.P. Morgan Chase Bank N.A., Sumitomo Mitsui Banking Corporation and MUFG Bank, Ltd. This bridge facility will be refinanced through diverse instruments (including, for example bonds, loans and hybrid bonds) and among a large group of financing institutions, through which the debt burden on the company will be reasonably reduced or mitigated over time.

The debt level has to be considered not in isolation, but in comparison to the new combined group's EBITDA. Although at the time of closing the ratio of net debt to EBITDA will be higher than it is now, we expect the combined group to de-lever quickly, using the substantial cash flow generation expected to result from the acquisition as well as the EBITDA growth. The recurring pre-tax cost synergies for the combined group are expected to reach a run-rate of at least $1.4 billion per annum by the end of the third fiscal year following completion. We reasonably believe we can therefore return to a target net debt to EBITDA ratio of 2.0x or less in the medium term. Note that this de-leveraging profile excludes any possible post-closing disposal of assets – a viable option that could be considered. De-leveraging quickly is indeed key in order to limit the company's exposure to macro-environment and market risks.

Last but not least, are we able to execute the integration of such a large company?

This is obviously a key consideration, and we of course carefully reviewed and discussed this before making a decision. Takeda's team is highly experienced across multiple M&A transactions, is highly diverse with 8 nationalities and is based mainly in Japan and the U.S. The management team has a proven track record of executing complex business integrations and large-scale transformations, and is well-positioned to successfully integrate Shire – with integrity – building on the expertise of the employees of both companies and maximizing the value of the combination. Integrating the U.S. business, R&D and the manufacturing & quality network will be the key and these areas are led by exceptional leaders. The detailed steps for the integration plan will be developed further, and following the closing, Takeda will warmly and respectfully welcome Shire employees into a new Takeda, which will maintain our Mission, Vision 2025, and our values which drive all that we do.

In conclusion, we want to emphasize, again, that Takeda's current strategy is working; we are executing and delivering as shown by our strong 2017 results. The Takeda Board, Takeda Executive Team and I are confident that the acquisition of Shire allows Takeda to accelerate our journey to become an agile, R&D-driven global pharmaceutical company – one that is well-positioned to deliver highly-innovative medicines and transformative care to patients around the world. All of this is driven by our four principles of always putting the patient at the center, building trust with society, reinforcing the reputation of the company and delivering superior business performance. These are not only the right values for a company committed to healthcare, but foundational to the Takeda business. Because of its financial strength and the quick de-leveraging, the new Takeda will be even more robust, and less exposed to risk than the current company.

I look forward to reporting progress against the opportunities set forth above, and to delivering on my promise of the benefits this acquisition will deliver to all of our stakeholders, including you, our shareholders.

Sincerely,
Christophe Weber
President & CEO

More information in relation to the offer to Shire shareholders is available at:
https://www.takeda.com/investors/offer-for-shire/